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Editorial

Sunlight helps Children from Developing Myopia.

What causes myopia has been a subject of controversy since many hundred years. It is a global epidemic to reach 52% by the year 2050 (WHO). In Asia, alone, 80% of the children are endangered from developing myopia in future. The genetic factor is inescapable especially with European heritage where the incidence is 40%. The question arise, should we select parents wisely?

Exposure to sunlight is one of the mysteries about its positive effect. Dr. Mutti from Ohio State University College of Optometry is an exponent of this hypothesis that if a child spends 2 hours outdoor every day with exposure to 1000 Lux of light, the chances of becoming myopic drops to 20% or at least it slows down the rate of progression. He further propounds that a child from both myopic parents, if he does not spend much time in outdoor activities, his chances to become short-sighted increases by 60%. He advises "Go outside and get the extra benefit of Sunlight." Bright light creates release of dopamine from the retina which slows down the growth of the eye, keeps the eye smaller and lowers the risk of becoming myopic. Exposing your eyes to sunlight also activates cytochrome oxidase, a part of the mitochondria in the cells which increases the cellular activity and anti-oxidant properties in the retina. A deficiency of cytochrome oxidase appears to contribute to macular degeneration.

There is some controversy over the role of reading and other close work on computers, smart phones, tablets—all the trappings of modern society. Dr. Aparna Ramasubramanian says "we

can't find any evidence that any aspect of what we call "near work" affects a child's risk of becoming nearsighted or its progression. Although everybody across the globe would agree with the above statement, but that's what our research shows in our study on 5,000 children.

She also made a randomized study on 276 students and encouraged them to spend 11 hours per week in outdoor activities through a school based program. She found that the rate of myopic progression was 54% lower as compared to the control group. "More time outside means less myopia" Taiwanese students spend 80 minutes' break each day outside, their myopic progression has dropped to 8-15%. Children with genetic tendency towards myopia were less likely to need glasses if they spend average of 2 hours/per day outside. Kids in Singapore believe "Keep Myopia away, go outdoor and play". In fact, our body is pre-programmed to need bright light. A hormone called melatonin regulates wake and sleep cycle. The hypothalamus uses sunlight as a cue for regulating hormone, temperature, thirst, hunger and blood pressure. According to Dr. Ian Morgan from Australian National University, 10,000 Lux of light for 3 hours/day may protect children from Myopia. Going outside on a sunny day will give you this much light. Indoor or in a class room usually gives 500 lux of light. Investigators noted that longer exposure to moderate sunlight reduced both myopic shift and axial elongation and the risk of rapid myopia progression was also 54% lower. The effects were significant in both non-myopic

and myopic children.

It is an established fact that excessive exposure to UVA and UVB radiation from sunlight contributes to the development of cataracts, macular degeneration and harmful effects to the skin. UV radiation and blue light cause oxidative stress, resulting in free radical damage. Hence, we use safety devices like sun-screens and sunglasses. If you wear glasses, avoid photochromic, light-adaptive, or variable tint lenses. They turn dark on exposure to light. They never give your eyes a chance to experience a short period of bright sun. If you wear glasses, ensure that the lenses have a UV coating.

When you are indoors, avoid using LED device which emanates blue lights, especially at night. Better use old-fashioned incandescent bulbs. LCD electronic screen like computers, TVs, smart phones and tablets, they emit excessive blue light. Instead of going outside to play, children are indoors, staring at one screen or another. Parents should set limits on total screen time for the day. Children should spend at least a couple of hours per day playing outdoors. Orange-amber lenses block 100% blue light. Install a blue light protecting screen over your monitor screen or wear computer glasses if you spend many hours per day on the computer. Many smart phones and tablets have a “block blue light” setting. Use this, especially at night. Adjust the brightness to prevent eye strain. If your device does not have a blue light setting, download a blue light filter app from the Google. We have discouraged the use of incandescent bulbs to save our electric bill and preferred the use of LED lights which are more efficient and cost-effective at the same time, though the risk is low but it’s still there. On the contrary, the incandescent bulbs produce infrared radiation – a wasted heat. Now this “wasted” heat from in-

candescent bulbs is helpful to the eyes in self-repairing of retina damaged from blue light.

For the treatment of myopia we are using multifocal contacts, gas permeable contact lenses to reshape the cornea, low-dose of atropine and various types of lasers. Now, atropine is something being used as an anti-myopia therapy for more than 100 years, but kids can’t tolerate high doses. However, researchers have found that very low doses are more tolerable to kids and also seems to have some benefit.

In Summary, in a the rapidly evolving electronic age especially with the advent of internet, it has become harder to imagine to keep away from the screens. In fact its free availability and numerous advantages have enslaved people of every age. We should try to eliminate the excessive use of electronic devices and replace it with the outdoor activities, closer to the nature in real life. We should plan for our children in such a way they can enjoy a variety of social, intellectual and physical activities essential for an all round development of a well balanced personality, minimizing the screen time through playing video games etc etc., In short they should have enough activities to balance the screen time.

Since ozone layer in the atmosphere has thinned out which allows more radiation from the sun. Hence, we draw a fine line for healthy sun exposure in order to avoid damaging effect of radiation. Researcher have advised to avoid maximum exposure between 10 AM to 2 PM in order to thwart the most common fears of sunburns, skin effects and cataract.

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Corneal Wavefront Measurement in Amblyopic Patients

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ABSTRACT

Objective: To assess the wavefront findings in an amblyopic eye

Method: A comparative cross-sectional study was done. A sample of 30 subjects with one eye as amblyopic was taken. Age ranges from 5 to 14 years. Females were 13 (43%) and males were 17 (57%). Corneal topography was done on each eye. The topography findings of normal eye was taken as standard for comparison with that of amblyopic eye in the same individual. Ziemer GALLIEI G2 was used for corneal topography. Machine print out was used as performa. Low order aberration (defocus and astigmatism) and high order aberrations (trefoil, spherical and coma) were studied. The research was conducted at College of Ophthalmology and Allied Vision Sciences, King Edward Medical University, Mayo Hospital Lahore, Pakistan. The study was conducted in December 2014. By applying Kolmogoro Smirnov test, it was confirmed that data was normally distributed so paired sample t-test was applied. P value less than 0.05 was taken as significant.

Result: There was a significant difference in third order vertical trefoil ($\rho=0.641$, $p=0.016$), third order vertical coma ($\rho=0.656$, $p=0.019$) and 7th order aberration ($\rho=0.475$, $p=0.041$). In all the other aberration such as 2nd order aberration, 2nd order oblique astigmatism, 2nd Order Defocus, 2nd Order Regular Astigmatism, 3rd order aberration, 3rd order horizontal coma, 3rd order horizontal trefoil, 4th order aberration, 4th order oblique quatrefoil, 4th order regular astigmatism, 4th order defocus, 4th order vertical astigmatism, 4th order regular quatrefoil, 5th order aberration, 6th order aberration and 8th order aberration there was no significant difference ($p \geq 0.05$).

Conclusion: There was significant difference in corneal aberrations between normal and amblyopic eyes.

Key Word. Amblyopia

INTRODUCTION

Amblyopia is a disorder of visual system which occurs during development in extra-striate cortex of visual pathway. It reveals as a decrease of visual acuity in eye which is amblyopic. Some other abnormalities of entire visual system e.g. contrast sensitivity and stereopsis may also decrease. Amblyopia occurs during development of brain. Amblyopia may be caused by organic pathology and functional abnormalities in visual pathway. It may occur mainly due to anisometropia or

strabismus. Confirmation of diagnosis of amblyopia depends on refraction by inducing cycloplegic, measurement of visual acuity and assessment of orthoptic problem. Screening and risk factor are also important in diagnosis. In the younger age, treatment is more effective. Treatment is done by occlusion or patching of good eye.¹

In order to determine, prevalence of amblyopia in Asian and Hispanic children with age group (6-72) months. A comprehensive study was done and clinical examination was conducted in which visual status and visual acuity was recorded. It was concluded that prevalence of amblyopia in both Asian and Hispanic was same but it seemed to be stable in Asian by age.²

There was significant difference in corneal aberrations between normal and amblyopic eyes.

Amblyopia may be unilateral or bilateral caus-

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ing decrease of vision. This problem is caused by underdevelopment of optic nerve causing the brain to favor one eye on the other. It is a leading cause of vision deprivation in children. The amblyopia is caused by following factors.

Anisometropia, Strabismus, Strabismic Amblyopia, Visual deprivation Organic amblyopia.³

Amblyopia can be classified as Strabismic amblyopia which is due to suppression of one eye, which is deviated, a result of disturbed interaction of both eyes. Anisometropic amblyopia which is due to difference in refractive status of both eyes. Amblyopia due to stimulus deprivation in which vision of one eye is deprived. It may be due to media opacities in one eye.

Ametropic amblyopia due to refractive error which is symmetrical. Meridional amblyopia occurs due to astigmatism. Due to abnormal visual status in early life, visual cortex disorder which results in amblyopia. Amblyopia causes vision loss in infants and children of young age. During the disturbance of normal visual development visual impairment occurs in amblyopia.

Amblyopia is an ideal model to understand how plasticity of brain may be harnessed. Due to ordinary viewing condition under amblyopia, results in impaired depth perception. Impairment of stereopsis has effect on visuomotor depending tasks. In Strabismic amblyopia, stereopsis affects more as compared to anisometropic amblyopia. The efficacy of treatment in Strabismic amblyopia is more than anisometropic amblyopia. The improvement of treatment in Strabismic amblyopia is more with dichoptic anisometropic training than monocular training.⁵

There is some capacity of binocular vision in amblyopic patients. It is important to quantify the suppression. There is some type of suppressive interaction at visual cortex, if we improve this then both monocular and binocular defects improves. It is necessary to investigate the measurement of binocular single vision in patients of Strabismic, anisometropic and amblyopia of mixed type.⁶ In amblyopia treatment it is important to measure the extent to which amblyopic eye suppresses the normal eye. Suppression is a binocular system binocularly but functionally monocular. Improvement in Strabismic amblyopia occur with reduction of suppression.⁷ In early childhood due to binocular disruption, amblyopia result. In amblyopia there is disorder extend from primary visual cortex to extra-striate visual cortex that is involved in visual integration.⁸

On the basis of geometrical optics, visual acuity at both distance and near would be same. However in amblyopic patients visual acuity at distance and near varies. In amblyopic eyes near vision is reduced than distance with reduced accommodation.⁹ The most important risk factors for unilateral amblyopia are strabismus and high refractive error. For the development of bilateral amblyopia important risk factors are bilateral astigmatism and hypermetropia of bilateral type.¹⁰

With increasing severity of amblyopia, there occur a decrease in visual functions and contrast sensitivity. There may be low processing of Parvocellular and Magnocellular pathway. There is some degree of damage at both these areas.¹¹ Amblyopia is unilateral or bilateral reduction of visual acuity. There is no abnormality of eye structures and in posterior visual pathways. Amblyopia treatment responds well in early life.¹² Amblyopia may occur as a result of abnormal visual interaction. The most common causes of amblyopia are strabismus, anisometropia and visual deprivation which may be as a result of congenital cataract and ptosis. In amblyopia there is difference of two lines of best corrected visual acuity between two eyes.¹³

Occlusion therapy is best method to treat amblyopia. It gives good overall success rate. But in this method there are chances of reoccurrence of amblyopia in severe cases. It is necessary to put compliances to parents.¹⁴ Accommodative performance of amblyopic eye should always be measured. Modified Nott Retinoscopy was used to measure the accommodative effort. When seen monocular accommodative effort is more as compared to both eyes results in retinal image to defocus.¹⁵ Full time patching gives best result on treatment of amblyopia of severe type. In these patients advised to patch good eye for six hours a week for three months. It gives best result in improvement of amblyopia. Patching in amblyopia improves visual acuity without any complication.¹⁶

Radii of curvature of cornea are both anterior surface and posterior surface. Curvature is measured in millimeter and also in diopter. Shape of cornea expressed in micrometers. Both of these identify corneal astigmatism. Surface should be optically smooth. Any irregularity results in degradation of image. Cornea is power dependent on its shape and refractive index. Thickness of cornea measured in micrometer. Corneal topography machine based on principle of Placido reflective analysis of image.¹⁷ A procedure used to measure the changes in shape of cornea of an eye. Corneal topographer emits a series of concentric rings of illuminated light on cornea of patient which are then reflected back on the instrument. This data analyzed in to machine and gives topographical map of that cornea. This is helpful in measuring the aberration of cornea.¹⁸

Corneal topography measures corneal aberrations. Optical aberration measures the wavefront error of entire eye. Analysis of wave front is done by aberroscope. This technique measures all type of aberration that is 2nd order, 3rd order, 4th order and high order aberrations.¹⁹ Three principles are used in corneal topography instruments. These are Placido disc reflection, scanning and scheinplung photography.²⁰

MATERIALS AND METHODS

A comparative cross-sectional study was done.

A sample of 30 subjects with one eye as amblyopic was taken. Age ranges from 5 to 14 years. Females were 13 (43%) and males were 17 (57%). Corneal topography was done on each eye. The topography findings of normal eye was taken as standard for comparison with that of amblyopic eye in the same individual. Ziemer GALLIEI G2 was used for corneal topography. Machine print out was used as Performa. Low order aberration (defocus and astigmatism) and high order aberrations (trefoil, spherical and coma) were studied. The research was conducted at College of Ophthalmology and Allied Vision Sciences, King Edward Medical University, Mayo Hospital Lahore. The study was conducted for a period of 2 months. By applying Kolmogorov Smirnov test, it was confirmed that data was normally distributed so paired sample t-test was applied. P value less than 0.05 was taken as significant.

RESULTS

TABLE NO 1.

Abberation of amblyopic and normal eye

	Mean	N	Std. Deviation	Std. Error Mean	
Pair 1	2nd order aberrations of amblyopic eye	1.8530	30	.68505	.12507
	2nd order aberrations of normal eye	1.7590	30	.84181	.15369
Pair 2	2nd order oblique astigmatism of amblyopic eye	.0003	30	.57885	.10568
	2nd order oblique astigmatism of normal eye	-.0192	30	.56722	.10356
Pair 3	2nd order defocus of amblyopic eye	-.6000	30	.28410	.05187
	2nd order defocus of normal eye	-.6263	30	.46751	.08536
Pair 4	2nd order regular astigmatism of amblyopic eye	-1.4080	30	1.02330	.18683
	2nd order regular astigmatism of normal eye	-1.3163	30	1.03858	.18962

This table shows the means and standard deviation of

compared pairs of 2nd order aberration of amblyopic and normal eye, 2nd order oblique astigmatism of amblyopic and normal eye, 2nd order defocus of amblyopic and normal eye and 2nd order regular astigmatism of amblyopic and normal eye. There was significant difference of means between these pairs.

TABLE NO 2: Correlation between paired sample of amblyopic and normal eye

	N	Correlation	Sig.	
Pair 1	2nd order aberrations of amblyopic eye & 2nd order aberrations of normal eye	30	.571	.001
Pair 2	2nd order oblique astigmatism of amblyopic eye & 2nd order oblique astigmatism of normal eye	30	-.530	.003
Pair 3	2nd order defocus of amblyopic eye & 2nd order defocus of normal eye	30	.509	.004
Pair 4	2nd order regular astigmatism of amblyopic eye & 2nd order regular astigmatism of normal eye	30	.573	.001

This table shows that there is strong correlation (rho=0.571) between 2nd order aberration of amblyopic and normal eye but the difference is not significant, strong correlation (rho=-0.530) between 2nd order oblique astigmatism of amblyopic eye and 2nd order oblique astigmatism of normal eye, strong correlation (rho=0.509) between 2nd order defocus of amblyopic eye and 2nd order defocus of normal eye and strong correlation (rho=0.573) between 2nd order regular astigmatism of amblyopic eye and 2nd order regular astigmatism of normal eye but difference is not significant.

This table shows that there is no significant difference between all of these groups. P value is (p ≥ 0.05) in all groups.

TABLE NO 3: Paired sample t- test

Mean	Paired Differences					t	Df	S i g . (2-tailed)
	Std. De- viation	Std. Error Mean	95% Confidence In- terval of the Differ- ence					
			Lower	Upper				
Pair 1 2nd order aberrations of amblyopic eye - 2nd order aberrations of normal eye	.09400	.72077	.13159	-.17514	.36314	.714	29	.481
Pair 2 2nd order oblique astigmatism of amblyopic eye - 2nd order oblique astigmatism of normal eye	.01953	1.00234	.18300	-.35475	.39381	.107	29	.916
Pair 3 2nd order defocus of amblyopic eye - 2nd order defocus of normal eye	.02633	.40518	.07397	-.12496	.17763	.356	29	.724
Pair 4 2nd order regular astigmatism of amblyopic eye - 2nd order regular astigmatism of normal eye	-.09167	.95270	.17394	-.44741	.26408	-.527	29	.602

This table shows that difference between the groups 2nd order aberrations of amblyopic eye - 2nd order aberrations of normal eye ($p \leq 0.05$), between 2nd order oblique astigmatism of amblyopic eye - 2nd order oblique astigmatism of normal eye ($p \leq 0.05$), between 2nd order defocus of amblyopic eye - 2nd order defocus of normal eye ($p \leq 0.05$) and 2nd order regular astigmatism of amblyopic eye - 2nd order regular astigmatism of normal eye ($p \leq 0.05$) is not significant.

TABLE NO 4: Comparison of paired sample means of amblyopic and normal group

	Mean	N	Std. Deviation	Std. Error Mean
Pair 1 third order aberration of amblyopic eye	.4795	30	.47920	.08749
third order aberration of normal eye	.5450	30	.23853	.04355
Pair 2 third order vertical trefoil of amblyopic eye	-.1058	30	.21224	.03875
third order vertical trefoil of normal eye	.0387	30	.23687	.04325
Pair 3 third order vertical coma of amblyopic eye	-.0083	30	.32029	.05848
third order vertical coma of normal eye	-.1200	30	.26172	.04778
Pair 4 third order horizontal coma of amblyopic eye	-.1733	30	.36026	.06577
third order horizontal coma of normal eye	-.0750	30	.46229	.08440
Pair 5 third order horizontal trefoil of amblyopic eye	-.1240	30	.30607	.05588
third order horizontal trefoil of normal eye	-.0597	30	.27278	.04980

3rd order aberration of amblyopic eye and normal eye,
 3rd order vertical trefoil of amblyopic eye & normal eye,
 3rd order horizontal coma of amblyopic eye & normal eye, and
 3rd order horizontal trefoil of amblyopic eye & normal eye. There was no significant difference between means of these pairs

TABLE NO 5: Correlation between paired sample of amblyopic and normal eye _____

	N	Correlation	Sig.
Pair 1 third order aberration of amblyopic eye & third order aberration of normal eye	30	-.031	.871
Pair 2 third order vertical trefoil of amblyopic eye & third order vertical trefoil of normal eye	30	.064	.737
Pair 3 third order vertical coma of amblyopic eye & third order vertical coma of normal eye	30	.656	.000
Pair 4 third order horizontal coma of amblyopic eye & third order horizontal coma of normal eye	30	-.053	.780
Pair 5 third order horizontal trefoil of amblyopic eye & third order horizontal trefoil of normal eye	30	.291	.119

There is strong correlation ($\rho=.000, p \leq 0.05$) between third order vertical coma of amblyopic eye and third order vertical coma of normal eye and the difference between groups is also significant.

TABLE NO 6: Paired sample t- test

Mean	Paired Differences					t	df	Sig. (2-tailed)
	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference					
			Lower	Upper				
Pair 1 third order aberration of amblyopic eye - third order aberration of normal eye	-.06553	.54188	.09893	-.26787	.13681	-.662	29	.513
Pair 2 third order vertical trefoil of amblyopic eye - third order vertical trefoil of normal eye	-.14443	.30777	.05619	-.25936	-.02951	-2.570	29	.016
Pair 3 third order vertical coma of amblyopic eye - third order vertical coma of normal eye	.11167	.24712	.04512	.01939	.20394	2.475	29	.019
Pair 4 third order horizontal coma of amblyopic eye - third order horizontal coma of normal eye	-.09833	.60101	.10973	-.32275	.12609	-.896	29	.378
Pair 5 third order horizontal trefoil of amblyopic eye - third order horizontal trefoil of normal eye	-.06433	.34570	.06312	-.19342	.06475	-1.019	29	.316

This table shows that there is significant difference between third order vertical trefoils of amblyopic eye - third order vertical trefoil of normal eye ($p \leq 0.05$) and between third order vertical coma of amblyopic eye - third order vertical coma of normal eye ($p \leq 0.05$).

TABLE NO.7 Comparison of paired sample means of amblyopic and normal group

	Mean	N	Std. Deviation	Std. Error Mean
Pair 1 fourth order aberration of amblyopic eye fourth order aberration of normal eye	.2193	30	.13266	.02422
	.2760	30	.22053	.04026
Pair 2 fourth order oblique quatrefoil of amblyopic eye fourth order oblique quatrefoil of normal eye	-.0187	30	.03830	.00699
	-.0167	30	.01348	.00246

Pair 3	fourth order oblique astigmatism of amblyopic eye	.0137	30	.02988	.00546
	fourth order oblique astigmatism of normal eye	.0260	30	.13622	.02487
Pair 4	fourth order defocus of amblyopic eye	.0950	30	.09637	.01760
	fourth order defocus of normal eye	.1030	30	.08918	.01628
Pair 5	fourth order vertical astigmatism of amblyopic eye	.0203	30	.05275	.00963
	fourth order vertical astigmatism of normal eye	.0067	30	.04080	.00745
Pair 6	fourth order regular quatrefoil of amblyopic eye	-.0580	30	.04046	.00739
	fourth order regular quatrefoil of normal eye	-.0407	30	.17354	.03168

4thorder aberration of amblyopic& normal eye,

4th order oblique quatrefoil of normal and amblyopic eye,

4thorder defocus of amblyopic& normal eye,

4thorder vertical astigmatism of amblyopic and normal eye, and

4thorder regular quatrefoil of amblyopic and normal eye.

Table no.8

Correlation between paired sample of amblyopic and normal eye

	N	Correlation	Sig.
Pair 1 fourth order aberration of amblyopic eye & forth order aberration of normal eye	30	.564	.001
Pair 2 fourth order oblique quatrefoil of amblyopic eye and forth order oblique quatrefoil of normal eye	30	.318	.086
Pair 3 fourth order oblique astigmatism of amblyopic eye and fourth order oblique astigmatism of normal eye	30	.476	.008
Pair 4 fourth order defocus of amblyopic eye & forth order defocus of normal eye	30	.713	.000
Pair 5 fourth order vertical astigmatism of amblyopic eye and forth order vertical astigmatism of normal eye	30	.074	.697
Pair 6 fourth order regular quatrefoil of amblyopic eye and fourth order regular quatrefoil of normal eye	30	.537	.002

This table shows that there is strong correlation between forth order aberration of amblyopic eye and forth order aberration of normal eye (rho=.001), forth order oblique astigmatism of amblyopic eye and fourth order oblique astigmatism of normal eye (rho=0.008),fourth order defocus of amblyopic eye and fourth order defocus of normal eye (rho=0.000), fourth order regular quatrefoil of amblyopic eye and fourth order regular quatrefoil of normal eye (rho=.002) but there is no significant difference between these groups.

TABLE NO 9: Paired sample t- test

Mean	Paired Differences	t	df	S i g . (2-tailed)					
					Std. De- viation	S t d . E r r o r Mean	95% Confidence Interval of the Dif- ference		
							Lower	Upper	
Pair 1	fourth order aberration of amblyopic eye - fourth order aberration of normal eye	-.05667	.18235	.03329	-.12476	.01142	-1.702	29	.099
Pair 2	fourth order oblique quatrefoil of amblyopic eye - fourth order oblique quatrefoil of normal eye	-.00200	.03633	.00663	-.01557	.01157	-.302	29	.765
Pair 3	fourth order oblique astigmatism of amblyopic eye - fourth order oblique astigmatism of normal eye	-.01233	.12481	.02279	-.05894	.03427	-.541	29	.592
Pair 4	fourth order defocus of amblyopic eye - fourth order defocus of normal eye	-.00800	.07063	.01290	-.03437	.01837	-.620	29	.540
Pair 5	fourth order vertical astigmatism of amblyopic eye - fourth order vertical astigmatism of normal eye	.01367	.06425	.01173	-.01032	.03766	1.165	29	.253
Pair 6	fourth order regular quatrefoil of amblyopic eye - fourth order regular quatrefoil of normal eye	-.01733	.15561	.02841	-.07544	.04077	-.610	29	.547

DISCUSSION

Amblyopia is an idiopathic disease in which there is reduction of visual acuity when no fundal pathology seen on examination. Amblyopia results due to strabismus, visual deprivation and due to unequal refractive status during early development of life. In young children and adults of middle age the common cause of visual impairment is amblyopia and it is increasing the risk of vision loss (1.2%).²¹

High refractive errors when occur in both eyes leads to an isometric amblyopia. Strabismus is also secondary cause of amblyopia. If there is large difference in refractive status of two eyes leads to anisometric amblyopia. As they play a potential role in image quality so high order aberration seems to be a causative factor in development of amblyopia.²²

The treatment outcome and management is difficult to treat in younger children, due to issue of compliance. Amblyopia can easily be treated in individuals above 10 years. Even after treatment completed successfully amblyopic patients when check give eye behaves as an abnormal eye for various visual functions.²³

There are following two types of aberration in eye. Low order aberration makes 85% of total aberration in eye. They consist of defocus and astigmatism. High order aberration makes 15 % of total aberration. They consist of spherical aberration, coma and trefoil. Order means complexity of wavefront shape. Order of aberration depends on complexity of shape.²⁴

High order astigmatism makes small contribution in eye's total wavefront, studies shoes that high order aberration has deleterious effect on image quality.

This study compared ocular aberrations in amblyopic eye and normal eye of same individual, the results showed that in amblyopic eyes third order vertical trefoil (p = 0.016),(p<0.05), third order vertical coma (p = 0.019),(p<0.05) and 7th order aberration (p = 0.041),(p<0.05). The differences were statistically significant.²⁵

In conclusion, high order aberrations are the main cause in the development of amblyopia. Further studies with larger sample sizes are required to further study the effect of HOAs in children with amblyopia.

CONCLUSION: There was significant difference in corneal aberrations between normal and amblyopic eyes.

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Effect of Cyclosporine a 0.05% in the Treatment of Sub-epithelial Infiltrates in Epidemic Kerato-conjunctivitis

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ABSTRACT

Purpose: Effect of Cyclosporine A 0.05% in the treatment of subepithelial infiltrates in epidemic keratoconjunctivitis

Patients and method: This was Descriptive Case series study conducted in Shalamar hospital Lahore. The age group from 15 to 45 years were included in this study. Who were not responding to the steroid therapy. Total of 100 patients were included in this study.

Results: Patients with corneal subepithelial infiltrates after epidemic keratoconjunctivitis, who were resistant to 3 months of steroid therapy were given topical cyclosporine A 0.05% for one month, 79 % improved

Conclusions: Results suggest that the Cyclosporine A 0.05% is safe and effective treatment for subepithelial infiltrates after epidemic keratoconjunctivitis who fails to respond with conventional steroid therapy.

Key Words: Cyclosporine A 0.05%, sub-epithelial infiltrates, epidemic keratoconjunctivitis, Adenoviral conjunctivitis. Epidemic keratoconjunctivitis, Corneal subepithelial infiltrate, Topical 0.05% cyclosporine A Epidemic keratoconjunctivitis, Corneal subepithelial infiltrate, Topical 0.05% cyclosporine A Epidemic keratoconjunctivitis, Corneal subepithelial infiltrate, Topical 0.05% cyclosporine A

INTRODUCTION:

Adenoviral conjunctivitis is highly contagious, most common viral disease of the eyes and is prevalent in the tropical areas and in hot climate. Adenovirus has many serotypes causing follicular conjunctivitis. But particularly serotype ^{3,4,7,8,19,37} are associated with kerato-conjunctivitis^{1,2}. Former three causes pharyngoconjunctivitis and rare three causes epidemic kerato-conjunctivitis and are 30% and 80% risk factor for keratitis respectively.

Patient present with redness, foreign body sensation, watering and discharge from the eye. on examination Injection of conjunctiva and predominant follicular reaction with few papillae are the common feature of early or milder disease. In severe cases lid swelling, Pseudo-membrane formation on palpebral conjunctiva, chemosis, hemorrhagic conjunctivitis, painful lymphadenopathy of pre-auricular lymph nodes, Mild Anterior uveitis can also be seen². Keratitis are usually in diffuse superficial punctate keratitis, focal epithelial punctate keratitis, and subepithelial infiltrates following conjunctivitis after 1 to 3 weeks. Subepithelial infil-

trates are small, round and grayish lesions. That may and may not be stained with fluorescein. They are histologically accumulation of dead antigen of virus and lymphocyte organized around stromal cells. These lesions completely disappear without any scarring. They can remain dormant in corneal tissue for years and can cause symptoms such as decrease in visual acuity, glare, halo, and photophobia¹.

Cold compression, artificial tears supplement and topical weak steroid in combination with antibiotic to prevent secondary bacterial infection are the main stay of treatment for adenoviral conjunctivitis. For sub-epithelial infiltrates conventionally topical prednisolone 0.5% is used but few of the patients unfortunately fail to respond. For these patients topical Cyclosporine A 0.05% can be used^{1,2,3}. With the limited studies on use Cyclosporine A 0.05% for the treatment of sub-epithelial infiltrates^{2,3,4} We hope this study will be useful to determine the effective treatment regime for post adenoviral sub-epithelial infiltrates in our settings.

Cyclosporine eye drops 0.05% is safe and effective treatment for subepithelial infiltrates after epidemic keratoconjunctivitis fail to respond conventional steroid therapy.

MATERIAL AND METHOD

This was a descriptive case series study. Both male and female patients were included in this study

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between the ages of 15 to 45 years, who had non responding post adenoviral keratitis. Total of 100 patients were included in this study. Informed consent was taken from every patient included in the study. Purpose and procedure was explained, and confidentiality of their personal information was ensured to the patient. Patient were also explained the pros and cons of the treatment. After Informed consent, personal profile was documented in part 1 of Performa and BCVA , IOP and subepithelial infiltrate count in part 2 of Performa.

Patient were prescribed Cyclosporine A 0.05% eye drops 4 times a day along with steroid for initial 2 weeks followed by Cyclosporine A 0.05% twice daily for the next 2 weeks along with steroid. All procedures, examination and documentations was done by the same ophthalmologist to prevent bias documentation of symptom. Follow up with Best corrected visual acuity, Intra ocular pressure and slit lamp examination for count of subepithelial infiltrates was documented for 4 weeks.

The data was entered and analyzed in SPSS Version 20.00. The quantitative data like visual acuity was presented as mean standard deviation. The qualitative data like subepithelial infiltrates count and improvement in visual acuity was presented in the form of frequency and percentage.

RESULTS

One hundred eyes of 100 patients were included in this study, of these 35 (35%) were male and 65 (65%) were female. The Patient’s were between 15 to 45 years of age. 40 patients had sub-epithelial infiltrates in their right eye and remaining 60 patient had Subepithelial infiltrates in their left eye. Before the start of the treatment BCVA in logMAR was recorded and it ranged from 1 to 0.2 logMAR. Likewise at the beginning of the study, average IOP was 15 ± 5 mmHg and average subepithelial infiltrate count was 4.83 (range from 2 to 10). All of the patients were nonresponsive to the steroid treatment after the initial 3 months of therapy. After the start of topical cyclosporine A 0.05% along with topical steroid. Patients were followed after every 2 weeks for 4 weeks.

At 4 weeks of therapy 79 patient were symptom free. In those patient the cyclosporine A 0.05% was stopped and steroid was tapered down to no medication. These patients recovered fully with no Subepithelial infiltrates and BCVA value of 0 logMAR. The remaining 21 patients showed variable degree of results. (4 patient had 2 Subepithelial infiltrates showed mild improvement, 3 patients had 3 Subepithelial infiltrates, 5 patients had 4 Subepithelial infiltrates, 9 patients had 6 or 8 Subepithelial infiltrates with severe visual impairment). These 21 non responders were continued with once daily or twice daily dose of cyclosporine A 0.05% along with steroids. 15 patient had raised IOP to 21 mmHg or more for which they were started on anti-glaucoma therapy along with reducing dose of steroid. At the end of 4 weeks out of 100 patients 79 (79%) were free from Subepithelial infiltrates and were symptom free and 21 (21%) patients remain resistant to therapy having variable degree of visual improvement.

Table 1 data sheet

Effect of Cyclosporine A 0.05% in the treatment of subepithelial infiltrates in epidemic-keratoconjunctivitis”

SR#	SEX	AGE	OD/OS	BCVA 0	BCVA END	IOP 0	IOP end	SEIC 0	SEIC 8 week
1	M	27	OD	0.8	0.3	20	20	8	2
2	F	43	OS	0.5	0	14	14	3	0
3	F	25	OD	1	0	20	18	7	0
4	F	45	OS	0.5	0	11	17	3	0
5	M	18	OS	0.3	0	12	12	3	0
6	F	19	OD	0.3	0	10	15	3	0
7	M	45	OS	0.8	0	14	15	6	0
8	F	43	OS	0.8	0	14	15	5	0
9	F	34	OS	0.5	0	15	14	4	0
10	F	32	OD	0.2	0	19	24	3	0
11	F	43	OS	0.8	0	14	15	5	0
12	F	32	OD	0.2	0	19	24	3	0
13	F	43	OS	0.8	0	14	15	5	0
14	F	32	OD	0.2	0	19	24	3	0
15	M	18	OS	0.3	0	12	12	3	0
16	F	19	OD	0.3	0	10	15	3	0
17	F	18	OD	0.3	0	12	14	2	0

18	M	21	OS	0.5	0	11	17	3	0
19	M	45	OS	0.8	0	14	15	6	0
20	F	34	OS	0.5	0	15	14	4	0
21	F	16	OD	0.6	0	13	15	4	0
22	F	25	OD	1	0	20	18	6	0
23	M	20	OD	1	0.5	14	20	8	6
24	F	45	OS	0.5	0	11	17	3	0
25	M	29	OS	1	0.5	15	18	10	6
26	F	18	OD	0.3	0	12	14	2	0
27	M	21	OS	0.5	0	11	17	3	0
28	M	45	OS	0.8	0	14	15	6	0
29	F	34	OS	0.5	0	15	14	4	0
30	M	18	OS	0.3	0	12	12	3	0
31	F	19	OD	0.3	0	10	15	3	0
32	F	25	OD	1	0	20	18	6	0
33	F	45	OS	0.5	0	11	17	3	0
34	F	43	OS	0.8	0	14	15	5	0
35	F	32	OD	0.2	0	19	24	3	0
36	F	42	OS	0.6	0	19	23	5	0
37	M	39	OS	0.3	0	18	18	2	0
38	F	18	OD	0.3	0	12	14	2	0
39	M	18	OS	0.3	0	12	12	3	0
40	M	27	OD	0.8	0.3	20	20	8	4
41	F	43	OS	0.8	0	14	15	5	0
42	M	21	OS	0.5	0	11	17	3	0
43	F	19	OD	0.3	0	10	15	3	0
44	F	43	OS	0.5	0	14	14	3	0
45	F	32	OD	0.2	0	19	24	3	0
46	F	42	OS	0.6	0	19	23	5	0
47	M	39	OS	0.3	0	18	18	2	0
48	M	18	OS	0.3	0	12	12	3	0
49	F	19	OD	0.3	0	10	15	3	0
50	F	16	OD	0.6	0	13	15	4	0
51	F	42	OS	0.6	0	19	23	5	0
52	M	20	OD	1	0.5	14	20	8	6
53	M	39	OS	0.3	0	18	18	2	0
54	M	29	OS	1	0.5	15	18	10	6
55	F	25	OS	0.8	0	14	16	5	0
56	F	18	OD	1	0.6	21	21	10	6
57	F	31	OS	0.5	0	13	17	3	0
58	F	25	OD	1	0	20	18	8	4
59	F	45	OS	0.5	0	11	17	3	0
60	F	42	OS	0.6	0	19	23	5	0
61	M	39	OS	0.3	0	18	18	2	0
62	F	25	OS	0.8	0	14	16	6	0

63	F	18	OD	1	0.6	21	21	10	6
64	F	31	OS	0.5	0	13	17	3	0
65	F	16	OD	0.6	0	13	15	4	0
66	F	18	OD	0.3	0	12	14	2	0
67	F	25	OD	0.5	0	20	18	2	0
68	M	27	OD	0.8	0.3	20	20	8	2
69	M	20	OD	1	0.5	14	20	8	4
70	M	21	OS	0.5	0	11	17	3	0
71	F	45	OS	0.5	0	11	17	3	0
72	F	43	OS	0.5	0	14	14	3	0
73	M	29	OS	1	0.5	15	18	10	4
74	M	45	OS	0.8	0	14	15	6	0
75	F	34	OS	0.5	0	15	14	4	0
76	F	25	OS	0.8	0	14	16	6	0
77	F	18	OD	0.3	0	12	14	2	0
78	F	18	OD	1	0.6	21	21	10	8
79	M	21	OS	0.5	0	11	17	3	0
80	F	31	OS	0.5	0	13	17	3	0
81	M	27	OD	0.8	0.3	20	20	8	2
82	F	43	OS	0.5	0	14	14	3	0
83	F	25	OS	0.8	0	14	16	6	0
84	M	27	OD	0.8	0.3	20	20	8	4
85	F	18	OD	1	0.6	21	21	10	8
86	F	43	OS	0.5	0	14	14	3	0
87	F	31	OS	0.5	0	13	17	3	0
88	F	42	OS	0.6	0	19	23	5	0
89	M	39	OS	0.3	0	18	18	2	0
90	M	45	OS	0.8	0	14	15	6	0
91	F	34	OS	0.5	0	15	14	4	0
92	F	16	OD	0.6	0	13	15	4	0
93	M	20	OD	1	0.5	14	20	8	2
94	M	29	OS	1	0.5	15	18	10	3
95	F	16	OD	0.6	0	13	15	4	0
96	M	20	OD	1	0.5	14	20	8	3
97	M	29	OS	1	0.5	15	18	10	3
98	F	25	OS	0.8	0	14	16	6	0
99	F	18	OD	1	0.6	21	21	10	8
100	F	31	OS	0.5	0	13	17	3	0

Table 2 Data sheet

	Before treatment	After treatment	p
BCVA	0.61	0.095	0.001
IOP	14.95	17.15	0.001
Subepithelial infiltrates count	5	1	0.001

DISCUSSION

Chemosis, photophobia, hyperemia, itching, eye pain and lid swelling can occur in epidemic keratoconjunctivitis (EKC) which can adversely affect the everyday life. Conjunctivitis can ensue after keratitis with subepithelial infiltrates count (SEIC) in approximately 80% of the patients^{5,6}. Photophobia, decrease of visual acuity, halo and irregular astigmatism can occur due to SEI. Decrease in visual acuity caused by SEIC can range from few weeks to some years as reported in some studies^{7,8}. Treatment by virus static agents such as ganciclovir, trifluridine and vidarabine were not effective in ocular adenovirus infections^{9,10}. Long term use of topical steroids is beneficial in adenovirus infections but can cause super-infections, cataract and glaucoma^{11,12}. Ocular surface lacrimal gland inflammation and T-lymphocyte proliferation and activation is suppressed by the use of topical CsA¹³. Topical CsA is effective in various concentrations in ocular inflammations such as ulcerative keratitis due to rheumatoid arthritis, anterior uveitis, corneal graft rejection, superior limbic keratoconjunctivitis, cogan syndrome, micotic keratitis, Behcet's disease, herpetic stromal keratitis, mooren ulcer and atopic keratoconjunctivitis^{14,28}. Topical 0.05% CsA was used successfully in the treatment of meibomian gland dysfunction, ocular graft-versus host disease, dry eye syndrome and pterygium surgery without any systemic or ocular side effects^{29,33}.

In the treatment of acute and chronic adenovirus infections CsA was effective in concentrations of 1% and 2% with majorly reduced or obliterated SEIC within 3 to 4 weeks^{7,5,34-35,8,14}. After an initial therapy of topical 1% CsA and steroids for a month, topical CsA 1% or 0.05% as a single dose per day or every other day was effective in treating SEIC a reported by Jeng and colleagues³⁵. 0.5% and 2% topical CsA were effective in treating SEIC as reported by Romanowski and colleagues, but it was claimed that this agent could facilitate the virus replication risking an epidemic³⁶.

In this study we included the patients who had no regression in SEIC for 3 months despite topical corticosteroids use. After two months with topical 0.05% CsA therapy, 79[79%] of eyes were cleared of SEIC, and in 21[21%] of eyes SEIC were not completely cleared but decreased in number. The treatment was discontinued in the eyes with completely cleared SEIC and continued in dose of twice daily in eyes which still had SEICs. From our experience, treatment with CsA should be continued until all SEIC are cleared. It cannot be foreseen that whether the SEIC will recur after treatment or when will it recur. Therefore, after the treatment patients should be followed up for long duration. Because of the impact of SEIC on patients daily life, control group who will be treated with placebo could not be constructed. Since our data were acquired without a control we cannot rule out the possibility of spontaneous resolution of SEIC as the natural history of the disease in this study.

CONCLUSION

Result suggest the Cyclosporine a 0.05% is safe and effective treatment for subepithelial infiltrates after epidemic keratoconjunctivitis who fail to respond with conventional steroid therapy.

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Sami Ullah

Frequency of Drug induced Hepatitis in recently Diagnosed Children with Pulmonary Tuberculosis

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ABSTRACT

Objective: To determine the frequency of drug induced hepatitis among newly diagnosed 119 children of pulmonary tuberculosis subjected to anti tuberculosis therapy.

Materials and methods: This cross sectional study was conducted at department of Pediatrics, Lady Reading Hospital, Peshawar from 4th November 2013 to 3rd may 2014 with total 7 months duration. All newly diagnosed children of pulmonary tuberculosis with normal baseline ALT of either gender and age up to 18 year were included while patients with Clinical evidence of hepatitis before initiation of ATT, deranged baseline LFT levels as measured in the laboratory, evidence of other causes of hepatitis on medical records, history of previous episodes of Jaundice, transfusions, operations and presence of non specific factors of liver dysfunction affecting the outcome of therapy were excluded from the study. Patients particulars and all variables of the study were documented according to proforma. SPSS version 16 was used for data analysis and tables were used to represent the data. The above mentioned conditions act as confounders and if included will introduce bias in the study results.

Results: The mean age group of our sample was 7.77 ± 2.7 years of which 59.7% were male and 40.3% were females. Mean baseline ALT level was 34.91 ± 5.8 . after 8 weeks of treatment with standard anti TB drugs, the hepatotoxicity was observed in 26.9% of patients with female children and children having baseline ALT above 30.00 were strongly prone to developing anti TB drug induced hepatitis.

Conclusion: Anti TB drug induced hepatitis is common problem in our population who are subjected to routine anti TB drugs.

Key Words: Pulmonary tuberculosis, hepato-toxicity, drug induced hepatitis

INTRODUCTION

Tuberculosis affected an estimated 8.8 million people and caused 1.4 million deaths globally in 2010, including a half-million women and at least 64 000 children. It also results in nearly 10 million cumulative orphans due to parental deaths. Moreover, it causes 6%-15% of all maternal mortality, which increases to 15%-34% if only indirect causes are considered¹. Unfortunately, despite causing nearly 10 million cumulative orphans due to parental deaths in 2009², tuberculosis prevention, diagnosis and treatment services are still

not acknowledged nor widely implemented by maternal and child healthcare stakeholders and implementers³. An accurate estimate of the global burden of tuberculosis in children is difficult mainly because of the challenges in case ascertainment, diagnosis and weak surveillance systems in many countries with a high burden of tuberculosis⁴.

Anti tubercular drug induced hepatitis is a common occurrence in children which needs further intensive studies before treatment.

Due to these reasons, children are often excluded from tuberculosis prevalence surveys¹, further hampering the collection of reliable information. It is estimated that children younger than 15 years contribute 15%-20% of the global tuberculosis burden⁵. In one study from South Africa, children <13 years of age contributed to 14% of the burden, with a childhood tuberculosis incidence rate of 407 per 100 000 population per year⁶. Currently available diagnostic tools for tuberculosis rely on AFB microscopy, culture growth, and molecular DNA detection (e.g. Xpert MTB/RIF test) of

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M. tuberculosis in specimens, largely in sputum⁴. However, children, especially those <5 year old, cannot expectorate sputum. Gastric aspirate, sputum induction, laryngeal swab and nasopharyngeal aspirate are methods used to obtain samples from children with positive AFB result ranging from 1% to 17% and culture growth ranging from 15% to 92%⁷.

The principles of treatment and the recommended regimens of drugs for each category of tuberculosis disease are generally similar between adults and children⁸. Children with suspected or confirmed pulmonary tuberculosis or peripheral lymphadenitis and living in HIV-prevalent settings or in settings with high isoniazid resistance, or both, should be treated with a 4-drug regimen consisting of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE) for 2 months followed by isoniazid and rifampicin (HR) for 4 months. Similarly, children with extensive pulmonary disease living in low HIV prevalence or low isoniazid resistance settings should also be treated with 2 months of HRZE followed by 4 months of HR⁹. Although tuberculosis drug metabolism, distribution and clearance are likely to be different from adults, especially in young children, drug recommendations for children were largely based on pharmacokinetic data obtained from adult studies¹⁰. Drug-induced hepatotoxicity can occur in children at any age or at any dosage of isoniazid, rifampicin, or pyrazinamide, but the incidence of this adverse effect is considerably lower in children than in adults¹¹. The pathogenic Mechanism of ant tuberculosis drug-induced hepatotoxicity (ATDH) is thought to involve drug-metabolizing enzymes including N-acetyl transferase2 (NAT2), cytochrome P4502E1 (CYP2E1) and glutathione S-transferase (GST) M1, T1. The associations between genetic polymorphisms of those genes and ATDH have been reported but with inconsistent results. Moreover, most studies were hospital-based retrospective studies and not prospective¹². Recent increases in the dosage of the essential and tuberculosis agents isoniazid (ING) 5-15mg/kg, rifampicin (RMP) 10-20mg/kg, pyrazinamide (PZA) 30-40mg/kg for use in children recommended by World Health Organization have raised concerns regarding the risk of hepatotoxicity¹⁰. In one study, drug induced hepatitis was observed in 52.9% of children subjected to anti TB therapy and jaundice occurred in 10.8% of children¹¹.

METHODOLOGY

Before starting of study approval from hospital ethical committee was taken and use of data for research and publication was explained to the guardians and informed consent was taken. The diagnosis of pulmonary tuberculosis was made upon strictly following operational definition as mentioned above. Detailed history was taken to exclude children with diseases mentioned in the exclusion criteria from our study. This will exclude confounders and possible bias in the study results. After a careful and detailed physical ex-

amination, laboratory tests were performed to record baseline levels of all relevant criteria. All the diagnosed children were put on standard anti tuberculosis treatment as per WHO guidelines. Follow-up clinical examination was done at 8 weeks after starting ATT and liver function tests was repeated to detect drug induced hepatitis. All the data was collected on a proforma by the investigator himself. All the laboratory investigations were done by single pathologist. Data was entered using SPSS version 10.0. Categorical variables like gender and drug induce hepatitis was described as frequencies and percentages. Quantitative variables like age, ALT at baseline and ALT at follow up was described as Mean \pm standard deviation. Drug induced hepatitis was stratified among age and gender to see the effect modifications.

RESULTS

A total of 119 newly diagnosed patients of pulmonary tuberculosis presenting in OPD were included in the study. The mean age and standard deviation of the sample was 7.77 ± 2.7 years. While distributing the cases of pulmonary tuberculosis observed here 32.8% in the age group up to 6.00 years, 53.8% were in the age group 6.01 to 12.00 years and 13.4% were in the age range 12.01 to 18.00 years. While distributing the sample with regards to gender, we observed that 59.7% were males and 40.3% were female cases. All the children of newly diagnosed pulmonary tuberculosis were subjected to measurement of baseline ALT levels. The mean baseline ALT level in our group of patients was 34.91 ± 5.8 . On categorizing the baseline ALT level in different groups, we found that we had 26.9% patients in the level of ALT up to 30.00, 52.9% were in the level between 30.01 to 40.00 and 20.2% were between the level of ALT between 40.01 to 50.00. All the patients were subjected to standard anti tuberculous treatment as per international protocols. 8 weeks after the treatment is continued, all the children were followed up and repeat ALT level was performed. On follow up, we observed that the mean ALT level was 85.5 ± 48.1 .

As per operational definition of Anti TB drug induced hepatitis, it was recorded that 26.9% of patients had their ALT level above 3 time upper limit of normal i.e. 50.00. While stratifying the ATDIH with regards to age, we observed that most of the patients who developed ATDIH were in the age group less than 12.00 years. On applying chi square test, the difference of ATDIH with regards to different age groups was statistically significant having a p value of 0.007. While stratifying the ATDIH with regards to gender, we observed that most of the female children developed as compared to male children. However, on applying chi square test, the difference of ATDIH with regards to gender was statistically insignificant having a p value of 0.192. While stratifying the ATDIH with regards to baseline serum ALT levels, we observed that most of

the children who developed ATDIH were in the group having baseline serum ALT level above 30.00 and advanced as the level increased. On applying chi square test, the difference of ATDIH with regards to baseline ALT level was statistically significant having a p value of 0.000.

DISCUSSION

All pharmacological interventions balance efficacy and toxicity; there are few efficacious agents that do not have some toxicity risk. In the case of anti-tuberculosis agents the major risk is hepatotoxicity and three agents identified by World Health Organization as essential, isoniazid (INH), rifampicin (RMP) and pyrazinamide (PZA), carry such a risk. In view of recent recommendations for increased dosages of INH (5–15 mg/kg), RMP (10–20 mg/kg) and PZA (30–40 mg/kg) for children.^{13–14} Frydenberg et al reviewed the toxicity of first line drugs for treatment of tuberculosis in children and concluded that children tolerate anti-TB drug severity well when using the standard recommended dosages.¹⁵ Liver being an important organ of drug metabolism is susceptible to drug induced injury and all 3 essential first line anti-tubercular drugs (isoniazid, rifampicin and pyrazinamide) can cause liver damage.^{16,17} The severity of liver damage varies from asymptomatic rise in liver enzymes to fulminate hepatic failure and death. Drug induced hepatotoxicity may be predictable and dose related in which all recipients will develop toxicity in a higher than recommended dose within fixed period of exposure or non-predictable drug toxicity, observed in few patients over variable period of use.¹⁸

Diagnosis of ATDIH is based on temporal relationship between drug intake and onset of symptoms, clinical features specific to particular drug and recovery of hepatic dysfunction on withdrawal of particular drugs.^{15,19,20} ATDIH is the major risk and if develops then warrants investigation and immediate withdrawal of all hepato-toxic drugs with substitution of alternative drugs.^{21–22} So it is important not only to monitor for clinical improvement but also for drug toxicity. This will help in early diagnosis and management since it is one of the reasons for ATT failure. The frequency of ATDIH varies depending upon a number of factors including age, weight and nutritional status, inter-current acute hepatitis, pre-existing liver diseases, severity of tuberculosis; and dosage and duration of ATT drugs.^{17,19,20,23,24} Amongst children treated for tuberculosis disease a different picture emerges as compared to adults. Although a similar proportion of children experience increased serum transaminase values, a considerably larger proportion presented with jaundice than amongst those managed for latent infection; this proportion varies from less than 1–50% in some studies of children treated for TBM. Several factors may be important in this regard. Disease severity plays a role in the frequency of ATDIH^{17,25} and underlying hepatic ab-

normalities^{26,27} before the start of treatment, especially in disseminated forms of tuberculosis, may be relevant in this regard; a large proportion of children will also have abnormal LFT before treatment. This is particularly likely in children with disseminated disease that might accompany Tuberculous meningitis.

We found that overall 26.9% of patients developed ATDIH and all during initial intensive phase of treatment. This is slightly higher than the previously reported mean incidence of 10% (8–39%) in a review by Donald PR in which has pointed out that among 8984 children treated for TB excluding TBM, 380 (9.9%) developed abnormal liver functions and in another group 717 children treated for TBM, jaundice was noted in 72 (10.8%) and abnormal liver tests were demonstrated in 172 cases (52.9%).²⁰ The frequency of 26.9% of ATDIH in our study is also slightly higher than two local studies in adults in which reported frequency varies from 8.4 – 20%.^{28,29} Most recent study in children from India has reported ATHID as 15.2% (n=7) among 46 children.³⁰ Drug induced liver injury in children constituted for 8.7% among 450 cases of ATDIH and combination anti-tuberculosis drugs were the most common cause (n=22) followed by anticonvulsants and 41% (16 patients) had of the studies report ATDIH during the initial intensive phase.^{18,28,29,31} Very young age and old age has been identified as risk factor for ATDIH.^{23,24,32} Mean age of patients who developed ATDIH in our study was 7.77. \pm 2.7 years which is lower than mean age of 16 yrs as reported by Devar-bhavi et al³³ but nearly close to 5.88 + 3.74 yrs in a recent study from India.³⁰ Young age (<3.5 yrs) has been found as vulnerable age group by Mansukhani but this was not observed in the present study.³⁰ In our study, ATDIH was more common in boys (59.7%) as compared to girls which are in contrast to a recent Indian study by Mansukhani et al in which only 20% of boys developed ATDIH compared to 11% in girls.³⁰

Although not reported in our series, but isoniazid has been reported to be major drug responsible for ATDIH.¹⁸ Main factor causing isoniazid hepatic toxicity is formation of hydrazines by the action of P450 enzymes, these hydrazines get bound to liver proteins resulting in hepatic damage. High dose of INH is not associated with risk of isoniazid associated hepato-toxicity. However, slow acetylation increases the exposure for longer duration and may result in increased risk of INH induced hepatotoxicity.¹⁸ In addition to acetylating, other factors like malnutrition viral hepatitis or preexisting liver disease as well advanced tuberculosis like TBM increases the risk of hepatotoxicity.^{32–34} Malnutrition is rampant in our country and in a recent report by Siddiqui et al showed that 51% of TB patients were malnourished.³⁵ But in a most recent study from India, the association of hepatotoxicity with malnutrition was not found.³⁰ The role of acute viral hepatitis has been documented from India that it may be a com-

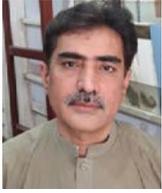
plicating factor in 10-15% of cases of ATDIH.^{19,24} However; we have excluded the cases of acute viral hepatitis as well as pre-existing liver diseases in the present study. Memon et al and Balouch et al in their studies on 215 and 119 adult patients reported that 18 (8.4%) and 26 (22%) patients developed ATDIH respectively. Our figure of 26.9% is higher than both Memon and Balouch et al; both studies are from adult population.^{27,35} Generally, it is said that ATDIH is much less in children compared to adults. Isoniazid was responsible for 5.4% (11 cases) followed by rifampicin (2, 0.9%).^{15,19} Rifampicin induces P450 enzymes thus it increases risk of INH induced hepato-toxicity, the reported hepato-toxicity rates due to rifampicin alone is 1%.²⁸ We have not observed mortality in this study as reported by others. A high mortality rates have been reported due to ATDIH and frequency varies from 1-50%.^{30,31,33} This is likely to be due to the close monitoring and withdrawal of culprit drugs and switching to alternative safer drugs.

CONCLUSION

Anti TB drug induced hepatitis is a common occurrence in our population of children who are subjected to routine anti TB treatment for pulmonary tuberculosis. In our study, we didn't take into account the risk factors which are involved in developing ATDIH, we recommend further larger studies also recording the risk factors for ATDIH before further recommendations can be drawn.

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Management of Acute Scrotum in Children at Pediatric Surgery Unit, Medical Teaching Institute Lady Reading Hospital Peshawar

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ABSTRACT

Objective: Acute scrotum is an emergency condition needs early intervention. The aim of our study has been to evaluate the findings in boys operated on acute scrotum.

Method and material: Descriptive study was conducted on 100 patients less than 14 years with acute scrotum admitted to MTI/LRH Peshawar from June 2016 to May 2018 data included history, age, primary symptoms/sign definite diagnosis, side involvement, clinical tests, imaging modalities, medical/surgical management and type of surgery.

Results: Diagnosis was made mainly by clinical signs and symptoms and surgical exploration. spermatic cord torsion (n=40) was the most common cause of acute scrotum, followed by incarcerated inguinal torsion (n=25) of testicular appendage (n=20) epididymo orchitis (n=10), idiopathic scrotal oedema (n=2), hematocele (n=3). Most 35% of patients were in the first year of life and the mean age was 5.5 years. the commonest signs were pain and swelling (70%) followed by pain, swelling and redness 20% and pain alone (15%). 60 patients consisting torsion of spermatic and torsion of testicular appendage, 25 patients with incarcerated inguinal hernia and 10 patients with epididymo orchitis underwent surgical exploration after care full physical examination. 10 out of 40 patients with torsion of testis had orchidectomy and orchidopexy of contralateral testis and the rest had detorsion and bilateral orchidopexy. 80% of the patients were referred to the hospital offer 12 hours of clinical onset of symptoms

Conclusion: Early exploration of acute scrotum based on care full physical examination is a relatively safe and simple procedure with good cosmetic results. It also allows an accurate diagnosis to be made.

Key words. Pediatric case, scrotal swelling, testicular torsion, epididymo -orchitis.

INTRODUCTION:

The acute scrotum is defined as scrotal pain, swelling and redness of acute onset¹. This is a serious condition because there is a risk of loss of testicular function. Acute pediatric scrotal pain sometimes requires prompt surgical intervention and there for accurate diagnosis of different etiologies of acute scrotal pain has great therapeutic and prognostic significance². In clinical practice, acute testicular torsion accounts for 70-80% of acute pediatric scrotum at presentation³. Torsion accrued when an abnormally mobile testis twists on the spermatic cord, obstructing its blood supply⁴. Patients present with acute onset of severe testicular pain. The ischemia can lead to testicular necrosis if not corrected within 5-6 hours of the onset of pain⁵. The in-

cidence of spermatic cord torsion among patients with acute scrotum varies from 20-60% depending on the age of patients, the type and location of the hospital, and the methods of diagnosis⁶. The incidence of torsion in children younger than 18 years is approximately one in 4000⁷.

Early exploration of acute scrotum based on careful physical examination is a relatively safe and simple procedure with good cosmetic results. It helps in confirming accurate diagnosis.

The pediatric acute scrotum can present right from the new born to adolescent patients. The peak incidence of pediatric testicular torsion is bimodal with the main peak between 12-18 years and smaller peak in the first year of life⁸. In a recent large study by Zhao et al⁹, looking at the incidence of testicular torsion confirmed that testicular torsion is uncommon but the rate of orchidectomy is high, especially in the youngest patients. Additional causes of the acute scrotum include of testicular appendage (hydatid of Morgagni), epididymo orchitis, idiopathic scrotal oedema, acute hydrocele, incarcerated hernia, and Henoch-schonlein purpura¹⁰.

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Torsion of testis or spermatic cord is undoubtedly the most serious affecting the scrotum that needs urgent diagnosis and treatment to save the affected testis and avoid testicular loss, fertility problem and medicolegal issues¹¹.

Testicular loss commences past twelve hours of initiation of symptoms. Beyond 24 hours of symptoms testicular loss will definitely happen and this is the main reason why in the absence of ancillary studies, surgeons immediately explore the acute scrotum¹². The two most common used preoperative studies are testicular scan and color Doppler ultrasound¹³. Testicular scans reliably show whether the testes have vascular flow or not, but are difficult to be obtained¹⁴. Doppler ultrasound is operator dependent and when done by experienced physician, can help reduce the number of emergency operations and hospitalization stay¹⁵. Clinical judgment by the surgeon is probably the most important factor in assessing testicular salvage. In the face of doubt the next step in management is immediate surgical exploration. Definite diagnosis of testicular torsion mostly can be confirmed by prompt scrotal exploration. Prognosis is good when detorsion of the affected testis is performed within first 6 hours¹⁶. The aim of this study was evaluate the role of early exploration in the management of acute scrotum, testicular torsion as the most common emergency in acute scrotal condition and often causes of common acute conditions such as torsion of testicular appendage, epididymo-orchitis and idiopathic scrotal oedema in patients reported to emergency department of MTI/LRH Peshawar during June 2015 – May 2018

METHODS AND MATERIAL:

This descriptive study was conducted on patients less than 14 years with acute scrotal pain or swelling referred to emergency/OPD pediatric surgery department MTI/LRH Peshawar, during June 2016 – may 2018. A total of 100 patients were evaluated in this study and a proforma was made for each case to collect the data in term of age, primary symptoms/sign, initial diagnosis, final diagnosis, side involvement, surgical treatment, conservative management, clinical presentation, time of hospital stay, orchidectomy, contralateral testicular fixation, complete blood count, urine analysis and other diagnostic tools, to evaluate the findings in children operated on acute scrotum.

RESULT:

100 patients were included in this study, aged one day to 14 years out of 60 patients with testicular torsion and appendix torsion, 20 patients had W.B.C count less than 1x10 10/1. Out of 10 patients with epididymo orchitis. 5 patients had W.B.C count from 1x10 10/1 through 1.5x10 10/1 W.B.C count greater than 1.5x10 10/1 was found in 53.3% of patients with incarcerated inguinal hernia. Most (34%) of the patients were in the

first of life (table I). the commonest signs were pain and swelling (60%), Pain swelling and redness (20%) and pain alone (15%), fever and vomiting was the less common (4%) symptoms in our patients (Table 2)

Table I: Age of patients with acute scrotum in MTI/LRH (2016-2018)

Age	Numbers	Percentage
0-1 year	34	34%
1-5 years	30	30%
5-10 years	20	20%
10-14 years	16	16%
Total	100	100%

Table II Primary signs/symptoms of patients with acute scrotum

Primary Symptoms/sign	Numbers	Percent
Pain & Swelling	60	60%
Pain+Swelling+redness	20	20%
Pain	15	15%
Fever	3	3%
Vomiting	1	1%
Total	100	100%

The diagnosis of 83 patients treated surgically were as follow: Torsion of testis 40, incarcerated inguinal hernia 25, torsion of testicular appendage 20, epididymo orchitis 10, and only 2,3 patients had idiopathic scrotal oedema and hematocele respectively. in 10 out of 40 patients with testicular torsion orchidectomy and contralateral orchidopexy was performed. In these 10 patients one was referred at the age of one month and with the duration time of 6 hours and others after 48 hours of onset.

In 14 out of 20 patients with torsion of testicular appendage surgical intervention was performed and appendectomy + ipsilateral orchidopexy carried out. A herniotomy was performed in 20 patients. other procedures were carried out in 5 patients. The post operative hospital stay ranged from 48 to 72 hours for more than half of the patients. Urine analysis was normal in 80% of patients. Abnormal urinary findings were found in 27 cases. Hematuria was found in 4 cases and all of them had epididymo orchitis. Hematuria pyuria was found in 4 cases and all of them had epididymo-orchitis. Pyuria was seen in 13 patients. Out of these patients 6 had epididymo orchitis; 4 patients had incarcerated inguinal Hernia; one patient had testicular trauma and 2 patients had testicular torsion. Other patients had normal urinary findings. Most of the patients with abnormal urinary findings had epididymo orchitis. Only 20 patients (9%) out of our 100 patients had pre operative ultrasonography. Sonography findings were not consistent with the final diagnosis. A positive sonographic finding was significantly higher

in patients with epididymo-orchitis compared with those with torsional disease. Doppler sonography was performed in 4 patients of these, 3 patients had findings consistent with the final diagnosis of torsion. In the rest of patients, sonography findings suggested torsion but the final diagnosis was epididymo orchitis. 50 patients (50%) with acute scrotum were referred to our hospital within 24 hours, 80% of which were treated surgically over 12 hours, and all of them had pain and swelling. In 50 patients clinical manifestation lasted greater than 18 hours. In 87 patients clinical manifestation were present from 12 to 18 hours.

Table III Etiology of acute scrotum.

Etiology	Numbers	Percentage
Torsion of spermatic cord	40	40%
Incarcerated Inguinal Hernia	25	25%
Torsion of testicular appendage	20	20%
Epididymo-orchitis	10	10%
Idiopathic scrotal oedema	2	2%
Hematocele	3	3%
Total	100	100%

DISCUSSION:

The most common symptoms in our series was pain and swelling (60%) to whereas in the series of Grandis et all with 33 patients, pain alone was the predominating symptom ¹⁶. Urinalyses were mostly normal in our patients, and diagnosis generally was established by clinical symptom and careful physical examination. Patients usually presented with scrotum pain. The duration of symptoms was shorter in testicular torsion (69% within 12 hours) compare to torsion of the appendix testis (62.7%) and acute epididymo orchitis (31%)¹⁷. In our study 50 (50%) patients with acute scrotum was referred to our hospital within the first 24 hours, 80% of which were treated surgically over 12 hours, pain and swelling.

Sidler et all¹⁸, in 1997 reported their series in which the most common (32%) etiology was testicular torsion, 70% in left testis, 31% torsion of testicular appendage and epididymo orchitis in 28% of the patients. Whereas in our series common etiology was torsion of spermatic cord (40%), torsion of testicular appendage (20%) and epididymo-orchitis (10%). In sidler series orchidectomy was performed in 61.2% within 24 to 48 hours of clinical onset, in our study it occurred in 10 (10%) patients within 12 to 24 hours and that was due to earlier diagnosis and surgical management¹⁸.

Mean age of patients in Sidler’s series for testicular torsion was 6.3 years and for torsion of testicular appendage it was 10 years, in our series it was 3 and 8.8 years respectively. Early diagnosis was the clue of successful management when a child is referred for scrotal redness and swelling, early surgical intervention is mandatory. Even in cases of torsion of testicular appendage, sur-

gical management is suggested, not to miss torsion of testis¹⁹. Sonography is the imaging modality of choice for the scrotum because it is simple, relatively inexpensive and quick (Carkaa S, et al)²⁰. Doppler ultrasound is able to differentiate between surgical emergencies and other etiologies. Schalamon. J et all reported 84% success in this differentiation²¹. Galejs et al in 1998 suggested that doppler sonography is very effective in torsion diagnosis, the accuracy being sometimes even 100%²². Radio-isotope is a useful diagnostic tool for acute scrotum²³. As pain and swelling of scrotum are the most common symptom is testicular torsion. and also there are paucity of diagnostic tool. So some studies early surgical exploration, as we have done this for the indicated patients in our study²⁴.

CONCLUSION:

Early exploration of the scrotum with care full physical examination excludes the risk of misdiagnosis and unnecessary delay by diagnostic techniques. Exploration of the scrotum is relatively safe and simple procedure which allows an accurate diagnosis to be made.

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Sami Ullah

Efficacy of Ampicillin plus Gentamicin with Ampicillin plus Cefotaxime in the Treatment of Suspected early Neonatal Sepsis

Sami Ullah FCPS¹, Haroon ur Rashid FCPS²,Bilal Khan FCPS(Ophth) FCPS(Vitreo Retina)³, Irfan Ullah MBBS⁴**ABSTRACT**

Objective: To compare the efficacy of ampicillin plus gentamicin with ampicillin plus cefotaxime in the treatment of suspected early neonatal sepsis

Materials and methods; This randomized controlled Trial was conducted in the Department of Pediatrics, Lady Reading Hospital, Peshawar from 1st April, 2013 to 20th October 2013 total 6 months and 20 days duration. All neonates with clinical suspicion of early onset neonatal sepsis presenting within 7 days after birth with either gender were included in the study while neonates who have received antibiotic of any type after birth were excluded from the study. Patient's particulars and data variables were documented according to the predesigned proforma. SPSS version 16 was used to analyze the data and tables were used to represent the data.

Results: 156 patients with suspected neonatal sepsis were included. Male to female ratio 1.36:1 Average age was 109.55 hours+ 56.94SD. Group A showed 69(88.5%) efficacy while non-effective in 9(11.5%) patients. Similarly Group B showed 59(75.6%) efficacy.

Conclusion: Ampicillin plus gentamicin is more effective than ampicillin plus cefotaxime for the Treatment of suspected early neonatal sepsis.

Key words: Efficacy, Neonates, Neonatal Sepsis, Ampicillin, Gentamicin, Cefotaxime.

INTRODUCTION

Neonatal infections are the leading cause of death among neonates and neonatal sepsis (NS) which keeps raising the red flag of remaining a major contributor to the neonatal morbidity and mortality¹. Neonatal sepsis is a global problem. Every year around 30 million neonates develop infections and 1-2 million of these neonates die². In developing countries mortality from neonatal sepsis is 10.4%, higher than that in the developed countries, with an incidence of 0.69 deaths/1000 live births³. The statistical data from Pakistan is largely unavailable but in India according to the data from National Neonatal Peri-natal Database, the incidence of neonatal sepsis is 30 per 1000 live births and it accounts for 30-50% of total neonatal deaths in developing countries. This sepsis related mortality can be lowered by adopting aggressive approach towards this disease⁴. Neonatal sepsis is a systemic inflammatory response to an infectious process with non-specific signs and

symptoms or focal signs of infection. It carries potentially fatal complications affecting major organ systems including cerebral edema or thrombosis, adrenal hemorrhages, bone marrow dysfunction and disseminated intravascular coagulation⁵. Without treatment the case fatality rate is high. Thus with non-specific initial presentation a high index of suspicion should always be kept for early diagnosis and favorable outcome⁶.

Ampicillin plus gentamicin is more effective than ampicillin plus cefotaxime for the treatment of suspected early neonatal sepsis.

Neonatal Sepsis is divided into two categories i.e. early neonatal sepsis (EOS) which occurs within first 7 days of birth (E Coli and Group B streptococci predominant culprits) and late neonatal sepsis which occurs after 7 days of life with (coagulase negative staphylococci and staphylococcus aureus predominant culprits)⁷. Risk factors for neonatal infection within the first 72 hours of life are well recognized and include maternal chorioamnionitis, advanced maternal age, high gravidity and prolonged rupture of membranes (PROM), maternal group B streptococcal (GBS) infection or colonization, and poor uptake of breastfeeding⁸. In the absence of sensitive and specific biomarkers of infection and lack of consensus on the interpretation of available markers, initiation of antibiotic therapy is still largely based on clinical judgment. Many facilities caring for neonates

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have established management guidelines to facilitate empirical antibiotic use^{9,10}. Regarding treatment of nosocomial infections with antimicrobials, the likely causative organisms, their antibiotic susceptibilities and the relative cost-effectiveness of available drugs and their side effect profiles should all be considered when developing guidelines¹¹ while the majority of studies of neonatal sepsis focus on causative organisms and prevention, there are few data on antibiotic use¹². As sepsis may be culture-negative and blood cultures may not be done routinely in secondary level facilities, the choice of antibiotic use may be a reasonable way to assess the extent and treatment of neonatal infection¹⁰ and a recent Cochrane review revealed the lack of randomized controlled trials in favor of a particular antibiotic for neonatal sepsis¹³.

The antibiotics routinely used in different clinical settings for the treatment of early neonatal sepsis included ampicillin, amoxicillin, aminoglycosides, cephalosporins and vancomycin. WHO has generally recommended the use of parenteral benzylpenicillin with aminoglycoside for EOS¹⁴ however, aminoglycoside have the potential to cause ototoxicity and nephrotoxicity and should be used with caution. Cephalosporins are attractive in the treatment of nosocomial infection because of their lack of dose-related toxicity and adequate serum and cerebrospinal fluid (CSF) concentration. Traditionally, the choice of antimicrobial agents is based on the local policy, and the duration of therapy is decided by the treating physician based on clinical symptoms and blood culture results¹⁵. In one study 80.8%¹⁶ of neonates with clinical suspicion of early onset neonatal sepsis recovered with ampicillin plus gentamicin while another study reported it to be 86%¹⁷. The projected effectiveness of ampicillin with cefotaxime reported in literature is 94% (79% for cefotaxime monotherapy)¹⁸.

Cefotaxime and ampicillin are commonly used as a substitute for ampicillin and gentamicin for the presumptive treatment of EOS. However, there appears to be an increased risk of death with the use of ampicillin and cefotaxime¹⁹

MATERIALS AND METHODS

The study was conducted after approval from hospitals ethical and research committee. All neonates presenting to neonatal ICU within 7 days after birth with high suspicion of EOS (as per operational definitions) were included in the study. The purpose and benefits of the study were explained to the parents of the neonate, they were assured upon the purpose and benefits of the study, the risks involved and they were explained that the study is done purely for research and data publication and if agreed upon a written informed consent were obtained from the parents of the neonate. All the neonates were subjected to detailed history and clinical examination. The neonates were randomly

located in two groups by lottery method. Neonates in group A were subjected to the combination of IV ampicillin (100mg/kg/day) plus IV gentamicin (5mg/kg/day) while neonates in group B were subjected to combination of IV ampicillin (100mg/kg/day) plus IV cefotaxime (50mg/kg/day). The rest of the treatment were kept uniform for all the neonates as per NICU guidelines and were decided by single expert pediatrician having minimum of five years of experience. All the neonates were followed till the 7th day of initiation of therapy to determine the efficacy of the combination therapy according to operational definition mentioned above. All the laboratory investigations were reported by single experienced pathologies having minimum of 5 years of experience. All the above mentioned information including name, age and gender were recorded on a pre designed proforma. Strictly exclusion criteria were followed to control confounders and bias in the study results.

All the collected data were analyzed in SPSS version 16. Mean + SD were calculated for numerical variables like age of the neonate at presentation. Frequencies and percentages were calculated for categorical variables like gender and efficacy. Efficacy in both the groups was compared by chi square test while keeping P value of < 0.05 as significant. Efficacies in both groups were stratified among age and gender to see the effect of modifications. All results were presented in the form of tables and graphs.

RESULTS

A total of 156 patients of suspected early neonatal sepsis were observed, which were divided in two equal groups A & B. Patients in Group A were managed with Ampicillin plus gentamicin and the patients in Group B with ampicillin plus cefotaxime. Sex wise distribution shows that out of 78 patients 48(61.5%) were male and 30(38.5%) were female while group B contains 42(53.8%) male and 36(46.2%) were female. Male to female ratio was 1.36:1. Sex distribution among the groups was insignificant with p-value=0.331. Average age was 109.55±56.94 hours with range of 24-208 hours. Group A contained 15(19.2%) patients in less than or equal to 50 hours, 25(32.1%) patients 51-129 hours and 38(48.7%) patients between the ages of more than 130 hours. While group B contained 22(28.2%) patients in less than or equal to 50 hours, 29(37.2%) in 51-129 hours and 27(34.6%) patients with age more than 130 hours. The age distribution among the group was also insignificant with p-value 0.175.

Efficacy wise distribution was significant with p-value = 0.030. Group A showed 69(88.5%) efficacy while non-effective in 9(11.5%) patients. Similarly Group B showed 59(75.6%) efficacy while non effective in 19(24.%) patients, although efficacy was significant and the Group A have greater efficacy than Group B. (Table 1). Age wise distribution of drug-efficacy shows that efficacy was greater in smaller age group and de-

creases with the increase of age. The patients having less than or equal to 50 hours of age have shown efficacy in 31(83.8%) patients while 6(16.2%) patients being non-effective. Patients with 51-129 hours of age have shown efficacy in 47(87%) of patients and 7(13%) have shown no efficacy. Similarly 50(76.9%) patients have shown efficacy and 15(23.1%) patients have no efficacy, with age more than 129 hours of age. The efficacy was insignificant with p -value=0.342. When efficacy was stratified among the gender it showed insignificance with p -value=0.555. There were 74(82.2%) male patients showing drug efficacy while non-effective in 16(17.8%) male patients. Similarly in female patients, 54(81.8%) gave efficacy while 12(18.2%) showed no efficacy.

DISCUSSION

Neonatal sepsis is the major and common cause of morbidity and mortality. The incidence is much higher in the developing world. Early diagnosis and effective treatment is the best way to lessen the mortality and morbidity associated. The delay in diagnosis and initiating therapy are the main reasons for high mortality. Despite great development in diagnostic and therapeutic procedures, neonatal sepsis still remains a major medical problem with a high morbidity and mortality rate²⁰⁻²¹. It represents for 30-50% of all neonatal deaths in developed countries²², while afflicting up to 10% of the neonate²³. Choosing the appropriate antibiotic drug for the empirical therapy should be based on the most frequent pathogens and the antimicrobial sensitivity in each hospital²⁴, because the frequency of pathogens may differ not only between various hospitals²⁵ but also between various times in a same hospital^{26,27}. Combination of Ampicillin and Aminoglycoside or Ampicillin and a third generation of Cephalosporins has been suggested as the drug of choice for neonatal sepsis²⁸. Thus, the regimens of ampicillin+amikacin or ampicillin+cefotaxime are the most commonly used antibiotics in our neonatal wards and Neonatal Intensive Care Unit (NICUs)²⁹. Although aminoglycoside achieves its bactericidal level very soon, it is associated with renal and ear toxicity³⁰. Neonatal sepsis must be treated with the first suspicion before determination of the responsible pathogen. Finding a surrogate antibiotic instead of the routine usage of ampicillin + amikacin or ampicillin + cefotaxime is necessary before appearing of bacterial resistance³¹.

Several studies about the effectiveness of ceftizoxime in the treatment of neonatal sepsis showed significant results^{32,33}. Ceftizoxime as a new third generation of cephalosporins has a broad spectrum effect on gram negatives like *E.coli*, *Klebsiella* species, *Proteus mirabilis*, *Hemophilus influenza* and *Anaerobes*. In addition to these effects, it covers streptococcal species, *Staphylococcus aureus* and has a good penetrance in cerebrospinal fluid³⁴. Our study also show significant difference between

the effectiveness of the two pairs of antibiotics. However 88.5% of the neonates who underwent antibiotic therapy by ampicillin plus ceftizoxime responded to the treatment and only 11.5% were non-responders who underwent other antibiotic regimens. Yamauchi et al., in a study on the effectiveness of ceftizoxime in the treatment of neonatal sepsis, reported an effectiveness of 90% for the drug³³. In another study ceftizoxime was reported to be effective in 87.5% of the patients; our results were comparable with both studies³⁴. Efficacy of combination therapy with ampicillin + amikacin in treatment of neonatal sepsis was reported to differ between 61% for *E. coli* to 100% for *Serratia*, with a mean of 70% for neonatal sepsis generally³⁵. A study from Kashan province (Iran) showed a comparable efficacy of 69% for combination of ampicillin and amikacin³⁶. Our study resulted in 88% efficacy for the combination (Ampicillin plus gentamicin) which was more than previous studies. In a recent study from Jordan, gram negative bacteria isolated from septic neonates were highly resistant to Ampicillin (82.8-100%), Gentamicin (41.4-79.5%), Ceftazidime (46-50%) and Piperacillin-Tazobactam (21.4-54.3%)³⁷. Only Imipenem and Ciprofloxacin showed good sensitivity. In the United States, resistance to ampicillin is the main concern (57%) for the gram negative bacteria that they have isolated³⁸. In Iran, *Klebsiella* isolates from neonates showed 100% resistance to ampicillin, 31% resistance to ceftriaxone, 46% resistance to Amikacin and 27% to gentamicin.³⁹ Dr. Darmstadt has recommended the following first line therapy in facility settings: for early and late sepsis: ampicillin and gentamicin; for early-onset meningitis: ampicillin plus gentamicin; and for late onset meningitis: ampicillin, gentamicin (or amikacin), and/or cefotaxime.³⁵ In Iran, some experts advocate using a third generation cephalosporin for treating *E. coli* and *Klebsiella* infections, and Vancomycin for *Staphylococcal* infections.⁴⁰ Clark et al., found that the mortality rate in neonates underwent treatment with ampicillin + cefotaxime was higher than those receiving ampicillin + gentamycin concluding that using the combination of ampicillin and cefotaxime in the first 3 days of birth might increase the risk of neonatal death²⁴. As ceftizoxime and cefotaxime are both a third generation cephalosporin, it is considerable that the concurrent use of ampicillin and ceftizoxime may also increase the risk of neonatal death. On the other hand several studies have shown the effectiveness of ceftizoxime in neonatal sepsis³³⁻³⁴.

CONCLUSION.

On the basis of our study results, we suggest that we should adopt giving ampicillin plus gentacin as 1st line empirical antibiotics in all our neonatal units, instead of ampicillin plus cefotaxime. We also suggest that more large scale Randomized Controlled Trials should be conducted to support our conclusion.

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Salva Shah

An audit of Fresh Frozen Plasma (FFP) Issuance in Tertiary Healthcare Level of KPK

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ABSTRACT

Objective: There is a universal concern about the inappropriate use of fresh frozen plasma. This study was done to determine the extent of unjustified use of fresh frozen plasma at tertiary healthcare level of Mardan.

Materials and Methods: A retrospective audit was conducted in Mardan Medical Complex and 100 consecutive requisitions forms for FFP during May to July 2018 were reviewed. Demographic data of patients, provisional clinical diagnosis, indication for FFP, department of requesting clinician, number of units transfused and coagulation profile were noted. The transfusion episode was classified as justified and unjustified according to BCSH guidelines.

Results Total 248 units of FFPs were transfused for 100 patients. Obstetrical and Gynaecology department requested the greatest amount (54 patients, 135 units). Most common justified indication for FFP use was massive transfusion followed by DIC. Most common unjustified indication for FFP transfusion was postoperative bleeding with normal coagulation profile. 60% of FFP issuance was justified in this study whereas 40% was unjustified.

Conclusion: The high rate of unjustified use of FFP transfusions indicates the need for strategies to improve transfusion practices. Periodic audit and training sessions for clinical specialities should be conducted about rational use of blood component.

Key Words: Fresh frozen plasma (FFP), transfusion, coagulation, disseminated intravascular coagulation (DIC)

INTRODUCTION

There is a shortage of blood and its components in the developing world. The resources are limited in terms of meeting the growing demands of blood components. Appropriate use of blood components is therefore required for ensuring their availability for needy patients as well as to avoid the unnecessary risk of transfusion transmitted diseases⁽¹⁾. Fresh frozen plasma (FFP) is a component separated from whole blood and frozen to 30C or below within 6 hours after collection. It is a good source of all coagulation factors including the labile factors V and VIII and plasma proteins⁽²⁾. It is life

saving in multiple conditions as patients with coagulopathy resulting from DIC, in patients of liver failure with active bleed, and in patients of thrombotic thrombocytopenic purpura (TTP)⁽³⁾. However there are many instances such as specific factor deficiency, as well as patients needing volume expansion, where FFP use is controversial.

The high rate of unjustified use of Fresh Frozen Plasma (FFP) transfusions indicates the need for strategies to improve transfusion practices. Periodic audit and training sessions for clinical specialties should be conducted about rational use of blood component.

FFP is conventionally prepared in the blood bank in the following manner ; fresh plasma is separated from donated whole blood, collected in citrate-phosphate-dextrose (CPD) solution, after centrifugation and subsequent removal of plasma (approximately 250 ml) within 4-6 hours after blood collection and then is frozen immediately at -40 C or lower⁽⁴⁾. The usage of FFP has significantly increased over the past few years despite the fact that plasma derived from allogeneic blood donation is finite and not risk free. FFP exposes patients to risk of transfusion transmissible diseases, allergic re-

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actions and haemolytic reactions caused by A and B antibodies. Rarely, antibodies against the patient's granulocytes may cause leukocyte aggregation in pulmonary vessels leading to transfusion related acute lung injury (TRALI Syndrome)^(5,6). Moreover excessive usage can lead to shortage in times of need as well as reduced availability for the production of albumin and immunoglobulins. Therefore, there is a need to use FFP only for specific indications. Monitoring FFP utilization is important to reduce not only all the above-mentioned risks and disadvantages but also wastage and cost. The aim of this study was to audit the clinical use of FFP against BCSH guidelines.

METHODOLOGY

We conducted a retrospective audit of FFP transfusion in Mardan Medical Complex which is a tertiary care hospital with 520 beds. This study was conducted during May 2018 to July 2018. Prior to the study, the approval was taken from the ethical board. 100 consecutive requisition forms during this time period were reviewed and data was collected. The component issue records available in the blood bank were initially scrutinized to identify the patients who had received FFP transfusions in 3 months from June 2018 to August 2018. Age, gender, ward requesting, primary diagnosis and indication for FFP transfusion was noted. We evaluated all FFP transfusions classifying them as justified and unjustified.

The audit of FFP use was evaluated according to the rules in British Committee for Standards in Hematology (BCSH). Data was analysed using SPSS.

Table-I: Criteria for the use of fresh frozen according to BCSH guidelines. Clinical indications for use of FFP.

Single-factor deficiencies where a specific or combined factor concentrate is not available.
Multiple-factor deficiencies and/or disseminated intravascular coagulopathy. Thrombotic thrombocytopenic purpura.
Need for urgent reversal of warfarin effect.
Following massive transfusion in presence of bleeding and prolonged coagulation.
Liver disease in presence of bleeding or prolonged prothrombin time (PT)-partial thromboplastin time (PTT)-international normalized ratio (INR) in the settings of invasive procedures.

RESULTS

A total of 248 units of fresh frozen plasma were issued for the 100 patients in our study group, including 44 males and 56 females with a mean age of 37 years (range 1-60 years). FFP was most commonly transfused in the patient age group of 19 to 38 yrs. Obstetrics and Gynaecology department requested most of the units of FFP (54 patients 135 units), followed by Medicine and Emergency departments. The most common justified indications for FFP use were massive transfusion,

followed by DIC. FFP transfusion was justified in 60 patients accounting to 150 Units. 40 patients received unjustified transfusion of FFP accounting to 98 Units.

Department wise distribution

DEPARTMENT	NUMBER OF FFP TRANSFUSIONS	PERCENT OF FFP UNITS CONSUMED
Obstetrics and Gynaecology	53	135 units (54.4%)
Medicine	26	60 units (24.1%)
Accident and Emergency	12	32units (12.9%)
Paediatrics	5	10units (4%)
Surgery	4	11units(4.4%)

Indications for fresh frozen plasma

Indication	No. of transfusion episodes
Justified Use	
Massive transfusion	38
DIC	6
Liver disease	5
Factor deficiency	5
Postoperative bleeding with deranged coagulation profile	4
Warfarin reversal	2
Unjustified Use	
Surgery related with normal coagulation profile	13
Hypoproteinemia	10
Hypovolemia	8
Bleeding with normal coagulation profile	6
Dengue fever	3

DISCUSSION

There are concerns regarding non-availability of blood components and transfusion-transmitted infections in developing countries, which makes it crucial to optimize FFP transfusions and reduce wastage. The situation is more critical in Pakistan where there is frequent shortage in blood supply, blood banks are not well regulated, poor blood testing facilities, relatively high frequency of transfusion-transmittable infections among apparently healthy individuals and hospital audit mechanisms are weak⁽⁸⁾. Sufficient guidelines and recommendations for the transfusion of FFP are available in medical literature, although mostly from other countries, but FFP usage remains often misused. Numerous studies have highlighted the need for and proven benefit of auditing the use of blood products as a reliable tool to uncover not only their inappropriate use but also to monitor the extent of compliance with the set guidelines for the use of these products^(9,10,11). In this study FFP transfusion was justified in 60% of

cases as per BCSH guidelines. A large proportion (40%) of transfusions were unjustified which was in accordance with other studies done worldwide. The percentage of justified use of FFP ranges from 31% to 63% worldwide⁽¹²⁾.

Massive transfusion was the most common appropriate indication for FFP transfusion followed by DIC and then chronic liver disease.

Bleeding related to surgery with normal coagulation profile were the most common inappropriate indication for FFP use followed by hypoproteinemia and hypovolaemia. FFP administration as volume expander or as nutritional supplement is not justified. Safer alternatives, such as crystalloids, synthetic colloids or human albumin solutions are available to serve purpose⁽¹³⁾. High cost of human albumin discourages its use in hypoproteinemia in developing countries. Efforts are therefore needed to establish infrastructure for large scale production of albumin in the country. In our study 10% of FFP transfusions were done for hypoproteinemia and 8% for hypovolemia. A previous study done by Nagarekha Kulkarni in 2012 showed incidence of FFP transfusions for hypoproteinemia and hypovolemia as 8% and 6% respectively⁽¹⁴⁾. The standard coagulation testing was mostly not done pre and post FFP transfusion and changes in coagulation profile were not assessed after FFP transfusions.

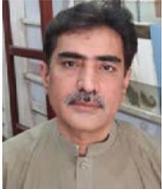
CONCLUSION

We have determined that FFP transfusions were used with improper indications at a high rate in the Obstetrical and Gynaecology department. As well as causing a serious economic burden and loss of sources, unnecessary FFP may be risky for the patients in terms of complications. Modification of FFP request forms with inclusion of laboratory evidence of coagulation defects, education of the staff at entry level and periodic audit of transfusion practices examined by the Hospital Transfusion Committee have been instrumental in curtailing the misuse of FFP.

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Malignant Abdominal Tumors in Children. (Our Experience at Lady Reading Hospital, Peshawar.)

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ABSTRACT

Objective: The objective of the present study was to observe the histopathological pattern and to know incidence of various pediatric intra-abdominal malignancies of Intra-abdominal tumors in children less than 16 years.

Material and Methods: This study was carried out at the department of Pediatric Surgery MTI/LRH Peshawar, over a period of 4 years from January 2014 to March 2018. Abdominal masses are often incidentally discovered by a parent while bathing the child, palpated unexpectedly on routine physical examination or detected on abdominal imaging. The commonly utilized techniques to aid diagnosis were ultra-sonography and computerized tomography scan and the commonly treatment modality was a combination of surgery and chemotherapy. Total of 63 intra-abdominal tumors of both sexes under 16 years of age was collected and analyzed to determine the various types of intra abdominal tumors in children in relation to histopathology, age and sex.

Results: Wilms's tumor was the most common tumor constituting 29.3 % of all cases. The others included non-Hodgkin's lymphoma (21.8%) neuroblastoma (12.3%), germ cell tumors and rhabdomyosarcoma (9%), Hepatoblastoma (9%) and a miscellaneous group. Majority of patient (65.2%) were under 5 years of age. The male to female ratio was 1.2:1

Conclusions: Wilm's tumor was the most common tumor. Most of the tumors were noted in children less than 5 years of age. Intra-abdominal tumors are more common in males.

Key words: Pediatric age, intra-abdominal tumors, Wilm's tumors, neuroblastoma.

INTRODUCTION:

Abdominal tumors, though relatively rare in children but after accidents still the greatest cause of death in children, are malignant tumors¹ during the past 20 years there has been a dramatic decrease in the death rate in children from infectious diseases, so that today the juvenile population has increased². With this increase, the number of children having an abdominal mass is potentially increased. The delay in diagnosis, and therapy can increase both the mortality and the morbidity due to the mass³. It is estimated that a child has 1:500 chances of developing cancer during the first 15 years of life⁴. There is geographic and ethnic variations among childhood cancer rates. The highest incidence is reported from Israel (30.6/100,000 males) and Nigeria, (22/100,000 males) and the lowest in India (6.8/100,000 males) and Japan (10.2/100,000)⁵. In Paki-

stan, the accurate incidence of cancers and malignant tumors in children is unknown.

Intra-abdominal tumors are common in male children, yet Wilm's tumor is a most common in children aging less than 5 years.

A report from the Pakistan Medical Research Council cancer study group, revealed that malignant tumors in under 15 years of age constituted 4.38% of all malignant tumors diagnosed⁶. The incidence can also be related to the reporting system of a country and its level of economic development. At presentation, patients may be a symptomatic or report a wide range of associated symptoms including fever, hematuria, pain, vomiting, constipation, Distention or less commonly hypertension and intestinal obstruction⁷. Abdominal masses are often incidentally discovered by a parent while bathing the child, palpated unexpectedly on routine physical examination, or detected on abdominal imaging.

The causes of pediatric abdominal masses are extensive, ranging from benign to neoplastic and often originating from organs within abdominal cavity. Earlier the diagnostic methods to identify these tumors of the primary stage were very disappointing. Now a days recent advances in diagnostic methods and the applica-

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tion of vigorous multidisciplinary treatment policies by special units combining pediatric surgery, radio therapy and multidrug chemotherapy regimens have made marked improvement in treating abdominal tumors of childhood, because if diagnosed earlier, these tumors are more responsive to treatment, resulting in good survival and prognosis⁸.The objective of the study was to review all patients under 16 years of age confirmed to have malignant abdominal tumors who presented at the MTI/LRH Peshawar between 2014 and 2018. An attempt was made to compare our experience with that reported in other studies.

METHODS AND MATERIAL:

The prospective observational study carried out at the

department of Pediatric Surgery, MTI/LRH Peshawar during a period of 4 years from January 2014 to March 2018. Total 63 intra abdominal tumors of both sexes under 16 years of age were collected and analyzed to determine the various types of intra abdominal tumors, age, sex and mode of presentation.

The commonly utilized techniques to aid diagnosis were ultrasonography and computerized tomography seen and the common treatment of modality was a combination of surgery and chemotherapy. For wilm’s tumor, the mean followup was 1 ½ years, the survival rate was 93.3% and there was no recurrence. with early diagnosis and multimodality treatment, the survival rates for childhood malignancies can be greatly improved.

RESULTS:

A total of 63 patients with abdominal tumors in pediatric age group were admitted in our Pediatric surgery Unit of MTI/LRH Peshawar, over a period of 4 years from January 2014 to March 2018. Study was a prospective one and all patients admitted were studied in details. The frequency of different Pediatric tumors are summarized in table 1. Table 1. Distribution of patients with abdominal tumors in pediatric age group in our study.

Serial No.	Type of Tumor	Numbers of Patients	Male	Female
	Wilms Tumor	24	17	7
	Neuroblastoma	12	9	3
	Lymphoma	14	10	4
	Rhabdomyosarcoma	4	2	2
	Hepatoblastoma	3	2	1
	Germ Cell	4	----	4
	Miscellaneous	2	1	1
Grand Total		63	41	22

Of 63 Patients, wilm’s tumor was the most common tumor (29.3%), followed by non Hodgkin’s lymphoma (21.8%) and neuroblastoma (21.3%). Germs cell and hepatoblastoma were less prevalent. Majority of patients (60.3%), presented under 5 years of age (Table II)

Table II. Age Distribution of all tumors.

Age (Years)	Frequency	Percent	Cumulative
<1	6	7.5	7.5%
1-5	30	52.8	60.3%
6-10	13	20.8	81.1%
11-14	5	5.7	86.8%
15-16	9	13.2	100%
Total	63	100%	

In our study of 63 patients, 41 were males and 22 were females, from table III, it is evident that the majority of patients were 3-6 years of age. The patients with wilm’s tumor presented in early age, whereas patients with lymphoma and hepatoblastoma presented above 4 years of age.

Table III age distribution of abdominal tumors in Pediatric age group in our series of 63 patients.

Age in years	Wilm's tumor (n=24)	Neuroblastoma (n=12)	Lymphoma (n=14)	Rhabdomyosarcoma (n=4)	Hepatoblastoma (n=3)	Germ Cell (n=4)	Misc (n=2)
0-2	6	3	-	-	-	1	-
2-4	8	3	-	2	2	1	2
4-6	8	2	8	1	-	-	-
6-8	3	1	2	-	-	-	-
8-10	-	-	2	-	-	-	-
10-12	-	-	1	1	-	-	-
12-16	-	-	1	-	-	-	-

Neuroblastoma also had its peak incidence in the age group of 1-3 years. NHL had its maximal incidence in the age group of 4-6 years (table III) Anaemia was present in a large percentage of patients and was the predominant finding on routine hematological investigation. (Table IV). As is evident from table 4, patients with wilm's tumors presented with swelling in the abdomen and flank .

Table IV. Incidence of physical signs and local abdominal examination in 63 cases of abdominal tumors in our study.

Physical sign	Wilm's tumor (n=24)	Neuroblastoma (n=12)	lymphoma (N=14)	Rhabdomyosarcoma (N=4)	Hepatoblastoma (N=3)	Germ Cell (N=4)	Misc (N=2)
Anaemia	6	7	7	3	2	1	2
Jaundice	2	-	-	-	2	-	1
Oedema	2	1	-	-	1	-	-
Distention	23	9	10	2	2	2	2
Visible Swelling	23	9	8	4	2	2	1
Crossed Mid-line	4	2	-	-	-	-	-
Tenderness	2	-	6	-	1	-	-
Splenomegaly	-	-	4	-	-	-	-
Ascites	3	2	-	-	-	-	-
Hepatomegaly	3	-	4	-	2	-	-

The abdominal masses palpated in the majority of our patients were nontender with other variably associated physical findings such as flank fullness, shifted umbilicus were also seen in few patients. Abdominal mass was present in all of the patients with soft tissue sarcoma accompanied with abdominal pain, fever, vomiting, weight loss, anaemia and breathlessness in varied distribution. Two children with diagnosis of teratoma presented with abdominal mass, abdominal pain, vomiting and constipation.

DISCUSSION:

The abdominal mass in an infant or child is most commonly an incidental finding first observed by a parent or at the time of a pediatric screening examination. According to the Dr. Sidney Sarber, "Every solid, semi solid or semi cystic mass in an infant or child should be regarded as a malignant tumor until its exact nature is determined by histological examination of the

removed tumors⁹.Of all child hood "surgical" abdominal masses, 70-80 % arise in the retroperitoneum and most are amenable to surgical excision if diagnosed early¹⁰.In our study of 63 patients, nephroblastoma or the wilm's tumor was the most common malignancy encountered, similar experience is reported by others¹¹. This is in accordance with the incidence reported by international classification of childhood cancer group for

0-9 years¹². The true incidence of Wilm's tumor in Pakistan remains unknown but may be similar to that in other countries as geographic and ethnic variations do not seem to affect its incidence. The highest incidence is reported in Finland, with 10 new cases per million per year¹³. Other studies indicate 7-6 per million new cases per year in the United States¹⁴ and 7.7, 7.2, 6.5, and 5.1 per million children per year in Sweden, Australia, Italy and England respectively¹⁵.

Most of the patients are under 5 years of age group with 70.6% which is similar with other studies¹⁶. Males are most commonly with 58.8% of total subjects with ratio of male: female of 1.2:1. Similar findings were observed by Hanif G, et al¹⁷, in the study "intra abdominal tumors in children" in 2004 in which majority of the cases were in the age group below 5 years with male to female ratio of 1.1:0.9. Wilm's tumors are most frequently diagnosed in the 2-5 years age group¹⁸, but the present study, unlike studies from the west¹⁹, 2 out of 15 patients (13.3%) were infants. The male to female ratio of 4:1 in this study differs from the equal distribution reported²⁰, and may reflect a preference of families in Pakistan to consult physicians for male offspring. It is evident from our study (table III) that the majority of patients were below 5 years of age. In series by Sharif et al²¹, majority (93.33%) of retroperitoneal tumors occurred in the first 5 years of life. Rai and Moazam²², also reported the majority (60.3%) of malignant abdominal tumors to occur under 5 years of life. In another study, median age of wilm's tumor is reported to be around 2-5 years²³. Another study reflects the mean age to be 3-5 years for wilm's tumor²⁴. Neuroblastoma also had its peak incidence in the age group of 1-3 years. Lymphoma had its maximal incidence in the age group of 4-6 years.

Majority of the patients in our study presented with abdominal mass (table IV) wilm's tumor has been reported to present as asymptomatic mass²⁵. Abdominal swelling was present in all of patients with neuroblastoma accompanied with abdominal pain, vomiting, fever, pallor, failure to gain weight, easy fatigability, loss of appetite, breathlessness, bowel and bladder dysfunction and diarrhoea. Neuroblastoma has been reported to appear typically as abdominal mass in young children²⁵.

Intestinal obstruction was the presenting feature in 62.5% of cases of abdominal lymphoma, accompanied with symptoms such as abdominal pain, fever, generalized weakness, vomiting, anorexia and loss of weight. Over the years, early diagnosis of abdominal tumors has significantly improved survival rates in children. Multimodality treatment strategies now result in over 60% survival of all children with malignant solid tumors, in case of wilm's tumor, the overall survival rates now approach 90%²⁶. In tumors with favorable histology, the NWTS-3 reported 96% four years survival rates for stage 1 tumors, 92% for stage II and

87% for stage III and for stage IV unfavorable histology the four years survival rates now 73%, long term survival for lymphoma has improved to 70% to 85%²⁷.

CONCLUSION:

General practitioners, family physicians and pediatricians must be made aware of the significance of an abdominal mass in the child; the high potential for malignancy in these masses and early referral to institutions best equipped to provide multimodality therapy. A national tumor registry is necessary to collect data on a sufficient number of patients to draw meaningful conclusions regarding the incidence and outcome of these tumors. The neonates, infant or child with an abdominal mass needs rapid clinical evaluation. Age, history and physical examination provide initial guidelines to diagnosis. If the initial evaluation indicates possible malignancy, more complex testing of blood, bone marrow, serum chemistries, urine and imaging studies may be required. Outcome varies widely depending on the malignant or benign nature of the existing mass but is generally more favorable in neonates.

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Naeem Mumtaz

Sub-cuticular Non-Absorbable Skin Suture give better result than Clips in Elective Open Colorectal Surgery? (A Controlled Randomized Study)

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ABSTRACT

Background: Varieties of methods are used to close the skin. Traditionally sutures (SS) have been used to close the skin but more recently metal staples (SC) were introduced with aim to reduce closure time and infection rates.

Objective: We aim to assess the difference between clips and sutures in elective colorectal surgery in terms of wound infection, cosmetic result and overall patient satisfaction

Methods: Prospective case controlled cohort study including all the patients who underwent elective open colorectal surgery, data collection was achieved through anonymous patient questionnaires.

Results: 218 filled questionnaires were received. 134 patients were allocated to SS group with median age of 67 (IQR 61, 74). SC group had a total of 84 patients with a median age of 69 (IQR 61, 71). 15% of SS group developed wound infection, compared to 20 % in SC group ($p=0.202$). Over all 61% of SS group claimed excellent results compared to 46% in SC group ($p=0.020$).

Conclusion: Our results showed that patients with non-absorbable sub-cuticular skin closure compared to clips had low infection rates, more satisfied with their scar and better cosmesis outcome. We therefore suggest using sub-cuticular sutures to close the skin in abdominal elective open colorectal surgery.

Key Words: Wound closure, Subcuticular suturing, skin staples.

INTRODUCTION

Good wound closure is effective skin healing with an acceptable cosmetic result to minimize complications such as wound dehiscence or infection. The method should be effective, efficient and comfortable for the patient.^{1,2} Commonly used methods for skin closure in abdominal surgery are metallic clips and subcuticular non-absorbable sutures. Some studies have favored the use of subcuticular sutures over metallic clips because of lower infection rates². Metallic clips are regarded as quicker and easier than sutures³⁻⁵, but they are less acceptable cosmetically⁶ and are more expensive.⁶⁻⁸

Majority of studies have been conducted in orthopaedic^{2,6,7,9,10}, obstetrics and gynecology¹¹⁻¹⁵, paediatrics^{16,17} and cardiothoracic surgery^{4,18} regarding methods of skin closure with clips versus sutures. Some studies have shown no significant difference in complications between the two methods but the cosmetic results were poorer in patients where metallic clips were used.¹⁹ Ranaboldo et al, in a study comparing the two

methods, concluded that the analgesic requirement was less when laparotomy wounds were closed with sutures.²⁰

Patients with non-absorbable sub-cuticular skin closure compared to clips had reduced infection rates and patients were more satisfied with their scar and the cosmetic outcome.

There has not been more information in recent literature on methods of skin closure following elective open colorectal surgery. Pickford et al reported that skin closure in abdominal operations with clips reduces the incidence of wound infection, in patients in whom operative parietal contamination had occurred.²¹ Subsequent trials have shown clips to be the preferred choice for abdominal wound closure in terms of time efficiency¹⁹, but no significant benefit has been demonstrated in cost effectiveness.²⁰

A meta-analysis published in the BMJ in 2010 compared clinical outcomes of staples versus sutures in wound closure in orthopaedic surgery. Data sources included Medline, Cinahl, Amed, Scopus and the Cochrane Library database. The conclusion was that the use of metal clips and especially in hip surgery, is associated with a significantly greater risk of wound infection than traditional suturing.²¹ We aim to assess the difference between clips and sutures in elective colorectal surgery in terms of wound infection, cosmetic result

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and overall patient satisfaction.

METHODS AND MATERIAL

This is a prospective case controlled cohort study including all the patients who underwent elective open colorectal surgery in Surgical Department of MTI, Lady Reading Hospital, Peshawar from May 2015 to May 2018. An ethical approval for the study was taken from the head of the Surgical Department.

A quality of life questionnaire was designed on European and local guidelines and approval was taken from clinical governance department. A questionnaire was sent to all the patients enquiring about scar, infection, pain and overall outcomes regarding cosmesis. Patients answered specific questions about infection (during their stay or after discharge from hospital), the use of antibiotics or the need for surgical management. Cosmetic results were assessed based on scar appearance, color, thickness, width and numbness.

Patients were divided into two groups depending upon the method of abdominal wound closure. Group 1 included the patient who had abdominal skin closure using sutures (skin sutures SS) and Group 2 included patients who had percutaneous staples for their skin closure (skin clips SC).

Inclusion Criteri. Patients underwent elective open abdominal colorectal surgery.

Patients with virgin abdomen

Exclusion Criteri. Elective open abdominal surgery for non-colorectal diseases. Previous laparotomy incision. Emergency open abdominal surgery for non-colorectal disease.

Technique of Wound Closure. Metallic clips, Non-absorbable subcuticular sutures

Quality of life and patient satisfaction. Robust questionnaire performa was used to assess the quality of life and patient satisfaction for abdominal skin closure after abdominal surgery.

Following parameters were considered:

- i) Size of scar:
 - a- Length
 - b- Width
 - c- Hypertrophy
- ii) Infection requiring:
 - a- Antibiotics
 - b- Dressing and debridement
- iii) Colour
 - a- colour of scar matching skin colour
- iv) Pain
 - a- types of analgesic medications used
 - b- duration of treatment
 - c- numbness
 - d- tension
- v) Cosmetic satisfaction score
 - a- Ranging from not satisfied to fairly and very satisfied

Data Collection. 369 patients were identified as having elective open colorectal surgery from May 2015 to

May 2018. Data collection was achieved through anonymous patient questionnaires. All patients were seen at the outpatient clinic at one week after surgery and then at six weeks and 3 months intervals for the first year after the surgery. Statistical package for social science (SPSS) version 16.0 was used to perform statistical analyses of the available data. Pearson chi-square test was used to analyze the data. Mean and median values were compared by standard statistical tests as appropriate. A P value of less than 0.05 was considered significant

RESULTS

369 patients were identified as having elective colorectal surgery from May 2015 to May 2018. A total of 218 filled questionnaires were received. 134 patients were allocated to SS group with median age of 67 (IQR 61, 74). SC group had a total of 84 patients with a median age of 69 (IQR 61, 71).

Infection rates were divided in two categories: infection as inpatient and overall infection rates. Only 7% of SS group patients developed infection while in-patients, as compared to 15% of SC group (p= 0.033). But overall 15% of SS group developed wound infection, as compared to 20 % in SC group (p= 0.202).

17% of SS group complained of scar thickness as compared to 28% in SC group (p=0.041), 30 % in SS group noticed widened scar and 45% in SC group (p=0.019). Only 38% of SS group could feel the scar as compared to 51% of SC group (p=0.040). Majority of patients in SS group 59% noticed that their scar matched the skin colour as compared to 45% of SC group (p=0.042). There was no significant difference noticed in prominence, swelling and tension of scar in both the groups.

78% of patients in SS group were very satisfied with scar formation as compared to 55% of patients in SC group (p=0.015). Over all 61% of SS group claimed excellent results compared to 46% in SC group (p=0.020). There was no significant difference noticed in pain and tension of scar in both the groups. The use of antibiotics, analgesics and ointments was also not significantly different. An equal percent of patients visited GP for scar problem.

	SS	SC	
Females	n= 56	n= 34	
Infection	19%	18%	P=0.5
Infection (IP)	9%	15%	P=0.3
Scar Thickness	11%	25%	P=0.08
Scar Width	13%	38%	P=0.04
Color Satisfaction	53%	51%	P=0.03
Scar felt	59%	41%	P=0.07
Outcome	72%	51%	P=0.043

Table 1. Overall result for female population of both

SS and SC groups. There was no significant difference noted in use of analgesics, antibiotics and ointments

	SS	SC	
Males	n= 78	n= 50	
Infection	11%	22%	P=0.05
Infection (IP)	9%	13%	P=0.042
Scar Thickness	16%	33%	P=0.02
Scar Width	13%	38%	P=0.04
Colour Satisfaction	92%	80%	P=0.035
Scar felt	36%	47%	P=0.0
Outcome	68%	49%	P=0.026

Table 2. Overall result for male population of both SS and SC groups. No significant difference was noticed in any group with regards to pain, numbness, tension in scar, use of analgesics and antibiotics.

	SS	SC	
Cohort	n= 134	n= 84	
Age	67 yrs	69 yrs	
Male	n= 78	n= 50	
Female	n= 56	n= 34	
Infection	15%	20%	P=0.202
Infection (IP)	7%	15%	P=0.033
Scar Thickness	17%	28%	P=0.041
Scar Width	30%	45%	P=0.019
Colour Satisfaction	59%	45%	P=0.042
Scar felt	38%	51%	P=0.040
Satisfaction	78%	55%	P=0.015
Outcome	61%	46%	P=0.020

Table 3. Comparison of results between SS and SC groups.

DISCUSSION:

Wound infection is one of the major causes of morbidity, prolonged hospital stay, discomfort to patients and increases the cost of the treatment. Only in 2009 wound infection had contributed additional 1 million inpatient days and \$1.6 billion in excess cost.²² Surgical site infection (SSI) is classified by the World Health Organisation (WHO) as any purulent discharge, abscess, or spreading cellulitis at the surgical site during the month after the operation.

With SSIs causing over one third of post-operative related deaths²³, pressure is placed on health care professionals and especially surgeons, in preventing the spread of infections amongst hospitalized patients.

Not only nosocomial infections carry a high mortality rate but also cause significant burden on morbidity, with 1.4 million worldwide suffering from infectious complications acquired in hospitals.²⁴

Our study suggests that metallic clips caused more wound infection and significant number of patients developed infection during hospital stay (p=0.033). Interestingly male patients with metallic clips developed more wound infection (p= 0.05) particularly during hospital stay (p=0.042). (Table 1 and 2). Earlier studies suggested that a reduction in infection rates could be achieved with skin staples because staples do not penetrate the incision but cross the incision site²⁵ and might cause less damage to the wound’s defenses than non-absorbable sutures.^{26,27} However recent meta-analysis suggested the higher risk of wound infection with use of metallic clips in orthopaedic surgery than sutures²¹ and favors the use of sutures to close the wound.

One of the current trials for SSI rates is ROSSINI (Reduction of Surgical Site Infection using a Novel Intervention) is underway to establish whether the use of a wound-edge protection device in adult patients undergoing laparotomy leads to a lower rate of surgical site infection (SSI).²⁸ Other clinical outcomes of SSIs include poor scars that are cosmetically not satisfactory, such as those that are widened, hypertrophic or keloid, persistent pain and itching, restriction of movement, and a significant impact on emotional wellbeing.²⁹

Our results showed that metallic clips increase the thickness (p=0.041), and width (p=0.019) of the scar as compared to non-absorbable sub-cuticle stitch. (Table 3) Similar results regarding thickness of the scar were reported by Clayer and Southwood³⁰ in hip surgery. A significantly higher number of patients in SC group claimed that the scar was palpable even after one year (p=0.040). Our results showed that patients in SS group noticed that their scar matches the skin colour after one year (p=0.042). Male patients in this study were more satisfied with the colour of scar than the female patients. The reason may be that females may have more aesthetic sense than males. (Table 1 and 2)

We also noticed that there was no significant difference in prominence, swelling and tension of scar in both the groups. Similar results in orthopaedic cases showed that there was no significant difference in patient’s satisfaction between SS and SC groups.⁹ However metallic clips are reported to be more painful than sutures.^{6, 28, 14, 31, 32} Ranaboldo et al also showed increase pain and increase use of analgesics with metallic clips is associated with more distress and morbidity.²⁰

Our results illustrate that the subcuticular sutures are superior to metallic clips in terms of cosmesis of the wound and patient satisfaction. Some studies suggested that poor results from clips is attribute to the poor technique of clips placement and it leads to not only poor healing but also the wound discharge leading to wound infection.^{5,7,31} Clips are considered to be more

expensive and the clips removal device pose extra burden to the cost.^{7,31} Also clips increase the rate of wound infection which ultimately means increase number of dressings and nursing cost. None of the studies have looked into the cost related to wound infection and further management in terms of antibiotic use, GP visits and further surgical interventions.

Patients with sutures were generally more satisfied with scar formation ($p=0.015$) and over all excellent ($p=0.020$) results compared to the clips. Lubowski et al showed no difference in complications between two techniques but there was convincing evidence that clips result in poor cosmetic results.¹⁹ In our study male patients complained less than female patients about cosmesis and pain and were more satisfied with general outcome. Bragg et al support this after a patient satisfaction survey performed following abdominoplasty³⁴.

CONCLUSION

Our results showed that patients with non-absorbable sub-cuticular skin closure compared to clips had reduced infection rates and were more satisfied with their scar and the cosmetic outcome. We therefore suggest using sub-cuticular sutures to close the skin in abdominal elective open colorectal surgery.

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Gulab Noor

Frequency and Causes of Conversion of Laparoscopic Cholecystectomy into Open Cholecystectomy

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ABSTRACT

Background: Symptomatic gall stone disease is a common health problem not only in developed nations its incidence is increasing in developing countries, because of changing dietary habits. Laparoscopic cholecystectomy is considered as gold standard method in its management.

Objective: To determine the frequency and causes of conversion of laparoscopic cholecystectomy into open cholecystectomy.

Subjects and methods: This descriptive cross-sectional study was conducted in surgical department of Medical and Teaching Institution (MTI) Lady Reading Hospital Peshawar from January 2016 to December 2017. 126 patients of symptomatic gallstones disease fulfilling the inclusion criteria were subjected to laparoscopic cholecystectomy and were followed throughout the procedure to see for any conversion and its cause.

Results: A total of 126 patients underwent Laparoscopy Cholecystectomy (LC) during the study period. The mean age was 41.32 years \pm 13.40 SD and age range of 18--68 years. The total no of cases converted to open cholecystectomy (OC) were 12 (9.52%).

Conclusions: One disadvantage of LC is the conversion into open procedure. But conversion should not be considered as complication of the procedure rather it is a mature decision by the surgeons to avoid unnecessary lengthening of the duration of surgery once they encounter any difficulty or intraoperative complication.

Key words: Laparoscopic cholecystectomy, gall stones, conversion, cholelithiasis.

INTRODUCTION

Cholelithiasis is a common disease with a prevalence of 10-15% in the USA and about 16% in Pakistan^{1,2} mostly remain asymptomatic but symptoms appear when any complication develops³ Ultrasonography is most useful investigation for diagnosing the gall stones and its complications e.g cholecystitis⁴.

Symptomatic gall stone disease cannot be managed with its complications without prompt surgical intervention. Carl-Langenbuch performed 1st successful cholecystectomy by open technique which remained the gold standard for the management of gall stones for about a century⁵. Then Philippe Moret brought a new advancement in its management by performing first successful cholecystectomy through laparoscopic technique⁶.

Laparoscopic cholecystectomy is preferable over open cholecystectomy for its lesser duration of

hospital stay, lesser mortality and morbidity, early return to work and better cosmetic results⁷. It is also considered for management of acute cholecystitis now a days⁸. Laparoscopic cholecystectomy is having certain disadvantages like its conversion into open cholecystectomy. According to some studies its conversion rate is 16-18%^{9,10}. Common causes for conversion mentioned in literature are dense adhesions 66.6% common bile duct injury 22.3% gut injury 11.1%¹¹ and hemorrhage 50%¹².

Laparoscopic cholecystectomy is the gold standard treatment modality. Its main disadvantage is the conversion into open procedure. But conversion should not be considered as complication of the procedure rather it is a mature decision by the surgeons to avoid unnecessary lengthening of surgery, once they encounter any difficulty or intra-operative complication. Moreover it can be avoided by proper case selection, improving hand eye coordination and meticulous dissection.

It will be the first study so far on this topic in our hospital which will provide local statistical data where adequate expertise is in the phase of development. By this study we will come to know that whether

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our results are comparable with national and international studies, which will reflect the level of our expertise in the field of laparoscopic surgery and may point out the need for further improvement.

MATERIAL AND METHODS:

This study was conducted in Surgical Department of Medical and Teaching Institution (MTI) Lady Reading Hospital Peshwar from January 2016 to December 2017. Approval of ethical committee were sought for this cross sectional descriptive study which was carried over 126 patients undergoing cholecystectomy. The cholelithiasis were diagnosed on the bases of episodes of pain and tenderness at right hypochondrium, aggravated by taking fatty meal and ultrasound abdomen suggestive of gall bladder stones. All the patients with diagnosis of cholelithiasis fulfilling the inclusion criteria were either through OPD or casualty. After taking informed consent for surgery, detailed history were taken and clinical examination were performed. Preoperative investigations and liver function tests were performed in all cases in order to confirm the diagnoses and exclude the patients with choledocholithiasis, empyems gall bladder, patients with previous abdominal surgery, cirrhosis of liver and gall bladder mass.

Preoperative antibiotics were given at the time of induction of anesthesia and we have followed the

patients throughout the procedure and were looked for conversion common bile duct injury, hemorrhage or gut injury results. Laparoscopic cholecystectomy was performed by the same surgeon of laparoscopic surgery. The data were recorded and analyzed into statistical package for social sciences. SPSS version 10.0). Results were presented as tables and graphs where appropriate.

RESULTS:

A total of 126 patients having cholelithiasis undergoing laparoscopic cholecystectomy were included in the study. Out of 126 patients, 102 (80.95%) were female and 24 (19.05%) male patients. Female to male ratio was found to be 1.12:1. The mean age was 41.32years+ 13.40 SD and age range of 18--68 yrs. Study population largely comprised of female patients of relatively younger age group. There were 45(38.9%) patients having age of 31-45 years followed by 47(37.3%) patients having age of less than or equal to 30 years.

Conversion rate from laparoscopic cholecystectomy to open was observed in 12(9.52%) while the rest of patients underwent laparoscopic surgery. The distribution of causes of conversion shows that the commonest cause being adhesions 10(7.9%) converted cases followed by hemorrhage 8(6.3%). Conversion rate and causes of conversion when stratified over age, it shows that higher age is more prone as that younger

TABLE # 01 Age wise stratification of conversion and its causes

			age (in years)			p-value
			<= 30.00	31.00 - 50.00	51.00+	
Conversion	Yes	Count	3	3	6	.081
		Column N %	6.4%	6.1%	20.0%	
	No	Count	44	46	24	
		Column N %	93.6%	93.9%	80.0%	
Adhesion	Yes	Count	2	3	5	0.121
		Column N %	4.3%	6.1%	16.7%	
	No	Count	45	46	25	
		Column N %	95.7%	93.9%	83.3%	
Common Bile Duct Injury	Yes	Count	0	2	0	0.203
		Column N %	.0%	4.1%	.0%	
	No	Count	47	47	30	
		Column N %	100.0%	95.9%	100.0%	
Haemorrhage	Yes	Count	3	1	4	0.136
		Column N %	6.4%	2.0%	13.3%	
	No	Count	44	48	26	
		Column N %	93.6%	98.0%	86.7%	
Gut Injury	Yes	Count	0	1	2	0.170
		Column N %	.0%	2.0%	6.7%	
	No	Count	47	48	28	
		Column N %	100.0%	98.0%	93.3%	

Table 2 Gender wise stratification of conversion and its causes

			Gender		p-value
			Male	Female	
Conversion	Yes	Count	4	8	0.185
		Column N %	16.7%	7.8%	
	No	Count	20	94	
		Column N %	83.3%	92.2%	
Adhesion	Yes	Count	4	6	0.079
		Column N %	16.7%	5.9%	
	No	Count	20	96	
		Column N %	83.3%	94.1%	
Common Bile Duct Injury	Yes	Count	1	1	.261
		Column N %	4.2%	1.0%	
	No	Count	23	101	
		Column N %	95.8%	99.0%	
Haemorrhage	Yes	Count	2	6	.658
		Column N %	8.3%	5.9%	
	No	Count	22	96	
		Column N %	91.7%	94.1%	
Gut Injury	Yes	Count	2	1	0.034
		Column N %	8.3%	1.0%	
	No	Count	22	101	
		Column N %	91.7%	99.0%	

ages although it was insignificant statistically. Table 1 Moreover conversion were more in male patients 16.7% as compared to 7.8% in females when stratified over gender. Table 2

DISCUSSION

Cholelithiasis is a common disease with a prevalence of 10-15% in the USA and about 16% in Pakistan^{1,2}. Patients mostly remain asymptomatic but symptoms appear when any complication develops³. Symptomatic gall stone disease can end up with its complications without prompt surgical intervention. Cholecystectomy was performed by open technique for management of gall stones disease which remained the gold standard for the management of gall stones for about a century⁵. But now this is an era of minimally invasive or key hole surgery, performing laparoscopic cholecystectomy for GBS has revolutionized its management^{15,16}

LC became an attractive treatment modality for cholelithiasis because of less scarring, shortened hospital stays, earlier returns to normal activities¹ Despite the fact that laparoscopic cholecystectomy has got many advantages but its conversion into OC is disappointing not only for patient but for surgeon as well. But conversion should not be considered as complication of

the procedure rather it is a mature decision by the surgeons to avoid un-necessary lengthening of procedure once they encounter any difficulty or inter-operative complication. The conversion rate of 3.6% to 13.9% is reported in literature.^{17,18} The frequency of conversion in this study being presented is 12(9.52%), which is according to that mentioned in literature.

In local literature most common cause of conversion was seen adhesions around the gall bladder. Adhesions made dissection difficult, although in most of the cases adhesions were separated with careful dissection with the help of cautery. In the national studies Pervaiz reported 2.38% and Tanveer reported 1.78% conversions because of adhesions.^{19,20} In our study adhesions (7.9%) were the most common cause which is a bit high with most of the local studies. However in majority of the international studies the reported rate is low comparatively. This is probably due to the fact that in majority of local studies, cases of acute cholecystitis were not included in the studies. Le VH reported conversion because of adhesions in 0.71% patients.²¹

However conversion to open laparoscopic surgery is still reported in the local literature as high as reported by Pervaiz in his study up to 2.94%. The most common causes of these conversions are use of refurbished laparoscope, lack of backup support and failure

of power supply.^{18,22} Our study population was younger, mean age 41.32 years + 13.40 SD. Daradkeh²³ reported mean age of 47.2 years, whereas Bingener et al²⁴ 40 years.

The reported conversion rates for acute cholecystitis range from 12% to 37.5%...¹⁶ However, the rate of conversion is high amongst studies from the Asian countries as compared to those from western world. In most cases, dense adhesion around the gall bladder and as uncontrolled bleeding were the main reasons for conversion to the open procedure.¹¹ Also in this study commonest cause being adhesions 10 out of 12 converted cases followed by hemorrhage 8 out of 12 conversions. Moreover conversion were more in male patients. 16.7% as compared to 7.8% in females. This was similar to Ibrahim et al, Brodsky et al²⁴ and Al Salamah also found male gender as a most significant determinant for conversion to OC.²⁵

Gharaibeh et al¹¹ reported 24% conversion rate in males vs. 4% in females, whereas Lim et al¹² reported 16.6% conversions in males vs 8.2% in females. Most conversions happen after a simple inspection or a minimum dissection, and the decision to convert should be considered as a sign of surgical maturity rather than a failure. Conversion should be opted for in the beginning and at the time of recognition of a difficult dissection rather than after the occurrence of complication.¹⁵⁻¹⁶

CONCLUSION

Laparoscopic cholecystectomy is the gold standard treatment modality in the management of symptomatic gallstones disease. Its main disadvantage is the conversion into open procedure. But conversion should not be considered as complication of the procedure rather it is mature decision by the surgeons to avoid unnecessary lengthening of the procedure once they encounter any difficulty or intraoperative complication. Moreover it can be avoided by proper case selection, improving hand eye coordination and meticulous dissection.

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Comparing the Efficacy of Ultrasound Guided Drainage VS Incision Drainage in Management of Breast Abscess

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ABSTRACT

Objective: To compare the efficacy of ultrasound guided drainage versus incision and drainage in management of breast abscess at Department of Surgery, Khyber Teaching Hospital, Peshawar.

Material and Methods: This Randomized controlled trial was carried out from July 2016 to Jan 2017 in the Department of Surgery, Khyber Teaching Hospital, Peshawar. A total of 184 patients with breast abscess (i.e. 92 in each group) were included in the study. Patients in group A were subjected to ultrasound guided drainage while women in group B were subjected to incision and drainage. Efficacy of both procedures was determined and then compared using chi square test. P value of less than 0.05 was taken as significant.

Results: The treatment modality in Group A was 93.5 % (86) efficacious while Group B showed an efficacy of 80.4% (74). The difference was significant between both the groups with p-value=0.007.

Conclusion: Ultrasound guided needle aspiration is an effective alternate treatment modality for both lactating and non-lactating breast abscess.

Key Words: Efficacy, breast abscess, ultrasound guided drainage, incision and drainage

INTRODUCTION

A breast abscess is a localized collection of pus within the breast that usually occurs as a complication of mastitis.¹ In most cases of breast abscess the organism most commonly cultured is *Staphylococcus aureus*.^{2,3} The patient presents with fever, chills, tenderness and breast erythema. Imaging with ultrasound can confirm the diagnosis, provides a means to drain the collection to tailor antibiotic therapy and can be safely used for regular follow up of abscess. Traditionally breast abscess has been treated by incision and drainage which is performed under general anesthesia and has led to possible unsatisfactory cosmetic outcomes, further more it requires regular dressings and prolonged heal-

ing time.⁴ Another treatment option for the treatment of breast abscess is repeated aspiration with or without ultrasound guidance and this has been reported to be associated with lower recurrence rates, excellent cosmetic outcomes and also lower costs. Recently a study reported a cure rate of 93% by ultrasound guided drainage.⁵ Two studies done reported cure rate of 82% by ultrasound guided drainage of breast abscess.^{6,7} Another study also reported a cure rate of 82% when done with needle aspiration as compared with open surgical drainage.⁸

Ultrasound guided needle aspiration is an effective alternate treatment modality for both lactating and non-lactating breast abscess.

Literature also shows that there is a success rate of 55.55% in ultrasound guided drainage of breast abscess with only a failure rate of 17.4% in which it was converted to open drainage, while open drainage was proved to be more painful and cumbersome.⁹ Previous studies have advocated the use of surgical drainage as primary treatment modality but recent studies have suggested that ultrasound guided drainage has both been successful with improved cosmetic and curative

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outcome.^{10, 11, 12}

A study was done in Dow medical college showing success rate of 76.6 per cent in incision and drainage and 93.3% in ultrasound guided.¹³ In another study, the cure rate was 88.57% in ultrasound guided, whereas patients managed by incision and drainage procedure had a cure rate of 93.44%¹⁴ In our study, randomized evaluation of efficacy in patients undergoing ultrasound guided drainage of breast abscess was done. The rationale of the study was to establish whether ultrasound guided needle aspiration is a feasible alternative treatment option for the breast abscess drainage in Khyber Teaching Hospital. Although many studies regarding breast abscess in women have been done, most of them were done on lactating women. There is lack of studies assessing the breast abscess and its treatment options in women in general.

MATERIALS AND METHODS:

This Randomized Control trial study was done in Department of Surgery, Khyber Teaching Hospital, Peshawar from July, 2016 to Jan, 2017. Total Duration of study was 6 months. A total of 184 patients were divided into two groups through Non-probability consecutive sampling technique (i.e. 92 in each group). All women presented with breast abscess having age between 15 -45 years were included in this study. Patients with recurrent or chronic breast abscess, those with necrotic skin overlying the abscess or abscess already draining, patients with clinical features of immune suppression (WHO clinical stage III and IV) and those known to be allergic to penicillin antibiotics were excluded from this study.

After getting approval from the hospital ethical committee to conduct the study, all patients with breast abscess attending outpatient department and emergency of this institute were invited to participate in the study. An informed consent was taken. Clinical diagnoses were made based on the presence of breast pain, swelling, ± fever and presence of a fluctuant tender breast swelling. The patients diagnosed clinically were subjected to ultrasound scan in the radiology department. The diagnoses were confirmed through ultrasound. The size of the abscess was estimated. After this randomization was done, and eligible participants were randomly allocated to receive ultrasound guided drainage and incision and drainage. After aspiration/ incision and drainage patients were started on co-amoxiclav. Follow-up period was 6 weeks. The exclusion criteria were strictly followed to control the confounders and bias.

Data were stored and analyzed in SPSS version 16. Mean ± SD were calculated for quantitative variables like age and duration of symptoms. Frequencies and percentages were calculated for categorical variables like efficacy. Efficacy was compared between the two groups using Chi Square test keeping P-value ≤

0.05 as significant. Efficacy was stratified amongst age and duration of symptoms to see effect modification. Poststratification chi square test was applied to determine effect modification. P value < 0.05 was considered significant. All results were presented in the form of tables and graphs.

RESULTS

A total of 184 patients of breast abscess were observed, which were divided in two equal groups A & B. Patients in group A were subjected to ultrasound guided drainage while women in group B were subjected to incision and drainage. Average age was 34.82 years+ 8.20SD with range of 15-45 years. The average age in group A was 34.11years+8.23SD and contained 16(17.4%) patients having age less than 25 years, 27(29.3%) patients between 25-35 years and 49(53.3%) patients having the ages of more than 35 years. While average age in group B was 35.52years+8.15SD and contained 12(13%) patients in ≤25 years, 25(27.2%) in 26-35 years and 55(59.8%) patients with age > 35 years. The age distribution among the group was also insignificant with p-value 0.608. (Table 1)

The average duration of symptoms in group A was 4.34 days+1.68SD and contained 15(16.3%) patients in less than 2 days, 56(60.9%) patients 3-5 days and 21(22.8%) patients having the duration of symptoms of more than 5 days. While average in group B, it was 4.88days+1.65SD and contained 8 (8.7%) patients in less than or equal to 2 days, 50(54.3%) in 3-5 days and 34(37%) patients with duration of symptoms of more than 5 days. The duration of symptoms distribution among the group was also insignificant with p-value 0.063. (Table 2) Efficacy wise distribution shows that Group A showed 86(93.5%) efficacy while non-effective in 6(6.5%) patients. Similarly Group B showed 74(80.4%) efficacy while non-effective in 18(19.6%) patients. Efficacy was significant in both the groups with p-value=0.007.

(Table 3) When efficacy was stratified over duration of symptoms in both the groups it shows also insignificance. (Table 4)

TABLE 1. Age wise distribution in both the groups

AGE IN YEARS	GROUP		TOTAL
	A	B	
≤ 25 years	16 17.4%	12 13.0%	28 15.2%
26 - 35 years	27 29.3%	25 27.2%	52 28.3

≥36 years	49 53.3%	55 59.8%	104 56.5%
TOTAL	92 100.0%	92 100.0%	184 100.0%
Mean±SD	.11±8.23	35.52±8.15	34.82±8.20

TABLE NO: 2. Duration of symptoms wise distribution of patients in both the groups

Duration of symptoms in days	no. of patients in group a	no. of patients in group b	Total no. of patients
≤ 2.00	15 16.3%	8 8.7%	23 12.5%
3.00 - 5.00	56 60.9%	50 54.3%	106 57.6%
6.00+	21 22.8%	34 37.0%	55 29.9%
Total	92 100.0%	92 100.0%	184 100.0%
Mean±SD	4.34±1.68	4.88±1.65	4.61±1.68

TABLE 3. Efficacy wise distribution of patients in both the groups

EFFICACY	GROUP		TOTAL	P-VALUE
	A	B		
YES	86 93.5%	74 80.4%	160 87.0%	0.007
NO	6 6.5%	18 19.6%	24 13.0%	
TOTAL	92 100.0%	92 100.0%	184 100.0%	

TABLE 4. Duration of symptoms wise distribution of efficacy in both the groups

Duration of Symptoms (in days)	GROUP				P-VALUE
	A		B		
	EFFICACY		EFFICACY		
	YES	NO	YES	NO	
≤ 2.00	15 94.6%	0 0%	7 87.5%	1 12.5%	0.6957
3.00 - 5.00	53 94.6%	3 5.4%	40 80.0%	10 20.0%	0.0639
6.00+	18 85.7%	3 14.3%	27 79.4%	7 20.6%	0.8342

DISCUSSION

Breast abscess is one of the commonest form of abscess at surgical emergencies usually seen in lactating woman.^{15,16} According to Haagensen “The conventional treatment of breast abscess has been surgical incision and drainage under general anesthesia, a curved incision in the skin line is used and a Penrose drain is left in a place for 72 hours”.¹⁷The gold standard of puerperal breast abscess drainage described by Haagensen is supported by Webster with addition of gauze packing¹⁸ patients requires hospitalization, breast feeding discontinuation and lactation suppression with tab bromocriptine 2.5 mg twice daily for 14 days.¹⁸ Breast distortion due to scarring and persistent fistula or sinus developed in some patients.¹⁹By placing the incision over inflammatory part of breast scarring can be avoided in visible part of breast.²⁰

Treatment of breast abscess traditionally has been incision and drainage however this has been found to be associated with possible unsatisfactory cosmetic outcome, difficult in breast feeding and needs general anesthesia, prolonged healing time, and regular dressing.²¹ Repeated aspiration with or without ultrasound guidance has been found to be another treatment option for breast abscess and this has been reported to be associated with less recurrence, excellent cosmetic result and has less cost.²²⁻²⁵

In our comparative study, we compared two groups, ultrasound guided aspiration and incision and drainage of the breast abscess in the management of it without control group. In the current report, patient’s age range has some similarity with the result of Dixon et al and Dener et al, who demonstrated that breast abscesses most commonly affects women aged 18-50 years.^{25, 26} Although breast abscess generally has

been associated with mastitis and breastfeeding, the results of our study and others indicate that abscess was also found in non-lactating women Crowe et al and Scholefield et al.^{27,28} There was 6.5% breast abscesses observed in the Ultrasound guided needle aspiration group during the study period. There was 19.6% abscess rate observed in the incision and incision group. However this rate was far less than 31% recurrence in the incision and drainage group which has been reported in another study^{25, 29}

Christensen et al have reported a very high rate of success, with 97% of patients with puerperal abscesses recovering after one session of ultrasound guided drainage.³⁰ However; the success rate of ultrasound-guided drainage might vary with different pathogens. In the report from Taiwan, 21% of MRSA-induced breast abscesses (11 of 52) required conversion to incision and drainage.³¹

Among the USG guided aspiration patients, the cure rate was 88% whereas patients managed by incision and drainage procedure with cure rate of 96%. Dixon JM et al reported success rate of 84%.³² Faisal Elagili et al reported success rate of 83.3% with USG guided aspiration of breast abscess.³³ Alphoncet al observed cure rate of 93.1% in ultrasound guided aspiration,³⁴ which are consistent with our study results. Patients who underwent aspiration, were satisfied with the cosmetic outcome, as there were no scars present after the treatment as similar to the studies of Singh et al and Kastrup et al.^{35,36}

CONCLUSION

The observation of our study shows that needle aspiration of the abscess with ultrasonography guidance combined with antibiotics has a great value in the treatment of breast abscess even in abscess with large volume; although repeated aspiration are needed to obtain complete resolution, this therapy is a well-accepted alternative to surgical treatment. Aspiration of the breast abscess through a wide bore cannula is thus a feasible and easy procedure, but may require multiple aspirations for cure. It does not require any mode of anesthesia and can be done on out-patient department basis. Breast abscess in selected group of patients with diameter of less than 7 cm can be treated by aspiration successfully and with a good cosmetic outcome. Aspiration of the breast abscess can be successfully done as initial mode of management in the treatment.

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Syed Waqar Hussain

Increase of 'Red-Cells Distribution Width (RDW)' Levels as Marker of Mortality in Patients with Septic Shock

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ABSTRACT:

Background: Sepsis is a clinical syndrome characterized by systemic inflammation due to infection. There is a continuum of severity ranging from sepsis to septic shock

Objective: To observe increase in RDW levels from baseline and to determine mortality in patients who have septic shock presenting to Medical ICU at Shifa International Hospital

Material and Methods: A Retrospective observational study was conducted at department of critical care medicine in Shifa International Hospital, Islamabad. Study duration was 6 months January 2018-June 2018. Data of patients admitted to Medical ICU from January 2017 to December 2017 were identified and reviewed. Ethical approval and consent forms were taken. Patients of age >18 years, both genders and diagnosed with sepsis requiring vasopressors were included in study. Exclusion Criteria was based upon patient's expiration within 24 hours and sepsis but did not require vasopressors. Data was analyzed using SPSS version 23. T test and ROC curve analysis was done. P value ≤0.05 was considered significant.

Results: Current study included 150 patients; 28.7% (n=43) were males while 71.3% (n=107) were females. Survivors and non-survivors were 35.3% (n=53) and 64.7% (n=97) respectively. Hospital outcomes of these patients divided them into 2 groups; survivor group and non-survivor group. Changes in Hemoglobin, TLC, Platelet count, CRP, Serum Potassium and creatinine levels were statistically significant (p-value <0.05). There was 1.9% increase per day of RDW among non-survivor group while there was 0.76% increase among survivor group. Sensitivity and specificity of RDW increase for predicting death in patients with septic shock were 85.6% and 73.6%, respectively.

Conclusion: During first 3 days of hospitalization in patients having septic shock, increase in RDW from baseline was associated with adverse clinical outcomes. Therefore, a dynamic change in RDW level over a period of time can be a very good independent prognostic marker for mortality in patients having septic shock.

Key words: Sepsis, RDW, Vasopressors

INTRODUCTION:

Sepsis is a clinical syndrome characterized by systemic inflammation due to infection. There is a continuum of severity ranging from sepsis to septic shock. Although wide-ranging and dependent upon the population studied, mortality has been estimated to be ≥10

percent and ≥40 percent when shock is present.^{1,2}

According to Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM), sepsis is defined as a life threatening organ dysfunction caused by unregulated host response to an infection. Organ dysfunction is defined as an increase in Sequential Organ Failure Assessment (SOFA) score equal or more than 2. Over a million ICU records from inside and outside USA helped derive the validity of SOFA score²

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During first 3 days of hospitalization in patients having septic shock, increase in (RDW) from baseline was associated with adverse clinical outcomes. There-

fore a dynamic change in RDW level over a period of time can be a very good independent prognostic marker for mortality in patients having septic shock.

The red blood cell distribution width (RDW) represents an index of the heterogeneity of the erythrocytes (anisocytosis), which is calculated by dividing the standard deviation of erythrocyte volume by the mean corpuscular volume (MCV) and multiplying by 100 to express the result as a percentage.³ A high RDW implies a large variation in RBC sizes, and a low RDW implies a more homogeneous population of RBCs. A very elevated RDW can be seen in iron deficiency, transfused anemia, myelodysplastic syndrome, and homozygous hemoglobinopathy, whereas slightly elevated RDW can be seen in thalassemia trait and anemia of chronic disease. The normal range for the RDW is 11.5 to 14.5 percent. There is no condition that regularly yields a RDW less than normal. Thus, in practice, the RDW is either normal or elevated. RDW is frequently increased in anemia caused by vitamin or mineral deficiencies (eg, folate, vitamin B12, iron).

Numerous observational studies have correlated a high RDW with adverse outcomes, including mortality.^{4,5,6} Increase in RDW from baseline during the first 72 hours after hospitalization is significantly associated with adverse clinical outcomes. Therefore, a combination of baseline RDW value and an increase in RDW of more than 15% can be a promising independent prognostic marker for mortality in patients with severe sepsis or septic shock.^{7,8}

Although the exact mechanism of association of RDW with mortality is not known but it is postulated that systemic inflammation response impacts bone marrow function, iron metabolism⁹, pro-inflammatory cytokines have been found to inhibit erythropoietin-induced erythrocyte maturation and proliferation, and to down regulate erythropoietin receptor expression, which are associated with RDW increases.¹⁰ High oxidative stress is present in sepsis through the generation of reactive oxygen species by activated leukocytes which can be a contributing factor of association of RDW and sepsis.¹¹

A 2 year study conducted at Shanghai District ICU found that serial increase in RDW was higher in non-survivors as compared to survivors on day 4 of admission.¹² Dynamic observation of RDW seemed more valuable in clinical practice, RDW and SOFA correlate with each other and are index of multiple organ dysfunction in sepsis. Present study aims to observe increase in RDW levels from baseline and to determine mortality in patients who have septic shock presenting to Medical ICU at Shifa International Hospital.

MATERIAL AND METHODS:

A Retrospective observational study was conducted at department of critical care medicine in Shifa International Hospital, Islamabad. Study duration was

6 months January 2018-June 2018. Data of patients admitted to Medical ICU from January 2017 to December 2017 were identified and reviewed. Ethical approval and Consent forms were taken from patients regarding their data utilization in study. Patients of age >18 years, both genders and diagnosed with sepsis requiring vasopressors were included in study. Exclusion Criteria was based upon patient's expiration within 24 hours of sepsis but did not required vasopressors. Data was analyzed using SPSS version 23. Frequency and percentages were calculated for qualitative variables. Mean and standard deviation calculated for Quantitative variables. T test and ROC curve analysis was done. P value ≤0.05 was considered significant.

RESULTS:

Current study included 150 patients; 28.7% (n=43) were males while 71.3% (n=107) were females. Survivors and non-survivors were 35.3% (n=53) and 64.7% (n=97) respectively. Among vasopressors, nor-epinephrine was given to 100% (n=150). Epinephrine was given to 68% (n=102) while vasopressin was given to 38.7% (n=58) patients. This is shown in table 1.

Table 1: Gender distribution, survivors, non-survivors and use of vasopressors among study population

Demographics	Percentage	Number
Female	71.3	107
Male	28.7	43
Non-survivors	64.7	97
Survivors	35.5	53
Nor-epinephrine	100	150
Epinephrine	68	102
Vasopressin	38.7	58

Hospital outcomes of these patients divided them into 2 groups; survivor group and non-survivor group. Changes in hemoglobin, TLC, platelet count, CRP, serum potassium and cretinine levels were statistically significant (p-value <0.05). On day 1, there was no significant difference noted in RDW levels and SOFA scores between non-survivor and survivor groups (p-value >0.05). RDW at day 3 was significantly raised in non-survivor group as compared to survivor group (p-value <0.05). No significant increase was noted in SOFA score at day 3 among non-survivors as compared to survivors (p-value >0.05). There was 1.9% increase per day of RDW among non-survivor group while there was 0.76% increase among survivor group. Table 2 elaborates the overall characteristics and laboratory values.

DISCUSSION:

This is the very first study of its kind, done

Table 2: Age, laboratory values, RDW, SOFA score and their dynamic changes between two groups

Characteristics	Non-survivors	Survivors	p-value
Age (Mean ± SD)	55.82 ± 14.10	56.17 ± 14.79	0.78
Hemoglobin (g/dL)	10.22 ± 1.55	10.99 ± 1.94	0.02
TLC (μL)	22358.76 ± 10368.69	13388.69 ± 2.76.67	0.001
Platelets (μL)	128804.1 ± 59205.44	166226.4 ± 32720.64	<0.001
C-Reactive Protein	177.90 ± 48.30	89.09 ± 29.34	0.002
Sodium (Na)	134.55 ± 4.35	135.15 ± 3.70	0.35
Potassium (K)	4.04 ± 0.54	3.95 ± 0.27	0.001
Cretinine	2.68 ± 0.84	1.64 ± 0.18	<0.001
RDW1	13.79 ± 0.92	11.82 ± 0.70	0.196
RDW3	16.49 ± 1.31	13.46 ± 1.13	0.773
RDW Increase	19.50 ± 2.75	14.11 ± 4.66	<0.001
SOFA	13.80 ± 2.61	9.35 ± 2.80	0.777
SOFA3	16.39 ± 1.99	9.01 ± 1.90	0.334

TLC: Total leucocyte count, rdw1: red cell distribution width on day 1, rdw3: red cell distribution width on day 3, SOFA: sequential organ failure assessment, sofa3: sequential organ failure assessment on day 3.

Sensitivity and specificity of RDW increase for predicting death in patients with septic shock were 85.6% and 73.6%, respectively. This is shown in figure 1.

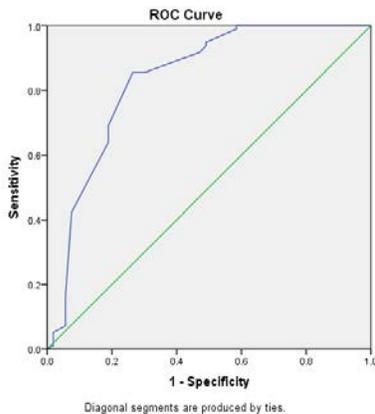


Figure 1: ROC curve of RDW Increase

in Pakistan. Previous studies regarding RDW only focused on usefulness of RDW in differentiating anemias.^{13,14} Present study is also unique in the sense that it has not only assessed the RDW at baseline among patients having septic shock but has also evaluated the dynamic change observed in RDW at third day and its correlation among non-survivors and survivors. Present study has come up with a notion that above RDW values of 17.5%, this laboratory test becomes a good predictor of poor outcomes among patients having septic shock. In one study it was observed that RDW values above 15% having dynamic changes after hospitalization were associated with poor outcomes.¹⁵ A large number of studies showed that high level of RDW was associated with possibility of poor outcome but there was an ambiguity to this observation as well. In clinical practice it was also noted that patients having high RDW levels still

survived.^{16,17} This led to the idea of observing dynamic change in RDW values and it was found that in septic patients, an increase in RDW from baseline during first 3 days after hospitalization was significantly associated with poor outcomes.¹⁸ Increase in RDW per day was more than double in non-survivor group as compared to survivor group in present study. This is because of the pro-inflammatory cytokines, inhibiting erythropoietin-induced erythrocyte maturation and proliferation, and down regulating erythropoietin receptor expression, which are associated with RDW increases.¹⁰ Malnutrition has also been postulated to be another explanation for this observation. Nutritional markers like cholesterol and albumin are believed to be significantly associated with RDW.¹⁹ Survival time is also noted to be highest in patients with low RDW at baseline and decreased increment in RDW per day during hospital

stay. This finding might be explained by resolution of inflammation and oxidative stress during initial treatment as pro-inflammatory cytokines inhibit erythrocyte maturation, systemic inflammation influenced bone marrow function and iron metabolism.²²

In present study different laboratory parameters were also observed to be significantly associated with poor outcomes among patients having septic shock. These included hemoglobin level, total leucocyte count (TLC), c-reactive protein (CRP), potassium and creatinine level. Sepsis induces hemolysis and can cause reduced hemoglobin levels and free hemoglobin can be used as a biomarker for diagnosis and outcome of severe sepsis in critical illness.²⁰ CRP level was also significantly associated with increased mortality in present study. In another study it was noted that changes in RDW were strongly correlated with CRP levels.²¹

Present study also showed that there was no significant association of SOFA score with RDW, neither was any dynamic change in SOFA score significantly associated with increased prediction of mortality in patients having septic shock. On the contrary in one study RDW level was shown to correlate with SOFA score.²² There were certain limitations in this study. This was a retrospective single center study. Only patients having septic shock were included in this study and RDW $\geq 17.5\%$ was associated with good predictor of increased mortality. We could not exclude the possibility that some mixing variables that would affect the outcome may have been missed. Erythropoietin, iron, vitamin B12 and reticulocyte count were not investigated which could affect RDW values.

In future, a large multicenter study with repeated RDW measurements is needed to generalize the role of RDW as a predictor of mortality in hospitalized patients.

CONCLUSION:

During first 3 days of hospitalization in patients having septic shock, increase in RDW from baseline was associated with adverse clinical outcomes. Therefore a dynamic change in RDW level over a period of time can be a very good independent prognostic marker for mortality in patients having septic shock.

Conflict of interest: There was no conflict of interest among authors

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