

Postoperative Complications of Trabeculectomy in Primary Open Angle Glaucoma Versus Primary Angle Closure Glaucoma

Erum Shahid¹, Uzma Fasih², Arshad Shaikh³ ¹⁻³Karachi Medical and Dental College & Abbasi Shaheed Hospital, Karachi

ABSTRACT

Purpose: To compare the frequency of postoperative complications of trabeculectomy in primary open angle glaucoma (POAG) with primary angle closure glaucoma (PACG).

Study Design: Comparative experimental study.

Place and Duration of Study: Department of Ophthalmology, Abbasi Shaheed Hospital, Karachi, from January 2017 to November 2019.

Methods: Seventy-one patients who underwent primary trabeculectomy without antimetabolites for primary open-angle glaucoma and primary angle-closure glaucoma during the given period were included in the study. Patients who had significant cataract, repeated trabeculectomy, failed argon laser trabeculoplasty and trabeculectomy done for congenital glaucoma, traumatic glaucoma, secondary glaucoma were excluded from the study. Patients were followed up for 12 months and complications were compared. Secondary outcome was reduction in IOP.

Results: Out of 71 patients, 52 had POAG and 19 had PACG. The mean age was 56.7 ± 10.9 for POAG and 52.2 ± 9.5 for PACG. The frequency of complications in POAG group was 28.2% and in PACG group was 21.1% (p >0.005).Complications were: cataract, uveitis, hyphema, choroidal folds, shallow anterior chamber, high IOP and positive Seidel test. Mean IOP reduction was from 31 ± 6.7 mm of Hg and 40 ± 14.8 to 15.6 ± 4.2 and 13.8 ± 4.7 in POAG and PACG respectively (p-value > 0.005).Trabeculectomy was successful in 80.7% POAG and 73.6% PACG patients (p value > 0.005).

Conclusion: No significant difference was observed in the frequency of complications in POAG and PACG patientsfollowing Trabeculectomy, over a period of 12 months. Trabeculectomy was equally effective in lowering IOP in both the groups.

Key Words: Glaucoma, Primary Open Angle Glaucoma, Primary Angle Closure Glaucoma, Trabeculectomy,

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Correspondence to: Erum Shahid Karachi Medical and Dental College & Abbasi Shaheed Hospital, Karachi Email: drerum007@yahoo.com

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INTRODUCTION

Glaucoma is the second leading cause of blindness after cataract worldwide and is accounted for 8%

blindness among 39 million blind individuals.¹ A meta-analysis by Tham has estimated a global prevalence of glaucoma of 3.54% between 40 to 80 years of age.² There was an escalation by 74% in number of patients suffering from glaucoma from 2013 to 2020 due to a change in aging population.² Pakistan has a burden of more than 1.8 million glaucoma patients and half of them have permanently lost their sight.³

Glaucoma refers to a group of disorders characterized by optic disc cupping and atrophy of

optic nerve head, with specific visual field loss, often, but not always with increased intraocular pressure.⁴ Elevated intraocular pressure (IOP) is a risk factor for developing glaucoma along with age, ethnicity, family history, thin corneas, myopia, and oxidative stress.⁵

Glaucoma is categorized into open angle and closed angle based on the visibility of angle structures on gonioscopy.⁶ Primary open-angle glaucoma (POAG) is chronic progressive optic neuropathy with a visual field defect, open-angle on gonioscopy and absence of secondary cause.⁶ Primary angle-closure glaucoma (PACG) is characterized by elevated IOP due to iridotrabecular contact and peripheral anterior synechia on gonioscopy.⁶

POAG is the most common subtype of glaucoma in all the regions accounting for 68.8% of all glaucoma cases.² PACG is the less common type but results in more blindness than POAG.⁷ POAG is dominant among Caucasian and African descendants while PACG is more common in the East Asian population.⁸

Trabeculectomy is the Gold standard treatment, when pressure reduction is unsuccessfully controlled by medical treatments or lasers. It is the most frequently performed procedure for lowering IOP in glaucoma patients worldwide.^{6,7} As compared to the medical treatment, trabeculectomy is more successful in achieving low IOP.⁹ It has the advantage of stabilizing IOP by minimizing diurnal fluctuation in IOP and by decreasing dependence on patient compliance with medication.¹⁰ Trabeculectomy has also been associated with several postoperative complications including wound leak, blebitis, endophthalmitis, shallow anterior chamber, hypotony, hypotony maculopathy, aqueous misdirection syndrome, malignant glaucoma, choroidal detachment and loss of vision.¹¹⁻¹³

Numerous studies have been published regarding post-operative complications of trabeculectomy but few have compared the complications of trabeculectomy in POAG patients and PACG patients.¹⁴⁻¹⁶ There is a dearth of data regarding complications of trabeculectomy from Pakistan. This study would be helpful to in adding data about this region. This study has been conducted to determine the frequency of postoperative complications of trabeculectomy in primary open-angle glaucoma compared to primary angle-closure glaucoma.

METHODS

This study was conducted in the Department of Ophthalmology, Abbasi Shaheed Hospital, Karachi, from January 2017 to January 2019. It was a comparative case series with consecutive sampling technique. The study was approved by ethical review committee and adheres to the tenants of the Declaration of Helsinki. All the patients who had undergone primary trabeculectomy without antimetabolites for primary open-angle glaucoma and primary angle-closure glaucoma with a 12 months follow up during the given period were included in the study. Patients who had significant cataract preoperatively, repeated trabeculectomy, failed argon laser trabeculoplasty and trabeculectomy done for congenital glaucoma, traumatic glaucoma, secondary glaucoma were excluded from the study. Patients who were lost to follow-up were also excluded. Surgeries were performed by the first two surgeons.

All the surgeries were fornix-based and done under retrobulbar anesthesia. Superior rectus suture was applied with 4/0 silk for adequate exposure of the superior sclera and limbus. A side port was made with a phacoemulsification knife 3.2mm for access to the anterior chamber. Conjunctiva was cut for fornixbased conjunctival flap near limbus along with radial relaxing incision using Westcott scissors. Non-tooth forceps were used for handling conjunctiva to avoid buttonholing. Conjunctiva and tenon capsules were separated from the episclera and sclera. Hemostasis was achieved with light wet field cautery to avoid shrinkage of the conjunctiva. A rectangular, partial thickness, a limbus-based scleral flap was outlined with a surgical blade no 11, measuring 3 X 4mm, within 2 o'clock to 10 o'clock hour of the limbus. The flap was lifted and dissected towards the limbus with a surgical blade no 16 till peripheral cornea. The anterior chamber was entered with a blade. A small window measuring 2 X 1mm was made by removing a piece of trabecular meshwork at the posterior edge of the anterior chamber incision with scissors. Peripheral Iridectomy was done by grasping the iris through this newly formed window with the help of iris scissors. The scleral flap was closed with interrupted nylon 10/0 sutures. Irrigation was done through the side port to wash the anterior chamber, check the functioning of the bleb and reform the anterior chamber with air. Conjunctiva and tenon capsule was also closed with interrupted 10/0 nylon suture. Subconjunctival steroids and antibiotics were given at the end of the procedure.

The dressing was done after applying antibiotic drop and ointment. Postoperatively topical steroid antibiotic drops (Moxifloxacin and dexamethasone) and antibiotic ointment were prescribed for 8 - 10 weeks. Systemic antibiotic ciprofloxacin 500mg twice daily and analgesic were given for 5 days. Atropine eye drops were also prescribed in eyes at risk for developing aqueous misdirection syndrome.

The dressing was removed on the first postoperative day. Patients were examined on a slit lamp biomicroscope. Visual acuity was assessed on Snellen's chart and intraocular pressure was checked by applanation tonometer on every visit. Patients were followed up postoperatively, day after surgery, at 1st week, 15th day, monthly for 3 months, and then at 6 months. They were assessed for complications, bestcorrected visual acuity (BCVA), and intraocular pressure (IOP). Siedel test was performed in every patient by putting a drop of 2% fluorescein over the wound site and then examining it under a cobalt blue filter. Early and frequent follow-ups were requested for complicated cases.

The primary outcome of the study was frequency of complications among the two groups. Hyphema, uveitis, wound leak, shallow anterior chamber, choroidal detachment, choroidal folds, hypotonic maculopathy, over filtering blebs, suprachoroidal hemorrhage, raised IOP, blebitis, endophthalmitis, malignant glaucoma and cataract were look for. The secondary outcome was the reduction of IOP after surgery, failed or successful trabeculectomy.

Encapsulated blebs or flat blebs with IOP of more than 21 mm of Hg that required medical treatment were considered as failed trabeculectomy. IOP of less than 21 mm of Hg without any medical treatment was referred as successful trabeculectomy.

Data was collected on a pre-designed proformaand analyzed on SPSS version 21. Frequencies were calculated for categorical variables like gender and complications. Means with standard deviation (SD) were calculated for numerical data including age and IOP. Reduction in preoperative and postoperative IOP was analyzed with a Pair t-test among POAG and PACG groups. Complications of trabeculectomy for POAG and PACG were compared with help of the Pearson chi-square test. Statistical significance was defined as a p-value of less than .005.

RESULTS

Out of 71 patients 52(73.3%) had POAG and 19 (26.7%) had PACG. There were 36 (50.7%) males for the POAG group and 6 (8.5%) males for the PACG group. Mean age of the patients for the POAG group was 56.7±10.9 and for the PACG group was 52.2±9.5 years. The age rangedfrom 33 to 74 years. The right eye was dominantly affected in the POAG group and left eye in the PACG group. The overall frequency of complications seen in POAG patients was 20 (28.2%) and in PACG patients was15 (21.1%). Patients with successful trabeculectomy in the POAG group were 42 (80.7%) as compared to 14 (73.6%) patients in the PACG group with a statistically non-significant pvalue (0.517). Failed trabeculectomy was seen in 10 (19.2%) patients in the POAG group as compared to PACG group i.e. 5 (26.3%) patients with a statistically non-significant p-value. Other demographic features are given in Table 1.

Table 1: Demographic features and clinical characteristics of the study participants (n = 71).

Variables	POAG	PACG
Mean age	56.7 ± 10.9	52.2 ± 9.5
Minimum	33	33
Maximum	74	65
Gender		
Males	36 (50.7%)	6 (8.5%)
Females	16 (22.5%)	13 (18.3%)
Laterality		
Right eye	32 (45%)	6 (8.5%)
Left eye	20 (28%)	13 (18%)
Diabetes	6 (8.5%)	0
Complications	20 (28.2%)	15 (21.1%)
Successful trabeculectomy	42 (80.7%)	14 (73.6%)
Failed trabeculectomy	10 (19.2%)	5 (26.3%)
Total	52 (73.3%)	19 (26.7%)

POAG – Primary open angle glaucoma, PACG – Primary angle closure glaucoma

There was no significant difference in reduction of IOP at follow-ups among the two groups as shown by the p-value given in Table 2.

Among the complications of trabeculectomy presented in Table 3, a shallow anterior chamber with high intraocular pressure was seen in 5 (7.0%) PACG patients as compared to 2 (2.8%) POAG patients with a statistically non-significant P value (0.015). Shallow anterior chamber with low intraocular pressure was more common in POAG patients i.e. 12 (17%) as compared to PACG patients i.e. 4 (5.6%) with

statistically non-significant p-value (0.86). Seidel test was positive in 10 (14.1%) POAG patients. Resuturing of the wound was also required in the POAG group in 6 (8.5%) patients only. Tenon cysts, uveitis, hyphema, and choroidal folds were seen in few patients among both the groups with a statistically non-significant pvalue. Cataract developed in 8 (11.3%) patients of the POAG group and 4 (5.6%) patients of PACG within 1 year of follow-up (p value > .005). A comparison of complications among the two groups with p values is given in Table 3.Sight-threatening complications blebitis, endophthalmitis, and malignant glaucoma were not encountered in our patients within the follow up period.

Table 2: Comparison of IOP before and aftertrabeculectomy in POAG and PACG patients.

Variables	POAG	PACG	P Value ^a
Pre-operative			
IOP	31 ± 6.7	40 ± 14.8	0.001
IOP 3 months	14.6 ± 3.2	17.0 ± 7.8	0.067
IOP 6 months	15.7 ±4.0	15.8 ± 4.7	0.589
IOP 12 months	15.6 ± 4.2	13.8 ± 4.7	0.353

^{a-}pair T test, IOP- intra ocular pressure, POAG-primary open angle glaucoma, PACG-primary angle closure glaucoma

Table 3: Percentage distribution of complications aftertrabeculectomy in both groups.

Complications	POAG	PACG	P-value ^b
Cataract	8 (11.3%)	4 (5.6%)	0.573
Choroidal fold	2 (2.8%)	0	0.386
Tenon cysts	2 (2.8%)	0	0.386
Block PI	0	2 (2.8%)	0.018
Uveitis	2 (2.8%)	2 (2.8%)	0.280
Hyphema	2 (2.8%)	3 (4.2%)	0.082
Shallow AC high IOP	2 (2.8%)	5 (7.0%)	0.015
Shallow AC low IOP	12 (17%)	4 (5.6%)	0.857
Seidel +ve	10 (14.1%)	0	0.039
resuturing	6 (8.5%)	0	0.122
Pressure patching	6 (8.5%)	6 (8.5%)	0.028

^bPearson chi square

POAG-primary open angle glaucoma PACG-primary angle closure glaucoma

PI- peripheral iridectomy

AC- anterior chamber

+ve- positive

DISCUSSION

In this study, 20 (28.2%) POAG patients and 15 (21.1%) PACG patients developed complications after trabeculectomy, within 12 month of surgery (p value > .005). Mahar had reported complications in 40% of

their PACG patients and in 30% of POAG patients; the difference was however, not statistically significant.¹² They had performed trabeculectomy augmented with antimetabolite and it was a small-scale study (n = 20).¹² Tan et al. have reported a frequency of complications in 8.7% POAG and 8.0% in the PACG group.¹³ This complication rate is comparatively lower than the present study.The trabeculectomy was done by 8 different surgeons on a total of 320 patients.¹³

The most frequent complication observed in our study was a shallow anterior chamber with low intraocular pressure (IOP), seen in 12 (17%) patients with POAG and 4 (5.5%) patients with PACG. Among them, 10 (14.1%) patients had a positive Seidel test in the POAG group. The most frequent complication reported by Mahar was flat bleb in 20% patients with PACG and 13% patients with POAG.¹² Flat bleb can be due to over or under filtration. Over filtration is a known complication of augmented trabeculectomy. The shallow anterior chamber was the most frequent complication encountered by Sihota et al in 40% of PACG patients and 30% in POAG patients (n = 64)within 10 year follow up.¹⁶ Divyalakshmi et al. have reported shallow anterior chamber with choroidal detachment in just one PACG patient.¹⁷ Tan et al. have reported shallow anterior chamber due to bleb leak in 0.9% of PACG group and 2.9% in POAG group.¹³ All of the above studies are common in reporting no statistically significant difference in complications among POAG and PACG patients.

In this study, shallow anterior chamber was treated with pressure patching in 8.5% of patients in both the groups. Resuturing and reformation of the anterior chamber (surgical intervention) were required in 8.5% of patients only in the POAG group. All the patients with the shallow anterior chamber in the study by Sihota et al were treated by non-surgical intervention.¹⁶ Resuturing was required in 1% of patients in the POAG group and 3.6% of patients in the PACG group in a study by Tan et al.¹³

Cataract is a well-known complication of trabeculectomy. Advanced Glaucoma Intervention Study (AGIS) has reported an increased risk of cataract formation by 78% after adjustment for age and diabetes.¹⁸ Cataract had developed in 8 (11.3%) patients in the POAG group and 4 (5.6%) patients in the PACG group in this study. Mahar had not reported cataract formation within 12 months follow-up period.¹² Cataract was the main complication (13%) after trabeculectomy with antimetabolite in Indian

studies.^{19,20} Study by Thatsnarong has reported cataract formation in 6 (16.7%) patients following trabeculectomy in PACG patients.¹⁵ The limited sample size of our study probably made the difference insignificant and longer duration follow up is also required. Development and progression of cataracts should be considered post trabeculectomy especially in patients with PACG.¹⁶

Choroidal folds and tenon cysts were observed in 2 (2.8%) patients in the POAG group while blocked PI was seen in 2 (2.8%) patients in the PACG group. Tenon cyst was seen in 3.3% and 6% of patients, post trabeculectomy, in studies by Divyalakshmi et al. and Borgreffeet al.^{17,21} The reported incidence of tenon cyst following trabeculectomy is about 9 - 15%.²²

The secondary outcome was the reduction in IOP in POAG and PACG patients. Preoperatively mean IOP in POAG was 31 ± 6.7 mm of Hg and 40 ± 14.8 mm of Hg in PACG patients. Post-operatively at 1 year, it was reduced to 15.6 ± 4.2 mm of Hg in POAG and 13.8 ± 4.7 mm of Hg in PACG patients. However, there was no statistically significant difference in the reduction of IOP between the two groups of glaucoma in this study. Mahar had reported a mean drop of 10.63 ± 3.2 mm of Hg in the POAG group compared to 9.42 ± 2.1 mm of Hg in the PACG group.¹² Mean postoperative IOP reductions was 14.63 mm of Hg after trabeculectomy by Suresh et al.²³ Sihota et al. did not find any significant difference in reduction of IOP with trabeculectomy.¹⁶

In this study successful trabeculectomy was observed in 42 (80.7%) POAG patients and 14 (73.6%) PACG patients with an insignificant difference. Other studies have reported success rates of 80% and 93.4% in trabeculectomies augmented with antimetabolites.^{19,20} Sihota have reported a 50% success rate in POAG and 54% in PACG after 10 years.¹⁶ There is a gradual decline in the success rate of trabeculectomy with longer duration of follow-up.

Primary open-angle glaucoma and primary angleclosure glaucoma are two different entities of the same disease. They have entirely different pathophysiology. There is a generalized impression that patients with PACG have a greater risk of developing postoperative complications as shallow anterior chamber, hypotony and malignant glaucoma following trabeculectomy as compared to patients with POAG.¹⁸ The results of our study and other studies of the region (ASIA) are consistent with the fact that surgical complications of trabeculectomy are independent of POAG and PACG.^{12,13,16,17} Early postoperative period is very crucial for prompt detection and management of complications. Surgical technique, surgeon's expertise and vigilant post-operative management are other important aspects to have a successful trabeculectomy in closed and open-angle glaucoma.

The limitations of the study are the retrospective design, and relatively small sample size of patients amongthe two groups. We have not analyzed complications based on ethnicity so our results cannot be generalized in our population. Further prospective studies are recommended with a large sample size from our region to study/analyze the long-term effects of trabeculectomy in our population.

CONCLUSION

The outcome of Trabeculectomy in terms of complications was not significantly different in the POAG versus PACG, over a period of 12 months. Trabeculectomy is equally advantageous in lowering IOP in POAG and PACG patients. Successful trabeculectomy is independent of the type of glaucoma as established by other studies in the literature.

Ethical Approval

The study was approved by the Institutional review board/Ethical review board (**OSP-IRB/2021/004**).

Conflict of Interest

Authors declared no conflict of interest.

REFRENCES

- 1. Bourne RR, Taylor HR, Flaxman SR, Keeffe J, Leasher J, Naidoo K, et al. Number of People Blind or Visually Impaired by Glaucoma Worldwide and in World Regions 1990-2010: A Meta-Analysis. PloS one, 2016; 11: e0162229.
- 2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology, 2014; 121 (11): 2081-2090.
- 3. Khan L, Ali M, Qasim M, Jabeen F, Hussain B. Molecular basis of glaucoma and its therapeutical analysis in Pakistan: an overview. Biomed Res Ther. 2017; 4 (03): 1210-1227.
- 4. **Thylefors B, Negrel AD.** The global impact of glaucoma. Bull World Health Org. 1994; **72 (3):** 323.

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- Levkovitch-Verbin H, Quigley HA, Martin KR, Valenta D, Baumrind LA, Pease ME. Trans-limbal laser photocoagulation to the trabecular meshwork as a model of glaucoma in rats. Invest Ophthalmol Vissci. 2002; 43 (2): 402-410.
- 6. European Glaucoma Society Terminology and Guidelines for Glaucoma, 4th Edition – Chapter 2: Classification and terminology Supported by the EGS Foundation. Br J Ophthalmol. 2017; **101:** 73–127.
- 7. Wells AP, Bunce C, Khaw PT. Flap and suture manipulation after trabeculectomy with adjustable sutures: titration of flow and intraocular pressure in guarded filtration surgery. J Glaucoma, 2004; 13 (5): 400-406.
- Foster PJ, Johnson GJ. Glaucoma in China: how big is the problem? Br J Ophthalmol. 2001; 85 (11): 1277-1282.
- 9. Wells AP, Cordeiro MF, Bunce C, Khaw PT. Cystic bleb formation and related complications in limbus-versus fornix-based conjunctival flaps in pediatric and young adult trabeculectomy with mitomycin C. Ophthalmology, 2003; **110** (11): 2192-2197.
- Schwartz K, Budenz D. Current management of glaucoma. Curr Opin Ophthalmol. 2004; 15 (2): 119-126.
- 11. Henderson HW, Ezra E, Murdoch IE. Early postoperative trabeculectomy leakage: incidence, time course, severity, and impact on surgical outcome. Br J Ophthalmol. 2004; **88** (5): 626-629.
- 12. Mahar PS, Laghari DA. Intraocular Pressure Control and Post Operative Complications with Mitomycin C Augmented Trabeculectomy in Primary Open Angle and Primary Angle-Closure Glaucoma. Pak J Ophthalmol. 2011; 27 (1).
- 13. Tan YL, Tsou PF, Tan GS, Perera SA, Ho CL, Wong TT, et al. Postoperative complications after glaucoma surgery for primary angle-closure glaucoma vs primary open-angle glaucoma. Arch Ophthalmol. 2011; **129** (8): 987-992.
- Maheshwari D, Kanduri S, Kadar MA, Ramakrishnan R, Pillai MR. Midterm outcome of mitomycin C augmented trabeculectomy in open angle glaucoma versus angle closure glaucoma. Indian J Ophthalmol. 2019; 67 (7): 1080.
- Thatsnarong D, Ngamchittiampai C. Outcome of Trabeculectomy in Primary Angle-Closure Glaucoma. J Med Assoc Thai. 2017; 100 (8): 907.
- 16. Sihota R, Gupta V, Agarwal HC. Long-term evaluation of trabeculectomy in primary open angle glaucoma and chronic primary angle closure glaucoma in an Asian population. ClinExp Ophthalmol. 2004; 32 (1): 23-28.

- 17. **Divyalakshmi KS, Ramakrishna R.** A comparative study of complications and its management following phaco-trabeculectomy in primary open angle glaucoma, primary angle closure glaucoma and pseudo-exfoliative glaucoma with cataract. Indian J Clin Exp Ophthalmol, 2019; **5 (1):** 121-126.
- Agis Investigators. The advanced glaucoma intervention study, 8: risk of cataract formation after trabeculectomy. Arch Ophthalmol. 2001; 119 (12): 1771-1779.
- Ramakrishnan R, Michon J, Robin AL, Krishnadas R. Safety and efficacy of mitomycin C trabeculectomy in southern India: a short-term pilot study. Ophthalmology, 1993; 100 (11): 1619-1623.
- 20. Lamba PA, Pandey PK, Raina UK, Krishna V. Short-term results of initial trabeculectomy with intraoperative or postoperative 5-fluorouracil for primary glaucomas. Indian J Ophthalmol. 1997; **45** (3): 173.
- 21. **Borggrefe J, Lieb W, Grehn F.** A prospective randomized comparison of two techniques of combined cataract-glaucoma surgery. Graefes Arch Clin Exp Ophthalmol. 1999; 237: 887–892.
- Vijaya L, Manish P, Ronnie G, Shantha B. Management of complications in glaucoma surgery. Indian J Ophthalmol. 2011; 59 (Suppl. 1): S131.
- 23. Suresh HH, Samhitha HR, Kishore H, Prasad K, Solse S, Divya P. Primary angle-closure glaucoma: A retrospective interventional case series in South India. Oman J Ophthalmol. 2016; 9 (1): 17.

Authors' Designation and Contribution

Erum Shahid; Assistant Professor: Concepts, Design, Literature search, Data acquisition, Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing, Manuscript review.

Uzma Fasih; Associate Professor: *Concepts, Design, Literature search, Data acquisition, Manuscript preparation, Manuscript editing, Manuscript review.*

Arshad Shaikh; Professor: Concepts, Design, Manuscript editing, Manuscript review.