

Logo

- **Editorial: Vision 2020: Did We Achieve the Objectives?**
- **Fluconazole Vs Amphotericin in The Management of Fungal Corneal Ulcer**
- **Barriers Towards Cataract Surgery**
- **Mechanical Implantation of Intracorneal Ring Segments**
- **Surgical Outcomes of Von Hippel Lindua Retinal Angiomas**
- **Eye Make-Up and Dry Eye Disease**
- **Comparison of Therapeutic Probing with and without Viscoelastic**

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2. Cochereau I, Goldschmidt P, Goepogui A, Afghani T, Delval L, Pouliquen P, Bourcier T, Robert PY. Efficacy and safety of short duration azithromycin eye drops versus azithromycin single oral dose for the treatment of trachoma in children - a randomised, controlled, double-masked clinical trial. Br J Ophthalmol. 2007;91:667-72.
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Editorial: Vision 2020: Did We Achieve the Objectives? 6
Tayyab Afghani

Comparison of Efficacy of Subconjunctival Fluconazole Injection Versus Topical Amphotericin B in The Management of Fungal Corneal Ulcer 9
Hamid ur Rehman, Muhammad Naeem Khan, Irfan Aslam Khattak, Adnan Ahmed

This study compared the efficacy of subconjunctival injection of fluconazole (2 mg/ml) with topical amphotericin B (0.5 mg/ml) eye drops in dealing with cases of fungal corneal ulcer. Patients with resistant corneal ulcers attending the outpatient clinic were divided into two groups. Group 1 included 37 cases treated with topical amphotericin B; Group 2 included 37 cases treated with subconjunctival fluconazole injection. Response to therapy and any complications resulting from it were compared between the two groups.

Barriers Towards Cataract Surgery Among Patients Visiting Tertiary Eye Care Hospital, Rawalpindi 16
Asifa Nawaz, Ume Sughra, Sultana Kausar, Maryam Firdous, Maheen Akbar

This study evaluated the barriers towards cataract surgery among patients visiting the Out Patient Department of a tertiary eye care hospital of Rawalpindi. Three hundreds and forty patients were interviewed by consecutive non-random sampling technique. Structured questionnaire was used with informed consent to collect the data. Major barriers reported in the study were non-availability of eye hospital, unwariness of cost effective treatment of cataract, fear of surgery, lack of knowledge about eye hospital in public/private sector and difficulty to visit an eye hospital.

Visual Outcomes and Ocular Attributes of Mechanical Implantation of Intracorneal Ring Segments-A Longitudinal Hospital Based Study 21
M Abdul Moqet Khan, Saad Alam Khan, Hina Sharif

It was interventional uncontrolled trial in which patients having manual implantation of Intra corneal ring segment were included. Visual acuity, spherical equivalent, maximum keratometric readings, corneal astigmatism and endothelial cell density was measured at fixed intervals. Any changes in visual acuity after surgery, spherical equivalent and K-Max were noted and statistically analyzed.

Surgical Outcomes of Von Hippel Lindua Retinal Angiomatosis **30**

Hussain Ahmed Khaqan, Hasnain Muhammad Baksh, Kashif Jahangir, Hafiz Ateeq Ur Rehman, Raheela Naz

This study was conducted to evaluate long term surgical outcomes of vitreoretinal surgery for retinal angiomatosis in VHL (von Hippel Lindua) syndrome. Eyes which underwent pars plana vitrectomy, retinectomy and endotamponade of 5000cs silicone oil for retinal angiomatosis and visual acuity was at least light perception (LP) were evaluated for outcome. All patients who completed three years follow up were included in the study.

Eye Make-Up and Its Association with Dry Eye Disease **36**

Munir Amjad Baig, Rabeeya Munir, Waleed Munir

This hospital based, cross sectional study was conducted to report the presence or absence of dry eye disease among eye make-up users. One hundred and forty-one female patients, with no history of dry eyes, putting an eye make-up > 3 times / week like mascara, eye shadow or eyeliner, attending eye OPD/refraction clinic were included. A questionnaire-based survey about dry eyes and eye make-up was done by a trained researcher while a single investigator performed various dry eye tests under same physical conditions. Dry eye diagnosis was made on three out of five tests.

Comparison of Therapeutic Probing with and without Viscoelastic Gel for Congenital Nasolacrimal Duct Obstruction **42**

Muhammad Sharjeel, Hafiza Sadia Imtiaz, Muhammad Abbas, Memona Mohiuddin

This study was conducted to determine the therapeutic role of probing in CNLDO and to compare the success rate and complication rate of probing with viscoelastic substance and probing without viscoelastic substance. Patients of either gender between 9-24 months of age, with unilateral or bilateral CNLDO that failed to resolve after 3 months of conservative treatment were enrolled into this study. Probing was performed in Group A with viscoelastic gel and in group B without viscoelastic gel. Complication rate and the differences between two groups in terms of success were reported.

Vision 2020: Did We Achieve the Objectives?

Tayyab Afghani

VISION 2020 was a global initiative aimed to eliminate avoidable blindness by the year 2020. Launched on 18 February 1999 by the WHO together with the more than 20 INGOs involved in eye care, it was a partnership that provided guidance, technical and resource support to countries that have formally adopted its agenda¹. Pakistan was one of the signatories.

There were three objectives. The first was to raise the profile among the key audiences of the causes of avoidable blindness and solutions, the second was to identify and secure the necessary resources, and the third was to facilitate three core Vision 2020 strategies. The core strategies were – Disease Control, Human resource development and infrastructure and appropriate technology development¹.

Around 20 years ago when we were learning about community eye health at iconic ICEH London, WHO had estimated that there were some 45 million people blind². About 60% of that was treatable; due to cataract and refractive error, 15% of causes in need of a public health intervention were Vitamin A deficiency, onchocerciasis, and trachoma. There were another 15% of conditions that at that time were difficult to manage and treat and that could not be cured: diabetic eye disease and glaucoma. Then there was a final 10% for which more or less nothing could be done including AMD and optic atrophy².

Did Vision 2020 met its aim to eliminate avoidable blindness by year 2020. Not at all, it was rather unrealistic and philosophical to even consider it as a time bound phenomenon. Pakistan, a signatory

to Vision 2020 {(Population of 221 million, per capita GDP 1285 USD (2019) and a medium human development index of 0.56 (2019)} has crude prevalence of blindness of 0.56% and all vision loss crude prevalence of 11.60%. The first National Survey of Blindness in 1987 to 1990 showed the prevalence of blindness in Pakistan was 1.78% and the second one after 15 years in 2005 showed the blindness prevalence to reduce to 0.9% (50% reduction)³. The third national survey is in progress currently. These figures had nothing to do with Vision 2020. It was rather a good planning at national level and strong leadership in eye health that resulted in this success.

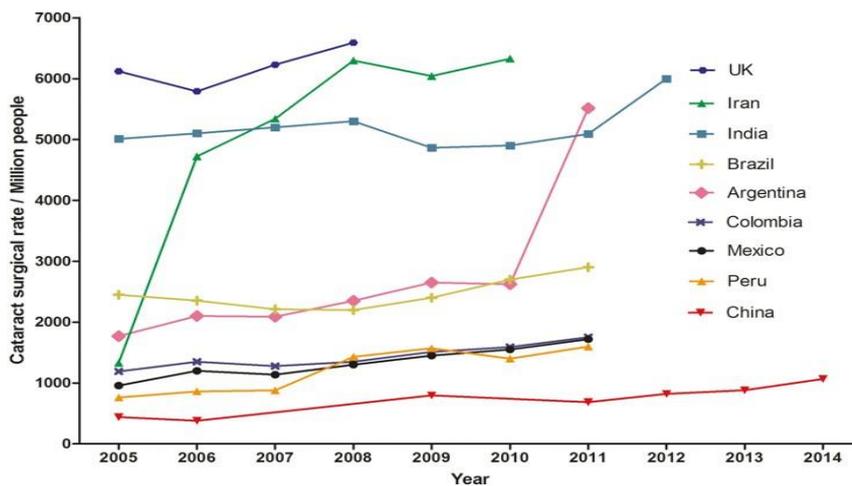
Let's see it from another angle. Vision Loss Expert Group has recently published its analysis in a landmark review stretching back to 1990 and projecting up to 2050⁴ (Table 1⁴).

Although the age-standardized prevalence of blindness and moderate or severe vision impairment decreased from 4.6% in 1990 to 3.4% in 2015, the number of people with avoidable visual loss has increased substantially because of growth and population ageing, and this trend is projected to continue up to 2050 and beyond. The authors⁴ estimated that 2.5% of the global population had avoidable vision loss due to cataract and uncorrected refractive error in 2010 and projected this figure to increase to 2.7% by 2020. Over the study period, most countries experienced an increase in CSR (such as China, India, Unites States, Brazil), with the greatest increase observed for Iran and Argentina, and a moderate increase observed for China. (See Figure 1⁴)

Table 1: Global magnitude of blindness- Past, Present and Future⁴

Year	Global number affected, all ages (millions)	
	Blindness	Moderate to severe visual impairment
1990	31	160
2000	32	176
2010	34	199
2015	36	217
2020	39	237
2030	55	330
2040	80	451
2050	115	588

From: Cataract Surgical Rate and Socioeconomics: A Global Study
 Invest. Ophthalmol. Vis. Sci.. 2017;57(14):5872-5881. doi:10.1167/iops.16-19894



Time changes of CSR in 10 countries with large population.

Figure 1 (Reproduced from Bourne et al⁴)

The study findings suggest that a substantial gap remains between the target set and what has been achieved so far and highlight the need for more coordinated efforts than have been made so far at global, regional, and country levels in terms of political and financial commitment, capacity building and training of more eye care personnel, improvement of access to eye care, enhancement of preventive and primary eye care services, sharing of best practices in implementation of programs for prevention of blindness, raising

community awareness through public-private partnership, and monitoring the progress by systematic data collection⁵.

A major shift from Vision 2020 objective of disease control to the concept of health care system-integrated eye care was the 2014-2019 Universal Eye Health Global Action Plan⁶. It set a global target of a 25% reduction in the prevalence of avoidable vision loss due to cataract and uncorrected refractive error by 2019 from the 2010 baseline level, a target not achieved so far.

In short, Vision 2020 has achieved success in its one of the three objectives only. The first objective in terms of advocacy and planning, the progress has been unprecedented. On two points, the global initiative failed to fully achieve its goals, the generation of adequate resources and infrastructure and appropriate technology development in local health care systems.

Although the last two decades have also witnessed unprecedented scientific and technological advances in terms of telemedicine projects, mobile-based applications, artificial intelligence and design and production of high-quality lens technology at a relatively low cost, we need dedicated professionals well placed in countries and supported in terms of finances and manpower to build processes and organize interventions. If there is anything that we can do, it is to select people, to make sure we have professionals who do understand that the community is responsible for its individuals and not just the government. If we have ophthalmologists who are serving only those who can pay the fee, which is one in 10, and don't feel ethically responsible for the other nine, we cannot expect significant progress. Similarly, industries should actively promote the use of low-tech alternatives rather than the expensive techniques and tools that can be afforded by no more than 5% to 10% of the population. For example, manual small-incision cataract surgery (MSICS), is a low-cost technique that uses simple tools but is not promoted much. Phacoemulsification may be the gold standard in USA, Europe,

Australia and Japan, but it is unaffordable for 70% to 80% of our population. As is famously quoted “Think Globally, but act locally”.

References:

1. WHO. Global initiative for the elimination of avoidable blindness. Geneva: World Health Organization, 2000.
2. Taylor HR. Global Blindness: The Progress We Are Making and Still Need to Make. *Asia Pac J Ophthalmol (Phila)* 2019;8:424–428
3. Jadoon MZ, Bourne RA, Shah SP, Khan MA, Johnson GJ, Gilbert CE, Khan MD. Prevalence of Blindness and Visual Impairment in Pakistan: The Pakistan National Blindness and Visual Impairment Survey. *Investigative Ophthalmology & Visual Science* November 2006, Vol.47, 4749-4755
4. Bourne RR, Flaxman SR, Braithwaite T, et al. Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: a systematic review and meta-analysis. *Lancet Glob Health* 2017; 5: e888–97.
5. Sabanyagam C, Cheng CY. Comment: Global causes of vision loss in 2015: are we on track to achieve the Vision 2020 target?. *Lancet Glob Health* 2017 Dec;5(12):e1164-e1165
6. Ackland P, Resnikoff S, Bourne R. World blindness and visual impairment: despite many successes, the problem is growing. *Comm Eye Health J* 2017; 30(100), 71-73.

Comparison of Efficacy of Subconjunctival Fluconazole Injection Versus Topical Amphotericin B in The Management of Fungal Corneal Ulcer

Hamid ur Rehman¹, Muhammad Naeem Khan¹, Irfan Aslam Khattak², Adnan Ahmed³

Objectives: The purpose of this study was to compare the use of subconjunctival injection of fluconazole (2 mg/ml) with topical amphotericin B (0.5 mg/ml) eye drops in dealing with cases of fungal corneal ulcer

Background: Fungal corneal ulcer is the most devastating eye infections which may cause loss of vision in severe cases, more commonly in the countries which are developing.

Materials and Methods: This study was carried out on 74 eyes of 74 patients with resistant corneal ulcers attending the outpatient clinic of department of Ophthalmology Khyber Girls Medical College, Hayatabad Medical Complex, Peshawar between July 2017 and February 2019.

Results: Group 1 included 37 cases treated with topical amphotericin B; the study showed amelioration of keratitis in nine cases (24%), and 28 cases (76%) developed complications. Group 2 included 37 cases treated with subconjunctival fluconazole injection; the study revealed statistically noteworthy result ($P < 0.01$) of amelioration of keratitis in 34 cases (92%), and in three cases (8%) complications developed.

Conclusion: Fungal corneal ulcer is the most devastating ocular infection and is a challenge for diseased, doctors and community. Most common cause we identified is diabetes and Plants eye trauma. Our study shows that subconjunctival injection of fluconazole was more efficacious than topical Amphotericin B eye drops, which is evident by effective healing of fungal keratitis and also less time to heal. *Al-Shifa Journal of Ophthalmology* 2020; 16(1): 9-15. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction

Fungal corneal ulcer is the most devastating eye infections which may cause loss of vision in severe cases, more commonly in the countries which are developing. [1] Fungal corneal ulcer is one of the main cause of visual loss in developing agrarian part of the world and is hard to manage. [1] Many patients who live in far flung poor areas gets late in presenting to hospitals; some are under diagnosed and injudiciously managed and develop serious complications. The corneal ulcer may worsen and lead to serious consequences like corneal staphyloma, descemetocoele, endophthalmitis, perforation, and visual loss. [2]

Fusarium and Aspergillus being the most common causes of Fungal corneal ulcer and are highly immune to most antifungal drugs.^[3] The fungal hypha can penetrate the unscathed Descemet's membrane and quickly enters the anterior chamber.^[2] The clinically dubious characteristics of fungal corneal ulcers are blurred vision, redness and pain, sensitivity to light, excessive discharge, and tearing^[1].

The topical administration of azoles, like fluconazole and voriconazole, has been demonstrated to be secure for eye structures and has fair perforation into corneal tissue.^[4] The types of fungal species isolated in patients with microbial keratitis are as follows:^[1]

Hyaline fungi: Fusarium solani, F. culmorum, Aspergillus flavus, A. fumigatus, A. terreus, A. niger, and other Aspergillus spp., Acremonium strictum, Scedosporium apiospermum, Clavulina humicola, Penicillium roqueforti, Phoma spp., and Rhizopus nigricans.

Molds dematiaceous fungi: Curvularia lunata, Curvularia spp., Bipolaris incurvata, Exserohilum rostratum, Cladosporium dominicanum, Lasiodiplodia theobromae, Alternaria alternata, Torula (Candida utilis), Aureobasidium pullulans, Nigrospora gallarum and Epicoccum spp.

Yeasts Candida albicans and other Candida spp.

As soon as one is diagnosed with fungal keratitis, immediate empirical therapy is required. Fungal corneal ulcer is a challenging ocular infection for Ophthalmologist. Natamycin is only ophthalmic antimycotic drug that is readily present in various regions of the world including Pakistan. Topical fortified antimycotic agents made from already available antifungal injections and it play a crucial part in management of fungal keratitis patients.^[5] Amphotericin B is one

of the wide-spectrum antimycotic drug. Topically it is efficacious for many cases of fungal keratitis^[6]. Topically strength of 0.05% in 5% dextrose (0.5 mg/ml) is used.^[1]

Shih-Hao Tsai et al used fluconazole subconjunctivally for management of intense mycotic corneal ulcer resistant to standard antimycotic medications and proved that it can be efficacious for intense fungal corneal ulcer and prevent early surgical intervention in acute phase of inflammation.^[7] Fluconazole is an effective antifungal agent against most cases of fungal keratitis.^[8] It is proven by the researchers that subconjunctival injection of fluconazole or intrastromal injection of voriconazole is effective against fungal corneal ulcer.^[9] Fluconazole used as subconjunctivally increase the potency of this medicine in management of mycotic corneal ulcer and has least side effects and it is also less hazardous for cornea and conjunctiva.^[10] Fluconazole 2 mg/ml injected subconjunctivally had lower rate of complications as compared to topical use of Amphotericin B and also has vast spectrum of antifungal coverage.^[11] Diagnosing corneal ulcer needs a detail history and complete ocular examination using slit-lamp biomicroscope. Sometimes only clinical signs are insufficient to diagnose an infection, but break in the corneal epithelium with staining on Fluorescein dye and stromal infiltrates should raise suspicion of infection until proven otherwise. There are no definite signs to identify the culprit microorganism but clinical experience and thorough slit-lamp examination can reveal the probable etiological agent in many cases.^[1] Fungal corneal ulcer has raised and dry slough, dense endothelial exudates, satellite lesions and stromal infiltrates with feathery margins.^[1]

Polyenes are amphotericin B, nystatin and natamycin and it destroy the cell by attaching to the mycotic cell wall ergosterol

and are efficacious against yeast and filamentous fungi. Amphotericin B is particularly useful against yeasts, but less effective against filamentous fungi; so it is the first line of choice against yeasts [12]. Amphotericin B (0.15%) drops can be used alone or in combination with natamycin in resistance cases; but their penetration through an intact epithelium is less than natamycin [12].

Azoles (imidazoles and triazoles) include ketoconazole, miconazole, fluconazole, itraconazole, econazole, and clotrimazole. Imidazoles and triazoles are synthetic chemical antifungal drugs. Azoles have good penetration in eye, so when it is given systemically they are helpful in management of ulcer caused by yeast and filamentous fungi. [13]

Materials and methods:

A prospective and follow-up study was conducted on 74 eyes of 74 patients with resistant corneal ulcers attending the outpatient clinic of department of Ophthalmology KGMC MTI Hayatabad Medical Complex Peshawar KP Pakistan between July 2017 and February 2019.

The patients were classified into two groups: group 1 included 37 eyes treated with topical amphotericin B (fungizone) eye drops at a concentration of 0.5% in 5% dextrose (0.5 mg/ml), prepared from the commercially available 50 mg vial with 5% dextrose dilution to obtain the 0.05% strength, every two hourly. For both categories topical 1% Cyclopentolate eye drops three times a day, 0.5% Moxifloxacin eye drops four times a day was used. Regular removal of the damaged tissue is done in both categories using keratome every 48 hours. Group 2 included 37 eyes treated with 1 ml subconjunctival injection having 0.5 ml of 2% lidocaine and 0.5 ml of fluconazole 2 ml made injectable form of fluconazole IV injection (Diflucan) injected every day for 10 injections and then every 48 hourly for another 10 injections.

Fate of ulcer in both groups was documented in both eyes and results were compared.

Results:

The ages of subjects in both categories was from 20 to 80 years, with a mean age of 45 years; 46 patients (62%) were under 45 years of age and 28 patients (33%) were older than 45 years of age (Table 1). As regards sex, 54 cases (62%) were male and 21 subjects (28%) were female (Table 1).

The study revealed that 36 cases (48%) were diabetic. Table 2 shows significant statistical difference ($P < 0.01$) in the presence of diabetes in relation to developing fungal corneal ulcer in both groups

On analyzing the occupation of the patients, it was found that 57 cases (76%) were farmers and 18 cases (24%) were from different occupations. A total of 57 patients complained of trauma with plant materials. No significant statistical difference was found in the origin of trauma in relation to developing fungal keratitis in both groups ($P > 0.05$) (Table 3).

As regards group 1, which was treated with topical amphotericin B for 37 cases, the study revealed healing of corneal ulcers in nine cases (24%), and 28 cases (76%) developed complications. There was significant statistical difference in the effect of the treatment on fungal keratitis; 86.7% of eyes of group 2 patients treated with fluconazole healed compared with 40.0% of eyes of group 1 patients treated with amphotericin B ($P < 0.01$) table 4.

As regards group 2, which was treated with subconjunctival fluconazole injection for 34 cases, the study showed statistically significant result ($P < 0.01$) of amelioration of keratitis in 32 cases (92%) and two cases (8%) developed complications. There was significant difference between the two

groups (before treatment) in terms of the ulcer size (P <0.05).

Table 1 Number and percent distribution of the patients based on sociodemographic data

Sociodemographic Data	Group (n(%))		Total n=74 (n (%))	Test of Significance
	Group 1 (n=37)	Group 2 (n=37)		
Age Groups (Yrs)				
< 45	24 (64.0)	22 (60.0)	46(62.0)	$\chi^2 =0.34 / >0.05$
>45	13 (36.0)	15 (40.0)	28 (38.0)	
Sex				
Male	25 (68.0)	28(76.0)	54 (72.0)	Fischer’s exact test=1.59 >/0.05
Female	12 (32.0)	09(24.0)	21 (28.0)	

Table 2 Number and percent distribution of the patients based on diabetes mellitus as risk factor data

DM	Group 1 (n=37) (n (%))	Group 2(n=37) (n (%))	Total (n=74) (n (%))	χ^2	P
Yes	9 (24.0)	27(72.0)	36(48.0)	46	<0.01)
No	28(76.0)	10(28.0)	38 (52.0)		

Table 3 Number and percent distribution of the patients based on the origin of trauma data

Origin of trauma	Group 1 (n=37) (n(%))	Group 2 (n=37) (n (%))	Total (n= 74) (n (%))	χ^2	P
Yes	27 (72.0)	30(80.0)	57(76.0)	1.75	>0.05
Non Plant	10 (28.0)	7(20.0)	18 (24.0)		

Table 4 Number and percent distribution of the patients based on the fate of ulcer

Fate	Group 1 (n=37) (n(%))	Group 2 (n=37) n(%)	Total (n=74) (n(%))	χ^2	P
Healed	9(24.0)	34(92.0)	43(58.0)	94.9	<0.01
Unheald	28 (76.0)	3 (8.0)	31 (42.0)		

Table 5 Mean and SD of the patients based on the size of ulcer before treatment

	Ulcer size (1 mm) (X- ±SD)		t test	P
	Group 1 (n=34)	Group 2 (n=34)		
Ulcer size (mm)	2.13±0.516	2.5±0.59	2.37	<0.05

Discussion:

The management of mycotic corneal ulcer is a difficult and hard task for ophthalmologists because the clinical signs are nearly similar in many cases, and many antifungal drugs are not readily available in many parts of the world. [1] Common antifungal used in different eye setups are polyene (natamycin and amphotericin B) and azoles (ketoconazole, fluconazole, itraconazole, and miconazole) [14]

Numerous elements were found that elevate the risk of fungal corneal ulcer. A study was conducted on 48 eyes and they observe that 58% of subjects with resistant keratitis, in which 38% were diabetic, and 21% got plant injury. [15] El- Sayed SH *et al.* reported that diabetes, plant eye injury and history of keratitis are the various predisposing elements for developing fungal keratitis. [1]

In our study, we found that diabetes mellitus and vegetative ocular trauma are the major risk factors for developing fungal corneal ulcer and we noted that 48% of the cases are diabetic and 76% cases have plant eye trauma. The present study conducted laboratory investigations to confirm the clinical diagnosis, same as Garg *et al* [6] who reported in their study that laboratory diagnosis is more supercilious to clinical identification in the treatment of fungal corneal ulcer. [16] Our study revealed that microscopic examination of corneal smear show only 38% of subjects with positive fungal results, but another study showed the sensitivity and specificity of gram staining for corneal smear as much as 61%. [17]

In the present study decrease sensitivity of detecting microorganism on direct microscopic detection is due to very intense insertion of mycotic organisms in the cornea, so it was not found in the scrapped tissue. However, we found that the positive culture result was reported to be around 75% and it is more accurate than direct gram staining and our results was comparable to another study conducted by

Nayak N who reported positive culture result to be 77.8% [18]

The present study was performed to compare the use of topical amphotericin B eye drops with the use of subconjunctival fluconazole injection in the treatment of fungal corneal ulcer. Our study showed that fluconazole used subconjunctivally may increase the effectiveness of this medicine in the management of fungal corneal ulcer and also increase the chance of least of side effects and hazardous for the corneal and conjunctival tissues. This is in agreement with that reported by Alsayed SH *et al* who stated that fluconazole 2mg/ml used subconjunctivally has the advantage of decrease incidence of complication as compared to the local use of amphotericin B and wider antimycotic spectrum. [1]

Avunduk *et al* reported that fluconazole is one of the safe and effective drugs when used as subconjunctival injection. Subconjunctival use of fluconazole is more effective than systemic use. [19]

Our study showed high percentage (92%) of curing of corneal ulcers in group 2, which was treated with subconjunctival fluconazole, compared with group 1, which was treated with topical amphotericin B (29%). Yilmaz and Maden [8] proved that subconjunctival fluconazole covers broader spectrum of fungi. Isipradit also showed that subconjunctival fluconazole was more effective compared with topical use. [20]

Conclusion:

On the basis of the findings of the present study, it is concluded that fungal corneal ulcer is the most devastating ocular infection and is a challenge for diseased, doctors and community. Most common cause we identified is diabetes and vegetative eye trauma. Our study shows that subconjunctival injection of fluconazole was more efficacious than topical Amphotericin B eye drops, which is

evident by effective healing of fungal keratitis and also less time to heal.

References:

1. El-Sayed SH, Wagdy FM, El-Hagaa AA, Mottawea EF. Topical amphotericin B versus subconjunctival fluconazole injection in the management of fungal keratitis. *Menoufia Med J* 2016;29:601-5
2. Jianzhang Hu, Jingjin Zhang, Yanling Li, Xiaoli Han, Weidong Zheng, Juan Yang, Guoxing Xu, "A Combination of Intrastromal and Intracameral Injections of Amphotericin B in the Treatment of Severe Fungal Keratitis", *Journal of Ophthalmology*, vol. 2016, Article ID 3436415, 7 pages, 2016.
3. H.-C. Lin, P.-H. Chu, Y.-H. Kuo, and S.-C. Shen, "Clinical experience in managing *Fusarium solani* keratitis," *International Journal of Clinical Practice*, vol. 59, no. 5, pp. 549–554, 2005
4. Nada WM, Al Aswad MA, El-Haig WM. Combined intrastromal injection of amphotericin B and topical fluconazole in the treatment of resistant cases of keratomycosis: a retrospective study. *Clin Ophthalmol*. 2017;11:871-874
5. Morand K, Bartoletti AC, Bochot A, Barratt G, Brandely ML, Chast F. Liposomal amphotericin B eye drops to treat fungal keratitis: physico-chemical and formulation stability. *Int J Pharm* 2007; 344 (1-2) :150-153.
6. Qu L, Li L, Xie H. Corneal and aqueous humor concentrations of amphotericin B using three different routes of administration in a rabbit model. *Ophthalmic Res* 2010; 43 (3) :153-158.
7. Shih-Hao Tsai, Yen-Chun Lin, Huan-Chen Hsu & Yan-Ming Chen (2016) Subconjunctival Injection of Fluconazole in the Treatment of Fungal *Alternaria* Keratitis, *Ocular Immunology and Inflammation*, 24:1, 103-106.
8. Yilmaz S, Maden A. Severe fungal keratitis treated with subconjunctival fluconazole. *Am J Ophthalmol* 2005; 140 (3):454-458.
9. Isipradit S. Efficacy of fluconazole subconjunctival injection as adjunctive therapy for severe recalcitrant fungal corneal ulcer. *J Med Assoc Thai* 2008; 91 :309-315
10. Shi W, Wang T, Xie L, Li S, Gao H, Liu J, Li H. Risk factors, clinical features, and outcomes of recurrent fungal keratitis after corneal transplantation. *Ophthalmology* 2010; 117 (5) :890-896
11. Prakash G, Sharma N, Goel M, Titiyal JS, Vajpayee RB. Evaluation of intrastromal injection of voriconazole as a therapeutic adjunctive for the management of deep recalcitrant fungal keratitis. *Am J Ophthalmol* 2008; 146 (1) :56-59.
12. Gokhale NS. Medical management approach to infectious keratitis. *Indian J Ophthalmol* 2008; 56 (3) :215-220
13. Johnson EM, Szekely A, Warnock DW. In-vitro activity of voriconazole, itraconazole and amphotericin B against filamentous fungi. *J Antimicrob Chemother* 1998; 42 (6) :741-745.
14. Xie L, Zhai H, Zhao J, Sun S, Shi W, Dong X. Antifungal susceptibility for common pathogens of fungal keratitis in Shandong Province, China. *Am J Ophthalmol*; 2008;146:260–265.
15. Mahdy RA, Nada WM, Wageh MM. Topical amphotericin B and subconjunctival injection of fluconazole (combination therapy) versus topical amphotericin B (monotherapy) in treatment of keratomycosis. *J Ocul Pharmacol Ther* 2010; 26 :281-285
16. Garg P, Gopinathan U, Choudhary K, Rao GN. Keratomycosis: clinical and microbiologic experience with dematiaceous fungi. *Ophthalmology* 2000; 107 (3) :574-580.

17. Sharma S, Kunimoto DY, Gopinathan U, Athmanathan S, Garg PR. Evaluation of corneal scrapping smear examination method in diagnosis of bacterial and fungal keratitis: a survey of 18 years of laboratory experience. *Cornea* 2002; 21 :643-647.
18. Nayak N. Fungal infections of the eye - Laboratory diagnosis and treatment. *Nepal Med Coll J* 2008; 10 (1) :48-63.
19. Avunduk AM, Wamei ED, Kaufman HE, Greer D. Comparison of efficacy of topical and oral fluconazole treatment in experimental *Aspergillus* keratitis. *Curr Eye Res* 2003; 26 :113-117.
20. Isipradit S. Efficacy of fluconazole subconjunctival injection as adjunctive therapy for severe recalcitrant fungal corneal ulcer. *J Med Assoc Thai* 2008; 91:309–315.

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Barriers Towards Cataract Surgery Among Patients Visiting Tertiary Eye Care Hospital, Rawalpindi

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ABSTRACT

Background: Cataract is one of the commonest cause of avoidable blindness in Pakistan. So Barriers that delay the surgical uptake in cataract patients become important investigation.

Objective: To evaluate the barriers towards cataract surgery among patients visiting the Out Patient Department of Tertiary Eye Care Hospital, Rawalpindi.

Materials and methods: It was a cross sectional study which was carried out at general OPDs (both paid and non-paid categories) of Tertiary Eye Care Hospital, Rawalpindi. Three hundreds and forty patients were interviewed by consecutive non-random sampling technique. Structured questionnaire was used with informed consent to collect the data.

Results: Major barriers reported in the study were non-availability of eye hospital near home 69.7% (237), unwariness of cost effective treatment of cataract 67.1% (228), fear of surgery 58.2% (198), lack of knowledge about eye hospital in public/private sector 56.2 (191), difficulty to visit an eye hospital 54.7% (186) and non-affordability of free surgery locally as 51.8% (176) pay more than thousand rupees fare for one turn to go an eye hospital.

Conclusions: Non- availability, lack of awareness, non-affordability, transport and fear of surgery were the major factors delaying cataract surgery. *Al-Shifa Journal of Ophthalmology* 2020; 16(1):16-20. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Cataract causes half of all cases of blindness and 33% of visual impairment worldwide. It is the leading cause of visual impairment and avoidable blindness in the world. The World Health Organization (WHO survey in 2002, estimated that cataract is cause of reversible blindness in more than 17 million (47.8%) out of 37 million blind individuals in the world. In a National Survey on Blindness (2004-5), 53% blindness was reported due to cataract.¹⁻³

Globally approximately 15 million cataract operations are performed annually with an estimated increase of 5 million from only 5 years ago. In 1994 approximately 500 ophthalmologists performed 140,000 cataract surgeries in Pakistan. Cataract surgery is not readily available in many countries, which is especially true for women, those living in rural areas, and those who are illiterate.⁴

The difference between cataract prevalence and its surgery done shows that there are some factors which cause delay in cataract surgery. Therefore, these barriers must be evaluated to get surgery in time so that normal functioning could be achieved by better vision. Cataract is most commonly due to aging but may also happen due to trauma or radiation exposure, can be present from birth, or may occur due to eye surgery for other problems.^{3,5}

Surgical treatment becomes necessary only if the cataract is causing problems which results in an improved quality of life. It is the most cost effective treatment of cataract. The procedures used for cataract surgery are extra-capsular cataract extraction (ECCE), intra-capsular cataract extraction (ICCE) and Pars planalensectomy.^{6,7}

Visual acuity is the most important need of daily life for normal functioning. Untreated cataract is the major cause of visual dysfunction throughout the world. In developing countries like Pakistan, cataract is the major cause of blindness. The purpose of this research is to find out the barriers towards cataract surgery among patients visiting the General OPD of Al-Shifa Trust Eye Hospital.

Materials and methods:

A cross sectional study was done at outpatient department (OPD) of Tertiary Eye Care Hospital, Rawalpindi to find out the barriers towards the uptake of cataract surgery. Study was done from October 2019 to January 2020. Sample size was calculated by following formula, $n = Z^2 \cdot pq / e^2$ according to which sample size was 340 with prevalence 33.2% at 95% confidence limit. Consecutive non-random sampling technique was used. Willing patients of both gender of age >35 years having visual acuity less than 6/18 without any ocular pathology except cataract were included in the study. An interview based structured questionnaire was used for data

collection. The questionnaire consisted of five sections, first section was comprised of sociodemographic data, second section consisted of visual acuity, third section had awareness questions, the fourth section had availability questions and fifth part had preference questions. All the individuals had visual acuity examination. For the detailed ocular examination, eyes of patients were dilated. After dilation patients were fully examined i.e. starting from eye lids till retina on ophthalmoscope by ophthalmologist to document cataract or any other pathology. Those patients who met the inclusion criteria were included in the sample. Informed consent was taken from each individual and each individual was interviewed to fill a structured questionnaire by the investigator. Data was entered in SPSS version 22. After entering data in the SPSS, data was cleaned by running frequencies, percentages and any discrepancy was removed. Descriptive analysis was done by running percentages & frequencies for the categorical variables and mean & standard deviation for continuous variables.

Results

Total 340 subjects included in this study. More than half of the patients were females comprising 53.8% in total data. Mean age of the subjects was 57.5 years ranging from 35 to 83 years. The educational level of majority of the respondents was primary 62.9%. More than half (192, 56.5%) respondents were not working due to poor vision.

Barriers towards Cataract Surgery:

Majority of respondents (280, 82.4%) had difficulty in vision due to cataract. More than 53.5% (182) subjects had no knowledge about cataract and 62.1% (211) subjects did not know about the treatment of cataract. One hundred and ninety-two (58.2%) were fear of cataract surgery (Table 1). More than half 69.7% (237) subjects had no eye hospital near their homes. Public transport was used by

70.0%(238) subjects while 51.8%(176) subjects paid fare more than one thousand for one turn. It was preferred by

34.1%(116) subjects that males should get their treatment first (Table:2).

Table 1: Awareness of Cataract & Its Treatment (N=340)

Awareness	Frequency (N)	Percentage, (%)
Cataract	40	100
Yes	116	34.1
No	182	53.5
Don't know	42	12.4
Treatment of cataract	N=340	100
Yes	129	37.9
No	211	62.1
Understanding of mature cataract	N=340	100
Yes	171	50.3
No	169	49.7
Is treatment painful?	N=340	100
Yes	152	44.7
No	100	29.4
Don't know	88	25.9
Vision improves after surgery	N=340	100
Yes	268	78.8
No	51	15.0
Don't know	21	6.2

Table 2: Availability of services for Cataract Surgery (n=340)

Availability	Frequency (n)	Percentage (%)
Eye hospital near home	N=340	100
Yes	103	30.3
No	237	69.7
Difficult to get eye checkup	N=340	100
Yes	186	54.7
No	154	45.3
Reason for difficulty to go eye hospital	N=340	100
Transport	130	38.2
Lack of time	53	15.6
Lack of attention	14	4.1
Other	143	42.1
Fare for one turn	N=340	100
500	104	30.6
1000	60	17.6
More than 1000	176	51.8
Payment of surgery charges	N=340	100
Yes	85	25.0
No	159	46.8
Hardly	96	28.2
Availability of free surgery locally	N=340	100
Yes	82	24.1
No	164	48.2
Don't know	94	27.6

Discussion:

Cataract is major cause of blindness in adults. It is treatable but still it is the most important eye health issue of the developing countries. In current study major barriers found were unavailability of hospital near home, no knowledge about cost effective treatment of cataract, fear of surgery, lack of knowledge about eye hospital in public/private sector, difficulty to get an eye hospital, lack of knowledge about cataract and people pay more than thousand rupees for one visit to an eye hospital.

Bettadapura et al reported that waiting for maturity of cataract to be the major barriers.⁸ Barriers related to patient attitude like (ability to manage routine work, cataract not mature, could see clearly with the other eye, busy with work), then to issues of service delivery or cost and affordability (insufficient family income) were found as barriers by Dhaliwal and Gupta.⁹

Bhagwan et al reported that 70.69% cases wanted operation only when able to see nothing.¹⁰ Rabi reported the main barriers for seeking cataract surgery were cost of the service (61%) and better vision in the other eye (18%).¹¹ Saikumar et al reported lack of escort, fear of surgery, socioeconomic reasons, adverse media reports of failures of surgery and surgery not needed to be the main barriers.¹²

Studies done in adjacent regions also found similar reasons for not taking surgical care as ours Yin et al reported lack of knowledge about cataract and concerns about the quality of local services as barriers.¹³ Snellingen et al in their study in Nepal found economic (48%) and logistical (44.8%) constraints followed by fear of surgery (33.3%) and lack of time (18.8%) to be the most frequent reasons for not accepting surgery.¹⁴

Vaidyanathan et al reported that 24% of people bilaterally blind and 33% of those unilaterally blind, found waiting for cataract to get mature. Second barrier they found (21.6% of the bilaterally blind) was "no one to accompany" and "Fear of operation" in 12.3% of the bilaterally blind population as a barrier. In our study the proportion of females was higher in almost all the reported barriers. Males mentioned waiting for cataract to get mature more than females while females (24.9%) stated "no one to accompany" nearly twice as frequently as males (14.2%) in other study.¹⁵

Addressing of barriers reported in the present study planning and policy making could improve utilization of services and cataract surgery uptake. However even when surgery is free and transport facility is available, cataract acceptance rates are low as indicated.

References:

1. Lens and Cataract. Italy: American academy of Ophthalmology: 2018 Nov 2.
2. World Health Organization. Priority Eye Diseases. [online] Available at: <<https://www.who.int/blindness/causes/priority/en/index1.html>>.
3. Cotter SA, Varma R, Ying-Lai M, Azen SP, Klein R, Los Angeles Latino Eye Study Group. Causes of low vision and blindness in adult Latinos: the Los Angeles Latino Eye Study. *Ophthalmology*.2018 Nov 13.
4. Jadoon Z, Shah SP, Bourne R, et al Cataract prevalence, cataract surgical coverage and barriers to uptake of cataract surgical services in Pakistan: the Pakistan National Blindness and Visual Impairment Survey *British Journal of Ophthalmology* 2007;91:1269-1273.
5. Jatoi M.S *Clinical ophthalmology*.5th ed. Karachi: Paramount Book
6. Marsa, L. What Are Cataracts? Understanding Symptoms And

- Treatment. [online] AARP. Available at:
<<https://www.aarp.org/health/conditions-treatments/info-2019/cataracts-eye-disorder.html>>.
7. Medicalnewstoday.com. Cataract Surgery: Types, What To Expect, And Recovery. [online] Available at: <<https://www.medicalnewstoday.com/articles/326346>>.
 8. Bettadapura GS, Datti NP, Donthi K, Ranganath BG, Ramaswamy SB, Sangeetha T. Barriers to the uptake of cataract surgery in a rural population of south Karnataka, India. *Int J Current Res Rev.* 2013;5:77-82.
 9. Dhaliwal U, Gupta SK. Barriers to the uptake of cataract surgery in patients presenting to a hospital. *Indian J Ophthalmol.* 2007;55:133–6.
 10. Bhagwan J, Rastogi IM, Malik JS, Dhull CS. Knowledge, attitude and practices regarding cataract surgery among senile cataract cases in Haryana. *Indian J Community Med.* 2006;31:668.
 11. International Agency for the Prevention of Blindness (IAPB). *International Year Book and Statesmen's Who's Who.* DOI: 10.1163/1570-6664_iyb_sim_org_38948.
 12. Sasikumar S, Naved M, Saikumar SJ. Cataract surgical coverage in Kolenchery, Kerala, India. *Community Eye Health J.* 1998;11:7.
 13. Yin Q, Hu A, Liang Y, Zhang J, He M, Lam DSC et al. A Two-Site, Population-Based Study of Barriers to Cataract Surgery in Rural China. *IOVS.* 2009;50:1069-75.
 14. Snellingen T, Shrestha BR, Gharti MP, Shrestha JK, Upadhyay MP, Pokhrel RP. Socioeconomic barriers to cataract surgery in Nepal: The south Asian cataract management study. *Br J Ophthalmol.* 1998;82:1424–8.
 15. Vaidyanathan K, Limburg H, Foster A, Pandey RM. Changing trends in barriers to cataract surgery in India. *Bull WHO.* 1999;77:104-9.

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Visual Outcomes and Ocular Attributes of Mechanical Implantation of Intracorneal Ring Segments - A Longitudinal Hospital Based Study

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Introduction: Intracorneal ring segments (ICRS) are used as a treatment modality in Low myopia and corneal ectasia with mechanical and non-automated surgery technique. In Pakistan, due to cost and availability based issues, mechanical method is preferred. It is important to evaluate its short and long term visual outcome.

Methodology: It was interventional uncontrolled trial conducted in cornea department, Al-Shifa trust eye hospital, Rawalpindi. The study duration was three years, from July 2016 to July 2019. Thirty-seven patients had manual implantation of Intra corneal ring segment and were included in the study. Visual acuity, spherical equivalent, maximum keratometric readings, corneal astigmatism and endothelial cell density was measured at fixed intervals. The intervals were Pre-Operative, 1 month follow up, 6 months follow up, 1 year follow up and 3 year follow up. Repeated measure ANOVA was used to detect statistically significant difference between pre-operative and post-operative intervals.

Results: There was statistically significant improvement in visual acuity after surgery and significant reduction in spherical equivalent and K-Max. No statistically significant difference was seen in visual outcomes for cases with and without a history of corneal cross linking.

Conclusion: Manual ICRS surgery is an effective treatment modality in mild to severe cases of Keratoconus. *Al-Shifa Journal of Ophthalmology 2020; 16(1): 21-29.* © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Intracorneal Rings Segments (ICRS) are synthetic polymethylmethacrylate (PMMA) rings which are inserted in the mid peripheral area of cornea. It has been used in low Myopia, Keratoconus, Pellucid marginal degeneration (PMD), Refractive surgery induced ectasia and Idiopathic irregular astigmatism^(1, 2). The rings have been observed to cause flattening in the central cornea leading to decrease in keratometric readings. The proposed mechanism involves arc shortening effect on cornea due to introduction of ICRS segments as spacer elements between the regularly placed corneal collagen fibers. However, unpredictable results have been frequently noted in keratoconus due to loss of regular orthogonal structure of collagen fibers⁽³⁾.

Currently two main surgical approaches are used for ICRS implantation based on the method used for formation of stromal channels or “pockets” for ICRS placement. Mechanical or Manual method involves mechanically creating the stromal channels with spatula after incising a partial thickness opening in cornea through calibrated diamond knife based on the established nomograms. Although this method decreases the cost but problems related to shallow or deep placement of rings have been reported ⁽⁴⁾. The other technique involves stromal tunnel formation by using femtolaser. Due to higher reliability, predictability and lack of complications, this is the method currently approved by FDA ⁽⁵⁾.

Although a less preferred technique due to procedure related accuracy and safety, manual ICRS have been used successfully in settings without facility of femtolaser. Multiple studies have reported positive visual outcomes with properly done manual ICRS implantation ⁽⁶⁻⁸⁾ and it becomes a feasible procedure for Keratoconus cases absolutely indicated for corneal transplant in low health finance countries like Pakistan. Although ICRS has been done for Keratoconus and Post refractive surgery ectasia in Pakistan no studies according to the best of our knowledge have been published describing visual outcomes of this surgery.

The objectives of current study were to measure visual acuity improvement after ICRS surgery and to determine relationship between achieved visual acuity, spherical equivalent, maximum keratometric readings and axial length in operated eyes.

Materials and Methods:

It was prospective follow up based study conducted from July 2016 to July 2019 in Cornea department of Al- Shifa trust eye hospital, Rawalpindi. All the cases that underwent manual ICRS surgery from in July 2016 were recruited in the study. All keratoconus cases with clear cornea, minimum corneal thickness 400µm at the sight of insertion of ICRS, no improvement with refraction, improvement of visual acuity up to 6/12 level or more with rigid gas permeable lens (RGP) (improvement with RGP is improvement with refraction) but associated absolute intolerance of RGP underwent ICRS implantation. Informed consent was taken from all patients before surgery. Informed consent was taken from the parents/ guardians and assent was taken from the patients in cases where respondents were minor.

Ferrara rings were implanted after creating a stromal tunnel manually. The depth for the tunnel, the thickness of rings, and angle of incision was selected based on the official nomogram calculation ⁽⁹⁾. All the cases were operated by a single surgeon. Single ring was implanted in asymmetric keratoconus and two rings were implanted in symmetric keratoconus. Asymmetry was defined as unequal distribution of cone between two halves when division was made by dividing the cornea into half from the most curved meridian on anterior axial curvature map in Galilei corneal imaging ⁽¹⁰⁾. All the patients were prescribed topical antibiotic steroid combination (tobramycin 0.3% and dexamethasone 0.1%) and topical antibiotics (moxifloxacin hydrochloride 0.5%) postoperatively for a week followed by weak steroid (florometholone 0.1%) and lubricants for one month.

Data collection was done pre operatively and on periodic visits of 1 month, 6 months, 1 year and 3 years. Data was collected after informed consent was taken based on the principles of Declaration of Helsinki. Study was conducted after

approval from the Institution review board and Ethical review board of Al- Shifa Trust Eye Hospital. The cases who had ring extrusion were operated for ICRS removal or ICRS repositioning. In cases of removal those cases were booked for Penetrating keratoplasty and subsequently operated and not followed up in the current study.

The main outcome variable was corrected visual acuity and the spherical equivalent of respective correction. It was measured with ETDRS chart in log MAR scale. Visual acuity was measured on every follow up. In addition, presenting complaint, corneal topography, specular microscopy, A- scan (immersion ultrasound technique) was done on every follow up. K max, corneal astigmatism was recorded from corneal topography. Endothelial cell density was recorded from specular microscopy. Anterior segment Optical coherence tomography was done to measure the depth of implanted ICRS after one week of surgery. It was calculated for two points from each ring and arithmetic mean of those reading was recorded. All the post-operative complications related to ICRS were noted and treated accordingly.

Preliminary descriptive analysis was carried out to describe the attributes of all respondents as well as to conduct normality analysis and check other assumptions necessary for inferential analysis. Repeated measure ANOVA (F-test) was used to determine the mean difference between data collected on different occasions. The variables assessed through F-test were Visual Acuity, Spherical equivalent (Refraction), K-Max, Astigmatism, and Endothelial cell density. Bonferroni test was used for Post Hoc comparisons for statistically significant variables. Mean difference between and calculated and observed depth of ICRS ring and last postoperative corrected visual acuity and pre-operative visual acuity with corneal RGP lenses was assessed through Dependent samples T-test. Independent

samples t-test was used to determine mean difference in visual attributes between participants with and without history of CXL. Pearson correlation was used to assess relationship between corrected visual acuity, spherical equivalent, and K-Max taken at the last follow up. All tests used p-value<0.05 as significant.

Results:

A total of 37 cases were included in the study. Majority of the patients were male (54.1%, N= 20). Mean age of the respondents was 21.00 years with a standard deviation of 6.42 years ranging from 12 years to 39 years. Less than half of the total respondents (40.5%) had a positive history of CXL. Mean visual acuity with RGP lenses was 0.34 ± 0.20 log MAR ranging from 0.18 log MAR to 1.00 log MAR. Majority of the cases (83.8%) had two rings implanted during surgery. (Table 1)

Mean calculated depth for ICRS rings was 447.08 ± 30.97 μm and mean observed depth was 324.73 ± 54.67 μm . Mean pre-operative visual acuity was 0.97 log MAR while it improved to 0.43 log MAR after one year. Similarly mean spherical equivalent of refraction improved from -8.82DS to -4.42DS (Diopter sphere) over the period of one year. There was reduction in K max as well from a mean pre-operative value of 60.01DS to 55.54DS after a period of six months.

A mean corneal astigmatism of 3.16DS was observed at the last follow up. There was a reduction in endothelial cell count density from mean pre-operative value of 2620.24 ± 405.18 per mm^2 to 2462.00 ± 343.23 per mm^2 at an interval of one month. (Table 2)

A statistically significant difference was observed between pre op attributes as compared to their subsequent follow ups (p-value <0.05). Mean pre-operative visual acuity was 0.97 log MAR and it improved to 0.38 log MAR at the last follow up.

Reduction in mean K Max reading from 59.99DS to 55.44DS was observed after one year of ICRS implantation. (Table 3)

Post Hoc test showed that there was no statistically significant reduction in mean corneal astigmatism up to first six months

of study after which a significant reduction was seen in the next six months (p-value= 0.001). However, a statistically significant reduction in spherical equivalent was observed after first month of implantation (p-value= 0.01). (Table 4)

Table 1: Demographic Characteristics and Ocular History

Variable	Frequency (N=37)	Percentage (%)
Gender		
Male	20	54.1
Female	17	45.9
History of CXL		
Positive	15	40.5
Negative	22	59.5
Number of Rings Used		
One	6	16.2
Two	31	83.8

Table 2: Visual Attributes of respondents

Variable (Unit)	Mean	Standard Deviation	Minimum Value	Maximum Value
Visual Acuity (log MAR)				
Pre-Operative	0.97	0.30	0.48	1.25
One Month	0.61	0.29	0.18	1.25
Six Months*	0.48	0.19	0.18	1.00
One Year*	0.43	0.19	0.18	1.00
Three year	0.39	0.20	0.18	1.00
Refraction (Diopter Sphere)				
Pre-Operative	-8.82	4.78	-0.50	-22.00
One Month	-5.84	3.64	-1.25	-14.00
Six Months*	-4.76	2.78	-1.50	-12.00
One Year*	-4.42	3.04	-0.25	-13.00
Three year	-3.78	2.31	-0.50	-9.50
Maximum Keratometric Reading (Diopter Sphere)				
Pre-Operative	60.00	4.71	51.13	67.15
One Month	55.54	4.87	43.90	65.87
Six Months*	55.54	7.65	45.88	64.44
One Year*	55.43	4.58	46.91	64.44
Three year	54.78	4.52	46.31	64.44
Corneal Astigmatism (Diopter Sphere)				
Pre-Operative	5.21	2.74	0.26	13.28
One Month	3.87	1.80	0.30	8.12
Six Months*	4.14	2.05	0.88	10.86
One Year*	3.71	2.01	1.00	10.86
Three year	3.16	1.71	0.71	8.50
Endothelial Cell Density (Cells per mm²)				
Pre-Operative**	2620.24	405.17	1845.00	3827.00
One Month***	2462.00	343.23	1736.00	3001.00
Six Months****	2401.31	350.07	1742.00	3284.00
One Year****	2393.78	360.42	1711.00	3147.00
Three year**	2360.33	380.12	1721.00	3212.00

*N=36, **N=33, ***N=31, ****N=32

Table 3: ANOVA test

Variables (N=36)	Mean±SD					ANOVA (Greenhouse-Geisser Test)		
	Pre Op	1 Month	6 Month	1 Year	3 year	F-value	p-value	Eta ²
Visual Acuity (log MAR)	0.97±0.31	0.61±0.29	0.48±0.19	0.43±0.19	0.38±0.19	53.17	0.0005	0.60
Refraction (DS)	-8.63±4.69	-5.89±3.68	-4.76±2.78	-4.42±3.04	-3.77±2.35	24.33	0.0005	0.41
K-Max (DS)	59.99±4.78	55.65±4.89	55.55±4.71	55.44±4.58	54.86±4.55	63.16	0.0005	0.64
Astigmatism (DS)	5.28±2.75	3.96±1.74	4.14±2.05	3.71±2.01	3.23±1.69	8.41	0.0005	0.19
Endothelial Cell Density (Cells/mm³)*	2596.26±403.10	2462.00±343.23	2400.65±353.79	2392.29±366.28	2331.71±359.25	10.16	0.0005	0.25

*N=31

Table 4: Bonferroni Post Hoc Comparisons

Variables	Mean Difference (I-J)	p-value	Confidence Interval (95%)	
Visual Acuity				
Pre Op & One Month	0.38	0.0005	0.20	0.55
Pre Op & Six Months	0.49	0.0005	0.33	0.65
Pre Op & One Year	0.54	0.0005	0.39	0.70
Pre Op & Three year	0.59	0.0005	0.42	0.76
Refraction				
Pre Op & One Month	-2.74	0.01	-5.01	-0.46
Pre Op & Six Months	-3.87	0.0005	-5.92	-1.82
Pre Op & One Year	-4.20	0.0005	-6.19	-2.21
Pre Op & Three year	-4.85	0.0005	-6.86	-2.85
K Max				
Pre Op & One Month	4.33	0.0005	2.95	5.72
Pre Op & Six Months	4.44	0.0005	2.97	5.90
Pre Op & One Year	4.54	0.0005	3.28	5.80
Pre Op & Three year	5.12	0.0005	3.70	6.55
Astigmatism				
Pre Op & One Month	1.32	0.12	-0.16	2.80
Pre Op & Six Months	1.14	0.30	-0.37	2.65
Pre Op & One Year	1.56	0.001	0.50	2.63
Pre Op & Three year	2.05	0.0005	0.98	3.12
Endothelial Count Density				
Pre Op & One Month	134.16	0.37	-52.09	320.41
Pre Op & Six Months	195.52	0.09	-15.58	406.61
Pre Op & One Year	203.87	0.003	52.56	355.19
Pre Op & Three year	264.45	0.0005	108.77	420.14

Discussion:

The main objectives of the study were to determine improvement in visual acuity after ICRS surgery and to evaluate if the difference shows statistical significance. It also involved establishing relationship of other ocular attributes within themselves and with final achieved visual acuity. Although the modern ICRS was first introduced by Professor Joseph Colin in the start of this century⁽³⁾ the notion of using an intracorneal device for changing corneal power goes as back as to 1960s⁽¹¹⁾. Mechanical ICRS in an established management regime of keratoconus in developed countries⁽¹²⁾ but few studies have been reported from low middle income countries like Pakistan with limited access to femtolaser^(7,13). To the best of our knowledge no research from our country has described results of manual ICRS for such a long follow up.

Significant improvement in BCVA was observed over the period of three years (p-value<0.05) In fact, improvement in BCVA was observed even after a relatively short interval of one month (p-value= 0.0005) but after this no two consecutive visits showed any improvement worth statistical significance with progressively increasing probability value. This shows that immediately after the surgery the rings cause prompt structural changes in the corneal curvature which in result leads to reduction or possible transformation of the existing irregular astigmatism leading to improvement of the BCVA. However, after that the changes within cornea occur at a more uniform and slow speed even though the size of interval in our study is larger after the first consecutive follow up. A possible explanation for this phenomena comes from the observation that the higher the grade of keratoconus the better is the postoperative visual outcome⁽¹⁴⁾. This points out to a logical hypothesis that the higher the irregularity observed in the cornea the more will be the curvatural flattening as ICRS somehow has a more

regularizing effect on corneas with higher ectatic properties. The internal mechanisms involved in this phenomena needs further researches to be conducted Different studies done previously have also reported statistically significant improvement in BCVA on a follow up as less as one⁽¹⁵⁾ and two months⁽¹⁶⁾.

A similar scenario was seen for changes in spherical equivalent as well with overall statistically significant reduction (p-value<0.05) and planned comparisons showing statistical significance only for the first follow up. In contrast, maximum keratometric readings show a different pattern. There is an early reduction in K-Max after the first month (p-value=0.0005), then there is a phase of minimal reduction over the next follow ups up to 1 year postoperatively with statistically significant reduction observed during the interval of 1 and 3 years. (p-value= 0.03) Similar results have been reported by other studies^(17, 18) for keratoconus ranging from mild to severe keratoconus.

It is concluded that manual ICRS is effective in improving visual outcome in keratoconus of all grades. If the predictability and safety involved in manual ICRS implantation can be improved, it will play a massively role in enhancing effectiveness of the procedure. It is also concluded that the mechanism involved in changes within cornea due to ICRS still needs research to be explored.

The study has few strengths. Due to its prospective study design, the changes taking place over time in the corneal refractive status were observed thoroughly. The surgeon related bias was minimum as all the surgeries were performed by a single researcher. Galilei based topography was used which is one of the few most accurate topography based instruments available.

The study had certain limitations. First of all, the overall sample size was small which

can be obstacle in generalizing the results. Secondly, detailed analysis of corneal aberrations was not conducted and thirdly we were unable to further depict the clinical significance of our results because of lack of a control group.

References:

1. Bakshi R. Intra-Stromal Corneal Ring Segments. Delhi J Ophthalmol [Internet]. 2013 [cited 2019 Aug 6];24(1):16–22.
2. Moshirfar M, Edmonds JN, Behunin NL, Christiansen SM. Current Options in the Management of Pellucid Marginal Degeneration. J Refract Surg [Internet]. 2014 Jul 1 [cited 2019 Aug 6];30(7):474–85.
3. Vega-Estrada A, Alio JL. The use of intracorneal ring segments in keratoconus. Eye Vis [Internet]. 2016 [cited 2019 Aug 6];3(1).
4. Monteiro T, Alfonso JF, Franqueira N, Faria-Correia F, Ambrósio R, Madrid-Costa D. Predictability of Tunnel Depth for Intrastromal Corneal Ring Segments Implantation Between Manual and Femtosecond Laser Techniques. J Refract Surg. 2018 Mar 9;34(3):188–94.
5. Mounir A, Radwan G, Farouk MM, Mostafa EM. Femtosecond-assisted intracorneal ring segment complications in keratoconus: From novelty to expertise. ClinOphthalmol [Internet]. 2018 May 22 [cited 2019 Aug 6];12:957–64.
6. Ferrara G, Torquetti L, Ferrara P, Merayo-Llodes J. Intrastromal corneal ring segments: Visual outcomes from a large case series. ClinExpOphthalmol. 2012;40(5):433–9.
7. D'Souza S, Ganesh S, Shetty R, Ramachandran S, Kurian M. Intrastromal corneal ring segments for management of keratoconus. Indian J Ophthalmol [Internet]. 2013 [cited 2019 Aug 6];61(8):451.
8. Albertazzi R, Ferlini L, Perrone L, Perrone D, Rao G, Alfonso J, et al. Combination of Intracorneal ring segments (Ferrara and Intacts) in the care of patients with Keratoconus. InvestOphthalmol Vis Sci [Internet]. 2013 Jun 16 [cited 2019 Aug 6];54(15):5291–5291.
9. Nomogram, AJL Ophthalmics [Internet]. [cited 2019 Aug 7].
10. Sandes J, Stival LRS, Pereira De Ávila M, Ferrara P, Ferrara G, Magacho L, et al. Clinical outcomes after implantation of a new intrastromal corneal ring with 140-degree of arc in patients with corneal ectasia. Int J Ophthalmol [Internet]. 2018 [cited 2019 Aug 7];
11. Blevatskaya ED. Intralamellarhomoplasty for the purpose of relaxation of refraction of the eye. Arch Soc Am OphthalmolOptom. 1968;6:311–25. translated from OftalmolZh 1966;7:530–537
12. Tunc, Z., Helvacioğlu, F., & Sencan, S. (2013). Evaluation of intrastromal corneal ring segments for treatment of keratoconus with a mechanical implantation technique. *Indian Journal of Ophthalmology*, 61(5), 218–225.
13. Jadidi, K., Mosavi, S. A., Nejat, F., Naderi, M., Janani, L., & Serahati, S. (2015). Intrastromal corneal ring segment implantation (keraring 355°) in patients with central keratoconus: 6-month follow-up. *Journal of Ophthalmology*, 2015, 1–8.
14. Alio, J. L., Vega-Estrada, A., Esperanza, S., Barraquer, R., Teus, M., & Murta, J. (2014). Intrastromal corneal ring segments: How successful is the surgical treatment of keratoconus? *Middle East African Journal of Ophthalmology*, 21(1), 3–9.
15. Amoozadeh, J., Rad, N. M., Beheshtnejad, A. H., Kheirkhah, A., & Hashemi, H. (2010). Effects of intracorneal ring segment on corneal biomechanics in keratoconic eyes. *Iranian J Ophthalmol*, 22(4), 25–30.
16. Kang, M. J., Byun, Y. S., Yoo, Y. S., Whang, W. J., & Joo, C. K. (2019).

- Long-term outcome of intrastromal corneal ring segments in keratoconus: Five-year follow up. *Scientific Reports*, 9(1), 315.
17. Al-Muammar, A. (2015). Comparison of visual, refractive and topographic keratometry outcomes of intacs and intacs SK in mild to moderate keratoconus eyes. *Middle East African Journal of Ophthalmology*, 22(1), 74–79.
18. Zare, M., Mehrjardi, H. Z., Afarideh, M., Bahrmandy, H., & Mohammadi, S. F. (2016). Visual, keratometric and corneal biomechanical changes after intacs SK implantation for moderate to severe keratoconus. *Journal of Ophthalmic and Vision Research*, 11(1), 17–25.

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Surgical Outcomes of Von Hippel Lindua Retinal Angiomatosis

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ABSTRACT

Purpose: To evaluate long term surgical outcomes of vitreoretinal surgery for retinal angiomatosis in VHL (von Hippel lindua) syndrome.

Methods: A total of 14 eyes underwent pars plana vitrectomy, retinectomy and endotamponade of 5000cs silicone oil for retinal angiomatosis. All the eyes in which other treatment options failed to improved visual acuity and visual acuity was light perception (LP) were included in the study. Study was conducted at department of ophthalmology, Lahore General Hospital/PGMI, Lahore. All patients who completed three years follow up were included in the study.

Result: In 7 (50%) eyes visual acuity improved from light perception (LP) to 6/60, in three (21.43%) eyes from light perception (LP) to 1/60, in two (14.29%) eyes from light perception (LP) to hand motion (HM), in one (7.14%) eyes vision did not improve from light perception (LP) and one (7.14%) eye vision decreased to no perception of light (NPL). Intraoperative or post operatively no significant complications observed.

Conclusion: Surgical treatment is a good option for Von Hippel Lindua retinal angiomatosis in patients with severe decrease in visual acuity, in whom other treatment options failed to improve visual acuity. *Al-Shifa Journal of Ophthalmology 2020; 16(1): 30-35. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

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Introduction:

The Von Hippel–Lindau (VHL) disease is an autosomal dominant disorder that implies a genetic alteration resulting in the loss of the tumor suppressor function of the VHL gene ^[1, 2] located on chromosome ^[3] (3p25.3). The protein encoded by this gene regulates the hypoxia-inducible factors (HIF) ^[4]. The incidence of the disease is 1/36,000 live births in the general population. ^[5, 6]

This disease has been classified into two types. Type 1 is characterized by retinal angiomas, CNS hemangioblastomas, renal cell carcinomas, pancreatic cysts, and neuroendocrine tumors, while type 2 includes pheochromocytomas, retinal angiomas, and CNS hemangioblastomas ^[7]. Half of the patients affected by VHL presents with ocular symptoms ^[8].

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The retinal lesions are often the first manifestation of VHL, and the natural course of these pathologically benign tumors most frequently leads to subretinal exudates, fibrovascular proliferation (FVP), exudative and tractional retinal detachment, and eventually to blindness of the affected eye if left untreated^(9, 10). Patients are typically diagnosed in the second or third decades of life, with a mean age of 25 years^[11].

Treatment can be challenging for many reasons, such as presence of multiple bilateral tumors and also potential for the growth of new tumors. Small lesions (up to 4.5 mm, but preferentially 1.5 mm or smaller in size) can be treated with laser photocoagulation^[12]. Peripheral and larger lesions can be treated with cryotherapy^[13]. A few successful outcomes are observed with photodynamic therapy^[14] and brachytherapy^[15]. Intravitreal injections of anti-vascular endothelial growth factor (VEGF)^[16], showed no effects on lesion size.

We conducted the study on patients with VHL in whom all other treatment modalities have been failed and we performed retinal surgery to assess whether pars plana vitrectomy (PPV) may offer the means of dealing with more complicated and advanced cases of retinal VHL disease with control of the disease and visual improvement.

Materials and Methods:

This is a retrospective review of the case notes for 14 eyes presenting with VHL disease, operated on for complicated retinal capillary hemangioblastoma (RCH) between 2016 to 2019. This study was conducted at Ophthalmology Department, Lahore General Hospital, Lahore. Institutional review board/ethics committee approval was taken for the study. Patients with light perception (LP) vision and those in which other treatments failed to improve vision were included in this study.

All patients had a comprehensive ocular examination, including Snellen visual acuity (VA) measurement, anterior segment examination, intraocular pressure (IOP) measurement, and fundus examination. Color fundus photographs of all 14 eyes were taken, and fluorescein angiography was performed as required.

All 14 eyes underwent 23-gauge pars plana vitrectomy, retinectomy and 5000cs silicone oil endotamponade. Core vitrectomy was completed and special attention was paid to detaching the posterior hyaloid from the retina. Triamcinolone was used intraoperatively to facilitate vitreous cortex visualization. Preretinal membranes, at both the posterior pole and periphery, as well as those covering the RCHs themselves, were carefully dissected, using the bimanual technique when necessary.

Surgery was then completed by resection of the RCH masses by retinectomy and endotamponade with 5000cs silicone oil. Patients were followed for three years.

Results:

In all the 14 eyes, the RCHs were too large or thick to be successfully treated by laser or cryotherapy alone and thus, failed to respond to one or both of these treatments. 7 eyes exhibited exudative and tractional macular detachment, 4 eyes exhibited peripheral exudative and tractional retinal detachment, 1 eye exhibited rhegmatogenous retinal detachment, and 2 eyes exhibited a combination of these conditions.

The mean follow-up period after the initial surgery was three years. In 7 (50%) eyes visual acuity improved from light perception (LP) to 6/60, in three (21.43%) eyes from light perception (LP) to 1/60, in two (14.29%) eyes from light perception (LP) to hand motion (HM), in one (7.14%) eyes vision did not improve from light

perception (LP) and one (7.14%) eye vision decreased to NPL.

The retina was flat in all the 14 cases and no significant intraoperative or postoperative complications were observed. No recurrence of the retinal capillary hemangiomas was noted.

Discussion:

Typical ocular manifestations of VHL disease consists of retinal capillary hemangioblastoma (RCH), which is identical to CNS hemangioblastomas histopathologically.^{17,18} They can be located anywhere within eye fundus, however, involvement of peripheral retina is typical. The probability of developing retinal angiomas increases with age, being 0.38 and 0.7 by ages 30 and 60 years, respectively.¹⁹ Small RCHs remain asymptomatic for years.²⁰ Many treatment modalities focus on shrinkage or removal of the tumors present in VHL disease, but no gold standard treatment has been established.

Spontaneous regression of RCHs was also reported.^{21,22} Most of them result in leakage, subretinal exudate formation leading to exudative retinal detachment and formation of hard exudates in macula, epiretinal membrane formation, and FVP starting in region of RCHs. Untreated RCHs will lead to loss of vision. Thus with early treatment, however, the vision can be preserved. Small to medium RCHs up to 2.0 DD can be successfully treated with focal therapy i.e., laser or cryotherapy.^{23,24} For large or multiple RCHs with preretinal fibrosis, advanced exudative, and tractional retinal detachment, this treatment is usually unsatisfactory and the ocular disease progresses.

Many different treatment modalities have been proposed for these cases. Anti-vascular endothelial growth factors either intravitreal or systemic did not cause stable RCHs regression.²⁵⁻²⁶ Brachytherapy and

external beam therapy have been used for larger RCHs but the results were no promising.^{27,28} Transpupillary thermotherapy and photodynamic therapy have also been used but success was not remarkable.²⁹⁻³⁰

The variability of the treatment results lead to the surgical intervention of the ocular VHL disease by Peyman et al in 1983, the first documented RCH excision.²⁷ Later in 1988, Machemer and Williams³¹ published their results for 2 cases in which they dissected an ERM to reattach the retina without any perioperative focal therapy i.e.0- laser or cryotherapy, with little or no success. Two cases treated by vitrectomy, with diathermy of the lesions and silicone oil tamponade were reported in 1987 for RCH associated retinal detachment.³² A trans retinal feeder vessel ligation is also documented in literature,³³ but resulted in revascularization because of the opening of adjacent vessels.

More recently, Liang et al in 2007³⁴ and Schlesinger et al³⁵ in 2008 also performed RCH excision during vitreoretinal surgery. In another series, vitreoretinal surgery was performed to remove an ERM an additional treatment to previous laser therapy, cryotherapy, or PDT.^{36,37,38,39} Last, fibrovascular proliferation from peripapillary angiomas was also addressed surgically in 12 cases.^{40,41,42}

Since then, 51 published cases of pars plana vitrectomy (PPV) in patients with VHL have been reported.⁴³⁻⁴⁴ Gaudric et al in 2011 published the largest cohort of 21 patients with VHL disease who underwent surgical intervention.⁴⁵

In our study, severe stages of the ocular VHL disease with exudative and tractional macular detachment were observed in 7 eyes, 4 eyes exhibited peripheral exudative and tractional retinal detachment, 1 eye exhibited rhegmatogenous retinal

detachment, and 2 eyes exhibited a combination of these conditions.

Our patient has had a good evolution so far, with gradual BCVA improvement, stability of RCH lesions and no need of further intervention. After a 3 years follow-up, the retina remains attached, and by now, there has been no development of new tumors. However, prospective studies with a larger number of patients and longer follow-up periods are required.

In conclusion, the results for the series reported indicate that vitreoretinal surgery with RCH resection should be considered a useful tool for salvaging eyes that develop large multiple RCHs. The goal of the treatment of RCH caused by VHL disease is not only to close the capillaries forming the hemangiomas but also to destroy the tumor cells present in the hemangiomas to avoid their recurrence. Pars plana vitrectomy in patients with VHL is a good treatment option in advanced ocular VHL disease, and in many patients, it allows to improve or preserve functional vision. RCHs excision should be reserved only for these cases where other treatment modalities like laser and cryotherapy are ineffective.

References:

1. Friedrich CA (1999) Von Hippel–Lindau syndrome. A pleomorphic condition. *Cancer* 86(11 Suppl):2478–2482
2. Kaelin WG (2007) Von Hippel–Lindau disease. *Annu Rev Pathol* 2:145–173. doi:10.1146/annurev.pathol.2.010506.092049
3. Maher ER, Neumann HP, Richard S (2011) Von Hippel–Lindau disease: a clinical and scientific review. *Eur J Hum Genet* 19(6):617–623. doi:10.1038/ejhg.2010.175
4. Maxwell PH, Wiesener MS, Chang GW, Clifford SC, Vaux EC, Cockman ME, Wykoff CC, Pugh CW, Maher ER, Ratcliffe PJ (1999) The tumour suppressor protein VHL targets hypoxia-inducible factors for oxygen-dependent proteolysis. *Nature* 399(6733):271–275. doi:10.1038/20459
5. Rasmussen A, Alonso E, Ochoa A, De Biase I, Familiar I, Yescas P, Sosa AL, Rodriguez Y, Chavez M, Lopez-Lopez M, Bidichandani SI (2010) Uptake of genetic testing and long-term tumor surveillance in Von Hippel–Lindau disease. *BMC Med Genet* 11:4. doi:10.1186/1471-2350-11-4
6. Maher ER, Yates JR, Harries R, Benjamin C, Harris R, Moore AT, Ferguson-Smith MA (1990) Clinical features and natural history of Von Hippel–Lindau disease. *Q J Med* 77(283):1151–1163
7. A review of Von Hippel-Lindau syndrome. Varshney N, Kebede AA, Owusu-Dapaah H, et al. *J Kidney Cancer VHL*. 2017; 4:20–29.
8. Ocular manifestations of von Hippel-Lindau disease: clinical and genetic investigations. Chew EY. *Trans Am Ophthalmol Soc*. 2005; 103:495–511.
9. Maher ER, Yates JR, Harries R, et al. Clinical features and natural history of von Hippel–Lindau disease. *Q J Med* 1990; 77:1151–1163.
10. Wong WT, Agron E, Coleman HR, et al. Clinical characterization of retinal capillary haemangiomas in a large population of patients with von Hippel-Lindau disease. *Ophthalmology* 2008; 115:181.
11. Maher ER, Yates JR, Harries R, Benjamin C, Harris R, Moore AT, et al. Clinical features and natural history of von Hippel-Lindau disease. *Q J Med*. 1990 Nov;77(283):1151–63.
12. Schmidt D, Natt E, Neumann HP. Long-term results of laser treatment for retinal angiomatosis in von Hippel-Lindau disease. *Eur J Med Res*. 2000 Feb;5(2):47–58.
13. Singh AD, Nouri M, Shields CL, Shields JA, Perez N. Treatment of retinal capillary hemangioma.

- Ophthalmology. 2002 Oct; 109(10):1799–806.
14. Schmidt-Erfurth UM, Kusserow C, Barbazetto IA, Laqua H. Benefits and complications of photodynamic therapy of papillary capillary hemangiomas. *Ophthalmology*. 2002 Jul; 109(7):1256–66.
 15. Kreusel KM, Bornfeld N, Lommatzsch A, Wessing A, Foerster MH. Ruthenium-106 brachytherapy for peripheral retinal capillary hemangioma. *Ophthalmology*. 1998 Aug; 105(8):1386–92.
 16. Wong WT, Liang KJ, Hammel K, Coleman HR, Chew EY. Intravitreal ranibizumab therapy for retinal capillary hemangioblastoma related to von Hippel-Lindau disease. *Ophthalmology*. 2008 Nov; 115(11):1957–64.
 17. Grossniklaus HE, Thomas JW, Vigneswaran N, Jarrett WH. Retinal hemangioblastoma. A histologic, Immunohistochemical, and ultra-structural evaluation. *Ophthalmology* 1992;99:140–145.
 18. Vortmeyer AO, Chan CC, Chew EY, et al. Morphologic and genetic analysis of retinal angioma associated with massive gliosis in a patient with von Hippel-Lindau disease. *Graefes Arch Clin Exp Ophthalmol* 1999;237:513–517.
 19. Maher ER, Yates JR, Harries R, et al. Clinical features and natural history of von Hippel–Lindau disease. *Q J Med* 1990;77:1151–1163.
 20. Wong WT, Agron E, Coleman HR, et al. Clinical characterization of retinal capillary hemangiomas in a large population of patients with von Hippel-Lindau disease. *Ophthalmology* 2008;115:181.
 21. Molina MC, Paulo JD, Donado JH. Spontaneous regression of a retinal capillary hemangioma. *Retina* 2008;28:1554–1555.
 22. Whitson J, Welch R, Green W. Von Hippel–Lindau disease: case report of a patient with spontaneous regression of a retinal angioma. *Retina* 1986;6:253–259.
 23. Lane CM, Turner G, Gregor ZJ, Bird AC. Laser treatment of retinal angiomatosis. *Eye (Lond)* 1989;3:33–38.
 24. Garcia-Arumi J, Sararols LH, Cavero L, et al. Therapeutic options for capillary papillary hemangiomas. *Ophthalmology* 2000;107:48–54.
 25. Wong WT, Liang KJ, Hammel K, et al. Intravitreal ranibizumab therapy for retinal capillary hemangioblastoma related to von Hippel-Lindau disease. *Ophthalmology* 2008;115: 1957–1964.
 26. Girmens JF, Erginay A, Massin P, et al. Treatment of von Hippel-Lindau retinal hemangioblastoma by the vascular endothelial growth factor receptor inhibitor SU5416 is more effective for associated macular edema than for hemangiomas. *Am J Ophthalmol* 2003;136:194–196.
 27. Kreusel KM, Bornfeld N, Lommatzsch A, et al. Ruthenium-106 brachytherapy for peripheral retinal capillary hemangioma. *Ophthalmology* 1998;105:1386–1392.
 28. Raja D, Benz MS, Murray TG, et al. Salvage external beam radiotherapy of retinal capillary hemangiomas secondary to von Hippel-Lindau disease: visual and anatomic outcomes. *Ophthalmology* 2004;111:150–153.
 29. Mochizuki Y, Noda Y, Enaida H, et al. Retinal capillary hemangioma managed by transpupillary thermotherapy. *Retina* 2004;24:981–984.
 30. Rodriguez-Coleman H, Spaide RF, Yannuzzi LA. Treatment of angiomatous lesions of the retina with photodynamic therapy. *Retina* 2002;22:228–232.
 31. Macheimer R, Williams JM Sr. Pathogenesis and therapy of traction detachment in various retinal vascular diseases. *Am J Ophthalmol* 1988;105:170–81.

32. Gaudric A, Korobelnik JF, Quentel G, Coscas G. Treatment of retinal detachment in Von Hippel angiomas: a propos of 2 cases [in French]. *Bull Soc Ophthalmol Fr* 1987;87:1357–8.
33. Farah ME, Uno F, Hofling-Lima AL, et al. Transretinal feeder vessel ligation in von Hippel-Lindau disease. *Eur J Ophthalmol* 2001;11:386–8.
34. de Klerk TA, Steel DH. Use of intravitreal bevacizumab in a patient with a Von Hippel-Lindau-associated retinal hemangioblastoma of the optic nerve head: a case report. *J Med Case Rep* 2008;2:182.
35. Schlesinger T, Appukuttan B, Hwang T, et al. Internal en bloc resection and genetic analysis of retinal capillary hemangioblastoma. *Arch Ophthalmol* 2007;125:1189–93.
36. McDonald HR, Schatz H, Johnson RN, et al. Vitrectomy in eyes with peripheral retinal angioma associated with traction macular detachment. *Ophthalmology* 1996;103:329–35; discussion 334–5.
37. Majji AB. Paramacular Von Hippel angioma with tractional macular detachment. *Ophthalmic Surg Lasers* 2002;33:145–7.
38. Laatikainen L, Immonen I, Summanen P. Peripheral retinal angioma like lesion and macular pucker. *Am J Ophthalmol* 1989;108:563–6.
39. Schwartz PL, Fastenberg DM, Shakin JL. Management of macular puckers associated with retinal angiomas. *Ophthalmic Surg* 1990;21:550–6.
40. Wong WT, Yeh S, Chan CC, et al. Retinal vascular proliferation as an ocular manifestation of von Hippel-Lindau disease. *Arch Ophthalmol* 2008;126:637–43.
41. Kreusel KM, Bechrakis NE, Neumann HP, Foerster MH. Parsplana vitrectomy for juxtapapillary capillary retinal angioma. *Am J Ophthalmol* 2006;141:587–9.
42. Garcia-Arumi J, Sararols LH, Cavero L, et al. The therapeutic options for capillary papillary hemangiomas. *Ophthalmology* 2000;107:48–54.
43. Dahr SS, Cusick M, Rodriguez-Coleman H, et al. Intravitreal anti-vascular endothelial growth factor therapy with pegaptanib for advanced von Hippel-Lindau disease of the retina. *Retina* 2007;27:150–158.
44. Schwartz PL, Fastenberg DM, Shakin JL. Management of macular puckers associated with retinal angiomas. *Ophthalmic Surg* 1990;21:550–556.
45. Schlesinger T, Appukuttan B, Hwang T, et al. Internal en bloc resection and genetic analysis of retinal capillary hemangioblastoma. *Arch Ophthalmol* 2007;125:1189–1193.

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Eye Make-Up and Its Association with Dry Eye Disease

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ABSTRACT

Eye makeup is a type of cosmetic which makes the eyes attractive. Cosmetics like eye shadow, eye liner, mascara are easily applied which improve self-confidence and one's appearance. Some eye make-up products, however, are supposed to have harmful effects on the eyes.

Purpose: To report the presence or absence of dry eye disease among eye make-up users.

Design: It is a hospital based, cross sectional, study.

Settings and Duration: Abbas Institute of Medical Sciences (AIMS) Muzaffarabad, Oct 2017 - Oct 2018.

Materials and Methods: We conducted a detailed eye examination of 141 female patients, with no previous history of dry eyes, putting an eye make-up > 3 times / week like mascara, eye shadow or eyeliner, attending eye OPD/refraction clinic of the hospital or referred from other departments. A questionnaire-based survey about dry eyes and eye make-up was done by a researcher while a single clinician performed various dry eye tests under same physical conditions. Dry eye diagnosis was made on the basis of positive results in three out of five tests. Statistical analysis was by simple frequencies/percentages.

Results: A total of 83(59%) women among 141 female patients had DE with positive symptoms and signs according to Japanese diagnostic criteria for dry eye. The main types of eye makeup were mascara used by 37% females, eye shadow by 33% and eye liner was used by 30% females. The main symptom was burning in 73% and watering in 61% of eyes. Regarding tests, 51% showed low tears break up time, 37% low Schirmer's test, 36% showed corneal fluorescein staining while 21% had lid hyperaemia or mucous threads.

Conclusion: Most common symptom among eye make-up users was burning sensation in eyes in our study. *Al-Shifa Journal of Ophthalmology 2020; 16(1): 36-41.* © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.

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Introduction:

Egyptians were the first to use perfumes and cosmetics. The word cosmetic derives from the Greek (kosmetikē tekhnē), meaning "technique of dress and ornament". Roman slaves used to bathe men and women in perfume as early as 10,000 BC. They changed their cheeks and lips, stained their nails with henna and their eyebrows and eyes with kohl made of antimony, lead, oxidized copper, burnt almonds, ash to please the aesthetics.¹

Dry eye (DE) disease is caused by either increased evaporation or decreased tear production.² In the United States about 33 million people suffer from dry eyes.³ Pakistani television played a crucial role in

encouraging women to look after their beauty⁴ according to Pakistan cosmetics market and industry forecast 2019-2026. Any type of cosmetics, which makes the eyes look attractive, is called eye makeup. Cosmetics such as eye liner, eye shadow and mascara are not permanent but improve one's appearance and are used by females for aesthetic purposes.⁵

Many of the present day makeup manufacturers were established during the 1920s and 1930s. Eugene Rimmel invented mascara, but the present form was developed by T.L. Williams in 1913. Eye makeup can cause or aggravate dry eyes by thinning the oily layer of the tear film.⁶

Vision scientists noted that when eyeliner was used to the inside of the lash line compared to outside, 15-30% more particles moved into the tear film^{7,8}. Most women know the eye problems associated with cosmetics but they still use it.⁹

Literature search shows that no local study has evaluated the relationship between eye make-up use and any dry eye problems related to it. The purpose of this study was to report the presence or absence of dry eye disease among eye make-up users presenting in an eye out patient department.

Materials and Methods:

This study was conducted after taking the consent and permission from ethical committee. Female patients, age group 24-44 years, attending eye OPD or referred from other departments putting an eye make-up > 3times/week were selected and screened for DE. Those putting <3 times /week, having any systemic disease or previous eye surgery, having pregnancy or using eye drops were excluded.

Dry eye questionnaire (DEQ-6) was administered to all female subjects and a questionnaire-based survey about eye make-up, its frequency, duration, mode of

application, type, removal and reason of use was done by a trained researcher. Basic demographics were recorded and various dry eye tests were performed under the same physical conditions by a single surgeon. DEQ 6 scoring, tear film breakup time (TBUT) of < or = 10 seconds in 1 or both eyes, Schirmer's test (ST) < or = 5 mm in 5 minutes, corneal fluorescein staining (CFS) score of > or = 1 (The staining area was graded from 0 to 3, with 0 meaning no punctate staining and 3 representing more than two thirds staining) presence of conjunctival injection, punctate epithelial erosions (PEE) and slit lamp examination for meibomian gland dysfunction (MGD) were recorded as positive signs according to Japanese Diagnostic Criteria for dry eye. The diagnosis was made on three out of five tests. The data was analyzed for frequencies / percentages.

Results:

Among 141 female patients, age group 24-44 years, mean age 31.6±7.2 years. Out of these, 92 women were of age 24-33years group while 49 were of 34-44years group. There were 29 postgraduates, 37 teachers, 30 computer workers, 23 office workers and 22 housewives.

The main types of eye makeup were mascara used by 37% females, eye shadow by 33% and eye liner used by 30% females. Only 64% (90) used to remove them by baby oil / other wipes. Based on Japanese Diagnostic Criteria for dry eye, 83(59%) women had DE. The main symptoms experienced often or all the times was burning sensation in eyes by 63% among age group 34-44 years while watering in 59% of eyes among age group 24-33 years. In addition, 51% showed low TBUT, 37% low ST, 36% showed CFS and 21% had lid hyperaemia or mucous threads. Regarding duration, 49% women wore eye makeup for 7 hours/daily, 31% for >5hrs while 20% were using for >3hrs/daily. Twenty-one percent of postgraduates and 19% of teachers using daily eye make-up had

severe dry eye symptoms. Twenty-three percent subjects using mascara had low TBUT, 27% of computer users showed CFS

suggesting unstable tear film. About 11% having refractive errors had DE symptoms.

Table-1: Baseline characters

Basics	(n=141)	Percentages
Age group		
24-33 years	92	65.2%
34-44 years	49	34.8%
Occupation		
Teachers	37	26.2%
Postgraduates	29	20.5 %
Computer users	30	21 %
Office workers	23	16.3%
Housewives	22	15.6%.
Eye makeup Usage		
5days /week	57	40.4%
3 days/week	84	59.6%
Mascara	52	37%
Eye liner	42	30%
Eye shadow	47	33%
Dry eye symptoms	89	59%
Eye lashes loss	33	23.4%

Table 2: Symptoms of dry eye after eye makeup

Symptoms	Never	Rarely	Sometimes	Often	All time
Burning	9%	8%	20%	32%	31%
Redness	12%	14%	15%	30%	29%
Watering	15%	17%	16%	25%	27%
FB sensation	22%	19%	17%	27%	15%
Grittiness	35%	23%	20%	16%	6%
Photophobia	51%	25%	16%	8%	10%

Table-3 DE tests among Eye make-up users

Test	Makeup (5days/wk) (n=57)	Makeup > (3days/wk) (n=84)
TBUT	23(40.3%)	9(11%)
ST	18(32.2%)	4(5%)
CFS	15(27%)	7(9%)
Lid margin hyperemia	8(13%)	6(8%)

Discussion:

Dry eye disease is defined as increased tear evaporation, decreased tear production or tear instability. These factors reduce lubrication of the cornea and conjunctiva. Risk factors for developing dry eyes include aging, medications, long computer work, contact lens wear and Lasik.¹⁰

The tear film is a three-layer solution covering the anterior ocular surface. Lipids are released from the meibomian glands through the holocrine mechanism. Studies confirm hormonal control of the glands.⁸

The Canadian DE study showed 27.8% prevalence as determined by patient questionnaires.⁷ Our study showed that 83(59%) women had DE based on Japanese criteria for dry eye.

About 23.4% (33) females using mascara complained loss of their eye lashes as they used to curl the eyelashes after applying mascara or they were not used to wipe out makeup before sleep. Drying out of mascara might have caused fall of eye lashes.

In our study 40 (30%) females used Kohl made of crushed antimony, burnt almonds, lead or combination as eye liner on the upper and lower eyelids with a small stick. In addition to reducing sun glare, it is generally believed that Kohl eyeliner could restore good eyesight and reduce eye infection. Kohl has been used in the past medicinally to treat eye related ailments, and the benefits are even shown in some scientific studies.²

Eye make-up aggravates or causes DE symptoms like burning, discomfort and foreign body sensations.¹¹ The present study noticed redness in 59% of eyes among age group 24-33 years while burning eyes was complained by 63% among age group 34-44 years similar to another study showing older age and longer

duration of eye makeup had higher DE impact.¹²

In this study interestingly, 26% subjects noticed more symptoms in the evening than in the morning which may be due to deposit formation during a day.¹³ Moreover, 34% patients had symptoms related to season, diet and time of the day. For others, they were constant.¹⁴

In the present study 21% had plugging of lid openings showing meibomian gland dysfunction (MGD). This is similar to another study showing MGD after eye makeup intolerance.¹⁵

In this study 10 (33%) computer workers of 35-44 years group complained about dryness after their usage and the symptoms were related to the duration of computer use similar to another study.¹⁶ Among 23(16.3%) office workers, 9(39%) makeup wearers faced more problems with air conditioning or central heating, confirming evaporative etiology of dry eye.¹⁷

Our study revealed that DE symptoms were severe in contact lens users when compared to non-contact lens users which was similar to another study,¹⁸ which reported that dryness was a frequent symptom while the least frequent was soreness among 83 contact lens wearers. Ocular surface symptoms such as dryness and discomfort were the main cause of discontinuation for contact lens in one study.¹⁹ One study showed that 12% of contact lens users discontinued permanently within five years of lens wear.²⁰

Our study showed that ocular FB sensation / irritation was more commonly reported by women of 35-44 years group, similar to other studies.^{21,22}

An article in the New York Times by Catherine Saint Louis mentioned that women wore makeup to increase their competence and trustworthiness. Other

literature showed that women waitresses received more tips using cosmetics than others who were not using cosmetics²³. When looking in the mirror, a woman focuses mainly on those parts of her face she wants to change.²⁴ In response to question of reason to use, 53% women in our study used it to improve their appearance and self-confidence, 31% used for aesthetic sense while 16% use it to be more attractive.

Conclusion:

Eye makeup can cause or aggravate dry eyes as most women wear it every day. It causes quick evaporation of the natural tears mostly by thinning outer oily layers. Considering the findings of this study, subjects using eye make-up should be educated to apply mascara at the tips of eyelashes and remove makeup before bed.

References:

1. Chaudhri, S. K., & Jain, N. K., History of cosmetics. *Asian Journal of Pharmaceutics*, 2009. 3, 164–167.
2. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the International Dry Eye WorkShop. *The Ocular Surface*. 2007;5(2):75–92
3. Galor A, Feuer W, Lee D J et al., "Prevalence and risk factors of dry eye syndrome in a United States Veterans affairs population," *The American Journal of Ophthalmology* 2011, vol. 152, no. 3, pp. 377–384.
4. Yasmin B, Rauf H, "Measuring the Underground Economy and its Impact on the Economy of Pakistan," *Lahore Journal of Economics*, Department of Economics, The Lahore School of Economics, 2004. vol. 9(2), pages 93-103,.
5. Dow, Bonnie J. "Feminism, Miss America, and Media Mythology". *Rhetoric & Public Affairs*. (2003). 6 (1): 127–149
6. Nichols KK, Foulks GN, Bron AJ, et al. The international workshop on meibomian gland dysfunction: executive summary. *Invest Ophthalmol Vis Sci* 2011; 52:1922–1929
7. Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. *Am J Ophthalmol*. 2014 Apr;157(4):799-806.
8. Jin X, Lin Z, Liu Y, Hormone replacement therapy benefits meibomian gland dysfunction in perimenopausal women *Medicine (Baltimore)*. 2016 Aug; 95(31): e4268
9. Millar TJ, Schuett BS, "The real reason for having a meibomian lipid layer covering the outer surface of the tear film a review," *Experimental Eye Research* 2015. vol.137, pp. 125-138,
10. Knop E, Knop N, Millar T, Obata H, Sullivan DA. The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. *Invest Ophthalmol Vis Sci* 2011; 52: 1938–1978.mgd-2
11. Zhuang SJ, Lei SC, Luo XD, Wang DL, Wen JJ, Deng DW, "Epidemiologic survey of dry eye in a community of Huidong County in Guangdong province," *Chinese Journal of Experimental Ophthalmology* 2012, vol. 30, no. 2, pp. 168–171
12. Abelson MB, McLaughlin J. Of biomes, biofilm and the ocular surface. *Rev Ophthalmol*. 2012 Sep;19 (9):52-4.
13. Benitez-del-castillo JM, Lemp MA. Anterior blepharitis. *Ocular Surface Disorders*. JP Medical Publishers. 2012;90(249):0.
14. Grubbs JR, Tolleson-Rinehart S, Huynh K, et al. A review of quality of life measures in dry eye questionnaires. *Cornea* 2014;33:215–18
15. Korb DR, Blackie CA. Debridement-scaling: a new procedure that increases Meibomian gland function and reduces dry eye symptoms. *Cornea*. 2013 Dec;32(12):1554-7.

16. Uchino, M., Yokoi, N., Uchino, Y. et al, Prevalence of dry eye disease and its risk factors in visual display terminal users: the Osaka Study. *Am J Ophthalmol.* 2013;156:759–766.
17. Hosaka E, Kawamorita T, Ogasawara Y, Nakayama N, Uozato H, et al. Interferometry in the evaluation of precorneal tear film thickness in dry eye. *Am J Ophthalmol* (2011) 151: 18–23 e11.
18. Stapleton F., Keay L., Jalbert I., Cole N. The epidemiology of contact lens related infiltrates. *Optom Vis Sci.* 2007;84:257–272
19. Keech, A., Senchyna, M., Jones, L. Impact of time between collection and collection method on human tear fluid osmolarity. *Curr Eye Res.* 2013;38:428–436.
20. K, Sinnott LT, Skadahl E, Nichols JJ. Frequency of and factors associated with contact lens dissatisfaction and discontinuation. *Cornea* 2007;26:168–74.
21. Truong S1, Cole N, Stapleton F, Golebiowski B. Sex hormones and the dry eye. *Clin Exp Optom.* 2014 Jul;97(4):324-36
22. Renfrew Foundation New Survey Results Indicate There's More to Makeup Use Than Meets the Eye. Renfrew Center Foundation Center. Web. (2012, February, 22). www.renfrew.org
23. Guegunen, N., & Jacob, C. Enhanced female attractiveness with use of cosmetics and male tipping behavior in restaurants. *Journal of Cosmetic Science*, (2010). 62, 283–290.
24. Tseelon, E. Fashion and the orders of masking. *Critical Studies in Fashion & Beauty*, (2012). 3(1&2), 3–9.
25. Chalmers RL, Begley CG, Caffery B. Validation of the 5-Item Dry Eye Questionnaire (DEQ-5): Discrimination across self-assessed severity and aqueous tear deficient dry eye diagnoses. - *Contact Lens and Anterior Eye*, 2010;33(2):55-60.

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Comparison of Therapeutic Probing with and without Viscoelastic Gel for Congenital Nasolacrimal Duct Obstruction

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ABSTRACT

Purpose: To determine the therapeutic role of probing in CNLDO and to compare the success rate and complication rate of probing with viscoelastic substance and probing without viscoelastic substance.

Materials and Methods: After IRB approval and informed consent, RCT was conducted at eye department of DHQ-UTH, Gujranwala for duration of 9 months containing 70 patients. Probing was performed in Group A with viscoelastic gel and in group B without viscoelastic gel. Patients of either gender between 9-24 months of age, with unilateral or bilateral CNLDO that failed to resolve after 3 months of conservative treatment were enrolled into this study. Probing was done under brief GA by one experienced ophthalmologist and follow up done till 6 months. All data recorded on proforma and analyzed by SPSS v.20.

Results: Mean age recorded was 16.5 ± 3.87 months with range of 9-24 months. Out of which, 48.6% were male while 51.4% were female. Left eye was involved in 50% patients, right eye in 38.5% patients while bilateral involvement was present in 11.4% patients. Cumulative success rate was found to be 97.1% in group A while it was 91.4% in group B with significant p-value of 0.032. Complication rate in group A was considerably lower (11.4%) than in group B (45.7%) and the difference between two groups was also statistically significant. (p-value=0.023)

Conclusion: In conclusion, probing is therapeutic in resolving CNLDO and also that probing with viscoelastic substance is associated with higher success rate and less complications rate than probing without viscoelastic substance. *Al-Shifa Journal of Ophthalmology 2020; 16(1): 42-50.* © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan

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Introduction:

Nasolacrimal duct obstruction (NLDO) is the blockade of tears outflow distal to the lacrimal sac manifested as excessive watering. Nasolacrimal duct (NLD) is 12-18 mm long membranous passage that starts at inferior end of lacrimal sac, descends and angles posteriorly and laterally to open into inferior meatus of nose, guarded by the fold of mucosa called valve of Hasner.¹

Congenital nasolacrimal duct obstruction (CNLDO) accounts for one of the most common causes of congenital abnormalities that affects around one in nine live births

with no gender predilection and is more common in Caucasians and in premature infants.² This condition presents with intermittent or persistent epiphora, recurrent infections and periocular skin excoriation. In most of cases, it's due to obstruction in the distal nasolacrimal duct at the level of valve of Hasner.

About 90% cases of congenital nasolacrimal duct obstruction resolves within 1 year. Initial treatment is conservative that involves NLD massage and topical antibiotics, failed response steps towards probing of membranous nasolacrimal duct that opens distal obstruction.³ Other treatment options include balloon catheter dilation,⁴ stents⁵ and silicone tube intubation.⁶ Ideal timings for NLD probing is controversial, some advocate early probing while others promote deferred probing.⁷

Congenital nasolacrimal duct obstruction (CNLDO) is classified into simple and complex. Simple CNLDO is characterized by membranous obstruction at distal end of nasolacrimal duct that is overcome easily during probing.⁸ While complex CNLDO is characterized by gritty sensation during passage of probe through nasolacrimal duct that can't be overcome easily.⁹ Probing is performed in office settings under topical anaesthesia or in operation theatre settings under general anaesthesia. Though it is aimed in helping to retrieve the distal obstruction of membranous nasolacrimal duct but it may not be successful if there is any bony protrusions or nasal pathologies present. Probing may also result in potential complications like bleeding, damage to puncti and canaliculi, false passage formation, pre-septal cellulitis, failure to resolve symptoms and recurrence.¹⁰

The Rationale of this study was designed to lower the complications rate associated with probing and thus to enhance final success rate of this procedure. For this, we designed this study to compare

complications rate and success rate of probing with and without viscoelastic substance as addition of viscoelastic substance during probing can help in smooth passage of probe and hence can reduce the incidence of complications like bleeding, damage to puncti or canaliculi, and false passage formation.

Materials and Methods:

After obtaining permission from institution review committee of DHQ-UTH, Gujranwala and getting written informed consent from guardians, a randomized controlled trial was conducted at eye department of DHQ-UTH, Gujranwala for duration of 9 months (June 2019-Feb.2020). Seventy patients (sample size calculated using 90% CI and 10% margin of error) were randomly and equally divided into two groups based on random number generator. Group A included patients in whom therapeutic probing was performed with viscoelastic gel while in group B patients, therapeutic probing was performed without viscoelastic substance. Patients of either gender between 9-24 months of age, with unilateral or bilateral congenital nasolacrimal duct obstruction that failed to resolve after 3 months of conservative treatment and who have completed 6 months post-op follow up, were enrolled in this study. Patients with previous history of probing/ NLD surgery/trauma, patients with craniofacial anomalies or Down syndrome and patients with punctual stenosis or agenesis, canalicular stenosis, complex CNLDO and congenital dacryocystocele were excluded from this study.

Patients fulfilling the inclusion criteria were admitted to Eye department through OPD after detailed ophthalmic examination. The procedure was performed under mask (brief inhalational anaesthesia without intubation) by one skilled ophthalmologist. After anti-septic measures, lower punctum was first dilated with dilator and in group A patients, 0.5ml of viscoelastic substance is used for

irrigation of lacrimal outflow pathway followed by smooth passage of Bowman's probe (0 & 00). While in group B patients no viscoelastic substance was used. In both groups, probe was first passed vertically for 2mm and then rotated at right angle to enter horizontal portion of canaliculus while applying gentle traction at lateral canthus. Probe was further passed until it touched the bony firmness where it is rotated again and probe passed downward and slightly laterally where any membranous resistance was retrieved by gentle forward pressure of probe until it emerged out at inferior meatus. At this stage, another probe was used to check the retrieval of first probe in nasal cavity. The same procedure was repeated in both groups through upper punctum. Post-operatively, topical antibiotic E/D were prescribed for 1 week. Any per-op complication was mentioned on specially designed proforma along with demographic variables.

Patients were followed at 1 week, 1 month, 3 months and 6 months period after

probing. If any patient developed post-op complications, it was mentioned and managed. Guardians were inquired about resolution or persistence of symptoms and patients were examined for epiphora, skin changes, mucous discharge and regurgitation. If no symptoms or signs observed in patient at each follow up, then complete resolution was labeled while the persistence of symptoms and signs of CNLDO, case was graded as unsuccessful. If parents reported symptoms of intermittent epiphora but on clinical examination, no positive finding was noted then it is graded as partial response.

Data was recorded and analyzed using SPSS version 20. Frequency and percentage was used for categorical data while Mean \pm SD and range was used for numerical variables. Primary outcome was success rate and secondary outcome was complications rate. Chi square test was used to compare results between two groups. P-value of <0.05 was considered statistically significant.



Fig.1: Instillation of viscoelastic gel



Fig.2: Bowman's probe 0 for probing

Results:

In this study, mean age recorded was 16.5 months with range of 9-24 months. In group A, mean \pm SD determined was 15.88 ± 3.74 months while in group B, it was 17.28 ± 3.93 months (Table 1). No statistically significant difference was found in age distribution between two groups. (p value= 0.36)

In general, 48.6% were male while 51.4% were female. In group A, 51.4% were male and 48.6% were female while in group B, 45.7% were male and 54.3% were female (Table 2). No statistically significant difference was found in gender distribution between two groups (p value= 0.25)

In general, left eye was involved in 50% patients while right eye in 38.5% patients. Mostly patients were unilateral (88.5%) while bilateral involvement was present in 11.4% patients. In group A, right eye was involved in 40% and left eye in 48.6% patients while in 11.4% patients, both eyes were involved. In group B, percentage for bilateral involvement was same as in group A (11.4%), while right eye involvement was in 37.1% patients and left eye in 51.4%. (Table 3, Figure 3)

In group A, where viscoelastic substance was used, complete resolution was seen in 32 patients (91.4%) with partial resolution in 2 (5.7%) and failure was noted only in 1 (2.9%) patient (Figure 4). So the cumulative success rate was found to be 97.1% in group A patients. While in group B, complete resolution was found in 28 (80%) cases, partial resolution in 4 (11.4%)

and failure was seen in 3 (8.6%) patients. And cumulative success rate for both complete and partial resolution in group B patients was noted to be 91.4%. P-value obtained was also statistically significant (p-value= 0.032)

Complications rate was also assessed between two groups (Table 4, Figure 5). Rate of bleeding was 5.7% in group A while it was 20% in group B. Damage to punctum or canaliculi was present in 2.85% in group A while it was 8.6% in group B. False passage was seen only in 1 patient of group B (2.9%) and pre-septal cellulitis was present in 2.85% of group A while 14.3% of group B patients. So net complication rate in group A was considerably lower (11.4%) than in group B patients (45.7%) and the difference between two groups was also statistically significant. (p-value=0.023)

Table 1: Demographic variables

	<u>Mean (Age in months)</u>	<u>S.D. (Age in months)</u>	<u>Range (Age in months)</u>
<u>Group A</u>	15.88	3.74	9-24
<u>Group B</u>	17.28	3.93	9-24
<u>Total</u>	16.58	3.87	9-24

Table 2: Gender distribution b/w groups

	<u>Male</u>	<u>Female</u>	<u>Total</u>
<u>Group A</u>	18 (51.4%)	17 (48.6%)	35 (100%)
<u>Group B</u>	16 (45.7%)	19 (54.3%)	35 (100%)
<u>Total</u>	34 (48.6%)	36 (51.4%)	70 (100%)

Table3: Laterality in both groups

	<u>Right</u>	<u>Left</u>	<u>Bilateral</u>	<u>Total</u>
<u>Group A</u>	14 (40%)	17 (48.6%)	4 (11.4%)	35 (100%)
<u>Group B</u>	13 (37.1%)	18 (51.4%)	4 (11.4%)	35 (100%)
<u>Total</u>	27 (38.5%)	35 (50%)	8 (11.4%)	70 (100%)

Table 4: Complications rate b/w two groups

	<u>Bleeding</u>	<u>Damage to punctum or canaliculi</u>	<u>False passage</u>	<u>Pre-septal cellulitis</u>	<u>None</u>
<u>Group A</u>	2 (5.7%)	1 (2.85%)	0.00	1 (2.85%)	31 (88.6%)
<u>Group B</u>	7 (20%)	3 (8.6%)	1 (2.9%)	5 (14.3%)	19 (54.3%)

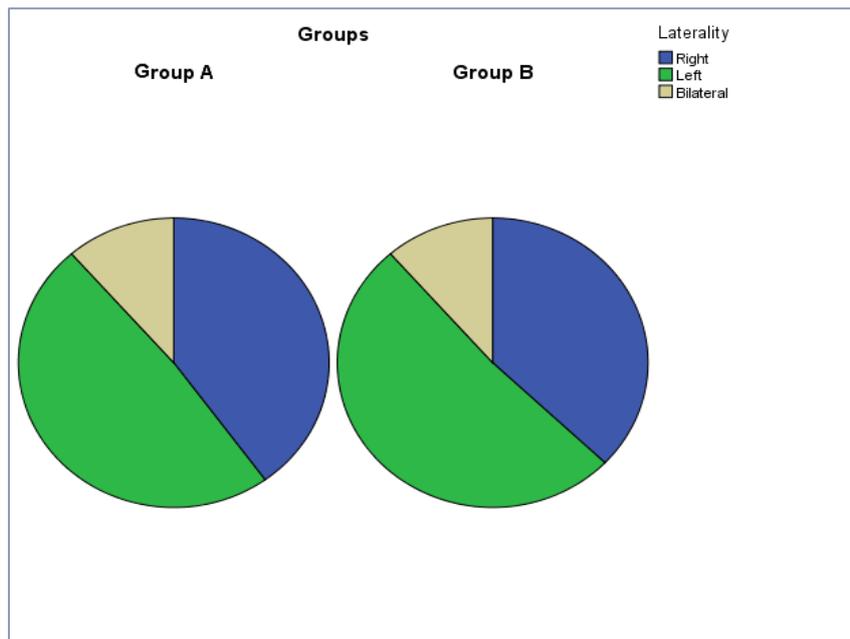


Fig.3: Pie chart showing laterality in both groups

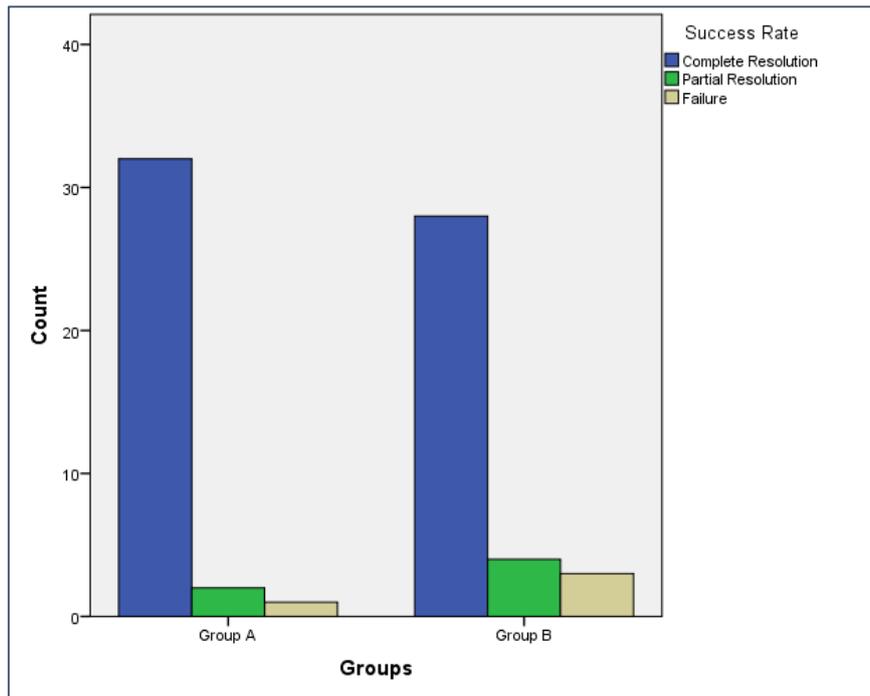


Fig.4: Clustered bar chart showing success rate in both groups

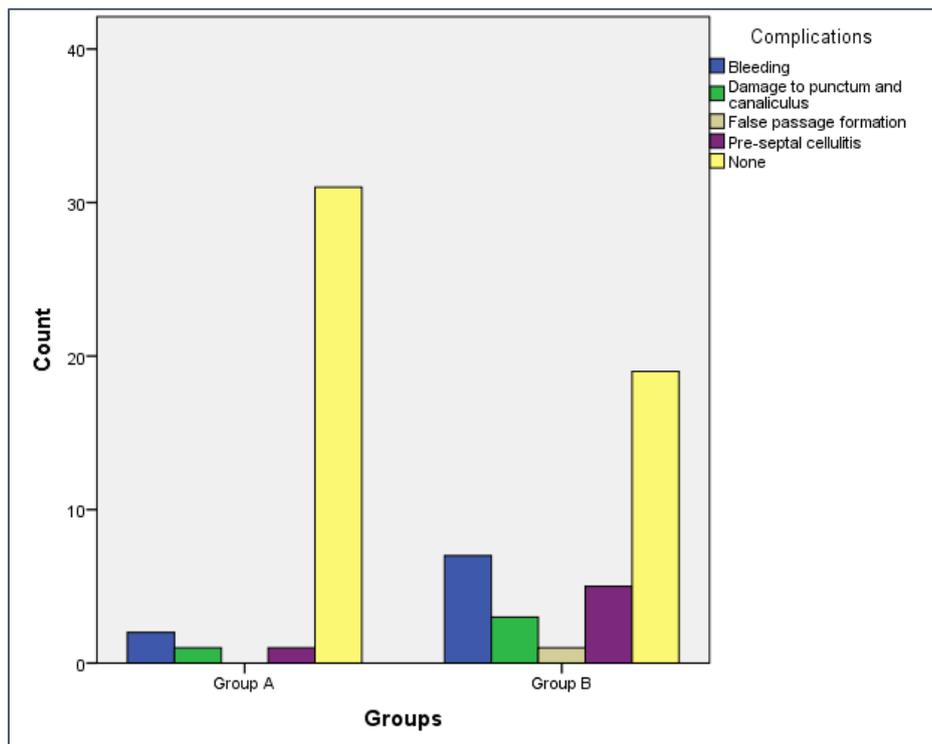


Fig. 5: Clustered bar chart showing different complications b/w two groups

Discussion:

Probing is considered an initial treatment option for congenital nasolacrimal duct obstruction when conservative management fails. Optimal timing for this procedure is still controversial.^{11,12} But

other than this factor, mechanical damage due to probe can result in certain complications and thus reduced success rate.

Mean age recorded in our study was 16.5 ± 3.8 months with range of 9-24 months. These values correlate well with similar local study conducted by Qamar et al, where mean age recorded was 17.0 months with range of 13-32 months.¹³ Age range was selected very carefully in this study so not to have any confounding factors related to fibrosis in late age and chances of spontaneous resolution in early age.

In our study, the proportion of females was higher than males that were 51.4% and 14.6% respectively. This is not in accordance with similar study conducted at Taiwan by Hung et al. who reported affected males population of 53% and that of females 47%.¹⁴ Another study published in JAMA reported the same contradicting results where male population affected was more (52%) than females (48%).¹⁵ These contradicting results compared to our study can be due to difference in ethnicity.

Our study reported unilateral involvement in 88.5% patients while bilateral involvement was present in 11.4% patients. Left eye was involved in 50% while right eye in 38% patients. These results correlate well with other studies carried out by Eshragi and H.R where unilateral involvement was more than bilateral and left eye was affected in slightly higher percentage than right eye.^{16,17}

Success rate in group A patients was found to be higher (97.1%) than in group B patients (91.4%) with statistically significant p-value. Success rate in group B correlates well with a study conducted by Shrestha et al, where overall success rate was 80.6% but it was 90.62% in patients below 2 years of age.¹⁸ Another study conducted by Rashid et al,¹⁹ reported similar success rate of 94.23% but none of these could meet the success rate of group A patients.

Overall complications rate was higher in group B (45.7%) than in group A (11.4%) with statistically significant difference. Among complications, bleeding was noted in more patients followed by pre-septal cellulitis, damage to punctum and false passage formation. Interestingly author couldn't find any specific study where these complications were discussed in detail and where relation of these complications was assessed with success rate. This makes our study quite innovative.

In our study, all probing cases were performed under brief inhalational general anaesthesia to reduce the risk of inadvertent trauma to delicate lacrimal drainage system and also to pay attention to the site and nature of obstruction as it would be more controlled and safe option under GA. Kotwal et al, also supports our views and he conducted similar study under general anaesthesia thus augmenting these facts.²⁰

Author has found few limitations of this study as its small sample and single center study. For more universal acceptance of these results, it should be multi-centered with large sample size and follow up period should be extended to more than 6 months to determine any recurrence.

Conclusion:

In conclusion, probing is therapeutic in resolving congenital nasolacrimal duct obstruction and also that probing with viscoelastic substance is associated with higher success rate and less complications rate than probing without viscoelastic substance.

References:

- 1- Vagge A, Ferro Desideri L, Nucci P, Serafino M, Giannaccare G, Lembo A, Traverso CE. Congenital Nasolacrimal Duct Obstruction (CNLDO): A Review. *Diseases*. 2018;6(4):96. doi: 10.3390/diseases6040096. PMID: 30360371; PMCID: PMC6313586.

- 2- Sathiamoorthi S, Frank R, Mohny B. Incidence and clinical characteristics of congenital nasolacrimal duct obstruction. *Br J Ophthalmol.* 2018;103(4):527-529.
- 3- Petris C, Liu D. Probing for congenital nasolacrimal duct obstruction. *Cochrane Database Syst Rev.* 2017;7(7):CD011109. doi: 10.1002/14651858.CD011109.pub2. PMID: 28700811; PMCID: PMC5580992.
- 4- Gazit I, Pras E, Or L, Hartstein M. Balloon catheter dilation as the primary treatment of congenital nasolacrimal duct obstruction. *Eur J Ophthalmol.* 2019;:112067211989590.
- 5- Tai E, Kueh Y, Abdullah B. The Use of Stents in Children with Nasolacrimal Duct Obstruction Requiring Surgical Intervention: A Systematic Review. *Int J Environ Res Public Health.* 2020;17(3):1067.
- 6- Okumuş S, Öner V, Durucu C, Coşkun E, Aksoy Ü, Durucu E et al. Nasolacrimal duct intubation in the treatment of congenital nasolacrimal duct obstruction in older children. *Eye.* 2015;30(1):85-88.
- 7- Repka M. Timing of simple probing for congenital nasolacrimal duct obstruction. *JAMA Ophthalmol.* 2018;136(11):1286-1287.
- 8- Ali MJ. Simple Congenital Nasolacrimal Duct Obstruction and Its Management. *Atlas of Lacrimal Drainage Disorders.* 2018:257-270
- 9- Ali MJ, Kamal S, Gupta A, et al. Simple vs complex congenital nasolacrimal duct obstruction: etiology, management and outcomes. *Int Forum Allergy Rhinol.* 2015;5(2):174–7.
- 10- Öztürk Karabulut G. Evaluation and Treatment of Congenital Nasolacrimal Duct Obstruction. *Beyoglu Eye J.* 2018;3(1):1-3.
- 11- A. Elbakary M, E. Shalaby O. Initial Late Probing for Congenital Nasolacrimal Duct Obstruction, Rate of Success and Factors Associated with Failure. *Int J Ophthalmic Res.* 2015;1(3):83-85.
- 12- Valcheva K, Murgova S, Krivoshiiska E. Success Rate of Probing for Congenital Nasolacrimal Duct Obstruction in Children. *Folia Medica.* 2019;61(1):97-103.
- 13- Qamar RM, Latif E, Tahir MY, Moin M. Outcome of Delayed Lacrimal Probing in Congenital Obstruction of Nasolacrimal. *Pak J Ophthalmol.* 2011;27(4):175-179.
- 14- Hung C, Chen Y, Lin S, Chen W. Nasolacrimal Duct Probing under Topical Anesthesia for Congenital Nasolacrimal Duct Obstruction in Taiwan. *Pediatr Neonatol.* 2015;56(6):402-407.
- 15- Sathiamoorthi S, Frank RD, Mohny B. Spontaneous Resolution and Timing of Intervention in Congenital Nasolacrimal Duct Obstruction. *JAMA Ophthalmol.* 2018;136(11):1281-1286.
- 16- Eshragi B, Fard MA, Masomian B, Akbari M. Probing for congenital nasolacrimal duct obstruction in older children. *Middle East Afr J Ophthalmol.* 2013;20(4):349-52.
- 17- H. R S, Mohan Kulkarni V. Study of outcome of late probing in congenital nasolacrimal duct obstruction. *IP International Journal of Ocular Oncology and Oculoplasty.* 2019;5(1):28-30.
- 18- Shrestha K, Bhattarai B, Manandhar L, Rai S, Pandey A, Gurung S. Outcome of probing and syringing in congenital nasolacrimal duct obstruction at various age groups in a tertiary eye center in Western Nepal. *Asian J Med Sci.* 2018;9(6):57-61.
- 19- Rashid W, Shaheen N, Zargar S, Ganie M, Kounsar H. Outcome of Syringing and Probing In Congenital Nasolacrimal Duct Obstruction in Children above Two Years of Age: A Prospective Study. *Annals of International medical and Dental Research.* 2017;2(5):1-3.

20- Kotwal DV, Kaur DH, Singh DV. To Study the Outcome of Bowman's Probing for Congenital Nasolacrimal

Duct Obstruction in Children under two years of Age. *J Med Sci clin Res.* 2017;05(04):20666-20670.

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