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EDITORIAL

## REFRACTIVE ERRORS: A CLINICAL PERSPECTIVE

The human eye is similar to an optical instrument<sup>1</sup>. A clear cornea allow slight to enter the eye and focus at a spot on the centre of retina, the foveal pit, which has a maximum concentration of cones, (the photoreceptors that are stimulated by light). Their maximal stimulation sends impulses via the optic nerve to the occipital cortex (a three neuronal pathway) to perceive a perfect image which is further analyzed by the prefrontal cortex. This perfect optical system has certain imperfections called aberrations as well as refractive errors; their additive affect not only degrades the retinal image but limits its clarity and spatial resolution.

### *The aberrations in the optical system of the eye:*<sup>2,3</sup>

The curved shape of the cornea, which is steeper at the centre, allows a straight beam of light to pass through while its flat periphery bends the light rays; the anterior and posterior surfaces of the cornea refract and bend light rays further. The bi-convex shaped lens has a similar affect (with minimal bending of light rays at the centre and more towards the periphery) and alterations in the size of pupil, all add up to defocus the retinal image. In bright light, the pupil constricts and its small aperture blocks the divergent, peripheral rays from both the cornea and lens, thus minimizing the affect of spherical aberration. However, as the pupil enlarges in dim light or at night, more divergent rays from the periphery of cornea and lens enter the eye and focus anterior to the straight beam of light passing through the centre of both these structures, not only producing glare but a defocused, blurred image<sup>4</sup>.

The affect of spherical aberrations increases as the fourth power of the diameter of the pupil i.e. if the pupillary diameter doubles, it increases the spherical aberration by 16 times. This results in haloes around point images and produces the condition of "Night Myopia", the affect of which is exaggerated after LASIK or surface ablation for myopia. In young eyes, the lens is an elastic structure and by altering its thickness, it plays a significant role in compensating for corneal aberrations by neutralizing them and improving the

quality of retinal image<sup>5,6</sup>. But with age, it hardens, loses its elasticity and this compensatory mechanism starts failing; rather it adds to the optical aberrations by the cornea, resulting in an image of poor quality.

**Impact of refractive errors:** all babies are born with some degree of refractive errors due to a mismatch between the optical components of the eye so that the resultant retinal image is out of focus to varying degrees. About 90-95% of babies are born with some degree of hypermetropia. Emmetropia, as described by Grosvenor<sup>7</sup> is the "normal" state of an eye in which parallel light rays focus on the retina when the accommodation is fully relaxed. Others consider the state of emmetropia to range between hypermetropia of +0.50 to +1.50 diopters<sup>8</sup>.

**The Process of Emmetropization:** It starts during the first 12-18 months after birth and by the first 5 years of life, 80% of both myopic and hypermetropic children become emmetropic<sup>9</sup>. This process has been postulated to result from an active as well as a passive mechanism.

**Uncorrected refractive errors in children result in Amblyopia and Strabismus, interfering child's development which can be avoided by early appropriate spectacle. Strabismus surgery is mostly required in congenital strabismus, while it can also be avoided in other types of strabismus by appropriate glasses. They not only restore a normal vision in either eye but also the muscular balance.**

The active mechanism<sup>10</sup> is a neural process regulated by the degree of blurring of the retinal image: the eye analyses the degree of retinal blur and shortens or elongates proportionately, by changing the axial length of the eye, till both the image and retina are conjugate.

A critical factor that regulates the axial elongation of eyeball is the alteration in the composition and amount of extracellular matrix of the sclera. The clarity

or defocus of an image at the neuroretina results in release of neurotransmitters (Dopamine and VIP) by retinal amacrine cells<sup>11</sup>; Dopamine increases the production of DNA and promotes the synthesis of proteins and proteoglycans in the sclera<sup>12,13,14</sup> making it thick and less stretchable thus reducing its elongation. On the other hand, Vaso-active Intestinal Peptide secretion (VIP)<sup>15</sup> stimulates choroidal blood flow and thickens the spongy choroid while at the same time, stretches, thins and elongates the sclera. Hence, the axial length of eyeball increases posteriorly. The sclera is also capable of altering its growth in a sector without altering the remainder. If a defocused image is present on one portion of the retina, only that part continues to grow to become myopic while the remainder with a clear image remains unaltered and emmetropic, resulting in myopic astigmatism.

This active neural control operates via a feedback mechanism from the brain, the evidence of which was provided by Troilo and Wallman<sup>16</sup>. They found a reversal of the original refractive error by severing the optic nerves of chicks: hypermetropic eyes became myopic, while myopic eyes became hypermetropic; with an intact optic nerve, the process of emmetropization was more accurate. This proved the theory that an active feedback provided by the brain regarding the quality of perceived image is essential for regulating emmetropization process. They further noted that by severing the Edinger Westphal nucleus (which controls accommodation), process of emmetropization slowed but it was not a prerequisite for it. Sorsby<sup>17</sup> has suggested that an increase in axial length occurring under genetic influence in high levels of ametropia; if one parent is myopic, the chance of a myopic child 22.5% while it increases to 42% if both parents are myopic<sup>18</sup>.

Similarly, visual deprivation in neonates due to severe congenital ptosis<sup>19,20,21</sup>, corneal opacity<sup>22</sup>, congenital cataract, vitreous opacification or haemorrhage<sup>23</sup>, and retinopathy of prematurity<sup>24,25</sup> causes the eye to elongate and become increasingly myopic. Another observation suggesting that emmetropization has an active component is the association of myopic progression in response to sustained near vision<sup>26</sup>.

This active mechanism works in close association with a **passive process** of emmetropization in which appropriate and proportional interactive changes occur in refractive components of the eye in response to a change in its axial length<sup>27</sup>. In a study on chicks, Troilo and Wallman<sup>28</sup> concluded that *corneal curvature* was a major contributor of astigmatic emmetropization.

Gernet and Olbrich<sup>30</sup> suggested *lenticular changes* were responsible for spherical emmetropization as myopic children have thin crystalline lenses, suggesting a mechanical relationship between growth of the eyeball and lens compensation. Larger eyes have a larger equatorial diameter, causing more tension and stretching of the zonular fibers. These stretched fibers consequently flatten the lens and reduce its optical power. The third factor is the changing choroidal thickness during active emmetropization process resulting in altering the *vitreous chamber depth* (a passive phenomenon)<sup>39</sup>. In myopia, the choroid is thin so retina moves backwards with it, resulting in an increased depth of vitreous chamber; in hypermetropia, the choroid thickens (active phenomenon) and pushes the retina forwards, thereby reducing the depth of vitreous chamber passively. Hence, the ocular structures responsible for causing large changes in refractive error are cornea, lens and the depth of vitreous chamber<sup>40</sup>, which is determined by the posterior growth of sclera.

**2-The Natural History of Refractive Errors:** Infants are born with a mild hypermetropia of +2.00D but a small number may have it in a moderate to high range of >3.5D. This is due to a relatively smaller size of eyeball as compared to the rest of the body. By the age of 4 years, the eyeballs and the brain attain 85% of their adult size while the rest of the body has grown to only 20%<sup>41</sup>.

The continued growth of eyeballs during these first few years of life results in a shift towards emmetropia and a gradual decrease in the level of hypermetropia in most individuals<sup>42</sup> so by the age of 5-6 years, 80% of the children are found to be emmetropic<sup>43</sup>. Ingram and Barr<sup>44,45</sup> stated that a child born with hypermetropia of less than +2.50 diopters of is likely to become emmetropic, whereas a child born with more than 2.50 diopters is likely become more hypermetropic by the age of 3.5 years<sup>46,47</sup>. By the age of 5 years, though the prevalence of refractive errors is reduced, its distribution still peaks towards a mild hypermetropia<sup>48</sup>. Over the next 10-15 years of life, the prevalence of hypermetropia is very much reduced though myopia is seen more frequently<sup>49,50</sup>.

Infants, with a family history of **myopia** (<5%), are born myopic which increases further as the axial length of eyeball continues to increase under the genetic influence. Some of them may exhibit a shift towards emmetropia by the age of 6 months but infants born with high myopia retain most of it in later years of life. Therefore, it is possible to predict refractive status in older children based on their earliest manifest refraction, with one year being optimal<sup>51</sup>. Myopic progression has

been found to be associated with other factors like ethnicity, female gender, younger age of onset, high IQ score, and prolonged study hours (by increasing the accommodative demand and eye strain)<sup>52,53</sup>. The evidence has been provided by Chua et al.<sup>54</sup>, who found that elongation of axial length and myopic progression can be slowed down by reducing accommodation with 0.1% atropine eye drops once a day.

At birth, the average amount of **astigmatism** is 2.00 D which decreases to 1.00 D by the age of 2.5-5 years<sup>55,56</sup> as a part of emmetropization process; 1/3 of spherical equivalent and 2/3 of the astigmatism reduces due to flattening of cornea during the first two years of life. This has been found in 90% of the children<sup>57</sup> in most races. Astigmatism of more than 1.50 D results in amblyopia if not corrected with glasses. Emmetropization process corrects "With"-the-rule astigmatism more than "Against"-the-rule astigmatism which is also a risk factor for becoming myopic at an earlier age and amblyopia. According to Abrahamson and Sjostrand<sup>57</sup>, low amounts of **anisometropia** (<2.50 D) is commonly found during the normal growth period of the eye<sup>58</sup>; children with 3.00 D or more anisometropia at one year of age have a 90% chance of retaining it at the age of 10, and a 60% risk of developing amblyopia<sup>59</sup>. The emmetropization process cannot correct >5.00 D of anisometropia<sup>60</sup> and may result in juvenile microtropia.

**Optics of Hypermetropia:** In emmetropia, parallel rays of light from a distant object are focused by the lens (without the need for accommodation) onto the retina (fovea) to form a clear image. In hypermetropia, because of a short axial length, they are focused behind the retina resulting in a blurred image. Therefore, accommodation is called upon to increase the curvature and thickness of the lens in order to increase its refractive power and focus the distant light rays upon the retina. The rays coming from a near object are more divergent and more accommodative effort is needed to see it clearly. Due to the phenomenon of accommodation/convergence synkinesis in the brain, the eyes converge as well resulting in an Esotropia (ET). According to Ingram, et al.<sup>61</sup>, infants with an esotropia or a microtropia do not show a spontaneous reduction of hypermetropia by the emmetropization process and were more likely to have accommodative problems. Both fixing and non-fixing eyes demonstrated accommodative abnormalities with poor convergence, showing that the underlying defect was congenital rather than refractive.

Children have a sufficient accommodative reserve to maintain a clear retinal image without producing asthenopia<sup>62</sup>. However a constant need for accommodative effort for near work results in

watery eyes, squinting and facial contortions during reading, frequent blinking, constant or intermittent blurring of vision, focusing problems, difficulty with or aversion to reading, decreased binocularity and eye-hand coordination. The presence and severity of these symptoms is variable and depends upon the degree of hypermetropia. Hypermetropia usually stabilizes by the age of 6-8 years<sup>63</sup> and starts reducing in amplitude with time. However, in children, who are constantly reading or doing close work for long periods, constant accommodation results in spasm of ciliary muscle and artificial myopia.

#### **Impact of Uncorrected Hypermetropia on Vision & Strabismus:**

- 1) A mild to moderate degree of hypermetropia or astigmatism is present in 90% cases of *infantile esotropia* and should be fully corrected as it may lead to *amblyopia*. A child with true, essential infantile ET should have a surgical correction of strabismus by 18 months age so that stereopsis can develop. Any astigmatic error should be corrected by glasses.
- 2) Anisometric hypermetropia (> 1.5D) or hypermetropic astigmatism of 1D, persisting beyond 2 years of age, results in *amblyopia*<sup>64</sup>.
- 3) If both eyes have the same degree of hypermetropia, then an *alternating ET* develops. Since the child fixates alternately with either eye, amblyopia does not develop.
- 4) If one eye is more hypermetropic, it accommodates more and converges more resulting in a unilateral, constant ET. A constantly in-turned eye loses foveal fixation, the child tends to prefer the emmetropic or less hypermetropic eye for seeing and the more hypermetropic eye (with a blurred image) is neglected by the brain. It is suppressed by the good eye, its neuronal connections to the brain shrink and it becomes *amblyopic*.
- 5) A large, constant ET results in an *eccentric fixation* as it never straightens to focus image on the fovea.
- 6) In a constantly esotropic eye, the MR never relaxes as the eye never assumes a primary position; its constant contraction results in its hypertrophy and contracture. Even if such an eye is given full hypermetropic correction, the hypertrophic muscle does not relax fully, a small amount of ET still persists and is erroneously labeled as a *partially accommodative ET*.
- 7) Uncorrected hypermetropia (>3.5 D in one meridian) results in blurring of vision, reduced binocular vision, constant accommodative effort, fatigability. These factors contribute to poor motor and cognitive development in younger children

(9 months to 5.5 years) and poor performance at school in older children. Screening by visual acuity testing in all preschool children is very important. Full optical correction of significant hypermetropia during infancy in the absence of strabismus, may interfere with the process of emmetropization<sup>65</sup> but partial spectacle correction is safe and reduces the incidence of subsequent strabismus.

- 8) In the presence of an esophoria or ET, no matter of how small a magnitude, full hypermetropic correction is mandatory to achieve a foveal fixation binocularly. This can only be achieved by full cycloplegia with atropine eyedrops as it neutralises even the latent hypermetropia (due to the tone of ciliary muscle = 1-1.50D). Cycloplegia with cyclopentolate eye drops does not neutralize the latent hypermetropia but only the manifest hypermetropia which an individual can correct by accommodating and is called **Facultative Hypermetropia**. If the error is large, then even by fully accommodating, the objects are not seen clearly, especially for near. This remaining amount of Hypermetropia that still remains uncorrected by accommodation is called **Absolute** and needs correcting glasses (Manifest= facultative + absolute).

**Optics of Myopia:** The term myopia means “I close eyes”, a myopic person sees distant objects with half closed eyes. Because of a large axial length, parallel rays of light from a distant object are focused in front of the retina resulting in a blurred distant image. Half-closed eyes create the affect of a pinhole, thereby reducing the extent of blurred image. Since the rays from a near object are divergent, they focus on the retina, producing a clear image. Hence a myopic person can see near objects clearly (short-sightedness); the farthest distance at which the vision is clear is called the Far Point (Punctum Remotum). In an emmetrope, the far point is at infinity while in a myopes, the higher the degree of myopia, shorter is this distance e.g. in myopia of 1D, far point is at 1 meter, in myopia of 2D, far point is ½ meter.

**Impact of Myopia on Vision & Strabismus:**

- 1) Myopia is mostly due to an increase in axial length of the eyeball; an increase in axial length of 1 mm produces myopia of 3D. Increase in corneal curvature by 1mm results in a myopia of 6D but this is seen less frequently as the normal emmetropization process encourages corneal flattening. It is seen in pathological conditions like keratoconus, keratoglobus. Index myopia (due to increased refractive index of lens) is seen in

diabetes and nucleus sclerosis.

- 2) Myopes usually have a limited horizon as they can see clearly till the far point, as their whole world is limited to that distance. This results in psychosocial problems in children with uncorrected myopia.
- 3) Eyestrain and diplopia for near work in myopes: The eyes normally converge when focused at a near object during reading, writing; convergence causes accommodation because of accommodation/convergence synkinesis in the brain (both reflexes operate together). The divergent rays from near objects focus clearly on the retina without the need for accommodation, but because of the synkinetic reflex, this extra accommodative effort focuses the light rays in front of retina producing a blurred near image. Hence the myope gives up the effort to converge allowing one eye to deviate outwards intermittently, resulting in diplopia for near and an exophoria initially, progressing later to an exotropia (XT), when the effort to converge is totally abandoned. In a study by Noha et.al.<sup>66</sup>, myopia was associated with intermittent XT in 90% cases by the age of 20 years. Intermittent XT is seen in 1% of healthy children in USA while esodeviation is more common, though the reverse is seen in Asian populations. Another study also showed a strong association between myopia and XT. The explanation given by the authors is that intermittent XT promotes the development of myopia through an increase in accommodative demand, as the reduction of accommodation slows myopic progression, thereby claiming that intermittent XT is a risk factor for myopia. This view does not sound rational as myopia sets in first and exophoria, progressing to an intermittent XT, and then a constant XT is noted at a later age.
- 4) In a study by Kushner<sup>67</sup>, intermittent exotropia was treated with over correcting minus lens therapy based on the principle that minus lenses in spectacles stimulate accommodative convergence, thereby, reducing an exotropic deviation. According to previous studies, excessive accommodation can result in myopic progression. However, in this study, it was found that the overcorrecting minus lens therapy did not result in myopic progression over the time. This study again refutes the view by Noha et al., that excessive accommodation results in myopic progression.
- 5) It has been found that increased outdoor activities<sup>68</sup>, including sports and leisure time, were



associated with less myopic progression (sunlight producing Dopamine by retinal amercing cells which increases scleral thickness and its rigidity). Myopic children should be discouraged to sit indoors on their cell-phones, laptops for long periods of time and promoted to spend more time outdoors. They should be encouraged to take a break intermittently during prolonged study hours.

- 6) Bad reading habits cause a constant eyestrain, raised IOP and stretching of the coats of an eyeball, thereby an increase in axial length and myopic progression. Children should be discouraged not to read while lying in bed, or stooping over their books, laptops, mobile phones.
- 7) Uncorrected anisometropic myopia of >4.50 D results in amblyopia because of a constantly blurred image in that eye.
- 8) Correcting glasses prescribed should be in the form of a weakest minus lens that gives a 6/6 vision for distance; over-correction of myopia interferes with the emmetropization process. Children should be encouraged to wear refractive glasses constantly to restore the convergence/accommodation balance for all distances, near as well as far.
- 9) In the presence of an exophoria or XT, Myopia should be fully corrected to stimulate accommodative convergence.
- 10) If an Esophoria is noted in a patient wearing his myopic correction, it means over-correction and the minus correction has to be reduced
- 11) In adults, the amplitude of accommodation decreases with age so it is important to decrease the minus correction for near.
- 12) High degrees of myopia at birth may produce esotropia in early childhood. In this case, an infant's far point is very close to the eyes making them converge all the time to see clearly at that distance; the vision for more remote distance is poor so the child avoids looking at far objects, the convergence is not relaxed, thus producing a constant esotropia.

## CONCLUSION

Uncorrected refractive errors result in a lot of visual morbidity in children by producing amblyopia and strabismus, thus interfering with a child's development. They can be avoided totally by early and appropriate spectacle prescription. Strabismus surgery is required only in congenital strabismus, while it can be avoided in other types of late onset strabismus by appropriate refractive correction and glasses: they not only restore a normal visual acuity in either eye but also

the muscle balance.

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Yacoub A. Yousef

## Chemoreduction of Progressive Intraocular Retinoblastoma by Systemic Topotecan

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Rasha Deebajah<sup>1</sup>, Imad Jaradat<sup>3</sup>, and Yacoub A. Yousef<sup>4</sup>

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### ABSTRACT

**Purpose:** To evaluate our experience with systemic Topotecan (TPT) chemotherapy as a second-line systemic chemotherapeutic regimen for treatment of refractory or recurrent intraocular retinoblastoma (RB).

**Methods and Materials:** A retrospective case series of 14 eyes from patients with intraocular Retinoblastoma (RB) who received systemic TPT as second-line chemotherapy from April 2008 until June 2010. The following data were collected: patient demographics, laterality, international intraocular retinoblastoma stage (ICRB) at diagnosis, treatment received before and after TPT, side effects related to TPT, eye salvage, and survival.

**Results:** The median age at diagnosis was 5 months (range, 1–16 months), and the median age at starting TPT was 10 months (range, 8–24 months). There were 6 (60%) females; all with bilateral retinoblastoma. The median number of TPT cycles was three per patient (range, 1–6), and the total number of administered cycles was 29. After TPT therapy; 4 (29%) eyes showed favorable response, 3 (21%) eyes showed minimal regression, 5 (36%) eyes had stable disease, and 2 (14%) eyes showed tumor progression. At a median follow-up of 48 months; 9 (64%) eyes were salvaged, 3 (21%) eyes received radiation therapy, and 3 (21%) eyes were enucleated (one was post radiation). Grade 3/4 neutropenia were noticed in a total of 59% of given cycles

and admission for febrile neutropenia was required after seven cycles.

**Conclusions:** Our report suggests that systemic TPT chemotherapy could be used as a salvage second-line regimen with low toxicity for patients with progressive intraocular retinoblastoma if systemic therapy is needed.

**Keywords:** Chemotherapy, enucleation, intraocular, retinoblastoma, salvage, topotecan

### INTRODUCTION

Retinoblastoma, a rare tumor arising in the developing retina, is the most common primary intraocular malignancy in childhood and infancy,<sup>1</sup> and the prognosis when the tumor is intraocular is excellent for long-term survival.<sup>1,2</sup> In 1954, external beam radiotherapy (EBRT) emerged as the first therapy to salvage eyes with advanced intraocular retinoblastoma,<sup>3</sup> but it was associated with increased lifelong risk of second cancers in children with a germ line RB1 gene mutation.<sup>4</sup> Systemic chemotherapy became standard primary treatment for intraocular retinoblastoma in the 1990s.<sup>5</sup>

While ineffective alone to eradicate retinoblastoma, systemic chemotherapy reaches adequate concentration to reduce tumor size and facilitate further treatment

with focal therapies, including thermotherapy and cryotherapy.<sup>6,7</sup> For patients who fail primary treatment, salvage relies heavily on focal treatment with intensive use of focal therapy with or without radiotherapy.<sup>6</sup> Concentrations of chemotherapeutic agents are being developed and tested. Among these, intra-arterial chemotherapy using super selective ophthalmic artery chemo embolization,<sup>8–11</sup> sub-tenon injection of chemotherapy,<sup>12,13</sup> and intra-vitreous delivery of chemotherapy<sup>14,15</sup> are all considered now appropriate for patients with refractory or progressive intraocular retinoblastoma.<sup>16</sup> Nevertheless, there is no standard second-line systemic chemotherapeutic regimen that can be used to salvage patients who cannot receive local chemotherapy. Herein we are evaluating our experience with Topotecan (TPT) as a single chemotherapeutic agent given to patients with refractory or recurrent intraocular retinoblastoma.

**Systemic chemotherapy of Topotecan (TPT) could be used as a salvage second-line regimen with low toxicity for patients with progressive intraocular retinoblastoma, if systemic therapy is needed.**

### METHODS

This was a retrospective study using data from

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retinoblastoma patients who received TPT from April 2008 till June 2010. Patient records were later reviewed, including patient demographics, the International Intraocular Retinoblastoma Classification (ICRB)<sup>17</sup> Group for each eye at diagnosis, treatments received before and after TPT, side effects and eye response after treatment. The used protocol for managing intraocular disease at our institution relies on chemoreduction using carboplatin and vincristine with or without etoposide; cycles are given every 3 weeks for 6–8 cycles. Consolidation focal therapy is started after the second cycle of chemotherapy. The indication for TPT was presence of active retinal or sub retinal tumor(s) that was not controlled after completion of CVE protocol combined with focal consolidation therapy. TPT was used to decrease tumor thickness to improve the response to focal therapy. Eyes with features of ICRB group E tumors were not offered this treatment. TPT was given to studied patients on a compassionate basis. The drug was given at 2.5mg/m<sup>2</sup> per day for 5 days. No adjustment in dose was done for younger patients. Paracetamol 15 mg/kg every 8 hours was given during the days of treatment to prevent fever with high dose TPT. Growth factors are not given routinely in our center except for patients with recurrent severe neutropenia or infections.

The tumor response was judged as favorable (FR) if the tumor clinically regressed (decreased tumor size, decreased number of seeds, or decreased tumor vascularity) to an extent that make the residual tumor controllable by focal consolidation therapy (laser therapy or cryotherapy) after systemic TPT. The response was judged as unfavorable response (UR) if there was no change in the tumor, tumor progression (increased tumor size, number of seeds, or tumor vascularity), or if there was partial regression in tumor size or thickness but not enough clinically to make the residual tumor controllable by focal consolidation therapy. For the purpose of analysis, the data was transferred to an excel sheet and calculations were performed using the software. All patients who received TPT in the period studied were included; however, eyes with no evaluable (NE) disease due to recent radiotherapy or inactive disease at time of initiating TPT were not included in the response analysis as indicated in the results below.

## RESULTS

The median age at diagnosis was 5 months (range, 1–16 months), and the median age at starting TPT was 10 months (range, 8–24 months). There were 6 (60%) females and all patients had bilateral retinoblastoma except one who had familial unilateral multifocal disease, and one patient who had active disease in

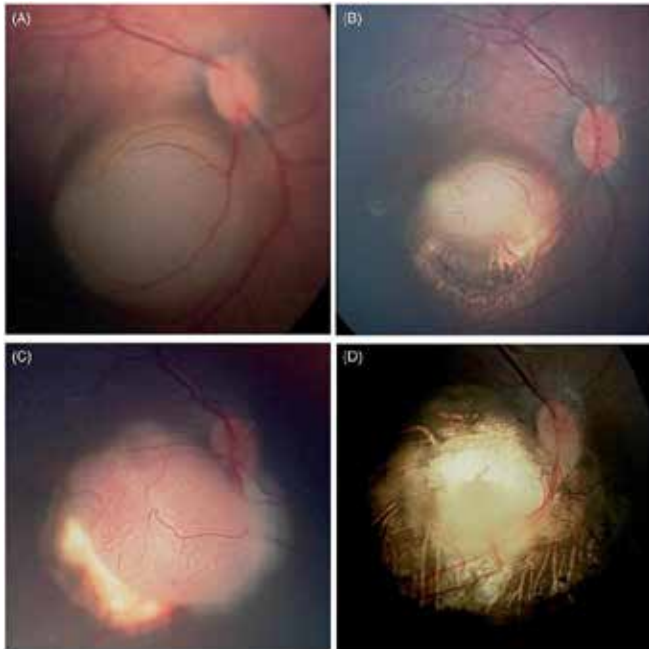
one eye with the other eye previously enucleated. Collectively, 18 eyes with retinoblastoma were evaluable. Only 14 were eligible for further analysis of response to TPT. Among the 18 evaluable eyes, 8 eyes had residual tumors with findings consistent with tumor viability following 6–8 cycles of standard chemotherapy. There were also 6 eyes with progressive disease at time of initiating TPT. Two patients (out of 6) were receiving chemotherapy (CVE protocol) at time of progression, while four patients were off therapy. Three eyes in three patients had inactive disease at time of initiating TPT which was started based on tumor status in the other eye. There was also one eye that was recently irradiated and tumor activity was not clear at time of initiating TPT. The three eyes with inactive disease and the one eye with recent radiation were not included in response analysis.

The median number of TPT cycles was three per patient (range, 1–6) after a median of 1 month (range, 1–5 months) following the last cycle of standard chemotherapy, and the total number of administered cycles was 29. Fever was documented during five cycles (17%). Grade 3 and 4 neutropenia were documented in 12 (31%) and 11 cycles (28%) respectively.

Thrombocytopenia was documented in four cycles (10%) and no one case had grade 4 thrombocytopenia. Admission for febrile neutropenia was needed in seven cycles (18%) while bacteremia was documented in only one case. No admission to the Pediatric Intensive Care Unit was needed. GCSF was used after two cycles only based on previous severe neutropenia. Vomiting requiring intravenous hydration was documented after two cycles (5%).

Among 14 eyes with evaluable disease, response was initially assessed after the first 1–2 cycles of therapy. After TPT therapy; 4 (29%) eyes showed favorable response (tumor thickness decreased to a level that can be controlled by focal consolidation therapy) (Figure 1). The other 10 eyes showed unfavorable response as follows: 3 (21%) eyes showed minimal regression (residual tumor still thick that cannot be controlled by focal consolidation therapy), 5 (36%) eyes had stable disease, and 2 (14%) eyes showed tumor progression (one was later salvaged). The median follow-up was 48 months (range, 36–65 months). Three eyes (21%) in three patients required external beam radiation therapy (EBRT) to control disease after 2, 12 and 12 months of initiating TPT. Three eyes (21%) in three patients were enucleated (one eye was enucleated following irradiation). Consolidation therapy was used for eight eyes after stopping TPT; trans-pupil thermal therapy (TTT) in eight eyes and cryotherapy in five eyes. At

time of analysis, out of 14 evaluable eyes, 9 (64%) eyes were salvaged, 3 (21%) eyes received radiation therapy, and 3 (21%) eyes were enucleated (one was post radiation). Interestingly, three of the eyes showed tumor progression after stopping TPT; one eye was controlled by consolidation therapy, one eye was enucleated 13 months after finishing the last TPT cycle, and one eye was irradiated 4 months after finishing TPT. Overall, there were 11 salvaged eyes with no need for EBRT among 18 eyes in the 10 studied patients.



**Figure 1.** A 7-month-old girl with bilateral retinoblastoma. (A) Ret-Cam images of the right eye at presentation. The tumor showed regression after six cycles of CVE chemotherapy and three sessions of thermal therapy. (B) 10 weeks after the sixth cycle of chemotherapy, the tumor progressed rapidly. (C) She received five cycles of systemic Topotecan therapy ( $2.5\text{mg}/\text{m}^2 = 1\text{mg IV in } 50\text{ ml N/S}$ ) with consolidation focal therapy and the tumor regressed significantly (D), and later on was controlled by multiple sessions of focal therapy.<sup>4,1</sup> Sultan et al. increasingly, they are used in the upfront treatment of retinoblastoma.<sup>8-15</sup>

## DISCUSSION

In this study we reviewed our institutional experience with TPT systemic therapy for patients with refractory or progressive intraocular retinoblastoma. In this analysis, favorable response to treatment was observed after 1-2 cycles of TPT in 29% of cases only. However, eye salvage was achieved in 64% of evaluable treated eyes in this series. The activity of TPT against retinoblastoma was first reported in single case reports.<sup>18,19</sup> Later, Chantada and colleagues<sup>20</sup> reported nine retinoblastoma patients who were treated with TPT for resistant/ progressive disease.<sup>20</sup> In that report, the response was noticed in three out of six patients

with extraocular disease, and in two out of three patients with intraocular disease. The dose used in that report was slightly lower than used in our patients ( $2\text{mg}/\text{m}^2/\text{dose}_5$  doses) and similar to our report, toxicity was not significant. Other forms of using TPT in retinoblastoma, including subconjunctival and intra-arterial administration of TPT, were used safely in patients with retinoblastoma with good activity. St. Jude Children Research Hospital has shown that therapeutic intraocular concentration of TPT follows systemic infusion in an animal model<sup>21</sup>

It seems that the blood-eye barrier is similar to the blood-brain barrier in its permeability to TPT. Recently, initial results of the institutional RET-5 protocol were published.<sup>22</sup> In this phase 2 study, single dose vincristine and five doses of TPT were given per cycle. The initial dose of TPT was  $2.25-3.5\text{mg}/\text{m}^2$ , depending on age. Two cycles were administered in a window phase and three more cycles were incorporated in the regimen of patients who showed response to the window phase before the introduction of focal therapy. TPT dose was adjusted depending on pharmacokinetic studies. Despite that, significant hematologic and non-hematologic toxicity, including two patients with typhilitis, made it necessary to use GCSF. Partial responses were seen in 24 out of 27 patients (89%), but the unacceptable high toxicity made this particular regimen highly toxic in comparison to other regimens used in retinoblastoma. It is probable that adding vincristine and the upfront introduction of the regimen in younger patients caused the obviously more toxic side effects in comparison to our report. Nowadays, focal administration of chemotherapy with intra-vitreous or intra-arterial chemotherapy are becoming more popularly used for patients with refractory/progressive retinoblastoma.

Nevertheless, there is still a need for a salvage regimen that can be used for patients with refractory or progressive disease. Giving more doses of standard chemotherapeutic agents will lead to more short and long term toxicities related to these drugs, and also lack of efficacy in patients who failed these agents previously.<sup>20-22</sup> This is particularly important in centers with no experience in the novel techniques mentioned above, or in patients who are not eligible for these methods, e.g. young infants where ophthalmic artery catheterization is technically difficult. Our report is retrospective in nature and evaluated a heterogeneous group of previously treated patients who needed salvage systemic chemotherapy at a time that modalities for focal administration of chemotherapy were not readily available. In our analysis, we used strict criteria

to define favorable response which might be a reflection of focal therapy as well.

Nevertheless, four eyes had a favorable response to treatment. Eye salvage was reported in a total of 9 out of 14 eyes with active disease at time of starting TPT. While it is hard to draw a definite conclusion, our report suggests that TPT could be used as a salvage regimen with low toxicity for patients with progressive intraocular retinoblastoma if systemic therapy is needed.

## CONCLUSIONS

Our report suggests that systemic TPT chemotherapy could be used as a salvage second-line regimen with low toxicity for patients with progressive intraocular retinoblastoma if systemic therapy is needed.

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کھول کر آنکھیں سرے آئینہ گفتار میں  
آنے والے دور کی دُھندلی سی اک تصویر دیکھ  
اقبال



Sadia Sethi

# Outcome of Anterior Transposition of The Inferior Oblique Muscle in The Treatment of Inferior Oblique Over-action

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## ABSTRACT

**Purpose:** To study the outcome of anterior transposition of inferior oblique muscle in the treatment of inferior oblique over action.

**Study Design:** This was a hospital based prospective study done at Department of Ophthalmology Khyber Teaching Hospital during January 2014 to June 2016.

**Methods:** A total of 35 patients were included in the study. Type of strabismus, ocular alignment, pre and post operative degree of Inferior Oblique over action were obtained using specified check list.

**Results:** A total of 35 patients were included in the study 57 eyes were operated. All patients had grade +3 inferior oblique overaction. Pre operative V pattern was present in 22 patients. After surgery it remained in only 5 patients. Overall 22 (62.8%) and 6 (17.4%) patients had preoperative esotropia and exotropia. While 7 (20%) patients had only IOOA Inferior oblique over-action improved in (91.4%). Residual hypertropia occurred in 2 (5%) and postoperative hypotropia was observed in 1 (2.8%) patient.

**Conclusion:** We concluded that anterior transposition of inferior oblique is effective for treatment of grade +3 inferior oblique over-action with minimum side effects.

**Key Words:** Anterior transposition, Inferior Oblique over-action, myectomy.

## INTRODUCTION

Over-action (or apparent over-action) of the inferior oblique muscle is a common aspect of new and recurring cases of strabismus. It is more appropriately described as over elevation in adduction in CEMAS classification system and by others.<sup>1,2,3,4,5</sup>

Primary inferior oblique over action (PIOOA) is usually associated with horizontal strabismus such as congenital esotropia or intermittent exotropia. Isolated PIOOA can occur without associated horizontal strabismus. Although PIOOA is bilateral in most of the cases but it is usually asymmetrical. Since the inferior oblique muscle is an elevator, abductor and extortor (the primary action of inferior oblique being extortion), these elements are exaggerated in direct proportion to over action. There is typical up shoot of adducting eye and shows V-Y Pattern.

Indirect ophthalmoscopy may show significant fundus extortion in both primary and secondary inferior oblique over action. One of the main secondary cause of IO over action is trochlear nerve palsy. Different surgical treatments have been done to treat inferior oblique muscle over-action.

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**Inferior oblique muscle transposition is successful and safe surgical procedure for treatment of grade +3 inferior oblique over-action.**

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## MATERIAL & METHODS

This study was conducted from January 2014 to June 2016 at Eye Department Khyber Teaching Hospital Peshawar. All patients were thoroughly examined including refraction, fundoscopy and squint assessment. Patients well excluded if had prior ocular disease or surgery, restrictive strabismus, history of trauma neurologic disease and craniofacial abnormalities. Patients with no vertical deviation in primary position but with +3 inferior oblique muscle overaction were selected. The inferior oblique was approached through conjunctiva and tenon's capsule by an inferior temporal fornix incision. A straight fine haemostat was placed across the inferior oblique muscle

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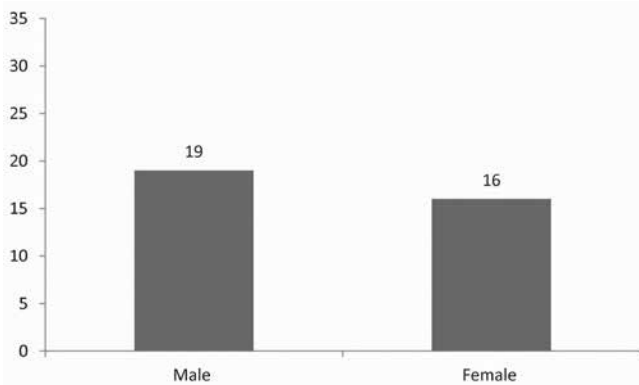
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as close as possible to its insertion. The muscle was cut near the haemostat and the cut end was cauterized. A 6 zero vicryl suture was passed through the stump and the muscle was reattached to the sclera lateral to the inferior rectus muscle insertion. The conjunctiva was then sutured. Patients were examined at 10 days, 40 days and 3 months post operatively. Final outcome was considered at 3 months.

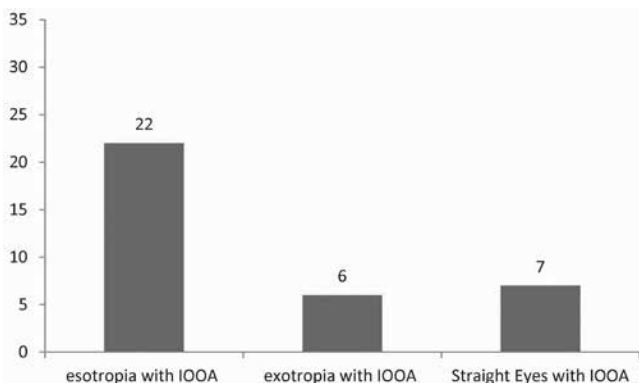
**RESULTS**

A total of 35 patients with grade +3 inferior oblique overaction were included in the study 57 eyes were operated. Out of 35 Patients 19 (54.2%) patients were male while 16 (45.7%) were female (Figure 1). Patients with minimum age of 5 years and maximum age of 30 years were included in the study. 22 (62.8%) patients had esotropia with IOOA 6 (17.4%) had exotropia with IOOA while 7 (20%) patients had only IOOA (Figure 2). Horizontal muscle surgery was performed in same operation where required. Out of 35 patients 32 (91.4%) patients achieved success, 2 (5%) had residual hypertropia while 1 (2.8%) had post operative inferior oblique under-action. (Figure 3)

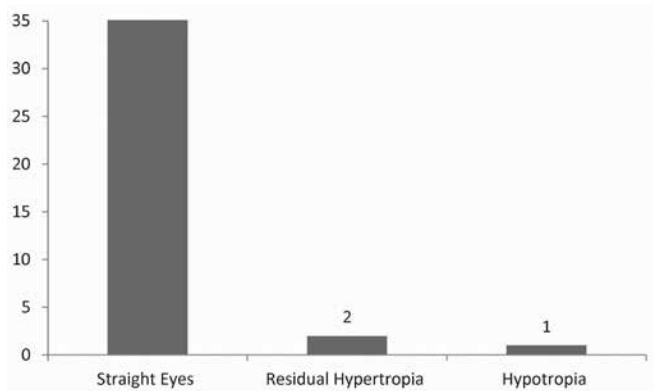
**Figure 1:** Gender Difference in Distribution of inferior oblique muscle over action



**Figure 2:** Horizontal Strabismus associated with Inferior oblique muscle over action



**Figure 3:** Out Come of Anterior Transposition of the Inferior Oblique Muscle In the treatment of Inferior Oblique Over Action



**DISCUSSION**

Different surgical treatments have been done to treat inferior oblique muscle over-action. In our study inferior transposition of Inferior oblique muscle was done for inferior oblique over-action with high success rate. Many studies have investigated the superiority of different surgical treatment for IOOA, however there are controversies in different studies.

In one study all the three procedures disinsertion, myectomy, and anterior transposition of inferior oblique muscle were effective for primary or secondary Inferior oblique overaction with minimum side effects.<sup>6</sup> In another study for the treatment of IOOA both myectomy and recession of Inferior oblique were used with similar success rates.<sup>7</sup> In a study conducted by Sadia Bukhari showed that isolated inferior oblique myectomy is highly successful and safe surgical procedure for correction of hypertropia.

Ghazawyet al study demonstrated that Inferior oblique myectomy has some advantage over anterior transposition in treating combined inferior oblique over-action and superior oblique underaction.<sup>8</sup> Graded IO recession by Fink’s method is an effective procedure to correct cyclo-vertical deviations due to primary inferior oblique over action. It also improves cyclo-vertical diplopia in selective cases.<sup>9</sup> While study conducted by Uncovskae et al showed that in patients with DVD and greater inferior oblique overaction anterior transposition of inferior oblique is more effective surgical treatment than myectomy.<sup>10</sup>

In our study inferior oblique under-action was present in 3% of the patients. These results are similar to another study where inferior oblique underaction was common, generally mild, persistent and usually asymptomatic 6 months following inferior oblique myectomy or recession.<sup>11</sup>



## CONCLUSION

Inferior oblique muscle transposition is successful and safe surgical procedure for treatment of grade +3 inferior oblique over-action.

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Sidrah Riaz

## Frequency of Hepatitis B & C in Previously Unscreened Patients Admitted for Elective Cataract Surgery

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Khalid Mahmood FCPS<sup>3</sup>, Prof. Dr. Saleem Akhtar FRCOphth, FRCS<sup>4</sup>

### ABSTRACT

**Objective:** To determine frequency of hepatitis B & C in patients admitted for cataract surgery.

**Methods:** A descriptive study conducted at Department of Ophthalmology in Akhtar Trust hospital, Lahore. The duration of study was 08 months from January 2015 to August 2015. All the patients admitted for cataract surgery were screened for hepatitis B surface antigen (HBsAg) and anti HCV antigen using immune-chromatography (ICT) method after taking informed consent from patients and hospital ethical committee. Diagnosis was made on basis of positive results for Anti HCV or HbsAg or both. Patient information was recorded on performs, data collected and analysed.

**Results:** 500 patients were admitted for cataract surgery from outpatient department (OPD) in Akhter Saeed Trust Hospital. Mean age of patients was 55 years out of these 273 were males (54.6%) and 227 were females (45.4%). 191 patients (38.2%) were carriers of either Hepatitis B or C. Hepatitis B accounted for 72 cases (14.4%) and Hepatitis C for 119 cases (23.8%). No patient was affected with B and C simultaneously.

**Key Words:** Hepatitis B, Hepatitis C, cataract surgery.

### INTRODUCTION

Viral Hepatitis is an infection of liver caused by viruses A, B, C, D and E resulting in its inflammation that can lead to hepatocellular carcinoma and liver cirrhosis.<sup>1</sup> Hepatitis B is a DNA virus and its liver infection is potentially life threatening, causing death of nearly one million people each year, around 2 billion people are affected by virus any time in their life time and 3 million are carriers.<sup>2</sup> Hepatitis B infection has worldwide distribution but vast majority of affected patients live in Asia, Africa and Middle East.<sup>1,3</sup> Annually 1.2 million people are dying from cirrhosis and liver cancer from chronic HBV infection.<sup>4</sup> A vaccine against HBV is available since 1992 which is 95% effective in preventing infection. HCV is RNA virus and it causes both acute and chronic liver infection. About 15-45% of infected person spontaneously clear the virus within 6 months of infection without any treatment. The remaining 55-85% people develop chronic HCV infection and risk of cirrhosis is 15-30% within 20 years.

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**Screening of every patient before surgery should be done, it can lead to early diagnosis and avoid cost of treatment and complications by early diagnosis. The doctors and operation theatre staff should follow proper ethical practice ensuring use of disposable syringes, blades and sterile instruments. The general population should be educated about disease risk factors and modes of spread.**

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The world health organization (WHO) estimated that 3% of world population is infected with HCV accounting for 120-170 million.<sup>5</sup> Both HBV and HCV share similar modes of transmission contaminated blood transfusion, prenatal, use of infected surgical instruments, dental surgery, sexual contacts and drug abuse.<sup>6</sup> Incidence of B and C is on rise.<sup>7</sup> Public and private sector hospitals where routine screening of hepatitis B and C is not done are posing serious threat to public.<sup>8</sup> In Pakistan prevalence of hepatitis B is 10%<sup>9,10</sup> and 4-7%<sup>11,12</sup> for hepatitis C. Health care providers specially surgeons and theatre staff are at high risk to get infected so study was conducted to have at least an idea about disease prevalence.

### METHODS

The descriptive study was carried out in AMDC Hospital. All patients admitted for cataract surgery were *included* in study. Patients with age less than

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20 years and other associated ocular morbidity like glaucoma, uveitis and retinal detachment were excluded. Informed and written consent was obtained from all patients and information was kept confidential. The study was approved by hospital ethical committee. Duration of study was 6 months and 500 patients were included, screened for AntiHCV and HbsAg using ICT methods. Data was recorded on performa and analyzed by SPSS version 20. Those patients who were positive were sent to physician in medical ward for ELISA, LFTs, PT, APTT and ultrasound abdomen. All patients who were not vaccinated and not suffering from hepatitis B were advised for vaccination.

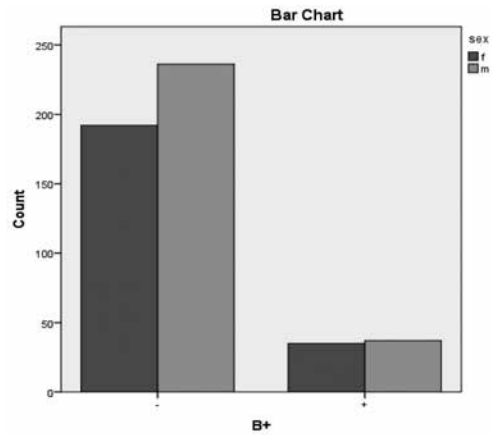
**RESULTS**

In this study 500 patients were admitted in 08 month period for cataract surgery, evaluated for presence or absence of HbsAg and antiHCV. 309 patients were operated for cataract and remaining, who were positive for hepatitis B and C, were sent to medical unit for further evaluation. Out of 500 patients males were 273 (54.6%) and 227(45.4%) were females. Mean age of patients was 65 years. Age ranged from 22 to 90 years. Total 191 (38.2%) had either hepatitis B or C. no one was affected with both viruses simultaneously. The patient who were found positive for hepatitis C were 119 (23.8%) and for HBV were 72 (14.4%).

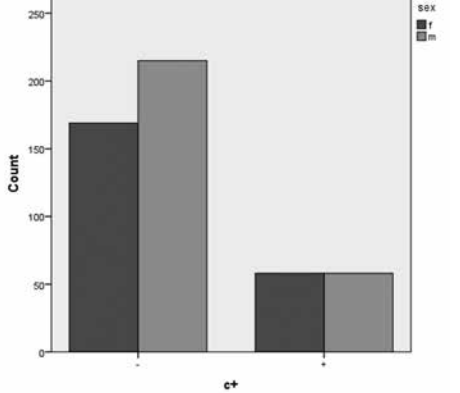
Hepatitis B was found in 37 (7.4%) males and 35 (7%) females. Hepatitis C was predominant in 63 (12.6%) males and 56 (11.2%) females. 91 (18.2%) out of 227(45.4%) female patients had either Hepatitis B or C, however 100 (20%) out of 273 (54.6%) male patients had hepatitis B or C. 173 (34.6%) male patients and 136 (27.2%) females had neither hepatitis B or C.

Data of Patients				
Data				
Number of patients	500			
Mean age	55 year			
Male patient	273			
Female patient	227			
Gender distribution of patients				
Gender	No disease	Hepatitis C +ve	Hepatitis B +ve	Total
Male	173(34.6%)	63(12.6%)	37(7.4%)	273(54.6%)
Female	136(27.2%)	56(11.2%)	35(7%)	227(45.4%)
Total	309(61.8%)	119(23.8%)	72(14.4%)	500

**Bar Chart showing patients with HbsAg+**



**Bar Chart showing patients with AntiHCV+**



**Bar Chart showing patients with AntiHCV+**

**DISCUSSION**

Hepatitis B and C are endemic in world now specially in developing countries like Pakistan. In rural areas unsafe, medical practice is common. In our study incidence of hepatitis B was 14.4% and 23.8% for HCV. The carrier state of HbsAg is around 10% in different segments of Pakistani people<sup>13</sup>, according to a study conducted in 2005 which is lower than our study conducted in 2015. Weis and co-workers reported 35% cases of HCV and 4% cases of HBV in their study in patients operated at John Hopkins.<sup>14</sup> In this study ratio of male is higher than female, in HBV 26.6% male and 25.2% female while in HCV 12.6 % males and 11.2% females are reported.

It is known that virus transmission is through blood and secretions. Most common route of transmission of hepatitis B and C virus is parenteral specifically blood transfusion, infected needle prick, injections by quacks, dental treatment, shaving by street barbers, sexual contacts and vertical transmission from mother to child.<sup>15,16</sup> More than 80% deliveries are conducted in our rural areas by traditional birth attendant in unhygienic

condition and without observing proper sterilization making mothers more vulnerable to HBV and HCV infection. 3 variables are significant regarding viral hepatitis prevalence which are intravenous drug abuse, blood transfusion and low socioeconomic status.<sup>17,18,19</sup> In order to prevent disease spread simple preventive measures can do a miracle, so awareness of disease and its risks should be known not only to patients but also to surgeons, theatre staff, nurses and paramedic staff. This is a hospital based study so application to general population could not be done but it highlights huge magnitude of disease burden that is not known by the patients.

### CONCLUSION

Prevention is better than cure so simple and relatively cheap screening method of every patient before surgery should be done because it can lead to early diagnosis and avoid cost of treatment and complications. The doctors and operation theatre staff should follow proper ethical practice ensuring use of disposable syringes, blades and sterile instruments. The general population should be educated about disease risk factors and modes of spread.

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جو ہے پردوں میں پنہاں، چشم بینا دیکھ لیتی ہے  
 زمانے کی طبیعت کا تقاضا دیکھ لیتی ہے  
 اقبال



Fatima Afzal

## Intraocular Pressure changes following Intravitreal Injection of Bevacizumab

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### ABSTRACT

**Objective:** 1. To determine the frequency of patients with age related macular degeneration that show a rise in intraocular pressure at least 5mmHg above their baseline value at 30 minutes after intravitreal injection of bevacizumab. 2. To determine the frequency of these patients in whom intraocular pressure returns to baseline at 24 hours.

**Materials and Methods:** This study was conducted in the department of ophthalmology Services Hospital Lahore, from July 2012 to December 2012. 100 eyes of 100 patients fulfilling the inclusion criteria were selected for this study. The prepared 0.05ml of bevacizumab (1.25mg/0.05cc) in a tuberculin syringe was injected with a 27- gauge needle through the pars plana at 4mm or 3.5mm away from the limbus. Then the intraocular pressure was measured using Goldman applanation tonometer 30 minutes post procedure, to determine the frequency of rise in intraocular pressure, and then after 24 hours to determine the frequency of those in whom intraocular pressure returned to baseline.

**Results:** The mean age of the patients was 76.4±4.9 years. There were 68 (68.0%) male and 32 (32.0%) female patients. The mean baseline intraocular pressure (IOP) of the patients was 12.2±2.0 mmHg. The mean intraocular pressure at 30 minutes of the patients was 13.2±2.0 mmHg. There were 8 (8%) patients who had rise in IOP at 30 minutes. There were 8 (100%) patients, whose IOP at 24 hours returned to baseline.

**Conclusion:** It was concluded from this study that intravitreal injection of bevacizumab is safe with respect to IOP changes, in case the IOP of patients rises after 30 minutes the majority of patients' IOP returned to baseline within 24 hours.

**Key words:** Intravitreal injection, age related macular degeneration, bevacizumab, intraocular pressure

### INTRODUCTION

Bevacizumab, is a full-length monoclonal antibody that recognizes and blocks all iso forms of vascular endothelial growth factor (VEGF).<sup>1</sup> It was approved by the US Food and Drug Administration (FDA) in 2004 for combination use with standard chemotherapy for metastatic colorectal cancer.<sup>2</sup> The drug was introduced to the international retina community in May 2005.<sup>3</sup> Its 'off- label' intravitreal use has grown exponentially ever since. Bevacizumab is being used for the treatment of retinal and choroidal neovascularization<sup>4</sup>, iris neovascularization, vitreous hemorrhage and macular edema<sup>5</sup> and has shown beneficial results. Because of its cost effectiveness compared to other anti VEGF agents, it has become the first line treatment for age related macular degeneration<sup>4</sup> with choroidal neovascularization which is likely to emerge as a major public health threat in our country in the near future. However existing literature on age related macular degeneration in the region is scarce. The Pakistan National Blindness and Visual Impairment Survey, in a report found that macular degeneration accounted for

2.1% of all blindness.<sup>6</sup>

**Intravitreal injection of bevacizumab is safe with respect to IOP changes, if the IOP of patients rises after 30 minutes in the patients it returns to the baseline within 24 hours.**

Other drugs used intravitreally include other anti-VEGF agents pegaptanib and ranibizumab; steroids like triamcinolone acetonide; antibacterial agents like vancomycin, ceftazidime, ceftriaxone; and antifungals like amphotericin B. The most commonly used doses are 0.1 ml (4mg) of triamcinolone, 0.09ml (0.3mg) of pegaptanib, 0.1 ml (1mg) of vancomycin, 0.1ml (2.0mg) of ceftriaxone, 0.1 ml (5to 10 ug) of amphotericin B.<sup>7,8,9</sup> A vitreous tap or paracentesis is usually required with administration of these drugs. Whereas the dose of ranibizumab used is 0.05ml (0.5mg) and that of bevacizumab used is 0.05ml (1.25mg).<sup>7</sup> The volume is about half that of any other drug used intravitreally and a vitreous tap is not routinely done.

With its growing popularity, assessment of safety of intravitreal bevacizumab is of fundamental importance. Documented complications of intravitreal bevacizumab injection are endophthalmitis, retinal tears, subretinal hemorrhage, vitreous hemorrhage, uveitis and lens injury.<sup>4,9</sup> Intravitreal injection of any drug, such as bevacizumab, increases the amount of fluid within the eye, and hence will increase IOP.

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Hollands et al in their study on 104 patients who underwent intravitreal injection of Avastin, found that 13.5% of patients had a rise in IOP at 30 minutes.<sup>10</sup> In the study, in 2 out of 3 patients (66.7%), IOP returned to baseline at 24 hours.

The rationale of this study is to evaluate intraocular pressure changes following intravitreal injection of bevacizumab as part of the efforts to establish its safety profile in terms of rise in intraocular pressure. Although ample research is available on its efficacy in the various diseases of the eye mentioned but little or no work has been done in our country to evaluate potential side effects of the intravitreal use of bevacizumab, especially its effect on intraocular pressure. As already mentioned, any intravitreal injection is expected to cause a rise in intraocular pressure by increasing fluid volume inside the eye. The very few international studies available have assessed the pressure changes only up to 30 minutes and patients were not followed beyond that. Our study will follow patients after the injection for up to 24 hours and evaluate the change in IOP, so that it can be ascertained whether a paracentesis or vitreous tap should be done, whether IOP monitoring is necessary after the procedure and to reassess the optimum amount of fluid to be injected into the eye. With more evidence and research done on its safety profile, the surgeons' confidence in the use of this drug will increase and patients will benefit greatly from this new treatment modality.

## MATERIALS AND METHODS

**Study Design:** Descriptive case series.

**Study Setting:** Department of Ophthalmology Unit 1, Services Hospital, Lahore

**Duration of Study:** Six Months (July 2012 to December 2012)

**Sampling Technique:** Non Probability purposive sampling

**Sample Size:** Sample size of 100 cases was calculated with 95% confidence level, 7% margin of error and taking expected percentage of patients who show a rise in intraocular pressure to 13.5% at 30 minutes of intravitreal injection of bevacizumab in patients with age related macular degeneration.

**Data Collection Procedure:** 100 patients fulfilling the inclusion criteria were selected from the outpatients department of Eye Unit 1, Services Hospital, Lahore. After getting informed consent, socio demographic data (name, age, gender) were noted. Pre-procedure evaluation included assessment of baseline intraocular pressure measurement using Goldman applanation tonometer. Intravitreal injection was given in the operation theatre under sterile conditions. Patients were prepared and draped in standard fashion. A solution of 10% povidone iodine was used for sterilization, a lid speculum for lid control and topical proparacaine hydrochloride 0.5% is instilled every 5 minutes, 3 times

before the procedure for anesthesia. The prepared 0.05 ml of bevacizumab (1.25mg/0.05cc) in a tuberculin syringe was injected with a 27-gauge needle through the pars plana at 4mm or 3.5mm away from the limbus if the patient is phakic or pseudophakic respectively. The needle was inserted approximately 1 cm into the globe and the drug was injected. After injection a sterile cotton swab was placed on the injection site to prevent the reflux of the medicine and a drop of an antibiotic, ciprofloxacin 0.3%, was instilled. The patient was advised to use ciprofloxacin 0.3% drops four times a day for ten days. Then the intraocular pressure was measured using Goldman applanation tonometer 30 minutes post procedure, to determine the frequency of rise in intraocular pressure, and then after 24 hours to determine the frequency of those in whom intraocular pressure returned to baseline. All the above information was collected on the proforma.

**Data Analysis:** Data was entered, and analyzed using SPSS version 10.0. The quantitative variables like age was measured in terms of mean and standard deviation. Qualitative variables like sex and raised intraocular pressure were presented as frequencies and percentages. P value  $\leq 0.05$  was considered significant.

## RESULTS

100 eyes of 100 patients with age related macular degeneration were included in the study. The mean age of the patients was 76.4 $\pm$ 4.9 years with age range from 20-80 years. There were 1 (1%) patients in the age range of 56-60 years, 4 (4%) patients in the age range of 61-65 years, 8 (8%) patients in the age range of 66-70 years, 21 (21%) patients in the age range of 71-75 years and 66 (66%) patients in the age ranging from 76-80 years (Table 1). There were 68 (68.0%) male and 32 (32.0%) female patients (Table 2). Based on occupation, 30 (30%) patients were housewives, 42 (42%) patients were laborers, 18 (18%) patients were retired, 6 (6%) patients were businessmen and 4 (4%) patients were farmers (Table 3). There were 24 (24%) patients had injection given to left eyes and 76 (76%) patients had injection given to right eyes (Table 4). The mean baseline intraocular pressure (IOP) of the patients was 12.2 $\pm$ 2.0 mmHg. There were 68 (68%) patients with IOP range of 10-12 mmHg, 29 (29%) patients had IOP range of 13-15 mmHg and 3 (3%) patients had IOP ranging from 16-18 mmHg (Table 5).

The mean intraocular pressure at 30 minutes of the patients was 13.2 $\pm$ 2.0 mmHg. There were 53 (53%) patients with IOP range of 10-12 mmHg, 33 (33%) patients had IOP ranging from 13-15 mmHg and 14 (14%) patients had IOP range of 16-18 mmHg (Table 6).

Considering the rise in IOP at 30 minutes, there were 8 (8%) patients who had rise in IOP and 92 (92%) patients had incidence of in IOP (Table 7). In the distribution of patients by IOP at 24 hours who returned to baseline, there were 8 (8%) patients, whose IOP at 24

hours returned to baseline (Table 8)

**Table 1:** Distribution of patients by age (n=100)

Age (Years)	No. of patients	Percentage
56-60	1	1.0
61-65	4	4.0
66-70	8	8.0
71-75	21	21.0
76-80	66	66.0
Mean ±SD	76.4±4.9	

**Table 2:** Distribution of patients by gender (n=100)

Gender	No. of patients	Percentage
Male	68	68.0
Female	32	32.0
Total	100	100.0

**Table 3** Distribution of patients by occupation (n=100)

Occupation	No. of patients	Percentage
Housewives	30	30.0
Labor	42	42.0
Retired	18	18.0
Businessmen	6	6.0
Farmer	4	4.0
Total	100	100.0

**Table 4 :** Distribution of patients by injection given (n=100)

Injection given	No. of patients	Percentage
Left eye	24	24.0
Right eye	76	76.0
Total	100	100.0

**Table 5:** Distribution of patients by baseline IOP (n=100)

Baseline IOP	No. of patients	Percentage
10-12	68	68.0
13-15	29	29.0
16-18	3	3.0
Mean ±SD	12.2±2.0	

**Table 6:** Distribution of patients by IOP at 30 minutes (n=100)

IOP at 30 minutes	No. of patients	Percentage
10-12	53	53.0
13-15	33	33.0
16-18	14	14.0
Mean ±SD	13.2±2.2	

**Table 7:** Distribution of patients by rise in IOP (n=100)

Rise in IOP	No. of patients	Percentage
Yes	8	8.0
No	92	92.0
Total	100	100.0

**Table 8:** Distribution of patients by IOP at 24 hours return to baseline (n=8)

IOP at 24 hours return to baseline	No. of patients	Percentage
Yes	8	8.0
No	0	0
Total	8	100.0

**DISCUSSION**

Intravitreal injection has become an increasingly common intervention in the treatment of retinal disease. With more than 15,000 annual intravitreal projected injections worldwide, bevacizumab is rapidly becoming one of the leading treatments for nonvascular age-related macular degeneration.<sup>11</sup> However, there is a growing evidence, of the benefits of bevacizumab for treating other ocular diseases associated with neovascularization, such as diabetic retinopathy.<sup>12</sup>

Previous studies support the use of intravitreal bevacizumab for treating various conditions of ocular pathology.<sup>13,14</sup> The largest collection of data concerning the safety of bevacizumab was compiled by the international intravitreal bevacizumab safety survey,<sup>1</sup> which reported on complications such as endophthalmitis, cataract progression, subretinal hemorrhage and retinal tears. However, as the report relied on voluntary reporting to ascertain complication rates, underestimation of these rates seems quite possible. Furthermore, the role of intraocular hypertension was not studied quantitatively.<sup>13,14</sup>

Numerous published reports highlight the potential for a significant rise in intraocular pressure (IOP) following intravitreal injections in general.<sup>15,16,17</sup> An acute rise in IOP has been shown in animal models to block axonal transport to the optic nerve head, in addition a higher rise in IOP is associated with more severe damage.<sup>18</sup> An acute rise in IOP has also been shown to decrease juxta papillary retinal and optic nerve head blood flow proportionally to the quantitative rise in IOP.<sup>19</sup>

Three recent studies have investigated the short term change in IOP following intravitreal injection of triamcinolone acetonide.<sup>15,16,17</sup> In the study by Benz et al<sup>15</sup>, the IOP normalized in most patients 30 minutes after injection, but 10% of patients, who did not have vitreous reflux after injection had an IOP greater than 25mmHg at 30 minutes. The mechanism for the short term IOP rise immediately after intravitreal injection of triamcinolone acetonide was thought to be a result of the increase in volume of the vitreous cavity after injection. As the intravitreal use of bevacizumab is growing exponentially, the safety of this procedure is of fundamental importance. Given the potential for significant IOP elevation in the immediate post injection period.

With its growing popularity, assessment of

safety of intravitreal bevacizumab is of fundamental importance. Documented complications of intravitreal bevacizumab injection are endophthalmitis, retinal tears, subretinal hemorrhage, vitreous hemorrhage, uveitis and lens injury.<sup>4,9</sup> Intravitreal injection of any drug, such as bevacizumab, increases the amount of fluid within the eye, and hence will increase IOP. Hollands et al in their study on 104 patients who underwent intravitreal injection of Avastin, found that 13.5% of patients had a rise in IOP at 30 minutes.<sup>10</sup> In the study, in 2 out of 3 patients (66.7%), IOP returned to baseline within 24 hours, so assume in my study that 50% of these patients will have normal IOP at 24 hours.<sup>10</sup>

In our study the mean age of the patients was 76.4±4.9 years. As compared with the study of Hollands et al<sup>10</sup> the mean age of the patients was 76±10.3 years, which is comparable with our study. In our study there were 68.0% male and 32.0% female patients as compared with the study of Hollands et al<sup>10</sup> there were 42% male and 58% female patients.

In our study the mean baseline intraocular pressure of the patients was 12.2±2.0 mmHg. As compared with the study of Hollands et al<sup>10</sup> the mean baseline intraocular pressure of the patients was 14.0 mmHg, which is comparable with our study. In our study, the mean intraocular pressure at 30 minutes of the patients was 13.2±2.0 mmHg as compared with the study of Hollands et al<sup>10</sup> the mean intraocular pressure at 30 minutes of the patients was 15.5 mmHg, which is comparable to our study. In our study there were 8% patients had rise in IOP at 30 minutes. As compared with the study of Hollands et al<sup>10</sup> 13.5% patients had rise in intraocular pressure at 30 minutes, which is comparable with our study. In our study 100% patients IOP at 24 hours returned to baseline. As compared with the study of Hollands et al<sup>10</sup> 66.7% patients intraocular pressure at 24 hours returned to baseline, which is comparable with our study.

On the above discussion, it is concluded that intravitreal injection of bevacizumab is safe with respect to IOP changes, the IOP of patients rise after 30 minutes as majority of patients' IOP returned to baseline within 24 hours.

**CONCLUSION**

It is concluded from this study that intravitreal injection of bevacizumab is safe with respect to IOP changes, if the IOP of patients rose after 30 minutes, it returned to baseline within 24 hours.

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Rabia Mobeen

## Determination of Best Regime for Administration of Atropine Eye Drops for Cycloplegia

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### ABSTRACT

**Objective:** Refractive error is a very common disorder of eye and it frequently causes reduced vision in children which can affect their daily life and academic performance. Hence, it is very important for children to have an eye examination. High accommodative power in children affects the refractive status of eye, so it is necessary to relax it fully while assessing their refractive error. In this regard cycloplegic drugs are instilled in eyes for accuracy in measurements. Atropine is the most efficient cycloplegic agent but its recommended regimen is of very long duration so we have to find the best regime for atropine instillation to achieve maximum cycloplegia.

**Methodology:** A cross sectional study was conducted to assess the best regime for administration of 1% atropine eye drops for cycloplegia and to see the effect of cycloplegia on different type of refractive errors. 30 patients of age between 0 to 12 years were assessed using a self designed performa. Patients requiring cycloplegic refraction were examined after installation of atropine 1 drop for 1 day and 3 drops for 3 days by autorefractometer and retinoscopy and results were compared to find out the difference in refractive error and the effect of cycloplegia on myopes and hyperopes.

**Results:** It showed most of the patients have no difference in refractive error between first day of atropine instillation and after three days. Few patients show little difference of +/-0.25 D after three days. Hyperopic patients showed less difference in refractive error found between first and third day of atropine instillation as compared to myopic patients. Atropine is an efficient cycloplegic drug and we can get effective cycloplegia on first day with even one drop of atropine instillation.

**Conclusion:** This may be beneficial for both the practitioner and child while doing cycloplegic refraction. It will greatly reduce the waiting time for parents and children, and will also lessen the adverse effects of atropine and allow for a better clinical service.

**Key words:** Atropine, Cycloplegia, Myopia, Hyperopia, Refractive error.

### INTRODUCTION

Refractive error is a very common disorder of eye, it occurs when the eye cannot focus light rays entering from infinity on the retina with accommodation being at rest. These errors may be classified into different categories that are: In Myopia one feels difficulty while seeing distant objects. In Hyperopia one cannot see near objects clearly. In Astigmatism, instead of one focal point on retina there are two points which causes distorted vision.

Such types of refractive errors are frequent cause of reduced vision in children so it is very important for children to have an eye examination. Symptoms include blur vision, squeezing the eyes, eye strain; headache The prevalence rate of visual impairment caused due to uncorrected refractive errors is estimated to be 153 million people, of whom eighty lacs are blind. Some

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**Cycloplegic refraction may be beneficial for both the practitioner and child. It will greatly reduce the waiting time for parents and children, lessens the adverse effects of atropine and allows for a much more efficient clinical service.**

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children can present with squint.<sup>1,2</sup> Such errors can be diagnosed by an eye examination and may be treated with best corrective glasses, contact lenses or refractive surgery.<sup>3</sup> Cycloplegic drugs produce paralysis of ciliary muscles which is called cycloplegia. These drugs can be instilled in the conjunctival sac, such as atropine, homatropine, tropicamide, scopolamine and cyclopentolate are known as cycloplegics. By paralyzing the parasympathetic nerve supply all accommodation can be abolished and refractive errors which before were latent become manifest. Atropine is an anti-cholinergic drug used to temporarily paralyze accommodation reflex in children and also as a mydriatic to dilate pupil. It is the most efficient cycloplegic agent. Although it is considered a relatively safe drug, some local and systemic side effects do occur. The recommended regimen for atropine Cycloplegia has been 7 to 10 applications within 3 to 4 days.<sup>4</sup>

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The purpose of this study is to find out the best regime for atropine instillation to achieve maximum cycloplegia. It will benefit both the practitioner and child while doing Cycloplegic refraction. The procedure of determining and correcting refractive errors is termed as refraction. The refraction comprises two complementary methods, the objective and subjective. In **objective refraction**, the examiner determines the type and degree of refractive error without active participation of the patient. The findings of objective refraction should always, wherever possible, be checked subjectively. The final refraction of the patient is much easier and is completed quickly if it is based on the objective estimate instead of its being only the subjective technique.<sup>5</sup>

High level of accommodation in children affects the refractive status of eye as lens optical power and shape can be altered by contracting ciliary muscles, so it is necessary to relax their accommodation fully while assessing refractive error. In this regard cycloplegic drugs are instilled in eyes for accuracy in measurements. It is called cycloplegic refraction. Some practitioners would argue that a cycloplegic examination should be carried out on all new patients. Indeed, in the Pediatric Clinic all children attending for the first time undergo a cycloplegic refraction. However, it is possible to highlight certain groups of children on whom a cycloplegic refraction is essential:

- Those in whom a satisfactory standard of acuity is not demonstrated.
- Those in whom a satisfactory level of stereopsis is not demonstrated.
- Those who present with a manifest squint, particularly an esotropia.
- Those who have an esophoria which appears significant or unstable.
- Those with a family history of squint, amblyopia or high hypermetropia.
- Those in whom pseudomyopia is suspected.
- Those who have a history of an 'eye turn' observed by the parent or guardian.
- Those who have anisometropia of greater than 1D.
- Those in whom poor accommodation is found.

A cycloplegic agent can always be used as an aid to refraction for a patient who shows poor co-operation during a standard routine refraction. A comparative study of refraction by atropine cycloplegia was held in children. They compared the refractive errors found after 2 drops one day and 9 drops three days atropine instillation and found that in 80-90% of the children after 3-day atropinization (9 drops per eye) the additional

cycloplegic effect of atropine is only 0.5 diopter compared to the application of 2 drops on the first day. So they concluded that for clinical purposes glasses can be prescribed on the basis of refractive data evaluated after 90-min atropinization.<sup>6</sup> Atropine is thought to produce the most effective cycloplegia in early childhood. Cyclopentolate and Tropicamide are the best known short acting cycloplegic agents. Phenylephrine is an adrenergic agent and has also a cycloplegic effect. In a study, combination of Cyclopentolate, Tropicamide and Phenylephrine with Atropine were compared and found no difference between them.<sup>7</sup>

#### RESEARCH DESIGN AND METHODOLOGY

A study was conducted on hyperopes in which refraction and wave front aberrations were evaluated before and after cycloplegia with topical administration of 1% atropine solution twice a day for a period of 1 week. Result showed significantly increased spherical equivalent refraction from  $+1.92 \pm 1.53$  diopters (D) to  $+3.10 \pm 1.61$ D. Corneal higher order aberrations did not alter after cycloplegia.<sup>8</sup> In another study 1% Atropine was used for cycloplegia. Results showed bilateral hypermetropia of +2.00 D or more in 12% of the children. Astigmatism of about +1.50 D or more in one or both eyes was found in 13.23% and anisometropia was found in 6.5% of children. Anisometropia was significantly associated with bilateral hypermetropia, but even more significantly associated with astigmatism.<sup>9</sup>

Further they compared the finding after atropinisation and found that cyclopentolate 1% is significantly less effective than atropine 1% at producing cycloplegia in 1-year-old children. If cycloplegic refraction is to be used for investigation or screening children for visual defects during the sensitive period, the more prolonged and profound cycloplegia following atropine could potentially have a disastrous effect on the development of vision. Cyclopentolate 1% would have to be used, and allowance made for its inadequacy as a cycloplegic.<sup>10</sup>

A quantitative, descriptive cross-sectional study was conducted to assess the best regime for administration of 1% atropine eye drops for cycloplegia and to see the effect of cycloplegia on different type of refractive error. 30 patients of age between 0 to 12 years were assessed using a self designed performa. Patients requiring cycloplegic refraction were examined after installation of atropine 1 drop for 1 day and 3 drops for 3 days by autorefractometer and retinoscopy and results were compared to find out the difference in refractive error and the effect of cycloplegia on myopes and hyperopes.

**RESULTS**

The great problem faced by an optometrist is instilling Cycloplegic drugs and waiting for one to two hours for refraction. This technique leads to lack of interest and cooperation especially in children. Further there are associated side effects with the prolong use of Cycloplegic drugs like pigmentation of the conjunctiva and cornea, lacrimal duct blockage, pigment in the anterior chamber, increased intraocular pressure, corneal endothelium damage, blurred vision, macular edema, allergy, discomfort, and hyperemia. This study was carried out on the determination of best regime for administration of atropine eye drops for cycloplegia. It was a cross sectional study. Data was collected through self designed performa. Patients requiring cycloplegic refraction were examined after installation of atropine for 1 day TID by autorefractometer and retinoscopy and results were compared with those found after 3 days of TID atropine instillation. The sample was drawn using non probability purposive study. Answers were taken on the performa, fed on computer using the SPSS version 20 software. The results were analyzed using the same software. The data is arranged in graphical form, where needed for the analysis of variables. These diagrams show the frequency distribution of the variables and their proportions among the patients and comparison of one day and three day cycloplegic findings of atropine instillation.

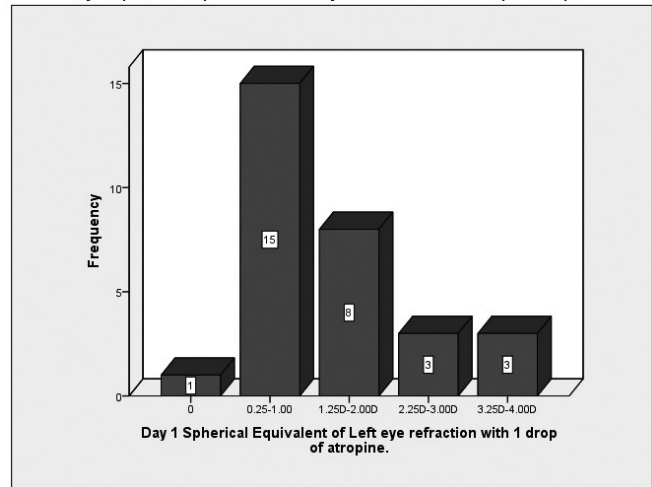
The data is divided into two parts each showing one profile.

Patients' profile

- History
- Clinical examination/ visual status

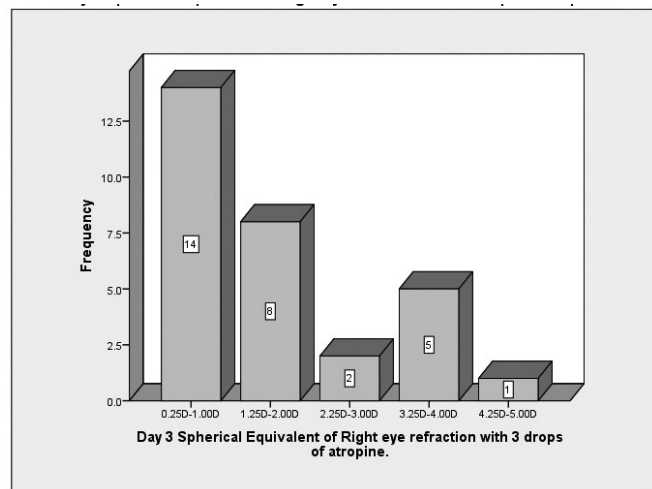
Mostly patients have spherical equivalent within the range of 0.25 to 1.00 D in right eye with one drop of atropine instillation and in some patients' refractive error found in the range of +1.25 to +4.00 Diopters.

**Day 1 Spherical Equivalent of Os Refraction with 1 Drop of Atropine**



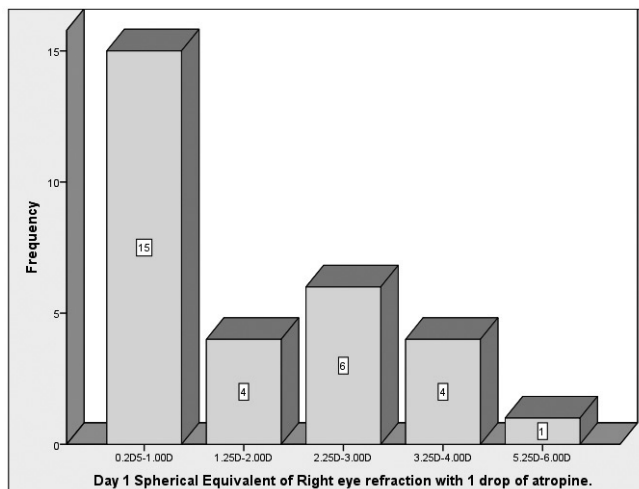
Mostly patients have spherical equivalent within the range of 0.25 to 1.00 D in left eye with one drop of atropine instillation. In some patients' refractive error found in the range of 1.25 to 2.00 D

**Day 3 spherical equivalent of od refraction with 3 drop of atropine**

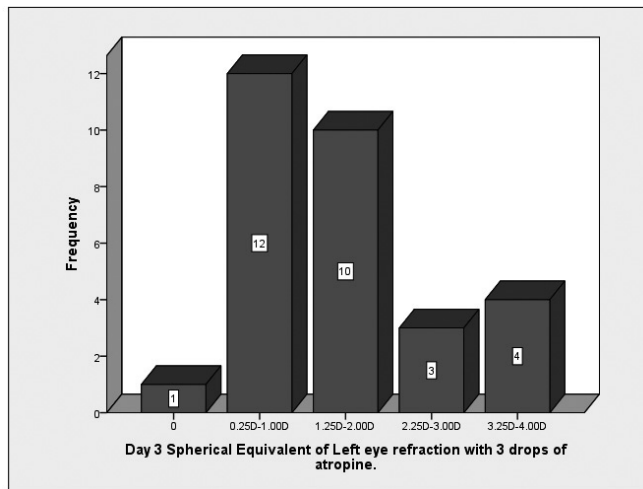


Mostly patients have spherical equivalent within the range of 0.25 Diopters to 1.00 D in right eye with three drops of atropine instillation after three days. Some patients also showed increase in refractive error at third day in the range of 1.25 to 2.00D and 3.25 to 4.00 Diopters.

**Day 1 spherical equivalent of Od refraction with 1 drop of atropine**



**Day 3 spherical equivalent of os refraction with 3 drop of atropine**



Mostly patients have spherical equivalent within the range of 0.25 to 1.00 D in left eye with three drops of atropine instillation after three days. Some patients also showed increase in refractive error at third day in the range of 1.25 to 2.00 Diopters.

**Difference according to type of refractive error found in left eye**



Hyperopic patients showed less difference in refractive error found between first and third day of atropine instillation

**DISCUSSION**

Refractive error is a very common disorder of eye, occurs when the eye cannot focus light rays entering the eye from infinity on the retina with accommodation being at rest. Such type refractive errors are frequent cause of reduced vision in children and it is very

important for children to have an examination. As high level of accommodation in children affects the refractive status of eye so it necessary to relax it fully while assessing their refractive error. In this regard Cycloplegic drugs are instilled in eyes for accuracy in measurements. Common Cycloplegic drugs are atropine, cyclopentolate, tropicamide, homatropine and scopolamine.

Atropine is an anticholinergic drug used to temporarily paralyze accommodation reflex in children and also as a mydriatic to dilate pupil.<sup>4</sup>

This study was conducted to determine the best regime for administration of 1% atropine eye drops for cycloplegia by comparing the efficacy of 1 day administration of atropine eye drops with 3 days total instillation dose and to compare the effect of atropine on myope and hypermetropes.

A study was conducted and results indicate that atropine 0.02% is the highest concentration that did not result in clinical symptoms and findings associated with higher dosages. Mean pupillary dilation was 3 mm, and mean accommodative amplitude was 8 diopters with this concentration. Further, reduction of the concentration of atropine from 0.02 to 0.01% did not seem to result in a decrease in clinical signs or symptoms associated with atropine. It was concluded that this would be an appropriate starting point in evaluating a low dosage of atropine to slow myopic progression.<sup>11</sup>

In a study it was showed that atropine has its greatest effect to accommodation and pupil size after 3 hours of installation. Accommodation returned to normal after 8 days of instillation and pupil size returned to normal after 12 days. It was concluded that one drop of Atropine affected accommodation for 8 days and near vision for 5 days. The results may impact on how Atropine penalization is prescribed to treat Amblyopia, both to minimize its impact on school performance and maximize atropine effectiveness.<sup>12</sup>

A study showed that complete suppression was caused with a single drop of 1% atropine with no significant recovery over the observation period. The fellow eye responses were reduced temporarily to about 75%. There was significant reduction in axial length of the eyes after daily atropine application, relative to fellow eyes treated with saline and refractions became more hyperopic/ less myopic. So it was concluded that a long lasting suppression of pupil responses in the eye was caused by one drop of atropine solution. It is also known that topical atropine also reduced axial eye growth.<sup>13</sup> Another study was conducted

to evaluate the long-term efficacy of a low-concentration atropine eye drop regimen (0.05%-0.1%) for controlling myopia progression in schoolchildren. The results demonstrated that long-term and regular instillation of low concentration atropine eye drops is effective for controlling myopia progression and provides a possible strategy for an initial myopia regimen.<sup>14</sup>

The results shows most of the patients have no difference in refractive error between first day of atropine instillation and after 3 days. Few patients show little difference of +/-0.25 D after three days. Hyperopic patients showed less difference in refractive error found between first and third day of atropine instillation as compared to myopic patients.

No studies were conducted to find the best regime of atropine administration by comparing the difference of first and third day refractive error and between 1 and 3 drops instillation.

### CONCLUSION

It was concluded that this may be beneficial for both the practitioner and child while doing cycloplegic refraction. It will greatly reduce the waiting time for parents and children, lessened the adverse effects of atropine and allow for a much more efficient clinical service.

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## Fractured Ozurdex™ implant in the vitreous cavity

A 58 yr old man presented with macular edema due to BRVO. Ozurdex was arranged for the affected eye. Immediately after injection broken Ozurdex™ implant was detected in the vitreous cavity, an unusual adverse event which has not been reported earlier. However this doesn't have any effect on efficacy of drug. Fractured Ozurdex™ implant is functionally stable despite its segmentation; it is difficult to say what exactly caused it and its possibility must be borne in mind by the treating physicians. Possible causes could be (i) implant got cracked during manufacturing/packaging and "broke" during injection, being unable to endure the force of the injection process and (ii) possible misalignment of implant within the injector, leading to shearing forces breaking it during injection.



*Pukhraj Rishi, Gaurav Mathur, and Ekta Rishi*



Shua Azam

## Risk Factors in Dry Eye

(A hospital-based study at Madinah Teaching Hospital, Faisalabad)

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### ABSTRACT

**Objectives:** (1) To determine the distribution of dry eye cases in different ages, genders and occupational groups. (2) To determine the possible relationship of the dry eye with its risk factors such as environment, systemic diseases and medications.

**Patients and Methods:** A hospital-based descriptive cross-sectional study at Madinah Teaching Hospital, Faisalabad was conducted including 100 diagnosed outdoor patients of age 10 years and above. Tear break-up time (TBUT), Schirmer's test II and Ocular Surface Disease Index (OSDI) was used to make a diagnosis of dry eye. Dry Eye Disease (DED) was defined as TBUT less than 10 seconds, Schirmer's test II less than 10mm wetting and OSDI score to be 33 or above.

**Results:** The prevalence of dry eye disease increased with age from 4% in age group 10-20 years to 33% in age group 51-60 years. Preponderance of females was found (60%) as compared to males (40%). The prevalence of DED was also higher among house wives, (49%), urban residents (57%) and those exposed to dust (29%). By using Chi-square test male smokers and computer users while females with systemic diseases and those who were using systemic medications significantly associated with a higher risk of DED with a p-value = <0.05.

**Conclusions:** Dry eye is common condition among older age subjects, house wives, urban residents and those exposed to dust. Smoking, computer use, systemic diseases (diabetes mellitus and hypertension) and systemic medications (anti-hypertensive and hypoglycemic drugs) were significant risk factors for dry eye.

**Key words:** dry eye disease, tear break-up time, risk factors

### INTRODUCTION

Dry eye is a multi-factorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.<sup>1</sup>

The flow of tears on ocular surface provides constant moisture and lubrication to maintain vision and comfort. The tear film which form smooth covering on the outer surface of the eye consist of three layers: outer lipid layer which is 0.1-0.2mm thick, next is aqueous layer which is 7-8mm thick and the last is mucous layer about 30mm thick. In human beings the goblet cells in the conjunctiva produce inner mucous layer, lacrimal glands and other accessory lacrimal glands produce the middle aqueous layer and the outer surface lipid layer is secreted by meibomian glands. The tear film has different nutrients that

nourish the corneal epithelium which is non-vascular. This tear film keeps the corneal surface humid which provides surface for the exchange of respiratory gases. It provides a clear optical path to the retina (inner most layer of the eye) by clearing debris from the transparent corneal surface and keeps the ocular surface safe from the attack of micro-organisms. It has a substance called retinol, which maintains the glassy nature of the cornea (Walcott, 1998). Stability of tear film is disturbed by decreased tear secretion, late drainage and change in tear ingredients and any other abnormality in the precocular tear film leads to dry eye.<sup>2</sup>

**Dry eye is a common condition amongst older age subjects, house wives, urban residents and those exposed to dust. Smoking, computer usage, systemic diseases (diabetes mellitus and hypertension) and systemic medications (anti-hypertensive and hypoglycemic drugs) are significant risk factors for dry eye.**

There are two categories: aqueous tear-deficient dry eye (ADDE) and evaporative dry eye (EDE). The category ADDE means that lacrimal glands failed to produce tear secretion. This category is further subdivided: Sjogren syndrome dry eye and non-Sjogren dry eye. EDE is caused by more evaporation of tears from the eye outer surface although rate of tear secretion is enough.<sup>1</sup>

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Signs and symptoms which present in dry eye are gritty sensation, pain, redness, ocular discomfort, fatigue, stringy mucous in or around the eyes, tearing, visual disturbance, photophobia, eye sensitivity to wind and smoke, discomfort when wearing contact lens<sup>1,3,4</sup>. Various risk factors like older age, smoking, arthritis, multivitaminosis, contact lens use, hormone replacement therapy, depression, hypertension, fibromyalgia, systemic lupus erythematosus (SLE), bursitis, ischemic heart disease (IHD) and diabetes are associated with dry eye disease.<sup>5,6,7,8,9</sup>

Drugs which are taken systemically like antihistamines, diuretics, beta-blockers, birth control pills, anticholinergics, nasal decongestants, antidepressants, tranquilizers and retinoids (isotretinoin) exacerbate dry eye symptoms.<sup>4,10,11,12</sup> Environmental pollutants like dust, exposure to sun and smoke are also risk factors for dry eye.<sup>13</sup> Localized disorders such as eyelid mal-position, lagophthalmos, and blepharitis causes dry eye disease. The neuromuscular disorders like Parkinson disease, Bell's palsy also affect blinking which finally leads to dry eye.<sup>14</sup>

Subjects with dry eye have problem with room gas heater, air conditioning room and shopping at the mall. Therefore, it is a big health condition which has a direct impact on the quality of vision and need to be addressed and it is important to know about DED signs/symptoms and different methods to manage this condition.

People with dry eye disease suffer problems during reading, writing, watching television or any other professional work like using computer and driving<sup>3</sup>. In Japan although public awareness about dry eye is high but less population seeks medical care for diagnosis and symptomatic relief.<sup>15</sup> In developing country like Pakistan a little public awareness has been observed about dry eye, its complications and factors associated with it. This study will draw the attention of public and health policy makers towards dry eye disease and its risk factors. A number of risk factors related to DED have been focused to study their impact on DED.

## PATIENTS AND METHODS

A hospital-based descriptive cross sectional study was conducted from 19 April 2016 to 21<sup>st</sup> May 2016, through convenient sampling to include 100 subjects with dry eye from age group 10 years and above, at the department of Ophthalmology at Madinah Teaching Hospital, Faisalabad.

**Inclusion criteria:** Subjects with dry eye. Aged above 10 years.

**Exclusion criteria:** Corneal/conjunctival pathologies, lid deformities/diseases.

Data were collected by getting signs from the subjects on an informed consent form. Only those subjects were included in the study who gave their consent. Visual acuity on Snellen chart was also recorded on an OPD slip of the patient by a trained technician. All the patients were evaluated for the diagnosis of the dry eye.

Two objective tests: tear break-up time (TBUT) and Schirmer's Test with local anesthetic and one subjective OSDI perform were carried out to assess the status of dry eye. A dry eye patient conformed to a tear break-up time (TBUT) less than 10 seconds, Schirmer's test with local anesthetic Alcaine less than 10mm wetting and OSDI score to be 33 or above. Examination was performed by using slit lamp first to exclude any corneal or conjunctival pathologies and lid deformities. All the tests and examinations were done following a standard technique.

The tear film stability was measured by TBUT and performed first to prevent effect of anesthetic. A fluorescein-impregnated strip wet with one drop of normal saline while the patient was looking up, the fluorescein strip was applied lightly touching the inferior fornix. As the patient was looking downward, fluorescein strip was applied on sclera to avoid contact with cornea which is highly sensitive. Under slit lamp (using a cobalt blue filter) the patient was asked to blink eye several times without squeezing while keeping the eye open for evaluation of the cornea. The time taken between the first blink and the first break (dry spot or disruption) appeared in the pre-corneal fluorescein-stained tear film was measured by using a stopwatch to calculate time accurately. TBUT of less than 10 seconds in one or both eyes was considered positive.

Schirmer's test II was used to measure tear secretion. The test was performed with topical anesthesia (Alcaine eye drops) and standardized Schirmer strip pre-calibrated Whatmann filter paper, 5mm wide and 35 mm long (TearFlo Sterile Strips, U.K). Firstly, one drop of proparacaine hydrochloride 0.5% (Alcaine) was instilled in the lower cul-de-sac. After two minutes, by using a clean tissue paper the surplus fluid was removed. The strip first folded around 5 mm from the 5 mm marking and was placed at outer side on the lower lid margin. The patient was instructed to refrain from talking during the procedure and not to close the eyes. After five minutes both the strips were removed from the fornices and dampness of the filter paper strip was noted. Wetting of filter paper less than 10 mm in five minutes was considered positive.

After objective tests performed, the Ocular Surface Disease Index (OSDI) questionnaire was used by interviewing patients face-to-face to assess symptoms

of ocular dryness. The OSDI is a 12-point scale used to quantify the dry eye symptoms to evaluate effectiveness of vision functioning as developed by the Outcomes Research Group at Allergan Inc. The OSDI has three subscales: vision-related functions (watching TV, reading), ocular symptoms (grittiness, blurred vision) and environmental triggers (low humidity, high wind). Scores of OSDI were calculated according to the formula given by Schiffman *et al.* (2000) as below:

OSDI = (sum of scores) x25 (number of questions answered)

Dry eye severity rates from 0 to 100 by the OSDI. For each question, subject selected a number between 0 and 4 to describe their symptoms as 4 indicates all of the time, 3 most of the time, 1 some of the time and 0 none of the time.

To find out the risk factors for dry eye, self-prepared Performa consisted of 14 variables was used in the end.

**RESULTS**

One hundred patients diagnosed with dry eye disease were included in this study. Forty subjects (40%) were male and sixty (60%) were female subjects (Figure 1). The ratio between male to female was 2:3. Majority of subjects were in age group 51-60 years (33%) followed by 41-50 years (22%) and 31-40 years (18%) (Figure 2). Most of the subjects in this study were resident of urban area (57%) (Figure 3). Subject’s history showed that 29% had excessive exposure to dust (Figure 4). Maximum frequency of DED was observed in house wives (49%) followed by laborers (39%) and students (5%) (Figure 5). Proportion of smoking was quite high among males (32.5%) as compared to females (1.66%). 25% males and 5% females were computer users. Obvious from the results that male smokers (Table 1) and computer users (Table 2) have DED (p-value <0.05). There were 25% males and 80% females presented with different systemic diseases including diabetes, arthritis and hypertension in the majority and 25% males and 73.33% females were using systemic medications. Female subjects with systemic diseases (Table 3) and systemic medications (Table 4) usage have DED (p-value <0.05).

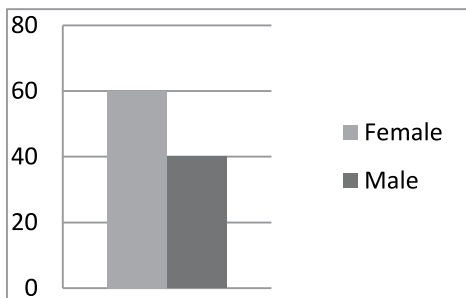


Figure 1: Gender wise distribution of DED (n=100)

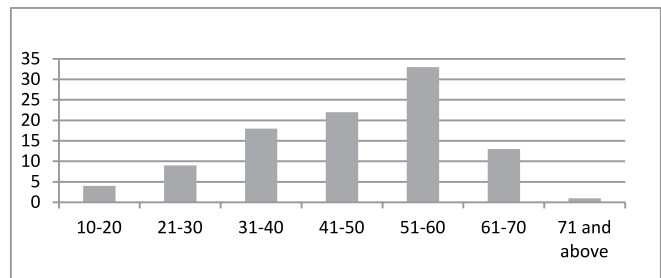


Figure 2: Age wise distribution of DED (n=100)

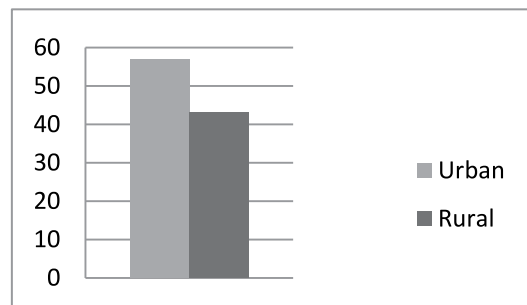


Figure 3: Residential area wise distribution of dry eye disease (n=100)

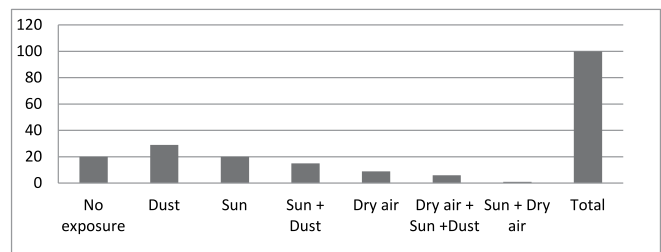


Figure 4: Distribution of Environmental pollutants (n=100)

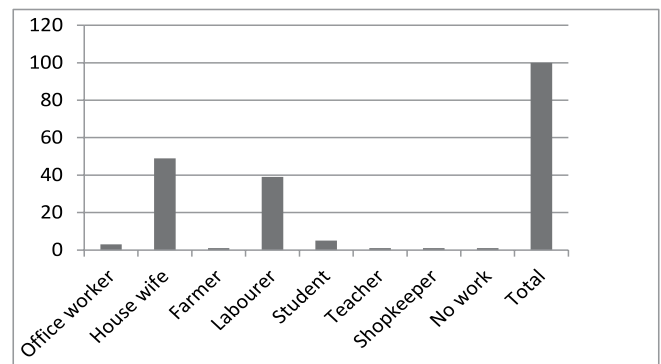


Figure 5: Occupation wise distribution of dry eye disease

Table 1: Association of smoking in different sexes

Gender	Smoking		Total
	Yes	No	
Male	27	13	40
Female	1	59	60
<b>Total</b>	<b>28</b>	<b>72</b>	<b>100</b>



**Table 2:** Association of computer use in different sexes

Gender	Computer Use		Total
	Yes	No	
Male	10	30	40
Female	3	57	60
<b>Total</b>	<b>13</b>	<b>87</b>	<b>100</b>

**Table 3:** Association of systemic diseases in different sexes

Gender	Systemic diseases		Total
	Yes	No	
Male	10	30	40
Female	48	12	60
<b>Total</b>	<b>58</b>	<b>42</b>	<b>100</b>

**Table 4:** Association of systemic medications in different sexes

Gender	Systemic medications		Total
	Yes	No	
Male	10	30	40
Female	44	16	60
<b>Total</b>	<b>54</b>	<b>46</b>	<b>100</b>

**DISCUSSION**

Diversity of dry eye disease, ranging from 7.8 % to 93.2% in the West and Asia, respectively is believed to be due to the regional location of the study population, randomly selected population and great variety of questionnaires which are used for dry eye, objective tests and various criteria for the diagnosis of dry eye.<sup>16</sup>

In our study, dry eye prevalence increased with age, which is similar with findings in other dry eye studies.<sup>17,18</sup> Nevertheless, Jeong<sup>19</sup> *et al.*, Sharma,<sup>20</sup> Magdum<sup>13</sup> *et al.* and Hashemi<sup>21</sup> *et al.* reported some contradictory results. Those different results may be attributed to different regional variations, genetic traits and environmental conditions. We found preponderance of females as compared to males and these results correlates with other studies.<sup>16, 18</sup> While Ranjan<sup>22</sup> *et al* reported that dry eye prevalence was higher among males than females. However, Jeong<sup>19</sup> *et al* contradict these results where gender is not associated with DED. Galor<sup>23</sup> *et al* reported that both males and females are equally affected by DED.

This study had 57% (57 subjects) residing in urban areas and 43% (43 subjects) residing in rural areas and similar to results reported by Sahai and Malik<sup>21</sup> and Han<sup>16</sup> *et al* and Sharma.<sup>24</sup> This similarity may be due to environmental pollution in urban areas which exacerbate DED. While Ranjan<sup>22</sup> *et al* reported that both urban and rural populations were equally affected by DED. The results show that the prevalence of DED is higher among house wives (49%) and contradict the findings reported by other studies,<sup>13,18,20</sup> where DED was

more common among laborers/farmers. On the other hand Sharma<sup>20</sup> reported that DED was more prevalent among home makers (24%) followed by students (19%), administrators (11%), teachers (10%) and farmers (9%). In this study proportion of smokers is quite high among males (32.5%) as compared to females (1.66%) and statistically significant association (p-value=<0.05) was observed. These results are in line with those illustrated by other studies.<sup>13,18, 20</sup> Nevertheless, Tan<sup>24</sup> *et al* and Lee<sup>25</sup> *et al* reported some contradictory results in which smoking is not associated with DED. The results show that 25% males and 5% females were computer user. There is a significant relationship (p-value= <0.05) and males were found more affected by DED. These results correlate with studies done in other countries.<sup>13,20</sup> The results show that 25% males and 80% females were presented with different systemic diseases including diabetes, arthritis and hypertension in the majority. There is a significant relationship (p-value= <0.05); females with systemic diseases were more vulnerable to having DED while results reported by Schaumberg<sup>17</sup> *et al.*, and Jeong<sup>19</sup> *et al.* showed that both genders with systemic diseases were prone to DED and Uchino<sup>26</sup> *et al.* reported that hypertension was a risk factor for DED only in men.

The results show 25% males and 73.33% females were using systemic medications and there is a significant relationship exists (p-value= <0.05) and show that females who were using systemic medication were more prone to have DED. On the other hand different studies reported by Schaumberg<sup>17</sup> *et al.*, Magdum<sup>13</sup> *et al.*, Tan<sup>24</sup> *et al.* and Ranjan<sup>22</sup> *et al.* (2016) showed that systemic medications equally affect both genders. Those different results may be attributed to different study designs, sample size, regional variations and genetic traits.

**CONCLUSION**

Dry eye is common condition among older age subjects, house wives, urban residents and those exposed to dust. Smoking, computer use, systemic diseases (diabetes mellitus and hypertension) and systemic medications (anti-hypertensive and hypoglycemic drugs) were significant risk factors for dry eye.

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## Urticaria multiforme

There is a history of recent viral respiratory but no exposure to allergies. The patient developed fever after one week, along with a generalized polycyclic annular rash with wheals. She also developed acral edema and the blanching arcuate urticarial rash as seen in the picture. On examination she was found to have dermatographism, characterized by the onset of welts and hives at the site of pressure or scratching. These clinical features together are most consistent with a diagnosis of urticaria multiforme. The patient was treated with diphenhydramine and the lesions resolved with no further sequelae.



D.D. **Erythema multiforme** Mastocytosis, Urticaria multiforme, Henoch-Schonlein purpura, Erythema migra



Junaid Hanif

## Effect on postoperative astigmatism by changing the axis of clear corneal incision in Phacoemulsification

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### ABSTRACT

**Objective:** To compare the mean post-operative astigmatism after phacoemulsification with superior clear corneal incision and temporal clear corneal incision in patients with cataract.

**Materials and Methods:** After approval from ethical review committee (letter attached) 80 patients with cataract, fulfilling the inclusion criteria were included from the outpatient department (OPD) of Layton Rahmatullah Benevolent Trust Eye Hospital, Lahore. Patients were divided into two groups A & B using random numbers (Table:1). Both the groups received retrobulbar local anesthesia. Group A were treated by Phacoemulsification through superior clear corneal incision and Group B underwent Phacoemulsification with temporal clear corneal incision approach. Wound size of 3.2mm was constructed with the help of keratome and foldable lens was implanted in both the groups. Informed written consent was taken and surgical procedure as well as the research details were communicated to the patient at the time of advice of surgery. To control bias, only one experienced surgeon carried out the procedures. These procedures are routinely done in this hospital and there is no ethical issue to carry out the study. All the information was noted. Post-op astigmatism was recorded at 4<sup>th</sup> week post-op as per operational definition.

**Results:** In our study, mean age was calculated 51.2±6.36 and 50.55±6.77 years in Group-A and B, 52.5%(n=19) in Group-A and 42.5%(n=17) in Group-B were male while 47.5%(n=21) in Group-A and 57.5%(n=23) were females, comparison of pre-operative astigmatism was calculated as 1.43±0.20 in Group-A and 1.47±0.22 in Group-B, p value was 0.31 showing insignificant difference, comparison of post-operative astigmatism was calculated as 1.06±0.16 in Group-A and 0.76±0.18 in Group-B, p value was 0.001 showing significant difference.

**Conclusion:** It is concluded from this study that the mean post-operative astigmatism after phacoemulsification with temporal clear corneal incision was significantly reduced when compared with superior clear corneal incision in patients with cataract.

**Key words:** Cataract, phacoemulsification, superior clear corneal incision, temporal clear corneal incision, post-operative astigmatism

### INTRODUCTION

Astigmatism is that condition of refraction wherein a point focus of light cannot be formed upon the retina because of unequal refraction of light in different meridians of cornea. It is measured in diopters (D) employing auto-refractometer or a keratometer.<sup>1</sup> Prevalence of with the rule astigmatism is 46.8% of eyes in general population.<sup>2</sup>

In Pakistan cataract contributes to 66.7% of the total blindness. Cataract surgery is the leading intraocular surgery being performed these days.<sup>3</sup> Phacoemulsification is considered the standard care

for cataract surgery.<sup>4</sup> There are several options for correcting astigmatism at the time of cataract surgery. They include incision placement on the steep axis of corneal astigmatism, single or paired peripheral corneal relaxing incisions, and toric intraocular lens implantation.<sup>5</sup> Correction of astigmatism is one of the main purposes of modern cataract surgery.<sup>4</sup> Several methods have been employed for this purpose including changing the size and site of incision, using corneal or limbal relaxing incisions.<sup>6</sup>

**Post-operative astigmatism after phacoemulsification with temporal clear corneal incision was significantly reduced when compared with superior clear corneal incision in patients with cataract.**

Multiple international studies have been conducted comparing different anatomical site incisions (Limbal Vs Clear corneal, Clear Corneal Vs scleral or scleral Vs Limbal ) or size of incisions if it was conducted at same anatomical site.<sup>7-9</sup> A study conducted with same

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size incision shows that the induced astigmatism was 1.44 D ( $\pm 0.31$ ) in patients who received superior corneal incisions, and 0.62 D ( $\pm 0.28$ ) in patients who had a temporal incision<sup>10</sup>. Other study shows postoperative astigmatism of 0.34 D in clear corneal temporal incision<sup>11</sup> and of 1.29 +/-0.68 D in superior clear corneal incision.<sup>12</sup>

**MATERIALS AND METHODS**

**Study Design:** Randomized control trial

**Study Setting:** Layton Rahmatullah Benevolent Trust Free Eye and Cancer Hospital, Lahore

**Duration of Study:** Six Months (28<sup>th</sup> July 2015 to 27<sup>th</sup> December 2016)

**Sampling Technique:** Non Probability consecutive sampling

**Sample Size:** Sample size of 80 cases (40 in each group) is calculated with 95% confidence level, 80% power of test and taking expected mean +/- S.D of mean astigmatism (Post-op) in both groups that is 1.44+/-0.31 (D) in superior corneal incision group versus 0.62+/-0.28(D) in temporal incisions group in patients with cataract undergoing phacoemulsification.

**Data Collection Procedure:** After approval from ethical review committee (letter attached) 80 patients with cataract, fulfilling the inclusion criteria were included from the outpatient department (OPD) of Layton Rahmatullah Benevolent Trust Eye Hospital, Lahore. Patients were divided into two groups A & B using random numbers table. Both the groups received retrobulbar local anesthesia. Group A were treated by Phacoemulsification through superior clear corneal incision and Group B underwent Phacoemulsification with temporal clear corneal incision approach. Wound size of 3.2mm was constructed with the help of keratome and foldable lens was implanted in both the groups. Informed written consent was taken and surgical procedure as well as the research details were communicated to the patient at the time of surgery.

To control bias, only one experienced surgeon carried out the procedures. These procedures are routinely done in this hospital and there is no ethical issue to carry out the study. All the information was noted. Post-op astigmatism was recorded at 4<sup>th</sup> week post-op as per operational definition.

**Data Analysis:** Collected data was entered and analyzed using SPSS version 17. As data is numerical so T test was applied with confidence interval of p = 0.05. The Quantitative variables like age, pre and post-operative astigmatism was presented as mean  $\pm$  SD. The Qualitative variable like gender was presented as frequency and percentage. The post-operative astigmatism was compared in each group, 4 weeks

after Phacoemulsification by using ‘t’ Test. Data was stratified for age, gender, duration of cataract and pre operative astigmatism to deal with effect modifiers. Post-stratification ‘t’ test was applied. P value 0.05 was considered significant.

**RESULTS**

A total of 80 cases fulfilling the inclusion/exclusion criteria were enrolled to compare the mean post-operative astigmatism after phacoemulsification with superior clear corneal incision and temporal clear corneal incision in patients with cataract. Patients age was recorded as 45% (n=18) in Group-A and 52.5% (n=21) in Group-B between 30-50 years while 55% (n=22) in Group-A and 47.5% (n=19) in Group-B were between 51-65 years of age, mean $\pm$ SD was calculated 51.2 $\pm$ 6.36 and 50.55 $\pm$ 6.77 years respectively. (Table No. 1) Gender distribution shows that 52.5% (n=19) in Group-A and 42.5% (n=17) in Group-B were male while 47.5% (n=21) in Group-A and 57.5% (n=23) were females. (Table No. 2) Comparison of pre-operative astigmatism was calculated as 1.43 $\pm$ 0.20 in Group-A and 1.47 $\pm$ 0.22 in Group-B, p value was 0.31 showing insignificant difference. (Table No. 3) Comparison of post-operative astigmatism was calculated as 1.06 $\pm$ 0.16 in Group-A and 0.76 $\pm$ 0.18 in Group-B, p value was 0.001 showing significant difference. (Table No. 4) The data was stratified for age, gender and duration of cataract and presented in Table No. 5, 6 & 7 respectively.

**Table 1:** Age Distribution (N=80)

Age (in years)	Group-A (n=40)		Group-B (n=40)	
	No. of patients	%	No. of patients	%
30-50	18	45	21	52.5
51-65	22	55	19	47.5
<b>Total</b>	<b>40</b>	<b>100</b>	<b>40</b>	<b>100</b>
<b>Mean<math>\pm</math>SD</b>	<b>51.2<math>\pm</math>6.36</b>		<b>50.55<math>\pm</math>6.77</b>	

**Table 2:** Gender Distribution (n=80)

Gender	Group-A (n=40)		Group-B (n=40)	
	No. of patients	%	No. of patients	%
Male	19	52.5	17	42.5
Female	21	47.5	23	57.5
<b>Total</b>	<b>40</b>	<b>100</b>	<b>40</b>	<b>100</b>

**Table 3:** Comparison of Pre-Operative Astigmatism (n=80)

Pre-operative astigmatism	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	1.43	0.20	1.47	0.22

**P value: 0.31**

**Table 4:** Comparison of Post-Operative Astigmatism (n=80)

Post-operative astigmatism	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	1.06	0.16	0.76	0.18

P value: 0.001

**Table 5:** Stratification for Age (n=80)

Age: 30-50 years

Post-operative astigmatism	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	1.08	0.12	0.75	0.21

P value: 0.001

Age: 51-65 years

Post-operative astigmatism	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	1.04	0.18	0.78	0.15

Z P value: 0.001

**Table 6:** Stratification for Gender (n=80)

Male

Post-operative astigmatism	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	1.07	0.12	0.80	0.17

P value: 0.001

Female

Post-operative astigmatism	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	1.05	0.19	0.74	0.19

P value: 0.001 <1 year

**Table 7:** Stratification for duration of cataract (n=80)

Post-operative astigmatism	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	1.09	0.10	0.74	0.15

P value: 0.001 >1year

Post-operative astigmatism	Group-A (n=40)		Group-B (n=40)	
	Mean	SD	Mean	SD
	1.04	0.21	0.71	0.23

P value: 0.001

**DISCUSSION**

Phacoemulsification has made cataract surgery through a small incision possible. Rapid and stable optical recovery is achieved by preventing significant

changes in corneal curvature. The smaller incision size induces less postoperative astigmatism. The clear corneal incision technique was introduced by Fine. This has led to increased safety, decreased pain, inflammation and surgically induced astigmatism (SIA). We planned this study with the view that local data is not available on these techniques, and to find out if there is any impact of same sized incisions but at different axis of a single anatomical site on post-operative astigmatism in our population. The technique that has better outcome may be used in future.

In our study, mean age was calculated 51.2±6.36 and 50.55±6.77 years in Group-A and B, 52.5%(n=19) in Group-A and 42.5%(n=17) in Group-B were male while 47.5%(n=21) in Group-A and 57.5%(n=23) were females, comparison of pre-operative astigmatism was calculated as 1.43±0.20 in Group-A and 1.47±0.22 in Group-B, p value was 0.31 showing insignificant difference, comparison of post-operative astigmatism was calculated as 1.06±0.16 in Group-A and 0.76±0.18 in Group-B, p value was 0.001 showing significant difference.

A previous study conducted with same size incision shows that the induced astigmatism was 1.44 D (±0.31) in patients who received superior corneal incisions, and 0.62 D (±0.28) in patients who had a temporal incision.<sup>10</sup> These findings are in agreement with our results. Other study shows postoperative astigmatism of 0.34 D in clear corneal temporal incision<sup>11</sup> and of 1.29 +/- 0.68 D in superior clear corneal incision.<sup>12</sup> Our findings are also supported by two other similar studies; small temporal incisions induced less change than superior incisions.<sup>13-14</sup> Muhammad Saadullah and other<sup>15</sup> assessed surgically induced astigmatism followed by phacoemulsification with clear corneal 3.2mm incision while using superior versus temporal approach and concluded that for a suture less clear corneal incision temporal approach results in considerably less degree of surgically induced astigmatism.

Most of the surgeons do not feel easy to sit on the temporal side while doing phacoemulsification irrespective of the preoperative keratometric results. They have a tendency to use superior approach for all the patients. It further increases the flattening if the incision is given in an already flatter meridian. Thus it may result in high degree induced<sup>16</sup> astigmatism postoperatively. This problem is increased as most of the surgeons like to leave the wound un sutured. This definitely affects the visual outcome postoperatively and increase in demand of spectacles to improve postoperative visual acuity.

One may find temporal approach to be a bit

difficult in the beginning. This is because of lack of support from the patient's forehead for surgeon's hands but with experience a surgeon can operate with equal ease using either approach and get the benefit of significantly reduced astigmatism.

In summary, the results of our study in accordance with other studies justify the hypothesis of the study that *"there is a difference between post-op astigmatism with superior versus temporal clear corneal incision in patients undergoing phacoemulsification."*

**CONCLUSION:**

We concluded that the mean post-operative astigmatism after phacoemulsification with temporal clear corneal incision was significantly reduced when compared with superior clear corneal incision in patients with cataract.

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**Cholesterol Embolization**

An 88-year-old man with a history of a quadruple coronary artery bypass grafting procedure and trans-apical trans-catheter aortic-valve replacement presented with this skin condition. What is the cause of this appearance?

1. Warfarin Necrosis
2. Subacute bacterial endocarditis
3. Cryoglobulinaemia
4. **Cholesterol Embolization**
5. Heparin induced Thrombocytopen





Rabia Mobeen

# Test & Re-test Reliability of Visual Acuity in Children using Lea Symbols Chart

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## ABSTRACT

**Objective:** The purpose of this study was to evaluate the reliability of Lea Symbols LogMAR Chart in 3-5years old children.

**Methodology:** Best corrected monocular visual acuity of a subset of children (n = 50) enrolled in the correction of refractive errors. At 1<sup>st</sup> visit visual acuity was measured at baseline after the correction of refractive error at Lea Symbol Chart and visual acuity was again measured after 3 days. Children started with LogMAR 0.4 (6/15 or 20/50) and read each letter on all subsequent lines until they missed all letters in 1 line.

**Results:** At baseline, the mean best corrected LogMAR visual acuity in the right eye and in the left eye was measured. The signed difference between VA measured at baseline and that measured after 3 days was significant in either eye. The age and gender of the subjects are other potential sources of variability. Given the limited age range of the subjects in this study (3 to 5years) it is showing that age was not associated with the significant difference in either eye. The variation was not associated with any specific age group. Almost each year child has an equal change variation in visual acuity. Gender is also has equal contribution for both eyes visual acuity. P value was less than 0.05 in both cases.

**Conclusion:** The reliability of Lea symbols chart in children age 3 to 5 years is logarithmic in principle. A mean difference of visual acuity measurements between the 2 visits is approximately 1 line difference or difference in letters in same line, equal to 0.1 log unit, if all other parameters like child's mood, environment etc is kept constant.

## INTRODUCTION

Early measurement of visual acuity is necessary to detect Amblyopia and to treat it. The reason for visual acuity assessment in children is to identify those whose visual development is not following normal patterns, to identify children who require spectacle correction, or who have developed, or are at risk of developing, amblyopia or strabismus, to detect pathology and other less common visual deficiencies. Visual acuity assessment in children is measured through different charts. The LogMAR crowded test was the first paediatric letter acuity test used specifically to improve the sensitivity and specificity of the test in identifying amblyopia deficiencies.

The Cardiff acuity test is used to identify children showing abnormal visual development. The data provided by the manufacturer of the Kay picture tests are derived from a study of 106 children having age 4-5 years and 118 children having age less than 4 year. These data are derived from a study using the Lea symbols

in single presentation. Crowded presentation may reduce the expected acuity levels a little bit, mainly in the younger age group, but in the absence of normative ranges for the crowded form of this test, these could be used to guide practitioners. Sonksen LogMAR Charts for both monocular and binocular acuity, allow the practitioner to identify children having normal acuity for age and those for whom acuity results fall within the bottom 10% for age.<sup>1</sup>

A study showed that if we measure the acuity on two visits there is a difference of two lines, which shows that its repeatability is relatively less and this difference is not so significant. While in the case of Bailey and Lovie chart by improving the contrast sensitivity repeatability increases. If there is difference of 5 letters or more between 2 visits then this difference is said to be significant. and a difference of 0.1 LogMAR indicated a real intraocular acuity difference.<sup>2</sup>

**The reliability of Lea symbols chart in children aged 3-5 years is logarithmic in principle. A mean difference of visual acuity measurements between the 2 visits is approximately one line or difference in letters in the same line, equal to 0.1 log unit, if all other parameters like child's mood, environment etc is kept constant.**

*Lea symbols chart:* For the measurement of inter-eye difference visual acuity Lea symbols chart is used

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in normal children. This is the best chart for the visual assessment in pre-school children. The Lea symbol and the Kay picture chart are the best picture matching tasks for children who are unable to match the letters.

### RESEARCH METHODOLOGY

Test A little work has been done on and retest reliability of measuring visual acuity and comparing methods of scoring. Many proves were given that visual acuity measurements give better result when recorded for second time but these studies were not aimed to assess variability and learning effect. Another study was conducted by Gibson and Sanderson to check repeatability, their sample included sixty four patients with lens opacities. The subjects visual acuity was measured two times on the same day (taken by a different nurse). They concluded that one third patients show no difference in measurement of visual acuity while 13% give visual acuity which differ by two lines and even more.

Test and retest reliability was measured by Arditi and colleagues on a standard acuity chart in highly trained normal subjects to minimize the variability. Their results also showed that letter-by-letter method show less variability then line-by-line method in spite of these two methods probit analysis can be used to score visual acuity at its best. This analysis defines visual acuity as the estimate of the letter size seen 50% of the time by the probit curve fitting function. Although the line assignment method has a higher variability than the letter-by-letter method and the probit method appears to have a low variability, these three methods have not been directly compared.<sup>3</sup>

The 1st priority of the World Health Organizations (WHOs) VISION 2020 is to control the amount of visual loss in children. There are several reasons for this. Children who are blind by birth or those who become blind after birth and survive, have lifetime blindness, with all the associated affects costs for the child, family and society. In fact, the amount of blindness due to all causes in children is almost equal to the amount of blindness due to cataract in elderly patients. Secondly, mostly visual loss in children can be treated. Thirdly, many cases of blindness also cause child death (e.g. premature birth, measles, congenital rubella syndrome, vitamin A deficiency, and meningitis). So child's survival is closely related to the control of blindness. As visual loss in children is rare, exact prevalence rate is difficult to get, because a large amount is required for population-based prevalence rate.

A clinically important measurement of visual functions is visual acuity. The method used in the ETDRS chart is that of letter-by-letter. In this procedure each letter presented is equal to LogMAR score. Charts

are presented five letters per line and progression is 0.10-logMAR increments therefore assigned a 0.02-logMAR score per letter. Another alternate of letter by letter is the line assignment method which shows that each line has a task psychophysically so an individual must proceed. But the line assignment method is more acceptable in clinical research and paediatric clinic and amblyopia treatment study. The benefit of letter by letter over line assignment method is that it measures 0.10 LogMAR change in acuity.<sup>4</sup> The outcomes of the current study demonstrates that the modified LogMAR chart with three optotypes gives a comparable result to the standard LogMAR charts for assessment of distant visual acuity in routine clinical examination set up with a much lesser testing time.<sup>7</sup> Visual acuity was assessed in normal and amblyopic children having age group from 4 to 12 years by line assignment method and interpolated threshold scoring. The significance in repeatability measurements was very little.<sup>4</sup>

Ninety five percent of vision measurements made with Bailey Lovie chart and Glasgow acuity cards are different by an amount of less than 0.07 log unit.<sup>5</sup> 95% population showed a wider difference between the Lea symbol and Snellen charts measurements as while visual acuity was better. LEA symbols and Snellen chart have showed good test retest reliability, although the variability between both measurements indicates that they are not interchangeable test.<sup>6</sup>

A high percentage of children aged 6 to 9 years (98%) can be tested with Landolt C's (8 positions) using three different visual acuity testing procedures. While using staircase method o decrease in test retest reliability was found starting from DIN via Best-pest.<sup>13</sup> The percentage of children whose unocular visual acuity could be measured were mostly having age of 3 to 3.5 years and give the same results in two types of charts. If we use crowded chart the results were better in HOTV in comparison with Lea symbol chart. These different types of charts tell us about the observed difference in the threshold acuity level.<sup>7</sup>

For the assessment of visual acuity by Lea symbol chart the youngest child should be at least of 1 year and 11 months of age. For the child age more than 2.5 years visual acuity could be assessed with this chart very easily. There are no chances of amblyopia if visual acuity by Lea Symbols chart is more than 1 line and inter eye difference is less than 2 lines. If the difference is 1 line above between two visits child should refer for reexamination.<sup>8</sup>

In the population of young children, in which the reason of reduced vision is astigmatism due to amblyopia, the Lea Symbols chart produced visual acuity results that were about 0.5 line better than obtained with



ETDRS charts.<sup>9</sup> In the children age less than 4 years the Worth 4 shape test is more successful than worth 4dot but the accuracy is almost equal. Worth 4shape is highly reliable so valid for the young children.<sup>20</sup> In younger age group from 7 to 13 years highest test retest repeatability was found by using ETDRS using the protocol EVA. It gives many potential benefits as better standard can be maintained across multiple sites, it makes easy to use automatic acuity score calculator so that data can be captured electronically, tester's role is also minimal in this case so data obtained is least biased, and visual acuity can be recorded from 20/800 to 20/12 by maintaining only a single distance. In age group 7 to less than 13 years computerized testing method should be taken as best when visual acuity is used as an outcome measure in eye research.<sup>10</sup>

**RESULTS**

A significant difference was found when intersession visual acuity was measured in AMD patients by using ETDRS charts. It can be contributed to both disease and measurement factors. This variability was found very useful for assessment and treatment of neovascular AMD in clinical trial design. Many efforts and research work is still required to find out the reasons of variability in measurements of visual acuity so that the appropriate criterion for measuring visual acuity can be implemented in this important group of patients.<sup>11</sup> In the patients with stable AMD the intersession test retest variability of reading performance give reasonable results to define the end point and to measure the variability.<sup>12</sup>

In a study it was found that automated system for measuring visual acuity was more practical by using Landolt rings. In this case the repeatability was found to be same to ETDRS charts which shows evidence that it can be used as another tool to measure its results in new clinical trial. In future its ability to give threshold curve of visual acuity will be proved very useful for new clinical research studies.<sup>13</sup> For the patients with maculopathy whose visual acuity is less than or equal to 20/200 the ETDRS chart has the advantage of giving better visual acuity results in comparison with the broken C visual acuity chart.<sup>14</sup>

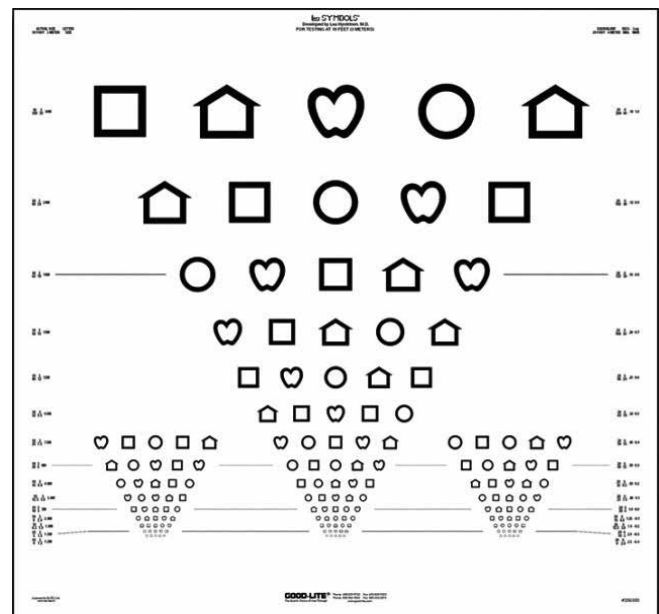
Landolt C charts gives poor VA results in comparison with letter and tumbling E charts in both young adults and visually impaired patients with Diabetic Retinopathy. These differences were more definite in patients with diabetic retinopathy who show poor VA. This study population should be considered in making comparison for the results from different clinical practices.<sup>15</sup> ETDRS visual acuity chart gives lesser amount of test retest variability in comparison with line assignment method chart.<sup>16</sup>

In the children age of 5 to 12 years ATS HOTV visual acuity chart gives better acuity in comparison with E-ETDRS chart but not better than a LogMAR level. When a child matures the practitioner should change the method for the assessment of visual acuity and should compare it with the previous results for the assessment of amblyopia.<sup>17</sup> According the 95% limits of agreement, the criterion for the change in visual acuity is not greater than 1 and half line. This value is like to that made for adults and shows that repeatability is often seen LogMAR visual acuity chart.<sup>18</sup> The repeatability measurements are often seen in early treatment of diabetic retinopathy study chart which is often recommended for the assessment of visual acuity in children in clinical practice.<sup>19</sup>

A quantitative, descriptive cross-sectional study was conducted to assess the test retest reliability of visual acuity in children using lea symbol charts. All the demographic data like age, gender, visual acuity and test retests results was collected through performa. A child's visual acuity was determined wearing trial frame with occluder on one eye using Lea Symbols chart at 3 meters. Test was performed 2 times with 3 days interval and we will determine that how many children give the same results before and after retesting.

Using SPSS version 20 the whole data was entered and analyzed. Quantitative variable like age was presented in form of mean ± SD. Significance was assessed at the *P* < 0.05 levels for all parameters. Categorical variables between groups were compared using Chi square test or Fisher's exact test; t test was used for continuous variables. All the data was presented in forms of frequencies, percentages and appropriate pie and bar charts.

**Lea Symbols Chart**



**Table :** Significance

One-Sample Test				
	Test Value = 0			
	T	Df	Sig. (2-tailed)	Mean Difference
Visual acuity of right eye	10.995	49	.000	2.08000
visual acuity of left eye	12.995	49	.000	1.88000

P value is less than 0.05 which shows that there is significant difference in visual acuity after three days interval.

**DISCUSSION:**

The clinicians all over the globe are in consensus about the type of VA chart to be used for research purpose. Disappointingly, for routine clinical use, the advantages of logarithmic progression acuity charts are conveniently eluded by blaming the time required to administer the procedure. The importance of having the same standard of acuity measurement in research as well as in clinical situation is highly significant when we apply the outcomes from clinical trials (which typically assess the VA with logarithmic charts) to predict the outcomes in clinical practice (which prefers to use Snellen’s chart).<sup>20</sup>

This study demonstrates the reliability of Lea symbols chart in children age 3 to 5 years. Lea symbol chart is logarithmic in principle. A mean difference of visual acuity measurements between the 2 visits is approximately equal 1 line difference or difference in letters in same line, equal to 0.1log unit if all other parameters like child’s mood, environments etc are kept constant. This observation is consistent with the previous studies.

A previous study showed that according the 95% limits of agreement, the criterion for the change in visual acuity is not greater than 1 and half line. This value is like to that made for adults and shows that repeatability is often seen LogMAR visual acuity chart.<sup>21</sup>

Above study shows a similarity with this study. The difference is that this has a difference of .15log unit, equal to 1 and half line difference, while we have 1line difference between two visits equal to 0.1log unit.

The age and gender of the subjects are other potential sources of variability. Given the limited age range of the subjects in this study (3 to 5years) it is showing that age was not associated with the significant difference in either eye. The variation was not associated with any specific age group. Almost each year child has an equal change variation in visual acuity. Gender is also has equal contribution for both

eyes visual acuity.

Another study showed that the youngest baby whose visual acuity could be measured with Lea symbols should be 23 months of age. The children above the age of 30 months could be assessed with Lea symbols chart easily. There are no chances of amblyopia if Lea Symbols visual acuity is higher than 1 and the difference between two eyes is less than 2 lines. Children with a difference of more than one line should be reexamined.<sup>8</sup>

Above study shows a similarity with this study both shows that if the difference between the two visits of visual acuity is higher than 1 line there are no chances for amblyopia.

The Lea Symbols and Bailey Lovie charts both provide a similar measure of inter-eye difference. However, the monocular acuity results were different in both charts and the difference depends on each individual’s visual acuity. Cooperation can cause significant variation in visual acuity. Monocular visual acuity assessment is possible. When monocular measurements are possible on both eyes, however, the intra individual inter ocular difference of visual acuity usually does not exceed one line.

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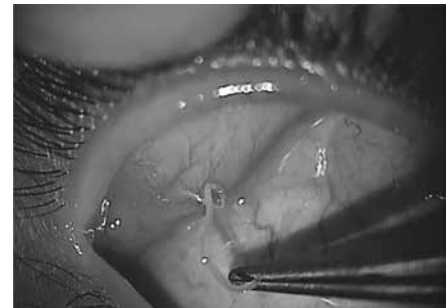
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## Worms in the Eye

A 21-year-old man presented with a 2-week history of itching in his left eye. He reported "seeing worms" in his eye. He underwent thorough irrigation of the conjunctival sac and lacrimal duct, during which three worms were removed. The worms were white, slender, and filiform nematodes, 10 to 12 mm long and 0.16 to 0.18 mm wide. The worms were morphologically characterized by the presence of a buccal capsule near the anterior end and cuticular striations over the whole tegumental surface. On the basis of these findings, the worms were identified as *Thelazia callipaeda*. These parasitic nematodes infect the lacrimal glands and ducts of mammals, including dogs, cats, and humans. They are endemic in some parts of Asia but have also been reported in Europe. Treatment of infection in humans involves mechanical removal of the parasites. To prevent infection, the fly vector should be avoided in areas in which the parasite is endemic. The patient has not reported any recurrence since the removal of the parasites.



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Courtesy: NEJM-UK



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## Sequelae of Reamed Interlocking Nail in the Tibial Fractures in terms of Union & Wound Infection

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### ABSTRACT:

**Introduction:** Tibia fracture is an orthopedic problem. It is commonly fractured because of its location and anatomy. The fracture may be either closed or open. The surgical choices for fixation are external fixator, open reduction and internal fixation with plate and ILN closed or open. Intramedullary nailing is the common surgical treatment option for open tibial diaphyseal fractures (type I, II and type IIIA). After intramedullary nailing, the postoperative complications in open fractures are different in literature.

**Objective:** To know the sequelae of reamed intramedullary interlocking nail in open tibial diaphyseal fractures in terms of union and wound infection.

**Material & Methods:** This study was conducted in orthopedic Department of Kabir Medical college Teaching Hospital Peshawar on 75 patients with open tibial diaphyseal fractures (Gustilo-Anderson classification type I and II). After reamed intramedullary nailing, patients were followed for wound infection at Two weeks postoperatively and union at 16 weeks.

**Results:** There were 57(76.00) males and 18(24.00%) female with the mean age of 40.50years  $\pm$  14.89SD. 69(92.00%) patients had no wound infection 06(8.00%) patients had wound infection at two weeks out-patient visit. Union of fracture at 16 weeks was noted in 72(96.00%) patients.

**Conclusion:** Reamed intramedullary interlocking nailing is a good mode of internal fixation in Gustilo-Anderson classification type I and II open fractures of tibia in terms of low infection rate and good union rate.

**Key Words:** Open Tibial diaphyseal fracture, Reamed intramedullary nail, Infection, Fracture union.

### INTRODUCTION

Tibia is more at risk to frequent injury because of its location. It is the most commonly fractured long bone and open fractures are more common in the tibia than in any other major long bone because of its anatomy. The blood supply to the tibia is more precarious than that of bones enclosed by heavy muscles. High energy tibial fractures may be associated with compartment syndrome or neural or vascular injury. Locked intramedullary nailing currently is considered the treatment of choice for most type I, type II, type IIIA open and closed tibial shaft fractures. Intramedullary nailing preserves the soft tissues sleeve around the fracture site and allows early motion of adjacent joints. Non union, Delayed union, Infective nonunion and wound infection are relatively common complications of tibial shaft fractures.<sup>1</sup>

These complication can be prevented by various treatment methods including acute delivery of I.V antibiotics, repeated debridement followed by early

local or free flap closure, rigid stabilization with external fixation or interlocking nailing and prophylactic bone grafting open reduction and internal fixation using plates.<sup>2,3</sup>

When surgically indicated interlocking nail at present is an attractive surgical option, as it is the only operative modality closest to the safe yet rewarding and time honored conservative treatment. Reamed interlocking nail is a good treatment for rapid union of tibial shaft fractures.<sup>4,5,6</sup>

The complications include cellulitis, superficial infection, deep infection, loose screws, broken screws, mal-union, minor knee pain and occasional fracture site pain after activity. The percentage of union of fracture shaft of tibia after reamed interlocking nailing is reported as 73% and wound infection 13.3% in literature.

**Objectives:** Objective of the study is to know sequelae of reamed interlocking nail in tibial diaphyseal fractures in terms of wound infection and union of fracture cases.

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**Reamed intramedullary interlocking nailing is a good mode of internal fixation in type I and II open fractures of tibia as it allows early weight bearing, minimizes the chances of infection and delayed union and has led to union in maximum cases.**  
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**MATERIAL & METHODS**

This descriptive study was conducted in orthopedic Department of Kabir Medical College Teaching Hospital, Peshawar during the period of 01.06.2014 to 31.05.2015 after permission from the Hospital Ethical Committee. Patients of both genders and age group more than 17 and less than 65 years with Gustilo-Anderson classification type 1 and II open fractures who presented in less than 12 hours were included in the study. Those patients who presented late after 12 hours, Gustilo-Anderson classification type III and IV, immune-compromised patients like diabetes mellitus and smokers were excluded from the study.

The study was explained to all patients and they were assured that the study is done purely for research and data publication for the benefit of other patients and surgeons. A written informed consent was obtained. The treatment offered to patients during the admission period in hospital was non-commercial, beneficial, non harmful and according to medical ethics.

All patients were worked up with detailed history and clinical examination followed by routine baseline pre operative investigations including full blood count with ESR, C reactive protein, blood grouping and cross match, urine routine examination, blood urea and sugar, serum albumin and serum electrolytes. All the patients were operated within 24 hours under general anaesthesia by same surgeon. Same preoperative antibiotics were given and reamed interlocking nail was done in all patients. They were kept in ward for 2 days with same antibiotic and analgesic cover and with regular temperature monitoring and nursing care. Wounds were examined after every 24 hours and regular dressing was changed. Patients were discharged to home 3rd post operative day. Patients were followed up in outpatient two weeks post operatively for wound infection and on 16 week for union of fracture. Union was clinically and radiologically defined as NO tenderness at fracture site, NO pain on weight bearing and obliteration of the fracture lines on x rays. Infection was defined as collection or discharge of pus from wound.

**Exclusion criteria** was followed strictly to control confounding variables and bias in the study results. All the collected data was entered and analyzed on SPSS 10. Descriptive statistics were calculated for all the variables. Mean and standard deviation was calculated for quantitative variables like sex and union of fracture.

**RESULTS**

There were 57(76.00%) males and 18(24.00%) female with the mean age of 40.50years ± 14.89SD shown in pie diagram. Youngest patient was 19 years old while

oldest one was 50 years of age.

Tibial shaft fractures encountered in this study according to their respective geometry were as follows; (table no. 1)

- Simple transverse fractures-----45(60.00%)
- Oblique fractures ----- 15(20.00%)
- Spiral fractures----- 09(12.00%)
- Segmental -----06(8.00%)

Results in terms of fractures according to gustillo and Anderson classification are shown in Table 2.

Outcome of the patients was based upon post operative wound infection at two weeks postoperatively and union at 16 weeks. 69(92.00%) patients had no wound infection 06(8.00%) patients had wound infection at two weeks post operatively . Table No. 3 Union of fracture at 16 weeks; 72(96.00%) fractures healed in 16 weeks while 03 (4%) patients showed no union. Table . 4

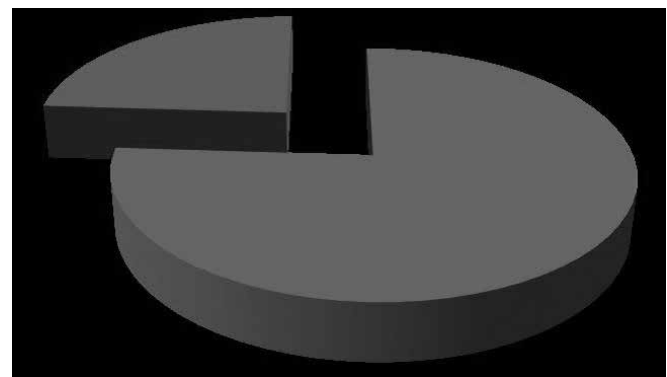


Figure 1. Red females and blue males

Table 1: Geometry of fracture distribution

Geometry of fracture	No of Cases	Percent
Simple transverse fractures	45	60.00
Spiral Fractures	15	20.00
Oblique fractures	09	12.00
Segmental Fractures	06	8.00

Table 2: Distribution according to Gustillo and Anderson classification

	No of Cases	percent
Type I	45	60.00%
Type II	30	40.00%

Table 3: Wound infection at two weeks

	No of Cases	Percent
No Wound infection	69	92%
Wound infection	06	08%
Death	0	0

**Table 4:** Union of fracture after 16 weeks

	No of Cases	Percentage
Union in 16 weeks	72	96.00%
No or delayed union in 16 weeks	03	04.00%

**DISCUSSION**

Tibia is more at risk to frequent injury because of its location. It is the most commonly fractured long bone and open fractures are more common in the tibia than in any other major long bone because of its anatomy

The blood supply to the tibia is more precarious than that of bones enclosed by heavy muscles. High energy tibial fractures may be associated with compartment syndrome or neural or vascular injury. Locked interlocking nailing currently is considered the treatment of choice for most type I, type II, type IIIA open and closed tibial shaft fractures. Intramedullary nailing preserves the soft tissue sleeve around the fracture site and allows early motion of adjacent joints. The results of interlocking nails shows that virtually all tibial diaphyseal fractures can be stabilized with an interlocking nail. Our results are comparable with most studies.

In one of the local study by Inam M et al<sup>2</sup> they studied 30 cases of tibia fractures treated with interlocking nail. In their study the average healing time was 19 weeks with no mal-union. Only one nail (3.3%) out of 30patients got infected. In our study the most important complication of infection and non union was evaluated after fixing fracture shaft of tibia with locked intramedullary interlocking nail. 75 patients with mean age of 37.24 including 57(76.00%) males and 18(24.00%) females falling in inclusion criteria were operated by same surgeons with same implant i.e interlocking nail .In our study we have healing in 16weeks of 96% and nonunion in 04%. We have male preponderance as is in their study.

Gosh K P<sup>9</sup> et all have compared the reamed ILN and conservative management of tibial fractures. In their study the mean time to union was nineteen weeks after management with a cast and thirteen weeks after management with nailing. The severity of soft tissue coverage are more important in the prevention of infection than is the type of implant used. Currently most orthopedic traumatologists in accept the use of reamed nail in type I and type II open fractures; however, the use of reamed nailing in type III open

fractures; is controversial. Finkemeier, etal<sup>10</sup> studied Ninety-four patients with unstable closed and open fractures of the tibial shaft. In their study there were no significant differences in the time to union or number of additional procedures performed to obtain union in patients with reamed nail insertion compared with those without reamed insertion for open fractures. A significant number of closed fractures were healed at four months after reamed nail insertion compared to unreamed nail insertion, but there was not a difference at six and twelve months. More secondary procedures were needed to obtain union after unreamed nail insertion for the treatment of closed tibia fractures, but the difference was not statistically significant.

**CONCLUSION**

On the basis of our study it is concluded that reamed intramedullary interlocking nailing is a good mode of internal fixation in type I and II open fractures of tibia as it allows early weight bearing, minimizes the chances of infection and delayed union and has led to union in maximum.

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Riaz Qadeer

## Autopsy of a Putrefied Body (An autopsy based study)

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### ABSTRACT

**Background:** Autopsy of a putrefied body pose a lot of problems in finding out the cause of death, mode of death, manner of death, time since death, personal identification and any crime associated with the death.

**Study Design:** This descriptive study is based on autopsy record and provides information regarding problems faced in autopsy of a putrefied body.

**Duration of Study:** From 1<sup>st</sup> January 2013 to 23<sup>rd</sup> May 2013.

**Methodology:** This study was conducted in the department of Forensic Medicine & Toxicology of Khyber Medical College, Peshawar. Data was collected from the record of autopsies performed from January 2013 to May 2013. It include all cases referred from urban as well as from rural area police stations of Peshawar district.

**Results:** Out of total 400 autopsies 13 postmortem (3%) were done on putrefied dead bodies.

**Conclusion:** It is very difficult to spend some time with a putrefied body to perform autopsy because of offensive smell so detailed study of the dead is done only by a dedicated and God fearing doctor and even then it is difficult to find out the cause of death, mode of death, manner of death, time since death or any associated crime with the death and most of the time personal identification is difficult even by the close relatives.

**Keywords:** Putrefaction, Autopsy, Peshawar, Pakistan.

### INTRODUCTION

Putrefaction or decomposition is the last stage in the resolution of the dead body from organic to inorganic state by the process of (1) autolysis and (2) bacterial action. It is the sure sign of death. The process of putrefaction starts after death and the rate of putrefaction depends on factors like the temperature of the environment to which the dead body is exposed, whether dressed or undressed, intact or mutilated, cause of death, age and sex of the dead, any embalming done or the death occurring in the snow covered high mountains and body remained buried in the snow or death occurred in the dry sandy desert or body recovered from the water.

Autopsy or postmortem is the scientific study of the dead according to the laws of the state. This examination is external as well as internal and it also includes the help of forensic science laboratory as and when required. The pre requisite for autopsy are (a) injury report as written by the police (b) first information report written by the police (c) written

request of police for autopsy. Police is the in charge of dead body to investigate all unnatural and suspicious deaths on behalf of the state and can ask for autopsy as and when required. Changes which occur in the dead after death are important, if carefully noted, these help the law in furthering justice so that no innocent to be punished and no culprit escape punishment awarded by the law.

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**All autopsies if done well in time can help in reconstruction of the story and helps the Government to do full justice. Better police training and early recovery of the dead body can reduce the miseries of the relations. Late recovery may be the reason of putrefaction which entails difficulty in conducting the justice.**

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These changes are grouped into immediate changes which prove death, early changes like fall in body temperature, post mortem staining and appearance of rigor mortis and late changes like appearance of greenish discoloration of skin in the right iliac fossa, marbling, swelling of the whole body due to accumulation of gases of putrefaction, loosening of hair, nails and teeth. Putrefaction is caused by two process (1) Autolysis which is self digestion of the dead body by its own enzymes and it starts within 3 to 4 hours (2) Bacterial action which produce a lot of enzymes which act on muscle proteins as well as on body fats and cause

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their breakdown. The micro organisms responsible for decomposition are both anaerobic and aerobic. Chief bacteria responsible for putrefaction are clostridium welchi, Strepto cocci, E.coli and B proteus. The worst offender is Clastridium Welchi as it produces lecithinase which hydrolyze the lecithin which is present in the cell membranes of almost all cells of body including blood cells.

Blood is a tissue and like other tissues of the body, it disintegrate into its components after death and these break down products of hemoglobin stain the endothelium of blood vessels. As 65% of blood is in the veins and veins are thin walled so 36 to 48 hours after death the superficial veins present in the and groin will give a mosaic appearance which is called **marbling** and it can be easily appreciated in fair skin people especially in females.

#### MATERIAL & METHOD

It is a retrospective descriptive study conducted in

the Department of Forensic Medicine and Toxicology of Khyber Medical College, Peshawar where all autopsies are carried out for the district Peshawar. A total of 400 autopsies were performed from 1<sup>st</sup> January 2013 to 23<sup>rd</sup> May 2013. All these cases were referred by the police from urban as well as from rural police stations to find out the cause of death and time since dead. Mode and manner of death or any other crime associated with the death to be mentioned in the autopsy report, issued to the police and a record of each case being maintained. From this record in a performa information like age, sex, and difficulties faced were noted and the results were analyzed as under.

#### RESULTS

Out of total 400 postmortem cases 13 dead bodies received (3%) were putrefied. Most of the dead bodies referred by police for postmortem were of male, were from rural areas and were in the age group 12 to 30 years. The results are tabulated as under:

S/ No.	Post mortem findings on dead body and presumed cause of death	Age	Sex	No. of cases	Remarks
1	Swollen body with foul smell, incomplete ligature mark around the neck noted, rectal prolapsed, eyes and tongue protruding out, skin slip condition present, joint between greater and lesser cornue of hyoid bone was loose (Presumed as asphyxia deaths)	8 to 11	Male	3	Sex determined from external genital, bodies recognized from dress
2	Body was swollen due to accumulation of gases of putrefaction, skin slip condition was present, marbling present in both axilla and groin, eyes were bulging out of the orbit, tongue was protruding out, rectum prolapsed, joint between greater and lesser cornue of hyoid bone was loose (Asphyxial deaths were presumed)	16 to 30	Male	5	Sex identified from secondary sex character, identification was done from dress and personal belongings
3	A lacerated wound with friable margin was present on the temporal region of both the dead bodies, both were of age about 20 to 22 years, both bodies were swollen and foul smelling with loosening of nails, teeth and hair and all other features of putrefaction were noted (Cause of death was fracture of skull)	21 to 22	One male and one female	2	Sex determination from secondary sex characters partial identification from appearance and some identification from dress,
4	Burnt partially disfigured dead body, blackening of the trachea respiratory tract and upper part of oesophagus was noted in addition to signs of putrefaction (Cause of death was ante mortem burns)	30	Female	1	Body recognized from extra digit of left hand, mole on right eye brow
5	Swollen dead body of boy, foul smelling, washer man skin seen, lungs were non oedematous, no rib markings seen on lungs, No water was present in the middle ear cavity (It was case of post mortem drowning) (Cause of death was not confirmed on autopsy)	11	Male	1	Body identified from his dress and scar mark on right knee
6	Mutilated body with some changes of caseation in the breast emitting rancid smell, other parts of body were mummified (Autopsy was negative)	28	Female	1	Body identified from his dress and his personal belonging (metallic ring)
Total				13	



Condition of body		Total	Sex		Total	Area		Total
Fresh	Putrefied		Male	Female		Urban	Rural	
387	13	400	357	43	400	134	266	400

## DISCUSSION

In our study the cases mentioned<sup>1,2</sup> were presumed as asphyxial deaths but it was difficult to comment as cases of throttling because process of putrefaction itself causes loosening of the junction between greater and lesser cornue of the hyoid bone. It was also difficult to comment that garroting was the cause of asphyxia simply because of the presence of ligature mark around the neck as this mark around the neck may be produced due to tightening of collar of the shirt under the effect of pressure caused by the accumulation of gases of putrefaction. More over due to prolapsed rectum it was not possible to say whether any sexual act like sodomy was done or not. The asphyxia was presumed as the cause of death keeping in view the age of victim, no poison was detected in the viscera and no weapon is required to mechanically interrupt the process of respiration and it is in the knowledge of almost everyone and easy to put pressure on neck to kill someone especially so if he or she is shouting for help. In two cases mentioned<sup>3</sup> death was caused due to fracture of skull as it was confirmed from radiology but it was difficult to say whether any or both of them were under the effect of alcohol or not because the process of putrefaction itself produce alcohol in the human body.

In the case mentioned<sup>4</sup> the cause of death was burning as she was breathing when put to fire so she inhaled and swallowed some carbon particles which caused blackening of the respiratory tract. More over level of carboxy haemoglobin in the viscera confirmed that it was case of ante mortem burns. Carbon mono oxide is a chemical which resist the process of putrefaction. Blisters are produced by burns and putrefaction also produce blisters. Ante mortem blisters contain more serum and electrolytes where as post mortem blisters mainly contain putrefactive gases and there will be no vital reaction. In the case mentioned<sup>5</sup> it was case of post mortem drowning as there was little water in the lungs so person was not breathing/ swallowing when he was thrown in the water to hide the crime.

Autopsy performed on fresh body can help in finding the cause of death, mode of death, manner of death, time since dead, any associated crime with the death, whether born alive or dead and it also help in personal identification of the dead. Autopsy performed on a putrefied body all these questions un-answered

or give a confused answer. Ante mortem injuries can be differentiated from post mortem injuries by **vital reaction** which is the reaction of the living tissues to any trauma. It is also difficult to comment that crime was committed at the place from where the body is recovered or body shifted to that place after killing or the circumstances of death/ position of body at the time of death. It is also difficult to say about the time since dead ie. post mortem interval. According to laws of the state benefit of doubt is given to the accused. Radiologist help in estimating the age, fracture and radio opaque material like bullet or coin in the pharynx.

In Pakistan Police is the in charge of dead body and is the investigating authority about death whether it is natural or unnatural. Death may be unnatural but if the concerned police station head officer (SHO) is satisfied that death is natural then he can issue order for burial of the dead. Death may be natural but concerned SHO is not satisfied so he will ask the medical authority for autopsy especially so when the relatives of the dead fail to accept the demand of police. Dead body is property of the state hence no consent of any one is required for autopsy. People avoid autopsy of their near and dear ones by request or by influence rather they are more interested in taking revenge so further creating un-rest in the society.

## CONCLUSION

All autopsies if done well in time by expert and God fearing doctor on fresh bodies can help a lot in reconstruction of the story and in furthering justice so that no innocent to be punished and no culprit how much influential, he may be, can escape punishment. Measures taken by the Government to improve social justice, better police training and early recovery of the dead body can reduce the miseries of the near and dear ones of the dead. Late recovery of dead body by the police either the culprit is clever or police is over stretched by its duties may be the reason of putrefaction of the dead and autopsy may not be so helpful and benefit of doubt is given to the accused.

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Sikandar Hayat

## Outcome of Ilizarov’s Technique in the Management of Congenital Pseudo-arthritis in Tibia (CPT)

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### ABSTRACT

**Purpose of the Study:** To assess the outcome of Ilizarov’s technique in management of congenital pseudo-arthritis of tibia.

**Patients & Methods:** We reviewed 18 cases of congenital pseudo-arthritis of the tibia (CPT) who were treated with Ilizarov’s apparatus between Jan.,2015 and Aug, 2016. The patients were evaluated clinically and radio graphically for ASAMI (association for the study and application of methods of Ilizarov scoring system) scoring.

**Results:** 14 patients achieved union out of 18. The main complication was re-fracture in 2 patients, and leg length discrepancy in 4 patients.

**Conclusion:** The Ilizarov technique was successful in achieving union with few complications, though this should be shown in long-term studies lasting until skeletal maturity.

**Key Words:** Ilizarov ex-fix, congenital pseudo-arthritis tibia.

### INTRODUCTION

The reported incidence of Congenital pseudo-arthritis of the tibia (CPT) varies between 1:140,000 and 1:250,000 and bilateral forms are extremely rare.<sup>1</sup> The tibia shows area of segmental dysplasia resulting in anterolateral bowing of the bone. The osseous dysplasia leads to a tibial nonunion and, because of tibial bowing and reduced growth in the distal tibial epiphysis, shortening of the limb usually occurs.<sup>2</sup>The disease becomes evident within a child’s first year of life. However, Andersen described a rare late onset type developing in a tibia, which is normal at birth but develops anterior bowing between the ages of 4 and 12 years.<sup>2</sup> The natural history of the disease is extremely unfavorable and, once a fracture occurs, there is a little or no tendency for the lesion to heal spontaneously.<sup>3</sup>

Treatment of CPT is still a challenge<sup>2,4-6</sup> Each treatment aims to obtain a long term bony union of tibia and fibula, to prevent limb-length discrepancy, to avoid

mechanical axis deviation, soft tissues lesions, nearby joint stiffness, and pathological fractures.<sup>7,8</sup> Invasive method of treatment that includes excision of pseudo-arthritis tissue including diseased periosteum with stable internal or external fixation with vascularized or non-vascularized graft is the conventional surgery for treatment of CPT. A noninvasive method, which includes electrical stimulation without surgery, is also described to enhance union. However, none of invasive or noninvasive method has yet proven its superiority. Conventional surgery is often associated with acceptable results,<sup>9,10</sup> and amputation may be proposed in failed cases.<sup>2,11-15</sup> Weber reported amputation of the calf in 9-14% of patients with CPT.<sup>16</sup> Treatment of this condition is associated with a substantial risk of non-union, refractures, leg length discrepancy (LLD), and malalignment of the tibia and the ankle.<sup>17,18</sup>

### The Ilizarov technique is successful in achieving union with few complications, until skeletal maturity.

Historically, Charnley (1956) first treated cases of CPT with intra-medullary rod.<sup>19</sup> Coleman added autogenous iliac bone graft to intramedullary rod for the treatment of CPT.<sup>14,20</sup> In 1974, Ostrup *et al.* demonstrated the presence of active osteocytes in vascularized bone graft and their absence in non-vascularized bone graft.<sup>21,22</sup> Taylor *et al.* (1975) succeeded in grafting the first vascularized fibula<sup>23</sup> and 3 years later, the same

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technique was applied by Weiland *et al.*<sup>24,25</sup> for treating patients with CPT. Shah *et al.* used cortical bone grafting with intramedullary nailing for the treatment of the CPT.<sup>26</sup> Cortical bone grafting from contralateral tibia resist resorption better than cancellous bone hence primary union rate is higher with use of cortical bone graft.<sup>27</sup>In summary, treatment procedures can be classified into 3 groups:

- (1) Intramedullary rodding (usually trans-ankle) with bone grafting<sup>28,29</sup>
- (2) Microvascular fibular transfer<sup>30</sup> and
- (3) The Ilizarov technique with its various modifications<sup>31,32,33</sup>. However, no single treatment has been shown to be uniformly effective.

Aim of this study was to know outcome of the management of congenital pseudo-arthritis tibia using Ilizarov technique.

## PATIENTS & METHODS

We prospectively analyzed all 18 patients with CPT who had been treated at our institute using a Ilizarov's technique between Jan 2015 and Aug 2016. None had bilateral involvement. Detailed preoperative clinical examination was performed, which included knee and ankle range of motion, limb length discrepancy, operative scars, limb alignment, and functional evaluation using ASAMI score system. Congenital pseudo-arthritis of the tibia treated with Ilizarov's technique

11 surgeries were performed by two senior surgeon (HRS) well trained with Ilizarov technique. The patients were operated keeping in mind some basic principles: i.e. excision of the pseudo-arthritis with the abnormal periosteum and surrounding tissues, removal of the dead and sclerotic bone ends until bleeding ends appear, and bone grafting in the intervening space. The sclerotic portion of the fibula, if present, was dealt with similarly. The Ilizarov frame was then mounted. The decision to apply the external fixator in compression mode or in bone transport mode was taken with respect to the limb length discrepancy. If the limb length discrepancy was less than 2.5 cm, we used compression at the pseudo-arthrotic site while if it was more than 2.5 cm or when there was a lot of fibrosis around the pseudo-arthritis due to previous surgery, a proximal corticotomy was performed with bone transport in order to prevent further LLD. Usually, 2 rings proximally and 1 ring distally were applied in the compression mode.

Bone transport (when needed) was started after 7 days of surgery at the rate of 1 mm/day. The patient was taught pin-tract care and partial weight bearing.

Physiotherapy with active and passive motion of the knee and ankle, and resting of the foot in shoes attached by elastic bands to the Ilizarov apparatus were advised to prevent joint contracture. The patients were followed regularly over a long period until clinico-radiographic union was obtained. The Ilizarov fixator was removed after radiographs had shown corticalization of at least 3 cortices, seen in radiographs taken in 2 planes

At final follow-up, patients were evaluated for union, knee and ankle motion, and limb length discrepancy. Union was labeled as being "primary" when it united after the present surgery without any need for secondary surgeries when additional surgery was required to obtain union. The need for additional procedures to achieve union was noted. Complications were categorized as minor or major. Minor complications were defined as being those complications or adverse effects that did not require any additional surgery or those that required only minor surgeries. Major complications were defined as being those that required complex surgeries for correction and those that adversely affected the final surgical outcome.

The results were classified as good, fair, or poor based on the presence or absence of these minor or major complications. A good result meant no or only minor complications that could be treated non-surgically, a fair result meant the presence of 1 or more minor complications that had to be treated surgically or the presence of a major complication after which the final surgical goal could be still achieved, and a poor result meant the presence of 1 or more major complications because of which the final surgical goal could not be achieved.

## RESULTS

A total of 18 cases included in this study prospectively between Jan 2015 till August 2016. Majority of the children belonged to age range 3-10 years. Age distribution is shown in table-1. Study population comprised of 8 (44.4%) male and 10(55.6%) female as shown in table-2.

All the subjects assessed according to ASAMI Scoring system shown in Table 3 and Table 4. According to ASAMI scoring system 4 patients (22.22%) turned out to be excellent, 10 patients (55.55%) good, 1 patient (5.55%) fair while 3 patients (16.66%) failed while none of the patients turned out to be poor.

Study population suffered from a number of complications including limb length discrepancy, infection, malalignment, refracture and failure to achieve union as shown in table 5. In one patient refracture was due to non compliance with brace wearing while in second patient refracture was through

proximal pin site due to infection and not through previous pseudoarthrosis site.

**Table 1:** Age distribution of study cases

S. No.	Age group	No of pts	Percentage
1.	3-10 yrs	14	77.70%
2.	11-20 yrs	02	11.10%
3.	21-30 yrs	02	11.10%
<b>Total</b>	(1-30) yrs	18	100%

**Table 2:** Gender distribution of study population.

S.No	Gender	No of pts	Percentage
1.	Male	08	44.4%
2.	Female	10	55.6%
<b>Total</b>		18	100%

**Table 3:** ASAMI Scoring Bone results

Bone results	Description	Score
<b>Excellent</b>	Union, no infection, deformity <7, limb length discrepancy <2.5 cm	<b>10</b>
<b>Good</b>	Union+ any two of the following: absence of infection <7 deformity and limb length inequality of <2.5 cm	<b>2</b>
<b>Fair</b>	Union+ only one of the following: absence of infection, deformity <7 and limb length inequality <2.5 cm	<b>0</b>
<b>Poor</b>	non union/refracture/union +infection+ deformity>7+limb length inequality >2.5 cm	<b>0</b>

**Table 4:** ASAMI Scoring Functional results

Functional	Description	Score
<b>Excellent</b>	Active, no limp, minimum stiffness(loss of <15 knee extension/<15 dorsiflexion of ankle), no reflex sympathetic dystrophy,insignificant pain	<b>6</b>
<b>Good</b>	Active, with one or two of the following: limp, stiffness, RSD, significant pain	<b>4</b>
<b>Fair</b>	Active, with three or all of the following : limp, stiffness, RSD, significant pain	<b>0</b>
<b>Poor</b>	Inactive(unemployment or inability to perform daily activities because of injury)	<b>2</b>
<b>Failures</b>	Amputations	<b>0</b>

**Table 5:** ASAMI Functional Outcome

Sr. No.	Outcome category	No. of pts	Percentage
1.	Excellent	4	22.22%
2.	Good	10	55.55%
3.	Fair	1	5.55%
4.	Poor	0	0%
5.	Failure	3	16.66%

**Table 6:** Complications.

S. No.	Nature of complications	No of pt	Total no pt	Percentage
1.	LLD	04	18	22.22%
2.	Infection	0	18	0%
3.	Non union	04	18	22.22%
4.	Refracture	02	18	11.11%
5.	Mal alignment	0	18	0%
6.	RSD	0	18	0%

Case of congenital pseudoarthrosis of tibia managed with the Ilizarov frame.



**DISCUSSION**

The treatment of CPT is controversial. Most series are small, non-comparative, and composed of heterogenous groups of patients.<sup>34</sup> Over the last few decades, intramedullary rodding with bone grafting and Ilizarov's technique have emerged as the most commonly used methods<sup>35-41</sup>

The Ilizarov technique, first introduced in the western world in the 1980s, has been widely used for CPT and has gained acceptance in various centers.<sup>42</sup> This method allows treatment of not only the pseudoarthrosis but also LLD, angular tibial abnormalities, proximal fibular migration, and foot contractures<sup>43,44</sup>.

According to the multicenter study of the European Paediatric Orthopedics Society (EPOS), the Ilizarov method has been found to be the gold standard for treatment of CPT<sup>45</sup>. The Ilizarov procedure is, however, associated with a high union rate, and also with a substantial refracture rate. In his series of 16 cases of pseudo-arthritis, Paley et al.<sup>46</sup> reported on refractures in 5 patients after initial union. Inam et al.<sup>47</sup> reported on 16 patients treated with Ilizarov. All the patients united but 10 patients had late axial mal-alignments and refractures. Cho et al.<sup>48</sup> reported on 23 patients with atrophic type of CPT who were treated with Ilizarov's technique. 20 of them suffered from refractures within 5 years of surgery.

The other important complication of the Ilizarov method is the late axial mal-alignment that may develop after radiographic union<sup>49</sup>. In one of the earliest series, Ilizarov and Gracheva (1971) had axial mal-alignments in 5 of 16 patients who were treated by the method. Kristiansen et al.<sup>50</sup> also noted similar rates of residual axial deformities. Our series has shown comparable results, with substantial symptomatic mal-alignments in 0 of 18 patients.

The relationship between these axial mal-alignments and refractures and the exact cause of refracture has been studied in great detail by several authors. Young age at surgery with a low cross-sectional area of the united segment of the pseudo-arthritis, ankle valgus due to fibular non-union, and non-compliance with bracing are all thought to cause refractures<sup>51,52,53</sup>. However, we feel that there are only 3 important causes of refractures, namely:

- (1) axial deviations leading to stress risers and fractures,
- (2) loss of intra-medullary support after removal of nails, and
- (3) non-compliance with external bracing regimen. Insufficient resection of the pseudo-arthrotic site is in itself a poor prognostic factor, but usually the poor result is because of a non-united pseudo-arthritis rather than a refracture.

22.2% of our patients had some residual limb length discrepancy after the surgery, at the last follow-up. However, union is the most important parameter, and limb length discrepancy can be tackled later on, if necessary. Even when the Ilizarov method was used for lengthening, the initial resection was so extensive in some patients, and even after substantial lengthening, some residual shortening was present.

The present study has some limitations. It is a pilot study with good medium-term results. Long-term studies until skeletal maturity are needed to evaluate

the benefit of this method

## CONCLUSION

Our method combines the qualities of two techniques and appears to provide lower refracture rates, fewer axial mal-alignments, and comparable functional outcomes than the methods used in other series.

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Roheena Wadud

## Effect of Single Intravenous Dose of Dexamethasone in Children undergoing Tonsillectomy/Adeno-tonsillectomy

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### ABSTRACT

**Objective:** To find the effect of single intravenous dose of dexamethasone in children undergoing tonsillectomy or adeno-tonsillectomy.

**Material & Methods:** This comparative study was conducted in the department of Anaesthesia LRH/MTI Lady Reading Hospital Peshawar from May 2015 to Oct 2015, children of both gender, age 5-12 years, undergoing tonsillectomy were divided into two groups of 50 each, one group D was selected to receive dexamethasone 0.5mg/kg (maximum 8mg), the second group C was given equivalent volume of saline, at the time of induction of anaesthesia. All the patients were observed in recovery and then in ward for post operative nausea and vomiting and also for need of anti-emetics for 24 hours.

**Results:** The frequency of nausea and vomiting was significantly less in dexamethasone group D  $P < 0.05$ , as compared with control group C. The need for rescue antiemetic was also significantly less in group D as compared to group C. Chi square test was applied.  $P < 0.05$ , which was considered significant.

**Conclusion:** Single dose of dexamethasone, given at the time of induction of anaesthesia, reduces the frequency of post-operative nausea and vomiting in children and the need for rescue anti-emetics in the first 24 hours.

**Key Words:** Tonsillectomy, post-operative nausea and vomiting, dexamethasone.

### INTRODUCTION

Post-operative nausea and vomiting poses problems for patients undergoing all types of procedures requiring anaesthesia or sedation. The incidence of post-operative nausea and vomiting ranges from 1% to 43%. It has led to one third of unexpected hospital admissions among paediatric patients after ambulatory surgery, delayed discharge and increase cost of care.<sup>1,3</sup>

Tonsillectomy with or without adenoidectomy is one of the most frequently performed surgical operations in children.<sup>4</sup> Among the anti-emetics used currently,<sup>5</sup> hydroxytryptamine antagonists such as ondansetron and granisetron are effective but their high cost limit their widespread use.<sup>6,7</sup> Other anti-emetics drugs used currently such as anti-cholinergics, dopamine receptor antagonists and antihistamine, although effective, possess clinically significant side effect, such as restlessness, dry mouth, tachycardia and extra pyramidal symptoms.<sup>8,10</sup>

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**Single dose of dexamethasone significantly reduces post operative nausea and vomiting after tonsillectomy in children. There are economic benefits because of reduced need for analgesia and anti-emetics and early return to normal diet.**

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Dexamethasone was first reported to be an effective antiemetic agent in patients receiving chemotherapy in 1981.<sup>11</sup> Since then, several studies have shown that dexamethasone is equal to or better than other antiemetic agents in preventing nausea and vomiting, associated with chemotherapy. Recently, dexamethasone has also been reported to have prophylactic effect on post-operative nausea and vomiting in patients undergoing tonsillectomy.<sup>12-13</sup> Thyroidectomy<sup>14,15</sup> or major gynaecological surgery.<sup>16,17</sup> Dexamethasone has also proved to be very effective in laparoscopic procedures.<sup>18</sup> The present study was conducted to assess the effect of a single dose of dexamethasone at time of induction of anaesthesia, on post-operative nausea and vomiting, in children undergoing tonsillectomy or adeno-tonsillectomy, using a standardized anaesthetic technique.

### MATERIAL & METHODS

This comparative study was conducted at department of Lady Reading Hospital /MTI Peshawar

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from May 2015 to October 2015. ASA PS I Children of both gender aged 5-12 years were listed for elective tonsillectomy or adeno-tonsillectomy. Written informed consent from the parents/guardians was taken.

Patients with history of preoperative nausea and vomiting in the 24 hours prior to anaesthesia/surgery, disease, prolonging gastric emptying e.g. pyloric stenosis, sleep apnoea and congenital anomalies were *excluded*. Patients with history of acute tonsillitis within six weeks, bleeding diathesis, those who received antiemetics or steroids 24 hours pre-operatively or with a known contraindications to steroids were also excluded. Because these are confounder of our study and make the results biased if included.

All baseline investigations were done pre-operatively. Children were kept fasting for 6 hours for solids and 2 hours for clear fluids. Children were divided into two groups. Each group consist of 50 patients group D received dexamethasone .5mg/kg (maximum 8mg), group C received equivalent volume of saline, was given after the induction of anaesthesia by the anaesthesiologist who was not involved in monitoring of patients post-operatively.

On arrival of patient in the operating room, preoperative vital parameter including pulse rate, blood pressure and O<sub>2</sub> saturation and respiratory rate were recorded. Anaesthesia was induced with oxygen, sevoflurane via face mask and intravenous line was established or in some cases, anaesthesia was induced, by first securing intravenous line and using propfol 2-3mg /kg, intubation of trachea was facilitated with atracurium 3.5mg/kg then anaesthesia was maintained with isoflurame 1% and O<sub>2</sub> 4L/min. Tramal 1mg/kg was used as analgesic agent. Then the study agent given. Patient vitals were monitored, and at the end of tonsillectomy, 0.75mg/kg Ketorelac was given. After the completion of tonsillectomy, neuromuscular blockade was reversed with neostigmine 0.04/kg and atropine .02mg/kg. Anaesthesia was discontinued and tracheal tube was removed in lateral position and then O<sub>2</sub> given via face mask. When patient recovered from anaesthesia, they were shifted to recovery. They were observed post-operatively for 2 hours in the recovery. Effect of dexamethasone was measured in term of nausea, vomiting which were recorded every 30 minutes in the recovery. Then the patient was shifted to ward, where they were monitored for nausea and vomiting for 24 hours. Nausea vomiting occurring more than twice was treated with meta-clorpomide 0.15mg/kg I/v over 15 minutes.

Also intravenous rehydration done with ringer lactate solution, when necessary in resistant cases.

Patient were discharged if they were free from morbidities like nausea and vomiting, pain and dehydration, after 24 hours. The frequency of post-operative nausea and vomiting in two groups were compared and also the need for rescue of anti-emetics were compared. Chi square test was applied, P value was less than .05, was considered significant.

**RESULT**

Data from 100 patients were analyzed, 50 received .5mg/kg (maximum 8mg) of dexamethasone and 50 received equivalent amount of saline. The two groups were similar as we found no significant difference between the 2 groups with respect to age, gender, duration of surgery and duration of anaesthesia. (Table-I). The effect in term of nausea and vomiting was significantly less in dexamethasone group (Group D) compared to normal saline group (Grouped C) with p-value=0.00004 by using Chi square test. Table II.

**Table 1:** Demographic characteristics of dexamethasone "D" groups and placebo "C" group

Characteristics	Group D (N=50)	Group C (N=50)	p-value
Age (Years)	8.25 + 2.08	8.02 + 2.19	0.5915
Gender M/F	26/24	23/27	0.3447
Duration of Anaesthesia (minutes)	48.7 + 9.44	46.55 + 9.53	0.2598
Duration of surgery (minutes)	38.34 + 5.89	39.29 + 4.16	0.3541

**Table 2:**

		Group		Total	p-value
		D	C		
Effectiveness	Yes	30	10	40	0.00004
		60%	20%	40%	
	No	20	40	60	
		40%	80%	60%	
Total		50	50	100	
		100.0%	100.0%	100.0%	

**DISCUSSIONS**

Post-operative nausea and vomiting (PONV) continues to be a common concern after tonsillectomy. It is a leading cause of dehydration and unanticipated hospital admissions in post-tonsillectomy patients which increases the total health care cost. To minimize PONV and improve oral intake, anaesthetologists have focused primarily on anaesthetic technique with minimal emetic potential.<sup>19</sup> Post-operative nausea and

vomiting continues to be a common complication of surgery especially tonsillectomy<sup>12,14</sup> thyroidectomy<sup>15,16</sup> laparoscopic cholecystectomy<sup>18</sup> and gynaecological procedures.<sup>17</sup>

It is a limiting factor in the early discharge of ambulatory surgery patients and a leading cause of unanticipated hospital admissions. Post-operative nausea and vomiting can lead to increase recovery room time and expanded nursing care. Equally important are the high levels of patient discomfort and dissatisfaction associated with post-operative nausea and vomiting. Post operative morbidity after tonsillectomy in children includes pain, vomiting, inadequate oral intake and dehydration.<sup>19</sup>

The incidence of PONV in children undergoing tonsillectomy ranges from 35%-75%.<sup>20</sup> Post-operative nausea and vomiting poses problems for patients undergoing all types of procedures requiring anaesthesia or sedation. The surgeries associated with increased incidence of nausea and vomiting in children include adeno-tonsillectomy, strabismus surgery, hernia repair and orchipexy. Anderson and Krohg have suggested post-operative pain as an important cause of post-operative nausea and vomiting and the relief of pain was associated with the relief of post-operative nausea and vomiting.<sup>21</sup> Also in another study, Stanke et al reported nausea and vomiting in 33% of patients on day 3, dropping to 11.6% by day 7 in patients undergoing adeno-tonsillectomy.<sup>22</sup>

Dexamethasone has recently been used as prophylaxis for post-operative nausea and vomiting in children undergoing tonsillectomy.<sup>23,24</sup> Our study was aimed at the pre-operative use of single dose of dexamethasone in cases of tonsillectomy and its effect on post-operative nausea and vomiting and improved quality of oral intake during the first 24 hours in children. Our study showed reduced post-operative nausea and vomiting. The age ranges in a study by Muhammad Ali Hashim<sup>25</sup> et al and Alajmi<sup>26</sup> M A et al, all the patients were from pediatric age group. In our study, majority of dexamethasone treated patient, did not require anti-emetic's in the first 24 hours of post-operative period. This indicates prolonged antiemetic effect of dexamethasone. These findings are also supported by other studies.<sup>26,27</sup> Systemic steroids have powerful anti-inflammatory effects and are expected to improve post surgical trauma. Several studies have shown that dexamethasone can decrease post surgical pain, nausea and vomiting post-operatively.<sup>28,29</sup>

In our study the anaesthetic technique, amount of intravenous hydration, analgesic dose and antiemetic therapy were standardized. The dose selected in

our patients was 0.5mg/kg(maximum 8mg) of dexamethasone intravenously at the time of induction of anaesthesia and it significantly reduces post-operative nausea and vomiting after tonsillectomy in children. Samar Kandi A.H. et al, had the same results.<sup>19</sup> The recent guidelines regarding tonsillectomy strongly recommend, the use of a single, intra-operative dose of intravenous dexamethasone to children undergoing tonsillectomy.<sup>30</sup>

Dexamethasone administration would not only lead to a decrease incidence of post-operative nausea and vomiting but would also decrease throat pain and time to resumption of oral intake.<sup>31</sup>

## CONCLUSION

Dexamethasone is considered safe and there were no adverse effects associated with single dose of dexamethasone. Dexamethasone significantly reduces post operative nausea and vomiting after tonsillectomy in children. Apart from markedly reduced post operative morbidity, there are economic benefits because of reduced need for analgesia and anti-emetics and early return to normal diet.

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## Amazing facts about Eye

- The human eye blinks an average of 4,200,000 times a year.
- Our eyes make 4.5 litres (8 pints) of tears a year.
- If an astronaut cry, his eyes will not produce tears due to affect of gravity.
- The human eye can distinguish about 10 million different colors.
- If the human eye is a digital camera it would have 576 megapixels.
- Our body needs sleep, keeping awake for 2 weeks can be enough to kill us.



Muhammad Khalid Khan

## Result of Two K-wire Fixation of Displaced Lateral Condyle in Humerus Fractures in Children

Muhammad Khalid Khan FCPS<sup>1</sup>, Dr. Misbah Durrani FCPS<sup>2</sup>, Samad Khan FCPS<sup>2</sup>, Muhammad Shoaib FCPS<sup>3</sup>

### ABSTRACT:

**Objective:** To assess the result of 2 k-wires at 45° fixation in displaced lateral condyle fractures of humerus, stabilized with K-wire fixation.

**Methods:** This study was carried out in department of orthopaedics at Kabir Medical College Hospital, Gandhara university Peshawar from February 2015 to February 2016 in one year. 15 children with lateral condyle humerus fractures Milch type II were studied. The condyles were treated by open reduction and fixed with 2- K.wires at 45°.

**Results:** Out of 15 patients, ten were boys (66.6%) and five(33.3%) were girls. The mean age was 7.5 years. 13(86.66%) were of right dominant elbow; while 2(13.33) were left elbows. Operation time was 45 minutes, neither minor nor major complications of anesthesia and surgery were observed. Clinical results were excellent in 14 (93.33) patients, good in 1(6.66%) and poor in 0(0.0%) patient according to Hard acre criteria.

**Conclusion:** From the results of this study we concluded that displaced lateral condyle fractures treated by open reduction and fixation with 2 k-wires at 45° is much more correct method to get the union and to avoid complication

### INTRODUCTION

Humerus fractures are very common in children.<sup>1</sup> Lateral condyle fractures of the distal humerus are the second most common fractures at the elbow in the paediatric population<sup>2</sup> usually between the ages of 6–10 years old making up 5–20 % of fractures in children.<sup>3,4</sup> Fracture usually occurs on out stretched hand and extension of elbow. The fracture patterns of the lateral condyle bear the name of Milch who in 1964 classified these fractures into Milch I and Milch II. In Milch type I, the fracture line enters the joint lateral to the ridge between the trochlea and capitellum while in Milch type II, the fracture extends into the trochlear groove.<sup>5</sup> The Jacob classification dictates whether surgical intervention is required. A. Jacob I is non-displaced, Jacob II is displaced by 2 mm, but not malrotated. Jacob III is displacement with malrotation.<sup>6</sup>

The diagnosis can be difficult both radiologically and clinically, with loss of function occurring, due to extension into the articular surface. The result of an incorrectly treated lateral condylar physeal injury may

not be evident until months or years after the initial index injury.<sup>7</sup>

Determination of the magnitude of displacement can be difficult. Some authors have suggested ultrasound, magnetic resonance imaging (MRI), arthrography, or multi-detector computed tomography (CT).<sup>8</sup> Many of these methods involve greater expense, time, radiation exposure, painful examinations, or even sedation.<sup>9</sup> Therefore, initial displacement assessment is often determined using plain radiographs.

Management of fractures showing little displacement remains controversial<sup>10</sup> Surgical treatment is recommended for fractures displaced more than 2 mm, either by closed reduction and percutaneous pinning<sup>11</sup> or open reduction and internal fixation.<sup>12</sup> For non-displaced and minimally displaced fractures closed treatment using a long arm cast or splint is usually effective.<sup>13</sup> The aim of this study was to know the result of open reduction and fixation with 2 K-wires at 45° in displaced lateral condyle fracture of humerus in children.

**Lateral condyle fracture of the humerus when dealt early and fixed with 2 k-wires yield excellent results.**

### METHODS

This study was carried out after permission from hospital ethical committee in Department of Orthopaedics at Kabir Medical College Hospital, Gandhara University Peshawar from February 2015 to February 2016 in one year.<sup>15</sup> children with lateral

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condyle humerus fractures were admitted from Out Patient and emergency department after complete clinical evaluation and assessment i.e history, examination, blood investigation, antero-posterior and lateral radiograph. Displacement of fracture identified from the lateral cortex of humerus at distal area towards the lateral cortex of fragment on the antero-posterior view, posterior cortex on the lateral view of radiograph. We included Milch type II closed fractures within 3 weeks. After counseling regarding the surgical procedure and consent from the parents for general anesthesia was taken, the pneumatic tourniquet was applied. After aseptic measures, limb was draped and through lateral approach, fracture opened through soft tissue dissection and then reduced under direct vision. After reduction stabilized with two K- wires one passed parallel to the joint and another at 45° to the 1st one.

For fracture stability, the elbow movements were checked per operatively and wound closed. Soft dressing, above elbow slab was applied and kept for three weeks'. Stitches removed after one week, pins removed after union achievement, i.e appearance and solidification of callus visible on the antero-posterior and lateral views of x-ray and on clinical assessment. K-wires removed after three to five weeks. Physiotherapy started earlier with removal of slab. Forearm movements i.e supination, pronation, flexion, extension and carrying angle were evaluated after full healing and were not changed as compared to the normal limb Hardacre et al<sup>14</sup>.

	Range of motion	Carrying angle	Symptoms
Excellent	No limitation	No alteration	No Symptoms
Good	Functional range of motion (no more 15 degree of complete extension.	Inconspicuous alteration	No, Arthritic, Neurologic symptoms
Poor	Disabling loss of function	Conspicuous alteration	Arthritic symptoms, ulnar neuritis, roentgen findings of nonunion, avascular necrosis

**RESULTS**

Total 15 children were evaluated. Out of 15 patients, ten were boys (66.6%) and five(33.3%) were girls. The mean age was 7.5 years. 13(86.66%) were of right dominant elbow; while 2(13.33) were left elbows (Table A).

Management was started as early as possible local circumstances of patient allowed. Operation time

was 45 minutes, neither minor nor major complications of anesthesia and surgery were observed. The patients were followed for five weeks period. The mean healing time was 5 weeks, the mean immobilization time was 4.5 weeks and K- wires were removed at mean time of 5 weeks Table B. Clinical results were excellent in 14 (93.33) patients, good in 1(6.66%) and no failure according to Hardacre criteria, Table

**Table – A**

Variables	Numbers	Percentage
Male	10	66.66%
Female	5	33.3%
Right elbow (dominant)	13	86.66%
Left elbow	2	13.33%
Age (mean)	7.5 years	

**Table – B**

Mean union time (mean)	5 weeks
Immobilization time (mean)	4.5 weeks
Removal of K-wire (mean)	5 weeks

**Table – C**

Union Rate	Outcome	Percentage
Excellent	14	93.33
Good	01	6.66
Poor	0	0.00
Total	15	100%



**DISCUSSION**

Injuries from a fall, motorcycle, cycle and games are common in children. The lateral condylar fracture is one of the most common fractures in children only second to supracondyler humerus fractures. It is often ignored and usually treated by the bonesetters in our society. Sometimes it causes serious complications and may lead to loss of elbow actions. Diagnosis of lateral condyle fracture sometimes may be difficult and MRI or Arthrography may be needed.

The gold standard in the treatment of displaced lateral condyle fractures of the elbow in children is open

anatomical reduction and internal fixation with K-wires followed by cast immobilization<sup>5</sup>. In a local study by Abdul Malik Shaikh and Muhammad Zaib Tunio<sup>1</sup> they have shown excellent result in 86.66% patients, good in 10% and poor in 0.33% using Hardacre criteria. In our study we have 93% excellent result and 6% good result with no poor outcome which is compatible with this local study.

The study by Khalid Mahmood, Faaiz Ali Shah, Ghulam Atiq<sup>5</sup> shows overall excellent results in majority (73.9%, n= 17) of patients while good, fair and poor results were reported in 3(13%), 2(8.6%) and 1(4.3%) patients respectively. They used the Agrawal modified criteria.

In the study by Andreas Leonidou, Krissen Chettiar, Simon Graham, Pouya Akhbar et al<sup>2</sup> One hundred and five patients with a displaced paediatric lateral humeral condyle fracture were identified and included in the study, 76 males and 29 females. The mean time to radiological union of the fracture and therefore removal of the wires was 33 days (4.7 weeks). Radiological union ranged between 21 and 56 days. (3–8 weeks). Follow-up ranged between 2 and 8 years with an average of 3.2 years. At the final appointment, all patients had achieved full range of movement of the elbow joint. Furthermore, there were no cases of residual pain, and all patients were happy performing daily life activities and participating in sports. Shen study 13 patients in 04 weeks, observed good outcome movements and cosmetic results<sup>15</sup>. Mazurek and Skorupki operated 07 years' old nonunion through olecranon osteotomy K-wire fixation observed good result after 06 months.<sup>16</sup> In another study of Baharuddin M, conducted in 2001, fracture were fixed with screw in 20 cases, 19 out of that were excellent at one year follows up.<sup>17</sup>

If lateral condyle fracture left untreated mal-union, non-union, proximal migration of fragment cubitus valgus, tardy ulnar nerve palsy, AVN, limitation of movement and cosmetic defects may occur. In our study the sample size is small and the duration of study is short. Larger sample size and longer period of follow up is needed for further evaluation.

#### CONCLUSION

We concluded from this limited study that lateral condyle fracture of the humerus when dealt early and fixed with 2 K-wires yield excellent results.

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خُدا نصیب کرے دائمی خوشی اُن کو  
عدم وہ لوگ جو ہم کو اُداس رکھتے ہیں



Roheena Wadud

## To Compare the Efficacy of Tramadol and Pethidine For Control of Intraoperative Shivering Under Spinal Anaesthesia in Elective Caesarian Section

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### ABSTRACT

To compare the efficacy of Tramadol and Pethidine for control of intra-operative shivering under spinal anaesthesia in elective Caesarian section.

**Methodology:** This double blind randomized study was carried out in Anaesthesia Department, Lady Reading hospital / MTI Peshawar from January 2015 to May 2015. Pregnant women undergoing caesarean section, who developed shivering following spinal anaesthesia with hyperbaric 7.5% bupivacaine were included in the study. All patients were randomly divided in two groups I & II. Group I received 1% tramadol 1mg/kg slow i/v and group II received 1% pethidine 1mg/kg slow i/v. The disappearance of shivering were assessed.

**Results:** stoppage of shivering took 10minutes in tramadol group while 20 minutes in pethidine group. P=0.03.

**Conclusion:** Tramadol is a more effective agent than Pethidine in the treatment of post spinal shivering with lower side effects in obstetric patients.

**Key words:** Spinal anesthesia, Tramadol, Pethidine, shivering.

### INTRODUCTION

Regional anaesthesia is a safe and popular anaesthetic technique for various surgeries. Around 40-60% of the patients under regional anaesthesia develop shivering.<sup>1,2</sup> Shivering can be very unpleasant and physiologically stressful for the patient after enjoying the comforts of modern anaesthetics.<sup>3</sup> Neuro-axial anaesthetic techniques are the most commonly indicated for caesarian sections, due to lower rates of maternal morbidity and mortality with less neonatal depression as compared with general anaesthesia.<sup>4</sup> Shivering may interfere with monitoring of electrocardiogram, blood pressure and pulse oximetry.<sup>5</sup> Post-anaesthesia shivering increase left ventricular systolic work index and oxygen consumption may be increased by 200% to 500%.<sup>6</sup>

Thus in patients with decreased myocardial function reserve, it may further compromise myocardial function. Shivering may also increase intraocular and intracranial pressure and may also contribute to wound pain.<sup>7</sup> The possible mechanism of shivering after spinal anaesthesia in pregnant women result

from central thermo-regulation disturbances, and predisposes patients to hypothermia which reduces the threshold for vasoconstriction and shivering.<sup>8</sup> Various pharmacological therapies such as pethidine<sup>9</sup>, ketamine<sup>10,11</sup> clonidine and tramadol<sup>13,14,15</sup> have been used to prevent shivering. Tramadol produces weak sedation effect and present low respiratory depression; It can be used safely in pregnant women.<sup>16</sup> This study was conducted to compare the efficacy of tramadol and pethidine for control of intra-operative shivering under spinal anaesthesia in pregnant women undergoing caesarean section.

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**Tramadol is a more effective agent than Pethidine in the treatment of post spinal shivering with lower side effects in obstetric patients.**

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### METHODOLOGY

It was a double blind randomized clinical trial. This study was done in Anaesthesia Department PGMI LRH/MTI Peshawar from January 2015 to May 2015. After obtaining departmental permission and informed written consent from 60 Obstetric patients with ASA physical status I-II who were candidates for elective caesarian section and who developed shivering after spinal anaesthesia. Patients with hypothyroidism or hyperthyroidism, cardiopulmonary disease, psychological disorders, a need for blood transfusion during surgery, an initial body temperature > 38°C or < 36°C with a known history of alcohol or drug abuse

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or medications likely to alter thermo-regulations were excluded from the study.

In the operating theatre, an 18 gauge venous cannula was inserted in the largest apparent vein on the dorsum of hand. Lactated ringer’s solution was infused at 10ml/kg/h over 30m before spinal Anaesthesia. Infusion rate was then reduced 6ml/kg/hr. Standard monitoring, including continuous ECG, pulse oximetry and NIBP were attached to the patient.

Spinal anaesthesia was given either at L3/L4 or L4/L5 interspaces. Hyperbaric bupivacaine 7.5mg/cc, 2cc, 15mg was injected using 25G spinal needles. The patients were immediately turned to supine position with lateral deviation of the uterus to the left, using a pad under the right hip. After blockade, hydration was maintained at 6ml/kg/hr. After birth 10 units of oxytocin in 500 ml of Ringer’s lactate were infused at 6ml/kg/hr. For treatment of hypotension, 5-10mg ephedrine was used. Patients who experienced shivering of grades 3 and 4 (Table: 1) were included in the study. All the patients who experienced shivering were randomly divided into group I and group II.

Group I received 1% tramadol of 1mg/kg in a dose of slow i/v and group II received 1% pethidine in a dose of 1mg/kg slow I/V for control of shivering. An observer was blinded to the study group. All the patient were observed for shivering grades and its disappearance. Patients were observed at interval of 1 min till 5 minutes and then after at 10, 20, 30, 40, 50 minutes. Patient is strictly monitored haemodynamically after spinal anaesthesia and also during shivering and then after the study drug administration at regular intervals. Statistical analysis was done P value < .05.

**RESULTS**

In this study, both the groups are comparable with regard to age, weight and ASA Physical status (Table-II). The onset of disappearance of shivering was found 1- minutes and 3 minutes in group I and group II respectively (Table III). There was statistically significant difference in the disappearance of shivering in both the groups Table-III. P=<0.01. Stoppage of shivering occurred earlier in group I in comparison with group II P < 0.001 which was significant. Table-III

**Table 1:** Control of Shivering

Grade: 0.	No Shivering
Grade: 1.	Mild fasciculation of face on neck. ECG disturbance in absence of voluntary activity of arms.
Grade: 2.	Visible tremors involving more than one group of muscle
Grade: 3.	Gross muscular activity involving the entire body, bed shaking.

**Table 2:** Demographic Data

Age in years	Group I N=30 27.4 ± 2.4	Group-II N=30 26.8 ± 10.8	PD-value 0.47 NS
Wt. Kg	65.8 ± 14.8	68.2 ± 12.7	≥ 0.3 N.S
ASA PS 1 11	14:16	13:17	≥ 6.05 N.S

N. S: not significant

**ASA PS 1 11:** (American society of Anaesthesiology Physical Status).

**Table 3:** Control of Shivering

Time Minutes	Group1 N =30	Group II N = 30	P value
1	16 (53.33%)	1 (3.33%)	< 0.05 S
3	27 (90%)	7 (23.33%)	< 0.05 S
5	27 (90%)	16 (53.33%)	
10	30 (100%)	25 (83.33%)	
20	30 (100%)	30 (100%)	
30	30 (100%)	30 (100%)	
40	30 (100%)	30 (100%)	
50	30 (100%)	30 (100%)	

**DISCUSSIONS**

Epidural and spinal anaesthesia decrease the vasoconstriction and shivering thresholds to a comparable degree.<sup>17</sup> but by lesser amount of 0.6°C than general anaesthetics when measured above the upper level of the block,<sup>2,18</sup> prolonged impairment of thermo-regulatory autonomic control under anesthesia along with cold environment of operating rooms and cold infusion fluids, contributes to a fall in core body temperature and hence cause shivering.<sup>19</sup> Other known causes of shivering included transfusion reactions, during sections, preexisting high grade fever or bacteremia, or infusion of contaminated intravenous fluid. Various method are available to control shivering during anaesthesia which include non pharmacological methods, like covering the patient with blanket, application of radiant heat and warming the operating room, use of warm local anaesthetics and warm intravenous fluids.

Pharmacological methods using drugs, opioids like pethidine, tramadol, nalbuphine, ketamine, imidazolam combination or ketamine alone.<sup>19,22</sup> In this study, we use tramadol for control of shivering after



spinal anaesthesia in pregnant women for caesarian section and we compare it with pethidine. Tramadol mechanism of action in the treatment of shivering is not clearly known. It can be noted that it has its effect through inhibition of nor-epinephrine and dopamine and thus facilitates the release of serotonin.<sup>23</sup> Pethidine exerts its thermoregulatory effects through kappa receptors.<sup>24</sup> However, pethidine probably acts directly on the thermoregulatory center.<sup>25</sup> In our study, tramadol was more effective agent for the control of post spinal shivering than pethidine. Our study supports the results of other studies indicating that tramadol is effective in the treatment of post anaesthetic shivering.<sup>26,28</sup>

Like previous study<sup>27</sup>, our study shows that the time of an end of shivering is significantly earlier than after pethidine administration. In a double blind randomized clinical trial study of pregnant women, who were candidates for elective caesarian section, it was shown that the control of shivering with tramadol was better than pethidine, like in our study.<sup>13,27,29,30</sup> The onset of disappearance of shivering was 1 minute in case of tramadol and 3 minutes in case of pethidine. One study shows, shivering reduced significantly at 1 minute after tramadol but the dose was 2mg/kg.<sup>1,2,29</sup>

In our study, the complete disappearance of shivering took 10 minutes in tramadol group and 20 minutes in pethidine group. Earlier studies have shown better results with tramadol.<sup>27,28,31</sup> One study showed the superiority of tramadol over clonidine for control of intra-operative shivering after spinal anaesthesia.<sup>32</sup> In our study, there was less haemodynamic disturbance and there were less side effects like nausea and vomiting as we infused drugs slowly intravenously.

## CONCLUSION

Tramadol is more effective in treating shivering under spinal anaesthesia in pregnant women undergoing caesarian section due to rapid onset, in a dose of 1mg/kg, slow i/v, when compared to pethidine.

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سب نے پوچھا خزاں کیا ہوتی ہے  
تم نے میری مثال دی ہوتی  
پوچھا موسم بدلتے ہیں کیسے  
تم نے اپنی مثال دی ہوتی  
پوچھا کیسے گھٹا برستی ہے  
میری آنکھوں کی بات کی ہوتی  
پوچھا رک رک کے کون چلتا ہے  
میرے دل کی مثال دی ہوتی  
کاش سب کچھ یوں نہ ہوا ہوتا  
بات تم نے سنبھال لی ہوتی ..... !!!  
پروین شاکر



Sikandar Hayat

## Outcome of Non-Union Tibia, Managed with Ilizarov Fixator

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### ABSTRACT

**Objectives:** To evaluate the outcome of tibial non-union managed with Ilizarov fixator.

**Methods:** The case series was conducted at Khyber Teaching Hospital, Peshawar, from January 2013 to January 2015. Patients with non-union tibia were included in this study. Patients of either gender, with complex non-union of the tibia were included. Outcome of the treatment was assessed to check bony union with application of Ilizarov fixator.

**Results:** A total of twenty cases with non-union tibia included in the study over a period of about 3 1/2 years. 50% (n=10) were aseptic non-union while 50% (n=10) infected non-union. 85% (n=17) were male while 15% (n=3) were female. Majority of the patients 60 % (n=12) belonged to age group 16-30 years. Left tibia was involved in 55% (n=11) while in remaining right tibia was involved. All the 100% (n=20) patients to whom ilizarov frame applied, already two or more than two surgeries had been performed .In 60% (n=12) patients osteotomy was performed while in 40% (n=8) no osteotomy performed. In majority of the patients time to union following Ilizarov application was one year. Only in 40% (n=8) patients bone grafting was needed. 95% (n=19) of non-union tibia united at the end of study period while only 5% (n=1) failed to unite. 20% (n=4) had shortening, 5 % (n=1) suffered from pin tract infection while 15% (n=3) suffered from equinus foot deformity at the end of study period.

**Conclusion:** Ilizarov fixator is an excellent device in tibial non-union whether infected or aseptic. It eradicates infection and allows bone to unite.

**Keywords:** Tibia non-union, Ilizarov external fixator.

### INTRODUCTION

Non-union of long bones is a source of functional disability along with economic hardships and loss of self-esteem. The incidence of non-union of long bones has been increasing, especially in view of increasing high-velocity trauma particularly road traffic accidents (RTA), which is more frequently treated with internal fixation.<sup>1,2,3,4,5,6</sup>

Chronic infection of the diaphysis of the long bones is the most challenging dilemmas in orthopedic surgery. To obtain eradication of the infection, bony union, and a functional extremity often requires courageous measures with increasing risks of failure or amputation. Standard principles of debridement and antibiotic therapy alone may result in an acceptable cure rate of less severe types of infections. Difficult or resistant infections usually require a more radical debridement of the septic bone and soft tissues in addition to the application of stable fixation to enhance soft tissue healing and bony union.

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**Ilizarov fixator is an excellent device in tibial non-union, whether infected or aseptic. It eradicates infection and allows bone to unite. Patients can be kept on weight bearing and mobilized during treatment.**

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A number of alternatives are available in the management of chronic diaphyseal infection comprising of, extensive debridement and local soft tissue rotational flaps, packing the defect with antibiotic impregnated beads.<sup>2,3,4,5,6,7,8</sup> Papineau-type open cancellous bone grafting, tibiofibular-synostosis, cancellous allograft in fibrin sealant mixed with antibiotics, and/or free microvascular soft tissue and bone transplants. All these treatments have variable rates of success and failure and are limited in their ability to re-establish extremity length and correct deformity. The definitive environment required for many of these techniques to achieve their maximum bone grafting potential prerequisites the extremity to be free of infection and have acceptable soft tissue coverage.<sup>2,3,4,5,6,7,8,9</sup> Many of these techniques also lack, to varying degrees, the ability to provide early functional rehabilitation of the limb during treatment.<sup>2</sup> There are many advantages of Ilizarov technique like fracture fixation and deformity

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correction which can be done in same sittings; it can be used in both closed and open fractures; bone transport/ limb length discrepancy can be corrected; repeated surgeries can be avoided; distraction and minor adjustments in the alignment of bones do not require anaesthesia; it serves as important tool in infected non-unions and polytrauma patients; and with the help of Ilizarov early ambulation of the patient is possible. Treatment with Ilizarov apparatus has been successful in managing most problems in these patients, but it is not a solution for each and every one patient.<sup>10,11</sup> The aim of this study was to assess the outcome of non-union of tibia treated with Ilizarov fixator.

### MATERIAL & METHODS

We conducted this study at the Department of Orthopedics and Traumatology, Khyber Teaching Hospital Peshawar and Abasin Medical Centre Dabgarri Garden, from January 2013 to January 2016, comprising of consecutive patients with non-union of the tibia managed with Ilizarov frame.

Patients of either gender, with complex non-union of the tibia were included in whom other ways of management had already failed. Thorough clinical history was obtained, complete physical examination was performed and investigations were carried out. All the patients were counseled about their conditions which necessitated an urgency of the surgical procedure they had to undergo. Informed consent was taken from all patients.

The patients had preoperative full-length radiographs of the affected leg for assessment of the level and type of fracture non-union, plane of deformity, bone quality and presence of sequestrum. Culture swabs from draining sinuses and open wounds were carried out in all patients.

The initial metal work was removed and the bone ends were debrided and deep tissue samples were taken for culture and sensitivity. The frame was then applied with trans-osseous wires and half-pins to preserve the anatomical axis and avoid any additional soft tissue damage. The frames were extended to the foot to minimize equinus deformity where necessary. Osteotomy was done in the same setting in majority of patients. Postoperatively, the patients were encouraged to bear weight with the aid of crutches. Physiotherapy within comfort with specific reference to joint mobilization and oedema control was attempted in all patients.

After the application of each fixator, radiographs were taken and patient were discharged on the second postoperative day. Physical therapy was continued throughout the treatment. Patients were educated

regarding bone transport and pin-site care and advised to change dressings daily. Outcome of treatment was fracture union. The criteria for union were the presence of bridging trabeculae on at least three cortices radiologically and absence of pain and no movement at fracture site clinically.

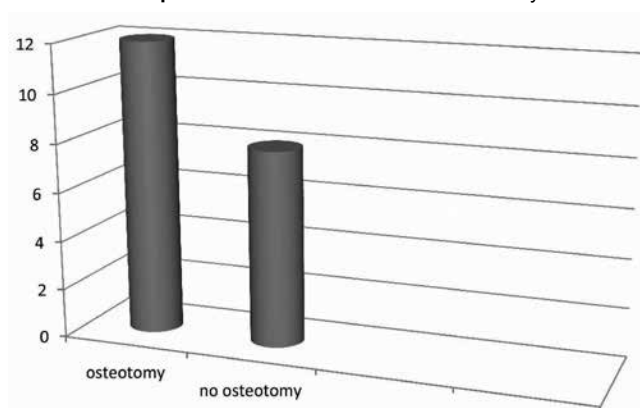
### RESULTS

A total of twenty cases with non-union tibia included in the study over a period of about 3 1/2 years. 50 % (n=10) were aseptic non-union while 50% (n=10) infected non-union. 85% (n=17) were male while 15% (n=3) were female Table-1. Majority of the patients 60% (n=12) belonged to age group 16-30 years. Left tibia was involved in 55% (n=11) while in remaining right tibia was involved Table 2.

In 95% (n=19) of cases middle and distal tibial diaphysis was involved while in only 5% (n=1) proximal tibial diaphysis was involved. 55% (n=11) of tibia fractures happened secondary to road traffic accident (RTA), 15% (n=3) due to bomb blast, 15% (n=3) due to fire arm injury while remaining occurred due to other reasons. 85% (n=17) of these fractures were fixed primarily with AO Ex -Fix, 5% (n=1) with interlocking nail (ILN) and 10% (n=2) with open reduction and internal fixation (ORIF).

To all the 100% (n=20) patients to whom illizarov frame applied, already two or more than two surgeries had been performed. In 60% (n=12) patients osteotomy was performed while in 40% (n=8) no osteotomy performed. Graph.1

Graph 1: Cases with and without osteotomy



In majority of the patients time to union following illizarov application was one year. Only in 40% (n=8) patients bone grafting was needed. 95% (n=19) of non-union tibia united at the end of study period while only 5% (n=1) failed to unite Table-3. 20% (n=4) had shortening, 5% (n=1) suffered from pin tract infection while 15% (n=3) suffered from equinus foot deformity at the end of study period.

**Table 1:** Gender and non union tibia

Gender	No of cases	%
Male	17	85
Female	3	15

**Table 2:** Side of tibia involved with non-union

Side of tibia involved	No of cases	%
Right	9	45
Left	11	55

**Table 3:** Outcome of ilizarov fixator in management of non-union tibia

Outcome	No of cases	%
United	19	95
Failed to unite	1	5

## DISSUSSION

Long-standing infected non-union and gap non-union is difficult to treat and is a challenging problem for orthopaedic surgeons. It may end up with residual deformity, persistent infection and contracture leading to a useless limb.<sup>9</sup> A number of ways and means has been employed to deal with such situation, particularly gap non-union is a significant problem. Ilizarov apparatus is a very good option for treating infected nonunion with a huge bone gap.<sup>10,11,12,13,14</sup> It can be done either by trifocal osteo-synthesis or bifocal osteo-synthesis. Usually, up to 5 cm of bone gap can be lengthened using bifocal osteo-synthesis.<sup>10,11,12,13,14,15</sup> When bone gap >5 cm, it is treated with bifocal osteo-synthesis, bony sclerosis occurs in fracture end during bone transportation which prevents union at the fracture site.<sup>10,11,12,13,14,15,16</sup> Hence, bone gap >5 cm may be treated with trifocal osteosyn-thesis to reduce time required for bone transportation as the treatment with Ilizarov ring fixator.

Ilizarov ring fixator provides with the ability of fracture compression and distraction and allows bone transport as well, hence very much effective in the management of infected non-union of the tibia where other types of treatment have failed. Patient can be weight-bear and joints can be kept mobilized while still on treatment which is an exceptional benefit of this device.<sup>17,18</sup>

We achieved 95% desired results in our study i.e., bony union. While in a study by Fleming,<sup>19</sup> ilizarov fixator in management of tibial non-union, showed excellent bone results in 60.87% cases, good in 26.09%, fair in 8.7% and poor in 4.35% cases. Functional results were excellent in 64% cases, good in 28%, fair in 4% and poor in 4% cases.

In another study<sup>20</sup> 58 patients with tibial non-union managed with Ilizarov fixator comprising of 38 (65.5%) infected non-union and 20 (34.5%) with clean non-union. At the end of study period bone results were excellent in 33(58.9%), good in 12(20.7%), fair in 8(13.8%) and poor in 5(8.6%) patients while clinical result was excellent in 33 (56.9%), good in 18(31.1%), fair in 4(6.9%) and poor in 3(5.1%) patients.

At the time of frame removal when bony union had achieved almost all the patients were infection free which is the great advantage of Ilizarov. Limb shortening occurred only in a couple of patients which was possible to correct and manage with the Ilizarov but on patients refusal post-pond. Similarly, correctable foot deformity mainly equinus occurred only in a few patients.

## CONCLUSION:

Ilizarov fixator is an excellent device in tibial non-union whether infected or aseptic. It eradicates infection and allows bone to unite. Patients can be kept weight bear and mobilized during treatment period.

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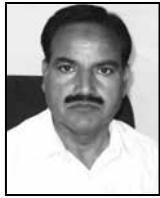
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## Yoshinori Ohsumi, Japanese Cell Biologist awarded the Nobel Prize in Medicine 2016

A Japanese Cell Biologist, was awarded the Nobel Prize in Medicine for his discoveries on how cells recycle their content, a process known as autophagy, a Greek term for "self-eating" which is a crucial process. During starvation, cells break down proteins and non-essential components and reuse them for energy. Cells also use autophagy to destroy invading viruses and bacteria, sending them off for recycling. Cells use autophagy to get rid of damaged structures. The process is thought to go wary in cancer, infectious diseases, immunological diseases and neurodegenerative disorders. Disruptions in autophagy are also thought to play a role in aging. What genes were involved, or its role in disease and normal development until Dr. Ohsumi began studying the process in baker's yeast.





Riaz Qadeer

## Medico Legal Importance of Post-mortem Interval (An autopsy based study)

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### ABSTRACT

**Background:** Medico legal autopsy is a valuable source of information about cause of death and time since dead, the story can be reconstructed on scientific bases.

**Study design:** This descriptive study is based on autopsy record and provides information regarding time since death and how to calculate this time.

**Duration of study:** From 1<sup>st</sup> January 2013 to 23<sup>rd</sup> May 2013.

**Methodology:** This study was conducted in the department of Forensic Medicine & Toxicology of Khyber Medical College, Peshawar. Data was collected from the record of autopsies performed from January 2013 to May 2013. It include all cases referred from urban as well as from rural area police stations of Peshawar district.

**Results:** Out of total 400 autopsies 59 dead bodies (15%) were received for postmortem within 1 to 2 hours of death, 191 dead bodies (48%) were received within 3 to 12 hours of death, 137 dead bodies (34%) received within 13 to 24 hours of death and 13 dead bodies (3%) were sent for the required autopsy quite late.

**Conclusion:** Quick referral of the dead along with required documents is important as it helps not only in calculating the time since death and helping in furthering justice by reconstructing the story on scientific bases. It also minimize the agony of the relatives by early burial of the dead in accordance with the injunctions of Islam.

**Keywords:** Post mortem interval, Autopsy, Peshawar, Pakistan.

### INTRODUCTION

Autopsy or postmortem is the scientific study of the dead according to the laws of the state and calculation of post mortem interval is one of the aims of autopsy. Postmortem interval is the time interval between death and post mortem done .It is important because it helps in reconstructing the story on scientific bases which may be different from the police investigations. An accused person according to police may be innocent but actually he is involved in the crime or vice versa. The subject of Forensic Medicine and Toxicology is important as it is about how medical knowledge helps the law in furthering justice.

*Thanatology* is an important chapter of Forensic Medicine and is related with the study of the changes occurring in the dead body after death. These changes depend on the age and sex of the person, cause of death and the temperature of the environment in which the dead body was lying. These changes are grouped into (i) immediate changes like absence of pulse and heart beat, non recordable blood pressure and flat or straight

line ECG. There is loss of spontaneous breathing and cyanosis .The pupils are fixed and mid dilated. There is cattle trucking of blood in the retinal blood vessels and dropping of lower jaw due to loss of muscle tone. (ii) Early changes which starts appearing within 2-3 hours of death and are fall in body temperature, post mortem staining and appearance of rigor mortis. (iii) Late changes which appear after 24 hours and are due to putrefaction/decomposition of human body in to its constituents under the action of bacteria and auto-digestion by the enzymes.

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**Calculation of post mortem interval is very important in all suspected homicidal cases as the required autopsies if done timely could help in justice and save the relatives from agony. It is difficult to conclude in a putrefied body as much time is wasted in unnecessary probing. Early referral of the dead is a legal requirement.**

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It includes changes like appearance of greenish discoloration of skin of the right iliac fossa, marbling which appears in the groin and axilla, loosening of hair, nails and teeth, swelling of body due to accumulation of gases of putrefaction thus making personal identification difficult. Mummification and Adipocere / saponification are two modifications of putrefaction. It is possible that some parts of the body may be mummified and adipocere may appear in other parts

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of the same dead body. After death changes occur in the whole body including eyes thus changes in the level of potassium in the vitreous humour also helps in calculating the time since death.

#### MATERIAL & METHOD

It is a retrospective descriptive study conducted in the Department of Forensic Medicine & Toxicology of Khyber Medical College, Peshawar where all autopsies are carried out for the district Peshawar. A total of 400 autopsies were performed from 1<sup>st</sup> January 2013 to 23<sup>rd</sup> May 2013. All these cases of suspicious and unnatural deaths were referred by the police from urban as well as from rural police stations to find out

the cause of death and time since dead. Mode and manner of death or any other crime associated with the death was also mentioned in the autopsy report and it was issued to the police and a record of each case was maintained. From this record in a performa information like age, sex, from rural or urban area and post mortem interval were noted and the results were analyzed as under.

#### RESULTS

Most of the dead bodies sent for autopsy were of male (89%) and were from rural areas (66%) as compared to (33%) from urban areas. The majority (35%) were in the age group 20 to 30 years.

S/No.	Post mortem findings on dead body	Post mortem interval	No. of cases
1	Body was warm, absent postmortem staining, absent rigor mortis	1 to 2 hours	59
2	Patches of post mortem staining present on dependent parts, rigor mortis present in the muscles of eye lids, Taches noires present on the sclera of the dead body	3 to 4 hours	22
3	Post mortem staining was present on the dependent parts but it was not fixed, rigor mortis was present in the eye lids and facial muscles of the dead body	4 to 5 hours	16
4	Post mortem staining was present and it was fixed, rigor mortis was present in the muscles of eye lids, face and neck muscles of the dead body	6 to 7 hours	23
5	Fully developed and fixed post mortem staining was present on the dependent parts, rigor mortis was present in the muscles of eye lids, face, neck, both the upper limbs and trunk of the dead body	8 to 9 hours	42
6	Rigor mortis was present in the muscles of the eye lids, face, neck, trunk, upper limbs and lower limbs along with fixed post mortem staining and body was cold	10 to 11 hours	40
7	Rigor mortis of the whole body including muscles of fingers and toes was present along with fully developed fixed post mortem staining	11 to 12 hours	48
8	The jaw, neck and extremities become fixed in position with the arms bent at elbows and legs at the knees and hips so movements at these joints was difficult	12 to 13 hours	42
9	Fully developed rigor mortis and post mortem staining along with appearance of yellowish green discoloration in the right iliac fossa	13 to 15 hours	66
10	Body was cold, post mortem staining present, rigor mortis starts receding, yellowish green discoloration present over the whole abdomen and spreading to the chest of the dead body	22 to 24 hours	29
11	Marbling of skin in the area of the axilla and groin was seen and it was due to the staining of the walls of superficial vein with altered haemoglobin, disappearance of rigor mortis and swelling of the body due to accumulation of foul smelling gases of putrefaction	36 to 40 hours	6
12	Trunk bloated, face discolored and swollen, blisters and skin slip condition was present	40 to 48 hours	3
13	Whole body grossly swollen and foul smelling and disfigured, hair and nails were loose and tongue was protruding out	70 hours	1
14	Soft viscera putrefied and maggots were present on the dead body	One week	1
15	Only more resistant viscera like prostate gland was present and most of the soft tissues were absent	Two weeks	1
16	Body was skeletonized and both mummification and adipocere were present	Three months or more	1



Condition of body		Total	Sex		Total	Area		Total
Fresh	Putrefied		Male	Female		Urban	Rural	
387	13	400	357	43	400	134	266	400
			89%	11%		34%	66%	

S/No.	AGE	No.	%age
1	1 to 10 years	15	4
2	11 to 20 years	48	12
3	21 to 30 years	141	35
4	31 to 40 years	83	21
5	41 to 50 years	52	13
6	51 to 60 years	41	10
7	61 years & above	20	5
<b>Total Cases</b>		400	

**DISCUSSION**

Out of total 400 autopsies 59 dead bodies (15%) were received for postmortem within 1 to 2 hours of death. These were the cases which were sent for medical treatment and died during treatment or were received dead in the hospital. Out of total post mortem done 191 dead bodies (48%) were received within 12 hours of death, 137 dead bodies (34%) received within 13 to 24 hours of death and 13 dead bodies (3%) were sent for the required autopsy quite late and this time period was ranging from days to weeks. The reason of this delay was difficulty in recovery of the dead body by the police as police may be over stretched/over burdened of its duties or the culprit was more clever to dispose off the dead body.

Many types of chemical changes to a body occur after death in fairly orderly manner. Some of those that can be used to estimate post mortem interval are Algor mortis, Livor mortis, Rigor mortis, Vitreous humour changes, Forensic entomology and changes in the dead body caused by autolysis and putrefaction.

Post mortem staining is one of the early signs of death as it starts appearing within 1 to 3 hours after death and gets fixed after 6 to 8 hours. It helps in calculating the time since death. It also gives information about the position of the body at the time of death and whether the position of the dead was changed or not within the time before it gets fixed and cause of death can also be determined from the color of postmortem staining. Distribution of post mortem staining suggests the circumstances or position of the body at the time of death eg. hanging , lying or reclining.

Rigor mortis also helps in calculating the time since death as it first appear in the muscles of eye lids, then in the muscles of face, neck, upper limbs, chest and trunk, lower limb. The muscles of fingers / toes are last to be affected. Rigor mortis disappear in the reverse order. Rigor mortis are fully developed in 12 hours, remain so for the next 12 hours and then starts receding and disappear in the next 12 hours to 36 hours after death secondary relaxation in muscles of body appear. In secondary relaxation the muscles do not respond to electrical / thermal stimulation and PH is alkaline due to accumulation of ammonia. In primary relaxation the PH of muscles is acidic and muscles respond to thermal and electrical stimulation. Primary relaxation is one of the early signs of death and appear within seconds and can easily be appreciated in the muscles of lower jaw as there will be dropping of lower jaw (opening of mouth) due to loss of muscle tone and this is a sign of death of central nervous system.

Results of our study is comparable to other studies done on this topic. Forensic science laboratory also helped in calculating the post mortem interval by confirming the potassium level in the vitreous humour. In Pakistan Police is the in charge of dead body and is the investigating authority of all unnatural deaths. Death may be unnatural but if the concerned police station head officer (SHO) is satisfied that death is natural then he can issue order for burial of the dead. Death may be natural but concerned SHO is not satisfied so he will use his authority and will ask for autopsy especially so when the relatives of the dead fail to accept the demands of police. Dead body is property of the state

hence no consent of any one is required for autopsy. People avoid autopsy of their near and dear ones by request or by influence. The aim is to avoid stigma / sarcastic remarks of society and save time and money by avoiding lengthy court procedures rather people are more interested in taking revenge so further creating unrest in the society. The actual number of un-natural deaths is much more than cases referred for autopsy because of the reasons mentioned above .

**CONCLUSION**

Calculation of post-mortem interval is very important in all suspected homicidal cases as the required autopsies if done timely by the expert and ethical doctor can not only help in furthering justice but also can reduce the agony of the relatives .It is difficult to find cause of death , mode of death, manner of death any associated crime with the death, identification of the dead and time since dead in a putrefied body. Much time is wasted by the police in completing the required investigations and some more time is wasted in negotiations with the near and dear ones of the dead in a developing country like Pakistan where some times the personalities and law makers are above the law. Early and quick referral of the dead along with the required documents to the medical authorities by the police seek attention of the Government. It also helps in early burial according to Islamic injunctions.

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**Congratulations**

The management and Board of Editors of Ophthalmology Update congratulate Dr. M. Amjad Chaudhary, who has recently been promoted and joined as Assistant Professor of Ophthalmology at K.E Medical University/Mayo Hospital, Lahore. We wish him a prosperous professional life and good health.....Chief Editor



Tallat Najeeb

## Role of Intra-tympanic Steroid in the treatment of Sudden Sensorineural Hearing Loss (SSNHL)

Tallat Najeeb FCPS<sup>1</sup>, Muhammad Ajmal FRCS<sup>2</sup>, Wajahat Ullah Khan Bangash FRCS, FCPS<sup>3</sup>

### ABSTRACT

**Objective:** It was to compare the treatment results of oral and intra-tympanic steroids in the management of sudden sensorineural hearing loss (SSNH) and to find out the effectiveness of intra-tympanic steroids in sudden sensorineural hearing loss.

**Study Design:** Randomized control trial.

**Place & Duration of Study:** Conducted at Holy Family Hospital and Social Security Hospital from Dec 2008 to Dec 2013.

**Material & Method:** All Patients were selected randomly with complaint of hearing loss for at least 3 days duration. PTA (pure tone audiometry) was advised to confirm SSNH. Patients were divided into Group A included patients who received oral steroid therapy dexamethasone 1mg/Kg body weight for three week and Group B included patients who received intra tympanic steroid injections, 1cc(4mg) of dexamethasone, every 7th day for 3 weeks. Any improvement in PTA of more than 20dB was considered significant. Follow up of patients was done for 6 months. Statistical evaluation of results was done by using window SPSS 16.

**Results:** Total number of patients were 30, divided into Group A and B. In Group A, total improvement in one month was seen in 9 out of 15 patients (60%). In Group B, total improvement was seen in 11 out of 15 patients (73.3%). Results were significant as p value was <.05.

**Conclusion:** Treatment should be started with oral steroids as early as possible; if the response to oral steroid is poor then intra tympanic steroid injections should be used as salvage therapy.

### INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is a common otology emergency<sup>1,2</sup> first described in 1944. It is defined as sudden unexplained hearing loss of more than 30dB developed over a period of three days in at least three contiguous pure tone frequencies.<sup>1,3,4</sup> In vast majority of cases it is unilateral, bilateral loss is very rare.<sup>6</sup> Etiology is unknown<sup>7,8</sup>, viral infection, vascular spasm or thrombosis, intracochlear membrane pathology and immune mediated disease may be considered.<sup>9,10,11</sup> Incidence is 2-20 per 100,000 populations.<sup>2,3</sup> It usually affects middle age group, common in 43-53 years of age. Male to female ratio is equal but slight male predominance in certain cases.<sup>4,12</sup> In majority of cases recovery is often spontaneous within few days of onset.<sup>3,4</sup> In others there is slow recovery, usually takes a week or two. 15% of patients do not recover, but continue to lose their hearing with time. Differential diagnosis should include ototoxicity, perilymph fistula, autoimmune diseases of inner ear, temporal bone fracture and acoustic neuroma.<sup>2,5</sup> No

specific treatment has been evaluated for SSNHL. Early administration of high dose of steroid has been proved beneficial.<sup>13</sup>

Overall steroid response rate is 60%. If left untreated only a minority of patients will show some degree of spontaneous recovery in first 2-4 weeks. Hearing rarely improves thereafter. In the last few years a number of studies have been undertaken to see the efficacy of steroids in the treatment of sudden sensorineural hearing loss and to see by which route it should be administered<sup>14</sup>. This study was done to find out if intra-tympanic steroids are more effective as primary therapy for SSNHL.

**Sudden Sensori-neural Hearing Loss is an otology emergency. All the efforts must be done to rule out any possible cause. As there is a high incidence of spontaneous recovery, treatment should be started with oral steroids as early as possible, if the response to oral steroid is poor then intra-tympanic steroid injections should be used as a salvage therapy.**

### MATERIAL & METHOD

All Patients were above age of 20 years, were selected randomly who presented to ENT department either in OPD or through emergency with complaint of hearing loss for at least 3 days duration and not for more than one month and tympanic membrane was

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found to be normal on otoscopy. If ENT examination revealed any middle ear infection or perforated drum, these patients were excluded from study. PTA (pure ton audiometry) was advised to confirm sudden sensorineural hearing loss. Only those were included having pure sensorineural loss of more than 30db in at least three contiguous frequencies. Patients with conductive or mixed hearing loss were also excluded from study. CT scan was advised in all these patients to rule out any retrocochlear pathology. Patients with any retrocochlear pathology and patients with any contra-indication of steroid therapy were also excluded from study. All selected patients were divided into two groups randomly. Group A included patients who received oral steroid therapy or who refused to get intra-tympanic steroid. Group B included patients who received intra tympanic steroid injections. All the patients were admitted. Pretreatment PTA results were recorded. Group A received tapering course of dexamethasone 1mg/Kg body weight for three week. Group B patients were given Intratympanic injection of 1cc (4mg) of dexamethasone, every 7<sup>th</sup> day for 3 weeks.

PTA was done in all patients after one week of therapy. Results were recorded. Any improvement in PTA of more than 20dB was considered significant. PTA was repeated after one month and then after 6 months to remove any chance of false results. Follow up of patients was done for 6 months. Statistical evaluation of results was done by using window SPSS 16 and descriptive analysis was done. Independent sample t test was applied for comparative study, results were considered significant if p value <.05.

**RESULTS**

Total of 30 patients were included in study. All were adults with age range 25 to 55 years, mean age was 40 years. 18 (60%) were male and 12(40%) were female. Group A and B further divided into A1, A2, A3 and B1, B2, B3 depending on severity of hearing loss. A1 included 3 patients with hearing loss up to >30-<40dB. A2 included 7 patients with hearing loss>40-<80dB and there were 5 patients in A3 with >80dB hearing loss. In B1 there were 5 patients with >30-<40 dB hearing loss, in B2, 5 patients with >40 and < 80db and in B3 there were only 2 patients with > 80dB loss.

In Group (A) after oral steroid therapy; one patient from A1 showed >20dB improvement in hearing, 2 patients from A1 did not show any improvement on PTA. In A2, 3 patients recovered with> 20dB, in group A3, only 2 patients showed > 20 dB improvement. Total of 6 patients out of 15 (40%) from group A showed >20dB improvement in hearing after one wk. Repeated PTA after one month, one more case from A1 and

2 more case of cases from group A2 showed >20dB improvement on PTA. None of the patient from group A3 showed further improvement in PTA and hearing. Total improvement in hearing in GA after oral steroid in one month was seen in 9 patients (60%). No further improvement was seen in these patients after 6 month.

In Group B after one week with intra-tympanic steroid, 4 patients from B1 showed >20dB improvement on PTA; in B2, hearing improved >20dB in 4 patients; in B3 only one patient showed >20dB improvement on PTA. Total of 9 patients out of 15 (60%) showed > 20dB in hearing on PTA. Repeated PTA after one month, further showed >20dB improvement in two patient; one from B2 and other was from B3. Total improvement was seen in 11 out of 15 patients (73.3%). No further improvement was seen in these patients after 6 months. Independent sample t test was applied for comparative study, results were significant as p value was <.05.

**Table 1:** Showing no of patients in each group with PTA results before therapy

Sr. No.	Group A			Group B		
	A1	A2	A3	B1	B2	B3
<b>Total number of patients</b>	3	7	5	5	8	2
<b>P. TA before therapy</b>	30-40 dB	50-80 dB	>80 dB	30-40dB	50-80dB	>80 dB

**Table 2:** Showing >20dB improvement in hearing after therapy in both groups

	Group A	Group B
<b>Total number of patients</b>	15	15
Number of patients showed igreater than 20 dB after 1 week	6	9
Number of patients showed greater than 20 dB improved after 1 month	9	11
Number of patients showed >20dB improved after 6 months	9	11

**DISCUSSION**

SSNHL is an emergency because there is very short period of time when the treatment may be effective.<sup>1,3</sup> History, clinical examination and proper use of investigations are mandatory to diagnose the

cause.<sup>4</sup> However in majority of the cases, no cause is identified and it is found to be idiopathic male to female ratio is equal in some studies but in majority there was male predominance.<sup>3,15</sup> In our study there is slight male predominance that was also common in previous studies. In our study it was mostly seen in middle age group with average of 40 years, in other studies it is also seen in this age group.<sup>2,16</sup>

There is 50% chance of improvement in hearing back to normal without any treatment.<sup>17</sup> Incidence of improvement is higher and quicker in patients when the treatment is started earlier as proved by previous studies.<sup>3,18</sup> High tapering doses of prednisolone over a period of 2 weeks is the treatment of choice.<sup>19,20</sup> In last few years a number of trials have reported that intra-tympanic steroids can achieve a significant rate of hearing improvement in SSNHL that failed to recover with primary oral steroid therapy.<sup>21</sup> Hyperbaric oxygen has been shown improvement in hearing and should be administered early.<sup>22</sup>

Many trials have been done to find out the efficacy of intra-tympanic steroid and consideration has been taken to take it as initial treatment as the results of intra-tympanic steroid are much better than oral steroid but in some studies there is no marked difference.<sup>19,23</sup> In recent studies oral steroid has been recommended the standard treatment, intra-tympanic steroid injection should only be used if systemic steroid therapy fails as there are also some risks with this procedure and patient inconvenience.<sup>24,25</sup> In our study slightly better results were seen in treatment with intra-tympanic steroid as compared to oral steroids that is compatible with previous studies but may be due to spontaneous recovery in these patients rather role of treatment. More detailed studies are required to see the intra-cochlear changes with steroid therapy and then the results should be compared.<sup>26</sup>

In our study better prognosis was seen in comparative young patients, in mild to moderate hearing loss and where the treatment started within a week. Better prognosis was also seen in otherwise healthy patients it means not having any other medical problem such as diabetes, anemia and hypertension and in patients without vertigo. These have been the same prognosis indicators in previous studies.<sup>27</sup>

## CONCLUSION

SSNHL is an otology emergency. All the efforts must be done to rule out any possible cause. As there is high incidence of spontaneous recovery, treatment should be started with oral steroids as early as possible, if the response to oral steroid is poor then intra-tympanic steroid injections should be used as a salvage

therapy.

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**Ophthalmology Update**

# A Review of Vitamin D in Pakistani Population

Rabail Javed, Farkhanda Ghafoor

## ABSTRACT

Vitamin D is a secosteroid which has an important function in bone metabolism and immune-modulation. Decreased levels of vitamin D are associated with many critical diseases like cardiovascular, cancer, diabetes, tuberculosis and osteoporosis. Low vitamin D can cause obesity and restrict bone growth and bone health in children and adults. Despite being near to equator, Pakistani citizens suffer from low vitamin D levels making them prone to many diseases and there is no guidelines for the treatment of vitamin D deficiency in general and diseased population of Pakistan. This review highlights the prevalence of vitamin D in different disease as well as healthy groups of Pakistani citizens through literature search. Further it also reviewed the literature available on knowledge of clinicians about vitamin D deficiency and its affects.

**Key words:** Vitamin D, Pakistan, level, deficiency.

## INTRODUCTION

Vitamin D is a hormone precursor involved in variant functions as calcium homeostasis, immune modulation, and anti-inflammatory process. Phytoplankton species (*Emiliani huxleyi*) as old as 750 million years ago, were the source of vitamin D production catalyzed by UVB rays.<sup>1</sup> Vitamin D insufficiency is a common finding worldwide. Levels vary in different areas depending on the demographic features, food fortifications, geographical locations, sun seeking behavior and seasons. It has been reported that a billion people globally have low serum vitamin D levels<sup>2</sup> but majority are asymptomatic, making, it clinically difficult to detect.

A large population of Pakistan is suffering from vitamin D insufficiency which may be occurring due to low intake of vitamin D rich food or less sun exposure or other co-morbidities like cancer, diabetes, osteoporosis and cardiac problems. There is scarce data on vitamin D deficiency/ insufficiency and its consequences, on Pakistani population.

### 1. Vitamin D Physiology:

Vitamin D is a secosteroid found in two major forms i.e. vitamin D<sub>2</sub> and vitamin D<sub>3</sub>. Vitamin D<sub>2</sub> is also known as Ergocalciferol which is present in plants, and a few fish, while vitamin D<sub>3</sub> also known as

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Cholecalciferol, is synthesized in the skin when exposed to the sunlight. There are two ways to fulfill vitamin D<sub>3</sub> requirements; one is through foods rich in vitamin D<sub>3</sub> such as mushrooms and sea foods and the other is by exposing skin to the UV light.<sup>2</sup> The time required to produce sufficient vitamin D<sub>3</sub> from the skin depends on the strength of the UVB rays, the time spent in the sun and the amount of pigment present in the skin.<sup>2</sup>

### 2. Synthesis of Vitamin D<sub>3</sub>

The synthesis of vitamin D<sub>3</sub> starts in keratinocytes and dermal fibroblasts. A precursor of vitamin D, 7-Dehydrocholesterol (7-DHC), is secreted on skin surface<sup>3</sup> and is converted by UVB radiations (290–315 nm) into pre-cholecalciferol (pre-D<sub>3</sub>). Pre-cholecalciferol forms cholecalciferol (D<sub>3</sub>) after undergoing thermal isomerization. Cholecalciferol is absorbed in the skin and blood and is transported to the liver by a transporter  $\alpha$ -2 globulin vitamin D-binding protein, VDBP.<sup>4</sup> In the liver, Cholecalciferol is converted into prohormone calcidol 25(OH) through an enzyme called vitamin D 25 hydroxylase.<sup>4</sup> Calcidol is converted into calcitrol (1.25(OH)<sub>2</sub>D) in the kidneys. Plasma calcitrol is transferred to targeted organs by the help of vitamin D binding proteins (VDBP).<sup>3</sup> Calcitrol is also synthesized by immune cells like monocytes and macrophages, where it acts as a cytokine.<sup>4</sup> Calcitrol is a potent ligand of the vitamin D receptor and mediates the majority of physiological actions of vitamin D.<sup>4</sup> Calcitrol is also synthesized by immune cells like monocytes and macrophages, where it acts as a cytokine.<sup>4</sup> Calcitrol is a potent ligand of the vitamin D receptor and mediates the majority of physiological actions of vitamin D.<sup>4</sup>

### 3. Role of Vitamin D<sub>3</sub>

Vitamin D and osteoporosis is caused by decrease in bone mineral density due to low calcium and vitamin D<sub>3</sub> in the body. Its prevalence is high in Pakistan. A study from Peshawar on 1000 post menopausal women

reported osteoporosis in 55% aged between 45-54 years and this increased to 97% in those aged between 75-84 years.<sup>5</sup> A previous survey reported 50% females from rural areas of Peshawar to be having low bone mineral density and low vitamin D3 status resulting in osteoporosis.<sup>6</sup> Another study on rural women from Peshawar reported osteoporosis/osteopenia in 75.6% with possible causes being low dietary intake of vitamin D3 and lack of sun exposure due to covering their body by "burqas".<sup>7</sup> A community based survey in Karachi on 305 premenopausal females aged above 18 years (mean age 31.97±8.0 years) showed vitamin D3 deficiency in 90.5%.<sup>8</sup> Vitamin D3 supplementation prevents bone loss, but this supplementation needs to be supported with increased calcium intake otherwise only vitamin D3 does not affect bone density and improve fractures caused by osteoporosis.<sup>7</sup>

#### 4. Vitamin D Status in Neonates and Children:

Vitamin D deficiency in mothers results in serious health issues in offspring like improper skeletal and brain development, diabetes, asthma and schizophrenia.<sup>9</sup> Its deficiency in childhood results in diseases like rickets, slow brain development and low immunity.<sup>9</sup> In Pakistan, vitamin D deficiency is seen in all age groups. A study on 349 pregnant women from Karachi having mean age 28.52±3.4 reported vitamin D deficiency in 70% with their 203 neonates also vitamin D deficient. Within the group, 155 neonates had mothers who were vitamin D deficient.<sup>9</sup> Another study from Karachi on 50 pregnant females reported 46% to be vitamin D deficient with 88% of their newborns also deficient in vitamin D. This study highlighted maternal vitamin D was significantly dependant on sun exposure ( $p < 0.007$ ) and diet ( $p < 0.01$ ).<sup>10</sup> Breast fed infants can also suffer from vitamin D deficiency if their mothers are deficient in vitamin D. A study from Islamabad on 75 infants (4-12 months) reported 66.6% to be vitamin D deficient with 41% mothers also deficient.<sup>11</sup> Rickets was reported in 85.3% breast fed children as compared to 40% formula fed based on x-rays, serum calcium, phosphorus and alkaline phosphatase levels.<sup>12</sup>

#### 5. Vitamin D and Cancer

In Asian countries, the role of vitamin D in breast, colon and prostate cancer has been widely studied. A study from Shaukat Khanam Hospital, Lahore on breast cancer patients assessed the relation of vitamin D with grade and stage of tumor and found no significant relationship.<sup>13</sup> Another study from Karachi in newly diagnosed leukemia patients (acute myeloid leukemia and acute lymphoblastic leukemia) aged 1-60 years, concluded that insufficiency of vitamin D was evident

in majority of patients which was further reduced after remission when compared with untreated group.<sup>14</sup>

#### 6. Vitamin D and Tuberculosis

Tuberculosis represents a major health issue in developing countries including Pakistan. Although there are various reasons of drug resistant tuberculosis and late sputum smear conversion.<sup>15</sup> A study on 100 TB patients reported a significant difference between vitamin D levels and sputum smear conversion time ( $p < 0.001$ ).<sup>15</sup> A randomized double blind multi centre placebo control trial on 259 smear positive patients aged  $\geq 16$  years concluded that high doses of vitamin D3 supplementation could lead to marked clinical and radiological recovery in TB patients along with immunity boosting in vitamin D deficient patients.<sup>16</sup>

#### 7. Role of Vitamin D in Cardiac Diseases and Diabetes

Over 25-33% of all deaths in Pakistan are related to heart diseases or diabetes.<sup>17</sup> A study from Lahore on non diabetic subjects (88) reported 98.5% to be vitamin D deficient and showed strong negative correlation between vitamin D3 level and LDL levels and a strong positive correlation between vitamin D3 level and HDL levels.<sup>17</sup> Another case control study from Aga Khan University Karachi on adult diabetic patients showed significant association between vitamin D levels of diabetic and non diabetic patients. Almost 63% cases were vitamin D deficient while rest had insufficient levels. Direct association was seen between socioeconomic status and vitamin D levels.<sup>18</sup>

#### 8. Vitamin D in General Population

Vitamin D levels in general asymptomatic population of Pakistan have also been studied extensively. A study from Islamabad on 737 people (mostly women=76.2%) showed 71.5% to be vitamin D deficient. Within gender, more females were deficient (56.2%) than males.<sup>19</sup> Another study from Islamabad reported 82.8% prevalence of vitamin D deficiency and concluded inadequate sun exposure as the possible cause.<sup>20</sup> A study from Karachi on healthy adults aged 16-62 years reported 77.7% females being vitamin D deficient with majority (76.6%) exposing only face and hands to sun for 1-2 hours.<sup>21</sup> Another study in 30-80 years reported 57.7% to be vitamin D deficient with significant association between low vitamin D levels and glomerular filtration rate.<sup>22</sup>

A study from Karachi on 54 participants working indoor or outdoor areas reported 98% indoor participants to be vitamin D deficient/insufficient and showed a strong relation between sun exposure and



**Table 1:** Frequency of serum vitamin D levels in various cities of Pakistan.

City	Sample Size (n)	Mean Age Years	±SD	Frequency of Serum Vitamin D Levels					
				Deficient (%)	Cut Off (ng/ml)	Insufficient (%)	Cut Off (ng/ml)	Sufficient (%)	Cut Off (ng/ml)
Islamabad	737	36.3(15-75)	----	71.5	----	11.3	----	17.2	----
Islamabad	351	46.03(13-65)	16.8	82.8	<20	-----	20-30	17.2	>30
Karachi	300	48(30-80)	-----	57.7	<20	26.6	20-30	15.7	≥30
Karachi	244	33.62(16-62)	12.6	76.2	<20	14.8	20-30	9.0	≥30
Sargodha	100	36.8(14-58)	-----	36	<20	10	21-29	54	>30
Lahore	80	47.2(40-60)	6.3	25	<10	73.7	10-29	1.3	>30

**Table 2:** Prevalence of 25(OH) vitamin D3 in Pakistan.

Ref	Place & Study Site	Study Year	Method Used	Number Tested	Deficiency <10ng/ml	Insufficiency 10-29ng/ml	Sufficiency >30ng/ml
19	FGSH, Islamabad	2014	Information not provided	351 both sexes	291	-----	60
23	Clinics, Sargodha	2013	ILMA	100 both sexes	36	10	54
10	Shifa Falahee, Shifa International Hospital, Islamabad	2013	Information not provided	75 infants 75 mothers	56 infants 71 mothers	9 infants 2 mothers	10 infants 2 mothers
--	Hayatabad Medical Complex, Peshawar	2013	CMIA	260 females	208	39	13
18	Kulsum International Hospital, Islamabad	2012	ECLIA	737 both sexes	527	83	127
8	Liaquat National Hospital, Karachi	2012	ECLIA	349 mothers 349 neonates	243 mothers 203 neonates	106 -----	----- 146
13	University of Karachi, National Institute of Blood Disease and Bone Marrow Transplantation, Department of pathology and Haem Oncology	2012	CMIA	86 (Leukemia) both sexes	27	55	04
16	University of Health Sciences, Lahore	2012	ELISA	88 both sexes	86	02	-----
5	Khyber Teaching Hospital, Peshawar	2011	ECLIA	107 (Post Meno) females	-----	99	08
7	Community, Karachi	2011	ECLIA	305 (Post Meno) females	276	16	13
21	Metropolis, Karachi	2011	RIA	300 both sexes	173	80	47
12	Shaukat Khanam Memorial Cancer Hospital, Lahore	2011	ELISA	180 females	86 breast cancer 69 control	4 breast cancer 17 controls	----- 04 controls
24	Shaikh Zayed Medical Complex, Lahore	2010	ELISA	80 both sexes	20	59	01
15	Agha Khan University Hospital, Ojha Institute of Chest Diseases and Dow University Hospital, Karachi	2010	ECLIA	250 (TB) both sexes	-----	250	-----
20	Hospitals, Karachi	2007	ECLIA	244 both sexes	186	36	22

ECLIA: Electro chemiluminescence immuno assay, ELISA: Enzyme linked immune assay, RIA: Radio immune assay, ILMA: Immunoluminometric assay, CMIA: Chemiluminescent microparticle assay

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Study from Sargodha showed vitamin D deficiency in 36% population irrespective of the gender but found significant difference in vitamin D levels of those working indoor and outdoor.<sup>24</sup> A study from Lahore on healthy asymptomatic adults found 25% to be vitamin D deficient while 73.7% had insufficient levels. They attributed this to sedentary lifestyle, low sun exposure and low vitamin D intake<sup>25</sup>.

### 9. Vitamin D and Obesity

There is an increasing number of obese population in Pakistan which is attributable to unhealthy foods and sedentary lifestyle. Genetic variation in vitamin D receptor have been correlated with body mass measurements<sup>26</sup> however, there is not much data on relation of vitamin D with obesity. In a genetic study on 100 subjects (50 obese, 50 non obese) between 18-45 years. vitamin D receptor, FOK 1 gene was mutated (ff=3) in 6% obese and was not mutated (ff=0) in any non obese person. Larger sample size was recommended to confirm this variation.<sup>26</sup>

### 10. Knowledge of Clinicians about Vitamin D and its Management

A survey on 400 practicing clinicians in Karachi showed only 62% knew the dietary sources for vitamin D, 85% for active form of vitamin D, 27% for conditions favorable for sunlight absorption and only 45% knew about importance of sun exposure for the production of vitamin D. Signs and symptoms, risk factors and diseases leading to vitamin D deficiency were known to 66%, 82% and 83% clinicians, whereas 63% were not aware of importance of vitamin D in cellular processes (such as immune system, anti proliferation etc) other than bone and muscle. Only 35% and 52% had knowledge about how to manage and treat (non affording) patients with vitamin D deficiency respectively.<sup>27</sup>

### 11. Critical Analyses on Vitamin D Status

Vitamin D status is assessed by the measuring its storage form 25(OH) D which has a half life of 3 weeks rather than active form 1,25(OH) vitamin D which has a short half life of 6 hours. It is unfortunate that most of the studies conducted in Pakistan published had no information regarding the time span between blood withdrawal and vitamin D test performance, questioning the variability in the results.

Vitamin D deficiency causing bone disease is linked with serum 25(OH) vitamin D levels of < 10 ng/mL worldwide<sup>28</sup> Most of the data from Pakistan has reported a deficiency of < 20 ng/ml. Sub optimal levels (10-30ng/ml) of vitamin D are termed as *vitamin D insufficiency*. Defining vitamin D deficiency/insufficiency on the basis of 25(OH) D levels is still a matter of debate. Optimal levels of vitamin D are  $\geq$  30 ng/mL, however this cut off is applied regardless of age group and gender. Since every age has its own vitamin

D requirement therefore, it is possible that optimal levels might differ. A large Pakistani population based study with age interval and gender is required to define the cut off levels for different age groups and diagnose deficient or insufficient individuals who have no evidence of disease. Scientists describe worldwide that "Population reference ranges for vitamin D vary widely depending on ethnic background, age, geographic location and the sampling season."<sup>28</sup> In northern latitude locations in particular, the level of vitamin D in 73% of the population is less than 20 ng/ml during winter season.<sup>29</sup> Thus, it is also important to determine geographical, seasonal, age, gender variations in 25(OH) vitamin D levels before describing vitamin D cut off levels. The cut off used by researchers in Pakistani population is given in Table-2.

**Conflict of interest:** None declared.

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ہر چند کہ ایجادِ معانی ہے خداداد  
 کوشش سے کہاں مردِ ہنر ہے آزاد  
 خونِ رگِ معمار کی گرمی سے ہے تعمیر  
 میخانہٴ حافظ ہو کہ بُت خانہٴ بہرادر  
 بے محنتِ پیہم کوئی جوہر نہیں کھلتا  
 روشن شررِ تیشہ سے ہے خانہٴ فرہاد  
 (کلامِ اقبال)



Prof. Liming Li

## Lower Heart Disease Risk Linked to Fresh Fruit Intake in a Chinese Study

### *A piece of fruit a day keeps the heart attacks away (China Kadoorie Biobank Study)*



Prof. Zhengming Chen,

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#### ABSTRACT

**Background:** In Western populations, a higher level of fruit consumption has been associated with a lower risk of cardiovascular disease, but little is known about such associations in China, where the consumption level is low and rates of stroke are high.

#### INTRODUCTION

New research revealed that people who eat fruit most of the week are significantly less likely to experience heart attacks and strokes compared to those who rarely eat fresh fruit. The latest findings come from a seven-year study involving half a million adults living in China, where people are less likely to eat fresh fruit compared to other countries like the United States or United Kingdom.

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**In Chinese adults a higher level of fruit consumption was associated with lower blood pressure and blood glucose levels and significantly lower risks of major cardiovascular diseases.**

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#### MATERIAL & METHOD

A seven-year study that involved more than 500,000 Chinese adults revealed that regularly eating fresh fruit significantly lowers the risk of heart attacks and strokes. Between 2004 and 2008, we recruited 512,891 adults, 30 to 79 years of age, from 10 diverse localities in China. During 3.2 million persons were followed up; 5173 deaths from cardiovascular disease, 2551 incident major coronary events (fatal or nonfatal), 14,579 ischemic strokes, and 3523 intracerebral hemorrhages were recorded among the 451,665 participants who did not have a history of cardiovascular disease or antihypertensive treatments at baseline. Cox regression yielded adjusted hazard ratios relating fresh fruit consumption to disease rates.

To examine the benefits of fruit consumption, researchers from the University of Oxford and Chinese

Academy of Medical Sciences looked at 512,891 adults aged 30 to 70 from 10 urban and rural localities in China. Researchers tracked the health and death records of participants through electronic hospital records between 2004 and 2008, noting that none of the participants in the study had cardiovascular diseases or high blood pressure at the beginning of the study.

#### RESULTS

Study analysis revealed that participants who ate 100 grams of fruit a day were a third less likely to die of cardiovascular-related conditions. Researchers said the findings were similar for men and women. The association between fruit consumption and cardiovascular risk seems to be stronger in China, where many still eat little fruit, than in high-income countries where daily consumption of fruit is more common. The study also revealed that apples and oranges consisted of most of the fruit consumed by participants in the study. Higher fruit consumption was also positively associated with other factors like education, low blood glucose, low blood pressure and healthy lifestyle habits like not using tobacco, according to researchers.

Overall, 18.0% of participants reported consuming fresh fruit daily. As compared with participants who never or rarely consumed fresh fruit (the "non-consumption" category), those who ate fresh fruit daily, had lower systolic blood pressure (by 4.0 mm Hg) and blood glucose levels (by 0.5 mmol per liter [9.0 mg per deciliter]) ( $P < 0.001$  for trend for both comparisons).

#### DISCUSSION

Among Chinese adults, a higher level of fruit consumption was associated with lower blood pressure and blood glucose levels and, largely independent

of these and other dietary and non-dietary factors, with significantly lower risks of major cardiovascular diseases. It's difficult to know whether the lower risk in people who eat more fresh fruit is because of a real protective effect, concluded Zhengming Chen, the study's senior author and a professor at the University of Oxford.

If it is so, then widespread consumption of fresh fruit in China could prevent about half a million cardiovascular deaths a year, including 200,000 before age 70, and even larger numbers of non-fatal strokes and heart attacks."



The adjusted hazard ratios for daily consumption versus non-consumption were 0.60 (95% confidence interval [CI], 0.54 to 0.67) for cardiovascular death, and 0.66 (95% CI, 0.58 to 0.75), 0.75 (95% CI, 0.72 to 0.79), and 0.64 (95% CI, 0.56 to 0.74), respectively, for incident major coronary events, ischemic stroke, and hemorrhagic stroke. There was a strong log-linear dose-response relationship between the incidence of

each outcome and the amount of fresh fruit consumed. These associations were similar across the 10 study regions and in subgroups of participants defined by baseline characteristics.

## CONCLUSIONS

Among Chinese adults, a higher level of fruit consumption was associated with lower blood pressure and blood glucose levels and, largely independent of these and other dietary and non-dietary factors, with significantly lower risks of major cardiovascular diseases.

## REFERENCE

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آج بھی ہو جو براہیم کا ایسا پیدا  
آگ کر سکتی ہے انداز گلستان پیدا



Usman Ali

## A Study of Sigmoid Volvulus Presenting to a Tertiary Care Hospital at Peshawar

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### ABSTRACT

**Objective:** Objective of the study was to enlist the various types of surgical management and postoperative complication of sigmoid volvulus in patients presented with sigmoid volvulus.

**METHODOLOGY:** In this study a total of 38 patients with sigmoid volvulus coming to Accident & Emergency Department were included. All the patients were admitted and investigated. The diagnosis was based on x-ray erect abdomen. Blood complete, urea, sugar, S. Electrolysis, x-ray and ECG were also done. All the patients were catheterized and a nasogastric tube passed for gastric decompression. All the patients were rehydrated and prepared for surgery as facilities for colonoscopic sigmoidoscopic decompression were not available and decompressions by rectal tube were unsuccessful.

**Results:** Among the cases with sigmoid volvulus there were 26 (68.42%) males and 12 (31.58%) were females. Majority 18 (47.4%) cases were in age range of 61-70 years. Eight (21.05%) patients had gangrene of sigmoid colon, 15 (39.47%) patients had resection and colostomy while 15 (39.47%) had resection and primary anastomosis. Among the postoperative complications, 05 (13.15%) patients had wound infection and 01 (2.6%) wound dehiscence. Two (5.26%) patients died because of sepsis and cardiopulmonary complications.

**Conclusion:** Patients presenting as acute abdomen should have urgent laparotomy as soon as possible. Colonoscopy is the gold standard procedure for stable patients with sigmoid volvulus. Sigmoidectomy and primary anastomosis is the procedure of choice as it not only avoids second admission and operation, but it also avoids the side effects and care of stoma which is major cause of morbidity.

### INTRODUCTION

Sigmoid volvulus is one of the commonest causes of large intestine obstruction.<sup>1</sup> It is the twisting or axial rotation of sigmoid colon about its mesentery. When complete, it leads to a close loop of obstruction with resultant ischemia, secondary to vascular occlusion.<sup>1,2</sup> Sigmoid volvulus is a life threatening condition resulting from rotation of sigmoid colon around mesenteries axis.<sup>3</sup> Sigmoid volvulus is common throughout much of Africa, India, Iran and Russia.<sup>4</sup>

Sigmoid volvulus is the third most common cause of large bowel obstruction in western world.<sup>5</sup> Rotation almost always occurs in anti-clockwise direction.<sup>1</sup> If volvulus with rotation greater than 180 degree produces obstruction of the intestinal lumen and mesenteric vessels.<sup>6,7</sup> The factors leading to volvulus are increased length of colon, distention of colon, a narrow base of mesentery and chronic constipation. The trigger factor causing volvulus is fecal impaction causing the

maximally distended colon to twist.

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**Acute abdomen is an emergency which needs urgent laparotomy with least time consuming. Colonoscopy is the gold standard procedure in sigmoid volvulus which must follow definitive surgery, otherwise recurrences are very common. Sigmoidectomy and primary anastomosis is the procedure of choice which prevents subsequent operation, complications and care of stoma a major cause of morbidity.**  
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Clinical presentation of sigmoid volvulus includes colicky abdominal pain with distension, which is relieved by passage of flatus and loose stool. In acute stage, abdominal pain, constipation and distension is the commonest presentation.<sup>8,9</sup> In gangrene sigmoid volvulus, blood in the rectum is found on digital rectal examination. Diagnosis is made on clinical and radiological finding. On radiological finding there will be bird beak deformity at the sight of torsion.<sup>10</sup> The conservative management of sigmoid volvulus is derotation by enema, endoscopic deflation, minimum invasive procedure mini-lap colopexy.<sup>10,11</sup> In all patients who are diagnosed as sigmoid volvulus, the first step should be to correct any fluid and electrolytes imbalance

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and use of broad-spectrum antibiotic in gangrenous sigmoid volvulus.

Colostomy for sigmoid volvulus was the operation of choice in the past. But such procedures were associated with increased morbidity, mortality repeated hospitalization.<sup>11</sup> To overcome such problems a single step surgery can be performed in the form of resection and primary repair of both the gangrenous and viable sigmoid colon.<sup>12,13,14</sup> Single stage surgery is better than two-stage surgery in term of morbidity and economy of the patients as well in addition to the psychological and social complication of colostomy.<sup>13,14</sup> Objective of the study was to enlist the various types of surgical management and postoperative complication of sigmoid volvulus in patients presented with sigmoid volvulus.

**MATERIAL AND METHODS**

After getting permission from the Hospital Ethical Committee, to conduct the study, data collection of the patients with sigmoid volvulus was started. This study was conducted in surgical A unit of Govt. Lady Reading Hospital, Peshawar from September 2009 to July 2010. All the patients with sigmoid volvulus coming to Accident & Emergency Department were included in the study. They were admitted and investigated after taking informed consent from the patients or their relatives, they were briefed about the surgical procedure and risks and benefits of the operation. The diagnosis was based on x-ray erect abdomen. Blood complete, urea, sugar, S. Electrolysis, x-ray and ECG were also done. All the patients were catheterized and a nasogastric tube passed for gastric decompression. All the patients were rehydrated and prepared for surgery as facilities for colonoscopic sigmoidoscopic decompression were not available and decompressions by rectal tube were unsuccessful. All the studied variables like demographic features, post-operative complications, like leakage, intra-abdominal abscess, ileus fistula and wound infection were analyzed for descriptive analysis. Mean ± standard deviation was calculated for age, sex male to female ratio was calculated. The results were expressed/ presented through tables, graphs and charts. All the data was analyzed by using computer program SPSS version 12.

**RESULTS**

A total of 38 cases with sigmoid volvulus were admitted during the study period, among these 26 (68.42%) were males while 12 (31.58%) were females with male to female ratio of 2.16: 1. Majority of patients 18 (47.4%) were in age range of 61-70 years, followed by 11 (28.9%) in the age range of 51-60 years, 8 (21.1%) were

in the age range of 71-80 years and 01 (2.6%) were in the age range of 41-50 years with mean age of 63.78±7.32 years. Minimum age was 50 years and maximum was 80 years (Table No. 1).

Eight (21.05%) patients had gangrene of sigmoid colon so Hartmann’s procedure was done in those patients. Fifteen (39.47%) patients had resection and colostomy while 15 (39.47%) had resection and primary anastomosis. No on table lavage was done in the resection and anastomosis group. The anastomosis was done in two layers inverting technique.

Among the postoperative complications, 05 (13.15%) patients had wound infection and 01 (2.6%) wound dehiscence. Two (5.26%) patients died because of sepsis and cardiopulmonary complications (Table No.2).

**Table1:** Various characteristics of patients (n=38)

Demographic data	No. of cases	Percentage
<b>Age:</b>		
41 - 50 years	01	02.60%
51 - 60 years	11	28.90%
61 - 70 years	18	47.40%
71 - 80 years	08	21.10%
<b>Gender distribution:</b>		
Male	26	68.42%
Female	12	31.58%

**Table 2:** Procedures and postoperative complications (n=38)

Procedures and postoperative complications	No. of cases	Percentage
<b>Procedures:</b>		
Resection and primary anastomosis	15	39.47%
Resection and Colostomy	15	39.47%
Hartmann’s procedure	08	21.05%
<b>Postoperative complications:</b>		
Wound infection	05	13.15%
Wound dehiscence	01	02.60%
<b>Mortality rate:</b>		
Patients expired	02	05.26%

**DISCUSSION**

Sigmoid volvulus is more common in India and Africa, constituting almost half of cases of intestinal obstruction.<sup>15</sup> The condition was also recognized by ancient Greeks. Hippocrates used a 12 inches long suppository and anal installation to untwist the bowel.<sup>16</sup> The patient presents with constipation, abdominal distention, nausea, vomiting and dehydration. The abdomen is tympanitic and sometime tender. The rectum is empty.

Plain x-ray abdomen is diagnostic however, magnetic resonance imaging and flexible endoscopy are more accurate.<sup>7</sup> Several radiologic diagnostic signs are described such as omega or horseshoe sign, bird’s

beak sign, liver overlap signs and empty left iliac fossa sign.<sup>17</sup> Surgeons would like to operate upon elective patient, so first ano-endoscopic derotation followed by an elective surgical operation would be a preferred choice of procedure.<sup>18</sup> Sigmoidoscopy is the initial procedure for those patients having no peritoneal signs of inflammation.

Decompression is successful in 70% to 90% of the cases. Flexible sigmoidoscopy is safe technique and it also allows direct visualization of mucosa, so that ischemia could be excluded.<sup>19</sup> Insertion of rectal tube should follow to allow further decompression. Barium enema has been described as another way of achieving decompression of sigmoid colon.<sup>7</sup> Non operative reduction of volvulus carries lower risk but the recurrence rates are high. Endoscopy is not definitive management as they were associated with 87% recurrences.<sup>7</sup> When surgery was done as semi elective procedure the mortality was zero.<sup>16</sup>

Following initial decompression definitive surgery can be performed on a patient who is rehydrated and not toxic, so avoiding complications. The permanent cure involves some sort of resection of sigmoid colon with or without anastomosis.<sup>20</sup> Less extensive procedure is not always successful and not recommended for gangrene and compound volvulus. Colonoscopy derotation and laparotomy with derotation and fixation of colon is associated with significant mortality.<sup>21</sup>

A recent report on laparoscopic rectosigmoidectomy after colonoscopy decompression on nine patients is a good authentic procedure.<sup>22</sup> The long colonic mesentery can be easily manipulated and resected by laparoscopy and the shortened base facilitates a stapled primary anastomosis.<sup>23</sup> The other advantage of laparoscopy is reduced blood loss, less post operative pain and less duration of post operative ileus.<sup>24</sup> A number of studies done on feasibility of one stage procedure using on table lavage.<sup>25</sup> The advantage of this procedure is to have a single operation having no colostomy and lesser hospital stay and avoiding a second operation on weak frail patients. The disadvantage is longer operative time and large quantity of irrigating fluid. Although an emergency resection and primary anastomosis is controversial subject, however there is growing acceptance of one stage procedure. Recent results of studies of primary anastomosis on unprepared bowel for malignant and non malignant colonic obstruction are promising.<sup>16</sup>

Hartmann's procedure and resection with primary anastomosis has got lowest recurrence rates.<sup>26</sup> Other technique used in management of sigmoid volvulus are sigmoidectomy and recently percutaneous endoscopic

colostomy.<sup>27</sup> The gold standard procedure for a clinically stable patient is endoscopic decompression with efficacy rates of 70%-90% and recurrence rates of 18%-19%.<sup>28</sup> If endoscopy fails or signs of peritonitis occur urgent laparotomy should be performed. Meso-sigmoidoplasty is associated with high rates of recurrence (10-70%) and mortality.

Sigmoidectomy and primary anastomosis is the procedure of choice for volvulus having a mortality of 8% and a morbidity of 13-26%.<sup>28</sup> In our series resection and primary anastomosis was associated with excellent results. All the patients with primary anastomosis had rectal tube place for 48 hours after surgery. Patients were selected for primary anastomosis on basis of variability and vascularity of colon. Our overall mortality was 5.26% and morbidity 15.75% which are comparable with another study.<sup>28</sup> In our series there was no anastomotic leak after resection and primary anastomosis.

Although we did not encounter a single patient with pregnancy and sigmoid volvulus. Sigmoid volvulus constitutes 25% to 44% of patients presenting with intestinal obstruction in pregnancy.<sup>29</sup> Sigmoidectomy with primary anastomosis is good one of definitive management of sigmoid volvulus.<sup>30</sup>

## CONCLUSIONS

- Patients presenting as acute abdomen should have urgent laparotomy as soon as possible.
- Procedure should be less time consuming in emergency.
- Colonoscopy is the gold standard procedure for stable patients with sigmoid volvulus some sort of definitive surgery must follow otherwise recurrences are high.
- Sigmoidectomy and primary anastomosis is the procedure of choice as it not only avoids second admission and operation, but it also avoids the side effects and care of stoma which is major cause of morbidity.

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آسماں ہو گا سحر کے نُور سے آئینہ پوش  
 اور ظلمتِ رات کی سیماب پا ہو جائے گی  
 پھر دلوں کو یاد آجائے گا پیغامِ سجود  
 پھر جبیں، خاکِ حرم سے آشنا ہو جائے گی  
 اقبال



Shaukat Ali

# To study the Association between Parental Consanguinity & Congenital Heart Diseases in Children at Mardan

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## ABSTRACT

**Background:** Congenital heart disease (CHD) is the most common congenital disorder in the newborns. Advances in cardiovascular medicine and surgery have enabled most patients to reach adulthood. Consequently, the prevalence of CHD is unclear and exceeding the number of patients seen in cardiology clinics. In Pakistan, the prevalence of CHD in neonates was found to be 4 per 1000 live births. Prevention of congenital cardiovascular defects has been hampered by a lack of information about modifiable risk factors for abnormalities in cardiac development. Over the past decade, there have been major breakthroughs in the understanding of inherited causes of CHD, including the identification of specific genetic abnormalities for some types of malformations. Consanguinity is widespread in Pakistan. The majority of studies on consanguinity in Pakistan have been carried out in urban metropolitan areas, and data on rural populations are scarce

**Objective:** To determine the association between parental consanguinity and congenital heart diseases in children.

**Setting:** Pediatric Unit Department of Pediatric Medicine, in D.H.Q hospital Mardan.

**Study Design:** Controlled case study.

**Duration of Study:** Six months (1/2/2015 to 2/8/2015).

**Material and Methods:** In this study sample size of 168 patients, 84 cases and 84 controls were calculated with 49% in cases with CHD and 29% in controls (without

CHD), considering odds ratio of 2.59, presenting to our hospital. Moreover, non-probability consecutive sampling technique was used for sample collection.

**Results:** Our study shows that in case group, mean age was 1 years with SD ± 1.07. Where as in control group, mean age was 1 years with SD ± 1.13. In case group, (62%) patients were male while (38%) patients were female. Where as in control group, (58%) patients were male and (42%) patients were female. In case group, (51%) patients had parental consanguinity while (49%) patients didn't had parental consanguinity. Where as in control group, (26%) patients had parental consanguinity and (74%) patients didn't had parental consanguinity.

**Conclusion:** Our study concludes that there is an association between parental consanguinity and congenital heart disease in children attending the children unit of D.H.Q Hospital Mardan.

**Key words:** parental consanguinity, congenital heart disease

## INTRODUCTION

Congenital heart disease (CHD) is the most common disorder in newborns. Advances in cardiovascular medicine and surgery have enabled most of the patients to reach adulthood.<sup>(1)</sup> Consequently, the prevalence of CHD is unclear, with estimates exceeding the number of patients currently seen in cardiology clinics.<sup>1</sup> In Pakistan, the prevalence of CHD in neonates was found to be 4 per 1000 live births.<sup>2</sup>

Prevention of congenital cardiovascular defects has been hampered by a lack of information about modifiable risk factors for abnormalities in cardiac development. Over the past decade, there have been major breakthroughs in the understanding of inherited causes of CHD, including the identification of specific genetic abnormalities for some types of malformations.<sup>3</sup>

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**There is a definitive association between parental consanguinity and congenital heart disease in children due to lack of information about modifiable risk factors for abnormalities in cardiac development, which can be avoided by social education of community to prevent congenital heart diseases.**

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Consanguinity is widespread in Pakistan, and the majority of studies on consanguinity in Pakistan have been carried out in urban metropolitan areas, and data on rural populations are scarce. First cousin unions had the highest representation (49.11% of all marriages), and marriages up to distantly related/*biradari* constituted 67.94% of all marriages.<sup>4</sup> Numerous articles have been published linking consanguineous marriage to an elevated prevalence of CHD, with ventricular and atrial septal defects, the most commonly cited disorders.<sup>5</sup>

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One study has reported that among cases of CHD, the consanguinity was present in 77.9% of the parents while among controls, consanguinity was present in 43.3% parents. The difference was found to be significant ( $P < 0.05$ ). The odds ratio was reported as 4.60 (95% CI: 2.53-8.43).<sup>6</sup> One more study has showed that among cases, consanguinity was present in 49% and among controls, consanguinity was present in 29% ( $P < 0.001$ ) with odds ratio = 2.59 (95% CI: 1.73-3.87).<sup>7</sup> But another study has reported that there was no association between CHD and consanguinity i.e. 22% among cases and 19.1% among control ( $P > 0.05$ ).<sup>8,9</sup> One more study has supported this evidence and showed that there was no association between CHD and consanguinity i.e. 3.9% among cases and 4.1% among control ( $P > 0.999$ ). and odds ratio=1.0 (95% CI: 0.4-2.7).<sup>10</sup>

Rationale of this study is to measure the association between parental consanguinity and CHD in children presenting to children unit of D.H.Q hospital Mardan. Literature has reported that CHD is significantly associated with consanguinity but controversy also exists. Consanguinity is a modifiable risk factor which can be avoided by social education of community to prevent congenital heart diseases. So we desired to conduct this study to confirm the association between CHD and consanguinity.

Congenital heart defect (CHD) may be defined as an anatomic malformation of the heart or great vessels which occurs during intrauterine development, irrespective of the age at presentation. Ventricular septal defect and coarctation of the aorta are typical examples of CHDs. Often viewed as a problem of adults, cardiovascular disease also exacts a terrible toll on the young. Congenital cardiovascular defects, also known as congenital heart defects (CHD), are the most common birth defect in the U.S.<sup>2</sup> and the leading killer of infants<sup>3</sup> The incidence of CHD ranges between 4 and 10 per 1,000 live births.<sup>4</sup> Tragically, more than 1,500 of them do not live to celebrate their first birthday.<sup>2</sup> Besides the terrible death toll, physical and mental suffering and lost potential of productivity that CHD causes, it also comes with a steep price tag. In 2004, hospital costs for all individuals with CHD totaled \$2.6 billion.<sup>5</sup>

But there is hope with research as most of them survive to adulthood, who formerly would have died.<sup>6</sup> However, the survivors particularly with more complex forms of CHD - are more likely to develop additional heart problems later in life. Young adults with CHD also face enormous barriers to effective health care, particularly when they are no longer covered by their parents' health plans. Few health and life insurance companies are willing to underwrite them as the cost is

prohibitive. The most common CHD are Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD)<sup>11</sup> Patent Ductus Arteriosus (PDA),<sup>11</sup> Tetralogy of Fallot (TOF)<sup>11</sup> Transposition of great arteries (TG)<sup>11</sup>

**RESULTS**

This study was conducted in Department of Paediatrics at D.H.Q Hospital Mardan, a total of 168 patients (84 cases and 84 controls) were observed to determine the association between parental consanguinity and congenital heart disease in children presenting to our hospital and the results were analyzed in which 56(67%) patients were in age < 1 year, 20(24%) patients were in age range 1-5 years, 8(9%) patients were in age ranged 6-10 years. Mean age was 1 years with SD ± 1.07. Where as in control group, 54(64%) patients were in age < 1 year, 21(25%) patients were in age range 1-5 years, 9(11%) patients were in age ranged 6-10 years. Mean age was 1 years with SD ± 1.13 (table 1). Gender distribution was analyzed as in case group, 52(62%) patients were male while 32(38%) patients were female. Where as in control group, 49(58%) patients were male and 35(42%) patients were female (table 2).

Status of parental consanguinity was analyzed as in case group, 43(51%) patients had parental consanguinity while 41(49%) patients didn't had parental consanguinity. Where as in control group, 22(26%) patients had parental consanguinity and 62(74%) patients didn't have parental consanguinity. (as shown in table no 3)

Stratification of parental consanguinity with respect to age and gender is given in table ( 4,5 )

**Table No 1. Age Distribution (n=168)**

Age	Cases N=84	Control N=84
< 1 year	56(67%)	54(64%)
1-5 years	20(24%)	21(25%)
6-10 years	8(9%)	9(11%)
<b>Total</b>	<b>84(100%)</b>	<b>84(100%)</b>
<b>Mean and SD</b>	1 years ± 1.07	1 years ± 1.13

Student T test was applied in which P value was 0.759. Cases: patients with congenital heart disease. Controls: patients without congenital heart disease

**Table No 2. Gender Distribution (n=168)**

Gender	Cases N=84	Control N=84
Male	52(62%)	49(58%)
Female	32(38%)	35(42%)
<b>Total</b>	<b>84(100%)</b>	<b>84(100%)</b>

Chi Square test was applied in which P value was 0.711.

Cases: patients with congenital heart disease Controls: patients without congenital heart disease

**Table No 3.** Parental Consanguinity. (n=168)

Parental consanguinity	Cases N=84	Control N=84
Yes	43(51%)	22(26%)
No	41(49%)	62(74%)
<b>Total</b>	<b>84(100%)</b>	<b>84(100%)</b>

Chi Square test was applied in which P value was 0.071. Odd ratio was ratio 2.16 . **Cases:** patients with congenital heart disease. **Controls:** patients without congenital heart disease

**Table No 4.** Stratification of Parental Consanguinity W.R.T Age (n=168)

Age	Parental consanguinity	Cases N=84	Control N=84	P values
< 1 year	Yes	29	15	0.230
	No	27	39	
<b>Total</b>		56	54	
1-5 years	Yes	10	5	0.381
	No	10	16	
<b>Total</b>		20	21	
6-10 years	Yes	4	2	0.377
	No	4	7	
<b>Total</b>		8	9	

**Cases:** patients with congenital heart disease. **Controls:** patients without congenital heart disease

**Table No. 5:** Stratification of Parental Consanguinity W.R.T Gender (n=168)

Gender	Parental consanguinity	Cases N=84	Control N=84	P values
Male	Yes	27	13	0.311
	No	25	36	
<b>Total</b>		52	49	
Female	Yes	16	9	0.238
	No	16	26	
<b>Total</b>		32	35	

**Cases:** patients with congenital heart disease. **Controls:** patients without congenital heart disease

**DISCUSSION**

Congenital heart diseases (CHD) are the most common congenital disorders in the new born in Pakistan is about 4 per 1000 live births<sup>(2)</sup> as consanguinity is widespread in Pakistan. The majority of studies in Pakistan have been carried out in urban metropolitan areas, and data on rural populations are scarce. First cousin marriages have the highest representation (49.11% of all marriages) and marriages up to distant related/*biradari* constituted 67.94% of all marriages<sup>(4)</sup> Numerous articles have been published linking consanguineous marriage to an elevated prevalence of CHD, with ventricular septal defects and atrial septal,

the most commonly cited disorders.<sup>5</sup>

Our study shows that in case group, mean age was 1 years with SD ± 1.07. Where as in control group, mean age was 1 years with SD ± 1.13. In case group, (62%) patients were male while (38%) patients were female. Where as in control group, (58%) patients were male and (42%) patients were female. In case group, (51%) patients had parental consanguinity while (49%) patients didn't had parental consanguinity. Where as in control group, (26%) patients had parental consanguinity and (74%) patients didn't had parental consanguinity.

One study has reported that among cases of CHD, the consanguinity was present in 77.9% parents while among controls, consanguinity was present in 43.3% parents. The difference was found to be significant (P<0.05). The odds ratio was reported as 4.60 (95% CI: 2.53-8.43).<sup>6</sup> One more study has showed that among cases, consanguinity was present in 49% and among controls, consanguinity was present in 29% (P<0.001) with odds ratio = 2.59 (95% CI: 1.73-3.87).<sup>(7)</sup> But another study has reported that there was no association between CHD and consanguinity i.e. 22% among cases and 19.1% among control (P>0.05)<sup>8,9</sup> One more study has supported this evidence and showed that there was no association between CHD and consanguinity i.e. 3.9% among cases and 4.1% among control (P>0.999). and odds ratio=1.0 (95% CI: 0.4-2.7).<sup>10</sup>

In South India, Bennett RL<sup>12</sup> aimed to maintain comparability in the ethnic and socio-economic backgrounds of the cases and controls groups in their study. They analyzed 144 cases of congenital heart disease ascertained from three major hospitals in Mysore in the state of Karnataka over two years versus 200 randomly-selected controls selected from the same region. To assess the potential risk of consanguinity on CHD, they interviewed all families and obtained family histories, and representative pedigrees from consanguineous families were shown. As with many studies, the details of the interviews to assess either consanguinity or CHD were not published, leading to an assumption that the ability to ascertain a family history of disease was similar in cases and controls. The authors also incorporated parental ages into a logistic regression analysis. The parents of 15.5% of the control group were consanguineous versus 40.3% of the CHD families, and it was concluded that the study suggested an approach to studying the recessive contributions to sporadic CHDs via consanguinity. Although patient age was utilized as a covariate in the analyses, further information regarding the specific characteristics of the case and control groups would have been even more helpful in interpretation of this study.

Yunis et al<sup>13</sup> in a study based in Beirut, Lebanon

studied 173 cases of CHD from a perinatal collaborative network, and their 865 controls were selected from the same hospitals' neonatal intensive care units. Mothers were interviewed in their native language and consanguinity was categorized by degrees of parental relationship. Data regarding neonatal variables and maternal factors were also assessed. At first-cousin level, after controlling for a number of factors an adjusted odds ratio (OR) for the effect of first cousin relationships ( $F = 0.0625$ ) on CHD of 1.8 (95% confidence interval (CI) 1.1–3.1) was reported. More distant consanguinity ( $F < 0.0625$ ) revealed an OR of 1.7 for CHD, although the 95% CI was 0.8–3.5. The study included control for a number of potential confounders, and the authors concluded that the study confirmed an association between consanguinity and CHDs among newborns in Beirut.

In a larger study, Chehab et al.<sup>14</sup> studied 1585 cases of non-syndromic CHD from a national pediatric heart disease registry also in Lebanon and 1979 controls without CHD from the same registry. An additional control group from a UNICEF study also was utilized. Although the details of the collection of registry information were not described in the article, the authors comparatively analyzed the data from these reasonably large groups. Consanguinity was present in a higher proportion of CHD cases versus controls when the analysis was performed on first-cousins (consanguinity in 19.4% of cases versus 14.4% in controls) and when first and second cousin parental relationships ( $F \geq 0.0156$ ) were co-analyzed. On the latter basis it was concluded that all degrees of consanguinity were greater in patients with congenitally malformed hearts compared to controls.

There is a possibility of some overlap in subjects in the studies by Yunis et al.<sup>13</sup> and Chehab et al.<sup>14</sup>, as both studies were conducted on individuals in Lebanon. In recognizing differences between cases and controls, the authors did address potential limitations of their study. They also acknowledged the importance of identifying the specific genetic risk factors in CHD and emphasized that the identification of genes involved in congenital malformations would improve counseling.

Some studies addressed the potential caveats in their data, e.g. Bassili et al.<sup>15</sup> performed a case-control study in Alexandria, Egypt using the public health system to select 894 cases of CHD and an equal number of controls. The mothers were interviewed and the authors noted that a half hour was dedicated to delineating the family history and detailed drawing of the family pedigree of cases and controls. In this study, the authors outlined the demographics of the case and control groups and described their methods in some detail. Of particular interest was the observation that

although the cases were similar to controls in many respects, they were more likely to be rural in residence and they tended to have less education. Interestingly, a history of consanguinity gave an adjusted odds ratio of 2.38 (95% confidence interval 1.92–2.96) for CHD. The authors discussed a number of potential sources of bias, including bias in selection, recall, and referral. It was concluded that consanguineous marriage was associated with an increased risk for CHD, and that further health education could help inform others about the potential effects of inbreeding.

## CONCLUSION

Our study concludes that there is an association between parental consanguinity and congenital heart disease in children presenting to children unit of D.H.Q hospital Mardan.

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