

LOW PRESSURE GLAUCOMA

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Background: To observe open angle glaucoma in the presence of low intra-ocular pressure.

Methods: A descriptive cross-sectional study was done on 150 patients who attended the glaucoma clinic during one year from January 2005 to January 2006. A detailed history was obtained and a thorough ophthalmic examination was performed, including gonioscopy, ophthalmoscopy, applanation tonometry and automated perimetry. **Results:** Out of 150 patients of Primary open angle glaucoma 33 patients (22%) were found to have glaucoma at intra-ocular pressure level below normal (low pressure glaucoma), with mean age 56 ± 9.21 years. Mean age of Primary open angle glaucoma group was $52.5 \pm 8.7\%$. Of the 33 cases of low-pressure glaucoma (22 patients) 66.6% were male and (11 patients) 33.4% were female, while in Primary open angle glaucoma (82 patients) 70% were male and (35 patients) 30% were female. Mean intra ocular pressure was 15.13 ± 3.60 mm Hg in low-pressure glaucoma and 28 ± 6.5 mm Hg in Primary open angle glaucoma. Maximum intra ocular pressure in Low-pressure glaucoma group was 21 mm Hg and minimum Intra ocular pressure was observed as 8 mm Hg, while these values observed as 50 mm Hg and 10 mm Hg respectively in primary open angle glaucoma. **Conclusions:** Low pressure glaucoma remains a difficult diagnosis for ophthalmologist who favors the argument that raised Intra ocular pressure is essential for the diagnosis of Primary open angle glaucoma. Low pressure glaucoma changes the definition of glaucoma and our concept of intra ocular pressure as a sole etiological factor is now out dated. The overall frequency of Low pressure glaucoma in the current study was 22% among suspected cases of Primary open angle glaucoma.

Keywords: Glaucoma, primary open angle glaucoma, low pressure glaucoma.

INTRODUCTION

Glaucoma is the second leading cause of blindness world wide.¹ Glaucoma cases are expected to hit 80 million by 2020; of these 74% will have primary open angle glaucoma² (POAG). POAG is an asymptomatic, progressive optic neuropathy characterized by enlarging optic disc cupping and visual field loss.³ It has been proven by many studies^{3,4} that POAG exhibits two patterns of visual field defects:

- A relatively diffuse and putatively more intra ocular pressure (IOP) dependant type.

- A localized and putatively less IOP dependent type.

Low pressure glaucoma (LPG) is a variety of POAG clinically defined⁵ as 'a condition in which IOP is less than 21 mm Hg associated with typical glaucomatous optic neuropathy and corresponding visual field changes'. This LPG also described as normal tension glaucoma and it is interchangeable with the term pseudo glaucoma. In glaucoma IOP is a major risk factor in the development and progression of disease, however, in LPG other risk factors are considered more important, as IOP, by definition, remains within statistically normal limits.^{6,7} We can say that, LPG simply a form of POAG in which one of the sign (IOP) is absent.³ LPG comprises a significant proportion of the generic grouping of POAG, although this proportion varies between samples and possibly between different populations.^{2,8} Many studies have been done

regarding LPG. According to those studies frequency of LPG is not low accounting for one third of POAG in west^{2,9,11} and two third among Japanese at the time of screening.¹² However, in our country we still lack epidemiologically valid data on LPG. Purpose of this study is to observe open angle glaucoma in the presence of low intra-ocular pressure.

MATERIAL AND METHODS

This was a cross-sectional study of descriptive type, conducted in the department of Physiology, Dow University of Medical and Health Sciences Karachi, Civil Hospital Karachi in collaboration with glaucoma clinic at Al-Ibrahim Eye Hospital Karachi. Among all glaucoma patients visited glaucoma clinic from January 2005 to January 2006, those who satisfied the following criteria^{13,14} were included in this study.

- Open angles of drainage.
- Glaucomatous cupping³ of optic nerve head and loss of neuroretinal rim.
- Visual field defects compatible with glaucomatous cupping.
- Absence of any secondary cause for glaucomatous optic neuropathy.

Those with cataract¹⁵ or any other eye disease producing optic neuropathy¹⁶, congenital eye diseases¹⁷, or previous medical, surgical or laser treated eyes were excluded from this study.

In all the patients presenting with history of glaucoma in glaucoma clinic visual acuity was checked using Snellen's chart¹⁸, and then eyes were examined using slit lamp¹⁹ to visualize anterior chamber of eye as well as interior of the eye either by using contact glass or direct ophthalmoscope¹³. Although contact glasses¹³ provide good view of chamber angles⁸, but to confirm the diagnosis a separate gonioscope^{19,20} was used. Later in all those patients with open chamber angles and glaucomatous optic disc changes¹³ IOP was measured using Goldmann Applanation Tonometer.²¹ Visual field were analyzed by the help of Humphrey Visual Field Analyzer²² 30-2 program, after calibration and standardizations according to manual of manufacturer. Consent of all patients was taken and confidentiality maintained. A detail questionnaire of all patients was filled, this Individual record sheet of the patients were than process for data analysis. The data collected for present study entered and verified by using the SPSS version 10.0 software packages. Descriptive statistics was computed. Relative frequencies (percentages) of groups was shown, result expressed as Mean±SD/SEM.

RESULTS

A total of 150 patients of all ages and both sexes were selected by convenient sampling. Out of these patients one hundred and four were male (69.4%) and forty six were female (30.6%). Of these 150 patients 33 were found to have glaucomatous optic neuropathy in the presence of IOP less than 22 mmHg (low pressure glaucoma), while rest of the population of POAG group is from high tension primary open angle glaucoma (HTPOAG) 117 cases (78%).

Table-1: Comparative analysis of frequency of low pressure glaucoma and high tension primary open angle glaucoma in various age groups

AGE (YEARS)	LPG GROUP (n=33)	HTPOAG GROUP (n=117)
≤40	3(9%)	20(17%)
40.1-50	5(15%)	30(25%)
50.1-60	15(46%)	57(49%)
>60	10(30%)	10(9%)

LPG = low pressure glaucoma, HTPOAG= High tension primary open angle glaucoma

In LPG group 22 (66.6%) were male and 11 (33.4%) were female, while in HTPOAG 82 (70%) were male and 35 (30%) were female. Age ranges from 35–75 years in total study population and mean age was found to be 56±9.21 years in the group of LPG and 52.5±8.7% in HTPOAG group. Comparison of frequencies of various age groups among NTG and HTPOAG was described in Table-1.

Mean IOP in LPG group was 15.13±3.60 mm Hg while it was 28±6.5 mm Hg in HTPOAG group. Maximum IOP level in LPG was 21 mm Hg and in HTPOAG it was found as high as 50 mm Hg, minimum IOP level was as low as 8 mm Hg and 10 mm Hg in LPGG and in HTPOAG respectively (Table-2).

Table-2: Ocular examination of study population

IOP	LPG GROUP	HTPOAG GROUP
Mean	15.13 mm Hg	28 mm Hg
SD	±3.60	±6.5
Minimum	8 mm Hg	10 mm Hg
Maximum	21 mm Hg	50 mm Hg

LPG = low pressure glaucoma, HTPOAG= High tension primary open angle glaucoma, IOP= Intra-ocular pressure

DISCUSSION

The type of POAG present in the IOP levels below normal was first observed in 1875 by a great ophthalmologist Von Graefes¹⁹, it was object of debate among many ophthalmologists who favors the argument that raised IOP is essential for diagnosis of POAG.¹⁴

In our study out of total 150 patients of POAG 33 patients (22%) have IOP less than 21 mm Hg and 117 (78%) patients had IOP more than 21 mm Hg. So the prevalence of LPG was about 22% in our study. According to another study carried out in Japan the incidence of glaucoma was much higher than the rest of the world, It has been reported that prevalence of LPG among Japanese at the time of screening was accounting for two third of cases, i.e., 2% of Japanese total population.²³ According to Tajimi study carried out in Japan by Iwase *et al* including randomly selected subjects of more than 40 years.¹⁴ Among these 3021 participants prevalence of POAG is 3.9% out of which 92% of patients had IOP less than 21 mm Hg which is about 3.6% of total population examined. This incidence is much higher than our results but this shows that prevalence of LPG is highest in Japan probably because of there tendency for IOP to fall with increasing age^{12,24} instead of lowering down like rest of the world.

In the west incidence of LPG is not low, accounting for one third to half of POAG cases.¹⁰ Sommer²⁵ states that 20–25% of glaucomatous neuropathy develops with normal or low IOP; this incidence is very near to our study.

In Rotterdam Study, which was a population based study carried out in Netherlands, out of 3062 eligible participants of 55 years of age or older, the over all prevalence of POAG was 1.10%. Of these patients about 39% had IOP's less than 21 mm Hg²⁶ with male predominance. The result of this study are comparable to ours, in our study frequency of LPG

among individuals between 50.1 to 60 years is 46% and 30% in patients more than 60 years of age.

The Swedish, Dalby study found LPG in 61% of the total POAG cases.²⁷ In another population based survey carried out in same set up including 760 people 65 to 74 years of age, 18% of individual of POAG had IOP less than 21 mm Hg.²⁸ In the Barbados eye study²⁹ including 3427 patients, about half of the newly diagnosed POAG patients had IOP less than 21 mm Hg which are about 1.2% of total population. In there study incidence rate of POAG increased from 1.25% at ages 40 to 49 years to 4.2% at ages of 70 years or more, tending to be higher in men than women (2.7% vs 1.9%). This study revealed high risk of low pressure POAG in the population of African origin, especially in older adults. In our present study incidence of both POAG and LPG increased with age so as observed in this study, though the incidence of LPG was much higher than our study but in Barbados study participation rate is much high though the diagnostic criteria was same.

As far as profile of POAG in a major eye hospital in India³⁰ is concern, in there five year study program including 2425 patients attending glaucoma clinic during this period, incidence of POAG is much less than angle closure glaucoma (ACG) (37:63). LPG accounting for 0.62% hospital referral, peak presentation in seventh decade. Mean age for presentation was 60.04 years, with male representing 74% cases. A remarkably low number of LPG cases were noted in this study as compare to rest of the world including ours, may indicate that most of the population were affected by ACG and over all rate of POAG is less. Though there is male predominance like our study but the mean age is bit more than ours indicating delay in diagnosis.

According to another study³¹ carried out at Al-Shifa Eye Hospital Islamabad, among total hospital admissions LPG was responsible for 3.0% of total Hospital visit. This study did not explain frequency of LPOG among POAG cases and demographics of study population, so lacking much valuable knowledge in this respect.

It is believed that LPGG occurs more commonly and severely in women, Levene review of the relevant studies found an over all higher female prevalence ranging from 6% to 75%.⁶ The Beaver Dam Eye Study³² found equal prevalence among both genders. There is a preponderance of females in Moorfield normal-tension glaucoma group with a ratio of 2:1 in all age groups¹⁴, while in Low-pressure Glaucoma Treatment Study³³ out of 190 patients with LPG 60% was females. In another study carried out in Moorfield eye hospital by Noureddin *et al*³⁴, out of 84 patients with low-pressure glaucoma 69% were

females. Fontana *et al*³⁵, also find the same in their clinical study on 54 patients out of which 34 (63%) patients were females. These studies show that prevalence of LPG is more common among females than male glaucoma patients, which has not been seen in our study. Although one study indicated that in younger samples, newly diagnosed males with LPG may show more severe field loss than in similar age females.³⁶ In our study there are more (64%) males with LPG than females 11 (26%). This may be because of our socio-economic setup and lack of visits to hospitals by females.

The incidence of normal-tension glaucoma increases with age.¹⁴ In our study mean age for LPG was 56 years (range 37–75 years). While Fontana *et al*³⁵, reported mean age around 59 years, Lake *et al*³⁷, reported 70 years, Plange *et al*³⁸, considered 51 years, Noureddin *et al*³⁴, found 66 years, Krupin *et al*³³, found mean age around 65 years.

A LPG is considered as a disease of elderly⁶, in our study maximum incidence of disease (46%) were between 51 to 60 years and 30% were more than 60 years of age. In the Beaver Dam Eye Study³² the prevalence of LPG increases from 0.2% in 43 to 54 years of age group to 1.6% in those over 75 years of age. However, there is significant minority of the patients who are below the age of 50 years. While in Japan, Shiose *et al*²³, observe that four times as many patients in the over 40 year age group have LPG accounting for 2% of the total Japanese population. This theory was also supported by Beaver Dam Eye Study³² but its frequency is less than that in Japan. Aung T *et al*³⁹, found in there study carried on 108 LPG patients that 66 patients were more than 60 years of age while only 42 were fall in less than 60 years category. In an Italian study of a population of over 40 years of age found a prevalence of 0.6%, showing that 33% had LPG out of POAG.¹¹

Though numerous data present regarding frequency of POAG in the world, thorough investigation regarding LPG still required. Due to financial constraints limited numbers of patients were enrolled in this study. Patients enrolled in this study are from different areas of Karachi only. Follow up of these patients have not been done which is very important to observe the pattern of progression of disease and differentiate LPG from other forms of glaucoma at different stages of disease. It was not a longitudinal study to establish strong conclusions but just an attempt to put some light on presence of this silent killer in our setup. Though incidence was much less than rest of the world but proper and timely diagnosis may be beneficial to save the sight. Public awareness on normal-tension glaucoma should be increase to address the challenges of disease and similar studies should be conducted in other areas to

established frequency of LPG in various cities of our country.

REFERENCES

- Resnikoff S, Pascolini D, Ale DE, Kocur I, Pararajasegaram R, Pokharel GP. Global data on visual impairment in the year 2002. *Bull of WHO* 2004;82:844–51.
- Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 2006;90:262–7.
- Distelhorst JS, Hughes GM. Open angle glaucoma. *Am Fam physician*. 2003;67:1937–44.
- Schulzer M, Drance SM, Carter CJ, Brooks DE, Douglas GR, Lau W. Biostatistical evidence for two distinct chronic open angle glaucoma populations. *Br J Ophthalmol* 1990;74:196–200.
- Baig MA, Akram A, Ishaq M. Normal Tension Glaucoma errors in diagnosis. *Pak J Ophthalmol* 2002;18:23–5.
- Levene RZ. Low tension glaucoma: A critical review and new material. *Surv Ophthalmol* 1980;24:621–64.
- Hitchings RA. Low tension glaucoma—its place in modern glaucoma practice. *Br J Ophthalmol* 1992;76:494–6.
- Collaborative Normal Tension Glaucoma Study Group. Natural history of Normal Tension Glaucoma. *Ophthalmology* 2001;108:243–53.
- Kroese M, Burton H. Primary open angle glaucoma. The need for a consensus case definition. *Epidemiol Community Health* 2003;57:752–4.
- Hollow FC, Graham PA. Intra ocular pressure, glaucoma, and glaucoma suspect in a defined population. *Br J Ophthalmol* 1996;50:570–86.
- Bonomi L, Marchini G, Marraffa M, Bernardi P, De Franco I, Perfetti S. Prevalence of glaucoma and intra ocular pressure distribution in a defined population. The Egna-Neumarkt study. *Ophthalmology* 1998;105:209–53.
- Iwara A, Suzuki Y, Araie M, Yamamoto T, Abe H, Shirato S. The prevalence of primary open angle glaucoma among Japanese. The Tajimi study. *Ophthalmology* 2004;111:1641–8.
- Khan MD, Islam Z, Ali SI, Khan AA, Saeed N. Glaucoma guidelines. Glaucoma Interest Group of Pakistan, Khy. Ophthalmological Society of Pakistan, 2002:1–27.
- Kamal D, Hitchings RA. Normal Tension Glaucoma- a practical approach. *Br J Ophthalmol* 1998;82:835–40.
- Roberts SS. Eye disease, understanding retinopathy. *Diabetes Forecast* 2005;58:25–6.
- Lee AG. Differentiating glaucomatous from non-glaucomatous optic atrophy. *Ophthalmology* 1999;106:855–7.
- Rosenberg LF, burde RM. Progressive visual loss caused by an arachnoidal brain-cyst in patient with an optic nerve colobomas. *Am J Ophthalmol* 1988;106:322–5.
- Miller SJH. Parson's disease of the eye. 19th ed. London: Churchill Livingstone; 1991. 75–86, 88–96, 107–11, 213–8.
- Weingeist TA, Liesegang TJ, Grand MG, Berlin MS, Hodapp EA, Lee DA. Glaucoma. Basic and clinical science course, San Francisco. American Academy of Ophthalmology, 1999;5–9, 22–54.
- Congdon NG, Spaeth GL, Augsburg J, Klanchnik J Jr, Patel K, Hunter DG. A proposed method for measurement in the anterior chamber angle biometric gonioscopy. *Ophthalmology* 1999;106:2161–7.
- Goldmann Applanation Tonometer. GAT instruction manual. Hagg-Streit Ophthalmic System Inc. Goldmann division. www.haag-streit.com 2003 Haag-Streit, Inc.
- Humphrey Visual Field Analyzer II-i. Carl Zeiss Ophthalmic System Inc. Humphrey division. www.humphrey.com 2003 Carl Zeiss Meditec, Inc.
- Shoise Y, Kitazawa Y, Tsukahara S, Akamats U, Mizokami K, Futa R. Epidemiology of glaucoma in Japan-a nation wide glaucoma survey. *Jpn J Ophthalmol* 1991;35:133–55.
- Nakano T, Tatemichi M, Miura Y, Sugita M, Kitahara K. Long term physiological changes of intra ocular pressure: a 10-year longitudinal analysis in young and middle aged Japanese men. *Ophthalmology* 2005;112:609–16.
- Sommer A. Glaucoma: facts and fancies. *Eye* 1996;10:293–301.
- Dielemans I, Vingerling JR, Wolfs RCW, Hofman A, Grobbee DE, de Jong PT. The prevalence of primary open angle glaucoma in and population based study in the Netherlands. The Rotterdam Study. *Ophthalmology* 1994;101:1851–5.
- Bengtsson B. The prevalence of glaucoma. *Br J Ophthalmol* 1981;65:46–9.
- Ekstrom C. Prevalence of open angle glaucoma in central Sweden. The Tierp Glaucoma Survey. *Acta Ophthalmol Scand*. 1996;74:107–12.
- Leske MC, Connell AM, Nemesure B, Li X, Schachat A, Hennis A. Incidence of open angle glaucoma: The Barbados Eye Studies Group. *Arch Ophthalmol* 2001;119:89–95.
- Jaychandra D, Sharad B, Zia C, Pankaj S, Arun N, Abhrajit D. Profile of glaucoma in a major eye hospital in North India. *Indian J Ophthalmol* 2001;49:25–30.
- Malik NM. Related incidence of different types of glaucoma in Pakistan. *Al-Shifa Med Bull* 1995;1:4–5.
- Klein BEK, Klein R, Spansel WE, Franke T, Cantor LB, Martone J. Prevalence of glaucoma: the Beaver Dam Eye study. *Ophthalmology* 1992;99:1499–504.
- Krupin T, Liebmann JM, Greenfields DS, Rosenberg LF, Ritch R, Yan JW. The low pressure glaucoma treatment study (LoGTS) study design and baseline characteristic of enrolled patients. *Ophthalmology* 2005;112:376–85.
- Noureddin BN, Poinosawmy D, Fietzke FW, Hitching RA. Regression analysis of visual field progression in low tension glaucoma. *Br J Ophthalmol* 1991;75:493–5.
- Fontana L, Armas R, Poinosawmy D, Haeth DF, Bunce CV, Hitchings RA. Unilateral field loss in normal tension glaucoma-a longitudinal followup study. *Invest Ophthalmol Vis Sci* 1997;2631:321–5.
- Shiraki R, Uchida H, Ishida K, Yamamoto T. difference of optic disc topography between low-tension group and high-tension group in normal-tension glaucoma patients. *Nippon Ganka Gakkai Zasshi* 2005;109:19–25.
- Lake S, Liverani E, Desai M, Casson R, James B, Clark A . Normal-tension glaucoma is not associated with the common apolipoprotein E gene polymorphisms. *Br J Ophthalmol* 2004;88:491–3.
- Plange N, Remky A, Arend O. Colour Doppler imaging and fluorescein filling defects of the optic disc in normal-tension glaucoma. *Br J Ophthalmol* 2003;87:731–6.
- Aung T, Okada K, Poinosawmy D, Membrey L, brice G, Child AH. The phenotype of Normal Tension Glaucoma patients with and without OPA1 polymorphism. *Br J Ophthalmol* 2003;87:149–52.

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