ORIGINAL ARTICLE

Determinants of Primary Open Angle Glaucoma: Review of records of patients attending University Teaching Hospital, Lusaka, Zambia

***M.K. I. Muma[1], C. Michelo[2], R. Bailey[3]**

[1]*Department of Surgery, University of Zambia*
[2]*Department of Public Health, School of Medicine, University of Zambia*
[3]*London School of Hygiene and Tropical Medicine*

ABSTRACT

Background: Primary open angle glaucoma (POAG) has continued to cause high disease burden globally and Zambia is no exception. We investigated the prevalence and socio-demographic determinants of POAG based on records of clients attending the eye clinic at University Teaching Hospital (UTH), Lusaka.

Methods: Data stem from serial hospital population based stored patients' records at the UTH eye clinic from 2008 to 2011 (n= 71,347). These records were examined for completeness in terms demographic information (specifically age, sex, residence and ethnicity) as well as ocular details that included the diagnosis based on full ocular examination and intra-ocular pressure. All the records that did not have any of this information were labelled as incomplete and excluded from final analysis. Multivariate logistic regression, stratified by age group and gender, was used to examine the association between demographic factors with POAG.

Results: Of the 71,347, 11.2% (7,968) did not turn up for appointments and 4.7% (3,323) records could not be found, hence the de facto eligible records that met the minimum eligibility criteria for the study 60,056 representing 84.1%. The aged ranged from 15 to 90 with a median age 47 years (IQR 42, 55). The prevalence of POAG was 4.2% (95% CI, 2.7%, 6.2%), distributed as 1.8% (95% CI 1.1, 2.9) in males and 2.4% (95% CI 1.9, 3.9) for females. The main determinants of POAG were age, sex, education and diabetic retinopathy. Females were more likely to have POAG than males (55.5% vs. 44.5%; OR 1.36, 95%CI 1.1,1.8); Similarly groups older than 55 years than younger (62.3% vs. 37.7%, P<0.001), with lower education status (45.9% vs 54.1. , P< 0.001) and those with diabetic retinopathy than without (34.0%, vs. 64.0%; OR1.2, 95%CI 0.9,1.39) had higher likelihood of POAG.

Conclusion: We found convincing evidence of POAG burden in the studied records. This finding suggests that POAG may be prevalent in the general population. This calls for setting up of both population as well as hospital based surveillance systems so as to know the exact national burden as it evolve over time. Such systems should incorporate health promotional sensitisation to promote early diagnosis as an ethical responsibility given the weight of disability associated with POAG.

***Corresponding Author:**
Mulenga K. I. Muma
Department of Surgery
Ophthalmology Unit
University of Zambia, School of Medicine
PO Box 50110, Lusaka, Zambia
Email: mkmuma@yahoo.com , drichengelo@gmail.com

INTRODUCTION

Preventable blindness has continued to be a significant contributor to disease burden and morbidity in eye health despite the most of the aetiology being in the category of avoidable causes[1]. Among the causes of preventable blindness is glaucoma which is a group eye diseases leading to optic neuropathies Of all the causes of blindness, POAG significantly affects the general population more than other forms of glaucoma [2].

Differentially, POAG varies with age, sex and race as demonstrated in several studies conducted in the Western world and Asia[3,4,5,6,7,8,9]. Although the disease prevalence in the Caucasian population is around 7%, in similar environments the black race has a 1.5 times higher chance of having POAG [10]. This may further suggest a bigger problem in black African populations. Despite this being the case, there is limited data on factors that are associated with the problem [1,2].

Although glaucoma has been associated with high morbidity, in Zambia there is no documented evidence on its exact magnitude and thus it has not been given the preventive or clinical management priority and urgency it deserves given this paucity of burden information. For example, the "Vision 2020: the right to sight" which is a key strategic WHO initiative to eliminate avoidable blindness does not mention glaucoma as one of its priorities [2]. Other global eye health partners have concentrated resources towards cataract eradication at the expense of glaucoma [2,3,4].

The study on which this article is based sought to address the gap highlighted above by determining the prevalence of POAG and the factors associated with it at the UTH. Knowing the burden and factors associated with POAG could help in designing primary preventive strategies of blindness nationally.

MATERIALS AND METHODS

Study area and population

The study was conducted at the University Teaching Hospital (UTH) in Lusaka, Zambia. The UTH is the national referral hospital with a bed capacity of more than 3 000 and provides both surgical and clinical services. Surgical services at this hospital include ophthalmological services through the 'eye clinic'. The UTH's eye clinic is estimated to cater for 21,000 clients annually for both routine and morbidity driven check-ups. The clients that attend this clinic virtually come from across the country, for all ages and for both self and system referrals.

There is another referral centre in Kitwe about 400 Kilometres north of Lusaka. However, and although many people are attended to there too, it remains small and by definition a second level facility.

Study design & selection

UTH was selected for the study on the basis of the high number of eye patients seen at the facility. Data stem from serial hospital population-based stored patients' records at the UTH eye clinic from 2008, 2009, 2010 and 2011 (n=14,060, n=18,609, n=18,681 and n=19,997 respectively) which gave an overall study population of 71,347. These records were examined for completeness in terms demographic information (specifically age, sex, residence and ethnicity) as well as ocular details that included the diagnosis based on full ocular examination and intra-ocular pressure. All the records that did not have any of this information were labelled as incomplete and excluded from final analysis giving a final sample of 60,056 adult eye patients aged between 15 and 90 years old. Poor vision was defined as vision worse than 6/18 in the better eye.

Data extraction

At UTH, all eye patients have to undergo a thorough eye examination which includes visual acuity, IOP measurement, fundus examination for nerve fibre layer and optic disc evaluation. In addition, gonioscopy (with a Volk 3 Mirror Gonio Lens) is also done by the ophthalmologists on all glaucoma patients who come with that as a provisional diagnosis; this is also done on other patients with this as a suspected or confirmed diagnosis from elsewhere. Glaucomatous-looking discs and glaucoma suspects are assessed by biomicroscopy with a 90D Volk lens. Visual field analyses are performed using Humphrey's visual field analyser using full threshold 30-2. Definition of glaucoma included IOP measured in mmHg by applanation tonometer and optic disc or retinal nerve fibre layer appearance suggestive of glaucomatous damage associated with diffuse or focal narrowing of the disc rim. The disc/rim asymmetric appearance between pairs of eyes are considered when the cup-to-disc ratio difference was > 0.3. Visual fields suggesting possible early glaucomatous damage were also considered. This standard of care is the routine at UTH and records were examined to ascertain if this standard was adhered to for us to label a record as truly with Glaucoma. Based on these inclusion and exclusion criteria, only 60,056 were included in the study.

Analysis

Extracted data was entered in Microsoft Excel (state version) and transferred using Stat Transfer (version 12) to Intercooled Stata version 11.0 (College Station, Texas, USA) for analysis. Prevalence was standardised for age using the national census (2010) in order to control for changes in the age structure between years. Multiple logistic regression analyses were used to assess and estimate the sex, age and gender on POAG. The distribution of age as a continuous variable conformed to normality as assessed by probability plots. Interactions were looked for using the likelihood ratio test and when identified, the terms were computed to allow estimation of the statistical effect of one of the variables separately for each level of the effect-modifying variable. Model diagnostics were done using the maximum likelihood estimation (MLE) and the Hosmer-Lemeshow goodness-of-fit. The variables in the model were age, residence, education and were stratified by sex and age group. Education level was equated to the number of formal school years attained. Although analyses were done in ages 15-90 years, the term “overall” was reserved for estimates in age group 15-90 years only. Multivariate logistical regression results were adjusted for age as continuous variable.

Ethical statement

The University of Zambia Research and Biomedical Ethics Committee granted ethical clearance number 013-08-12 for the study. Further approval was obtained from Ministry of Health of Zambia through the UTH. Given the known standard of care, records with diagnosis of glaucoma were examined to ascertain if clients were managed for POAG accordingly. Where this was missing, the in-charge was informed so as to explore follow up possibilities. Record examination was handled and guaranteed using the hospital confidentiality norms and practices as outlined in the Standard Operating Procedures (SOPs) when dealing with records.

RESULTS

Participation and distribution

Of the 71,347, a total of 7,968 did not turn up for appointments due to various reasons and 3 323 records could not be found or were incomplete. Therefore, the total number of adult eye patients actually seen in the eye clinic in the study period was 60,056. In total, 17,354 adult eye clients were diagnosed with poor vision. This represents 24.3% of the total adult eye patients seen in the eye clinic during the study period. Of these, 6,045 (34.8%) patients were screened for glaucoma.

A total of 60,056 of eye patients' records, representing all the patients that were seen at the UTH eye clinic from 1st January, 2008 to 31st December, 2011, were considered for the study.

A total of 11,291 (10.2%) files could not be considered for the study because the patients either did not turn up for scheduled appointments (7.2%) or their records could not be traced or were incomplete (3.0%).

Of the 60,056 adults recruited in the study, 30,847 (49.7%) were females and 30,208 (50.3%) were males; the ages ranged from 15 to 90 years with a median age of 47 years. With regard to education, most of the patients had primary school education (41.2%), 23.2% had secondary school education, 21.8% had tertiary education

Table 1: Prevalence of POAG, diabetic retinopathy and blindness among patients with glaucoma according to age groups and gender

AGE GROUP	< 40		40 - 44		45 - 49		50 - 54		55 - 59		60 - 64		≥ 65		TOTAL
	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	MALE	FEMALE	
PATIENTS SCREENED FOR GLAUCOMA; PREVALENCE POAG	n = 1377 0.8% (0.6,0.9)	n = 1312 1.4% (1.1,1.9)	n = 1413 4.8% (3.9,4.9)	n = 1002 9.7% (9.5,9.9)	n = 1167 15.1% (14.9,15.3)	n = 1345 13.1% (12.7,13.5)	n = 1429 12.3% (11.9,12.7)	n = 1234 16.8% (16.2,17.1)	n = 1099 18.8% (18.2,19.3)	n = 1178 20.3% (19.7,20.8)	n = 1345 15.1% (14.7,15.6)	n = 1023 26.5% (25.5,27.1)	n = 1387 18.6% (18.3,18.9)	n = 1043 36.3% (35.8,36.7)	n = 17354 8.6% (77.7,10.3)
DIAGNOSED WITH GLAUCOMA	11	19	69	97	176	176	177	207	207	239	203	271	258		2489
NO GLAUCOMA	1358	1301	1316	933	991	1169	1222	1057	860	971	1087	810	1116	664	14855
GLAUCOMA ASSOCIATED WITH DIABETIC RETINOPATHY	0	0	0	0	9	12	15	20	23	22	21	28	26	37	213
GLAUCOMA ASSOCIATED WITH BLINDNESS	0	1	1	2	1	2	19	20	25	26	35	35	52	73	292

Notes: 1. Sample sizes was 60,056 (30,847 females and 30,208 males) and 13.3% had no formal education at all.

A total of 2,499 patients were diagnosed with POAG. This represented 4.2% of 60,056 eye patients. When considered for causation of poor vision the patients with POAG represented 8.6% of the patients diagnosed with poor vision as compared to 14,855 (91.4%) who had poor vision due to other causes (Table 1).

The number of glaucoma cases by age and gender is summarised in Figure 1. The number of cases increased with age and women appeared to be more affected than men.

Figure 1: Number of glaucoma cases (n=2,499) by age and gender seen at UTH, Zambia from 2008 to 2011

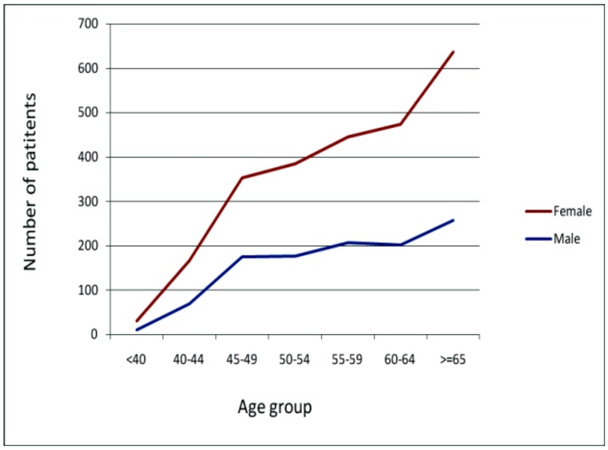

Table 2: Determinants of glaucoma at University Teaching Hospital's eye clinic in Lusaka, Zambia (2008 to 2011)

Factor	Description	Proportion (%)	Odds Ratio (95% CI)
Sex	Male	44.2	1
	Female	55.8	1.36 (1.02, 1.83)
Age	<40 years	1.3	1
	40 – 44	6.7	0.78(0.57, 1.06)
	45 – 49	14.1	0.98 (0.78, 1.22)
	50 – 54	15.4	0.97 (0.79, 1.20)
	55 – 59	17.9	0.81 (0.67, 0.99)
	60 – 64	19.0	1.47 (1.24, 1.74)
	≥65	25.6	1.20 (1.01, 1.44)
Education	Primary	55.4	1
	Secondary	34.4	0.76 (0.64, 0.91)
	Tertiary	10.2	0.55 (0.37, 0.72)
Diabetic retinopathy	No glaucoma	90.7	1
	Glaucoma	9.3	1.23 (0.93, 1.64)
Blindness	No glaucoma	87.3	1
	Blindness	12.7	1.74 (1.21, 2.45)

Of the participants who were diagnosed with glaucoma, 292 (12.7%) were blind due to this condition. This was found to be associated with a high co-morbidity with diabetic retinopathy

DISCUSSION

This study has revealed a high burden of POAG observed largely in lower educated older males aged 40 years and above in the studied records. This burden seem to have a non-differential distribution pattern by all other social demographic factors except for age and education, suggesting an increasing risk as populations get older especially after 40 years. Surprisingly there was a marked and significantly higher burden in disease in females compared to their male and this seem not to have been influenced by unequal distribution of health seeking behaviour in that proportion of males and females seen at the eye clinic was almost equal (50.3% vs. 49.7). This is similar to observations reported elsewhere even where the health seeking behaviour was differentially distributed by gender with females tending to seek health care much more than males [8,9]. The reasons for this were unclear and were beyond the scope of this study.

It is possible that differential disease patterns among non-participants in the general population could have biased our estimates, but the magnitude and direction of this effect can only to some extent be assessed [11]. The non-participation due to missing or incomplete records among the clients attending eye care services at this hospital were significantly high (34%).

We further note that this does not capture clients who either sought health care services elsewhere or indeed did not seek care at all. A counter argument is that eye care problems are so critical that when they do occur, one tends to seek care earlier for fear of being blind. If this argument is upheld, we argue therefore that if non-participation bias due to delayed or deferred health seeking behavior was present, its effect was very minimal in that this could only represent a small proportion of non-participants. Not withstanding the presence of all such selection biases due to non-participation, we are convinced that they are unlikely to be an important factor explaining the high prevalence of POAG in the studied records. Further the consistent observation that as the age increases, the odds of ailment increased has also been documented elsewhere, suggesting biological consistence and plausibility[8,9,11]. We are thus persuaded to believe these findings especially in the absence of any other study examining burden on POAG in this population. For that reason we also think that although external validity is a critical challenge when data from such selected communities are extrapolated to the whole population, yet in such conditions such as PAOG where diagnosis is often at a tertiary health center, one could be persuaded to extrapolate such findings to the general population especially if demographic factors are controlled for.

We thus find it possible to extrapolate these findings particularly given the high number of records reviewed in this study which suggests a possible high power to estimate, not withstanding the compromise it may potentially have on accuracy. The study showed prevalence of POAG at 4.2% was high at the UTH in Lusaka, Zambia. The prevalence was slightly lower than what was reported in the USA in the Baltimore and the Barbados eye surveys as well as the study in Accra, Ghana by Ntim-Amponsah et al.[5,7,9]

This could be attributed to the fact that the study on which this article is based was hospital population based and was therefore limited to a hospital population while a community-based population study can potentially capture more cases.

Comparatively higher prevalence rates of POAG have been documented in black populations in the West Indies, particularly St Lucia: 8.8%,[16] Barbados: 7.1%,[9] and also in Baltimore, USA: 4.74%.[7] The Barbados study also found a prevalence of 0.8% in white populations, although the population had a relatively small white sample size of 133 while our study did not have any white population. Indeed, it has been speculated that although the population of Barbados was derived from West Africa, there may be nutritional, environmental or genetic influences in Barbados that may be different in Africa and in particular Southern Africa.[9] However, the findings of this study compare well with the findings of Rotchford et al. in South Africa and Rudnicka et al. in the United Kingdom, who found that the overall prevalence of POAG was 2.7% and 2.4% respectively.[17,18]

All the 2,489 cases involved in the research reported in this article were diagnosed with POAG, with 49 (2.0%) of them having neovascular glaucoma due to proliferative diabetic retinopathy. In all, 63% were newly diagnosed, while the rest were known POAG patients. This is worrying as most glaucoma diagnosis was made during an eye examination for other eye complaints, hence the need for screening programmes. A total of 292 (12.7%) had vision of 3/60 or worse in the better eye and were considered to be blind.

This explains further the need for the glaucoma screening programmes. Most patients (95.4%) were on treatment with timolol eye drops and a few (4.6%) with xalatan eye drops due to few available options of anti-glaucoma drugs in government health facilities were young patients aged below 40 years implying that POAG significantly ($p<0.001$) occurs in this age group.

About 51.0% of the POAG patients had had surgery performed on them. The high rate of surgery could be due to lack and cost of anti-glaucoma drugs prompting the option of surgery as the first line of treatment in many cases. The 8.6% of patients with poor vision who were diagnosed with POAG represent a significant proportion which shows the high contribution of glaucoma to poor vision. This could reaffirm glaucoma as a cause of poor vision and blindness in the country. Also, many glaucoma patients present very late as the disease is symptomless in the early stages [5, 18]. Furthermore, it was suggested in the Barbados study that the prevalence of POAG could be directly influenced by genes, especially in those with an African ancestry [7]. This prevalence of glaucoma observed in the records of these clients seem to be significantly associated with educational attainment and with increasing age.

Education seemed to have a protective effect against the disease in that patients who were less educated were more likely to develop POAG as compared to their educated counterparts (Table 2). The reasons for this where beyond the scope of this article. However there could be two possible and plausible explanations for this.

Firstly, educated people are more likely to have a higher and better lifestyle assuming they have higher earnings and could be better informed about eye diseases and health in general. This might mean such educated POAG patients would also afford and seek treatment from private practitioners outside UTH and may not be fully captured in these records.

Secondly and on the other hand, It may also follow that upon being diagnosed with glaucoma, they are referred to the UTH eye clinic for further specialised management and follow up meaning they are attended early and could avoid complications or even depending upon mitigating factors for the glaucoma, they could recover. In fact they may even be reporting much earlier even at UTH thereby avoiding worsening the situation or increasing the chances of recovery. We are not aware of any programs targeting prevention of glaucoma but blindness. It may therefore be that the preventive programs on blindness have had an effect on general health seeking patterns but differentially by educational attainment with higher educated groups responding positively. If this is the case we further hypothesise that such preventive messages and activities that have been reported to have had a positive impact in reversing HIV risk patterns, beginning with higher social groups in this population, diffusing to lower social groups as proposed in the Diffusion of Innovation theory, may in similar manner do so for eye challenges like glaucoma, with higher educated groups as catalysts of positive health seeking behavior. [19,20,21]

Whilst describing the changing dynamics regarding HIV infection patterns in Zambia, Michelo, et al argues that "lifestyles, cultural practices and communication patterns may significantly differ by educational attainment; However, whenever change happens, it does most probably begin with the higher educated groups" [22]. Therefore the lower risk levels of glaucoma seen among higher educated groups may be a stage of progression. On the other hand we are aware that there is no other study that has made this observation on the association of education and prevalence of POAG, thereby calling for additional observational studies on this factor.

Finding an association of glaucoma with increasing age was not totally surprising as this has well been documented in literature [9, 12, 13]. What was surprising was the prevalence of glaucoma in the younger age group at 1.3%. This is against what is documented in literature where it has been categorically stated that any form of glaucoma is only possible after the age of 40 years old. This study has actually demonstrated that this is actually not true. Whereas Figure 1 and Table 1 show an increase of POAG with age as compared to the determinant analysis, it seems that there is a decrease in ages 40-44 years and 45-49 years relative to less than 40 years. This could be due to the small number of those seen with glaucoma below the age of 40 years. The question would therefore be that could it be that glaucoma could be missed out in the younger population because of the myth that it does not occur below the age 40. There was a statistically significant difference in gender prevalence of POAG from ages 40 years upward (CI; 0.67, 0.99, p=0.004). The standardised age-specific prevalence was 1.3% for ages below 40 years and 18.7% for ages 40 years and above.

This age group contributed 98.4% (2,549) of the total eligible sample population and only 115 were found ineligible. Prevalence rose significantly after the age of 65 years and above, giving a high average level of 16.8% (95% CI 12.11%, 19.55%) in this age group that formed only 3.7% (637) of the eligible sample population. This could be attributed to high number of Zambian people reaching advanced age due to better living.

The above finding has been reported in studies such as the Barbados and Baltimore eye surveys [5,7,9]. POAG has also been reported to be common among patients aged 40 years and more [8,9,12,13]. In this study it was found to increase rapidly from the age of 45 years, especially in women (Figure 1). Although the prevalence was low in those aged below 40 years, finding that 2.4% of patients diagnosed with glaucoma were below the age of 40 years, could suggest that early but active screening even fifteen years earlier could yield positive preventive outcomes.

This therefore means that health promotion messages in higher educated college students just in their twenties could help them and the communities they will serve to undergo screening regularly in the same way young women go for cervical cancer screening. In fact the screening of both cervical cancer and prostatic enlargement could be re-packaged and integrated to include glaucoma and lifestyle disorder screening - a comprehensive and integrated approach to preventive screening.

Therefore, it is important that all adults be screened for glaucoma regardless of age in order to have the young ones diagnosed early, so as to enable early commencement of treatment thus potentially preventing blindness as the disease progression will be controlled. This will also entail fewer years of debilitation as blindness will be significantly delayed.

Lastly but not the least, we also observed that there was an association between presence of POAG among clients with history of or reported diabetes. The study also demonstrated a weak association between the prevalence of glaucoma and its increase in age with diabetic retinopathy (DR), $p=0.04$ whose prevalence also increased with age. This could be possible because DR may lead to increased IOP and promote apoptosis of neuronal tissue due to increased vascular compromise that occurs in DR. The significant of this finding is that screening for DR and glaucoma can be performed at the together and under one programme.

CONCLUSIONS

We conclude that the prevalence of PAOG in the studied population is high and this may even be an under-estimate because this study only reports results from one hospital site. However and further finding differential burden patterns by education, age and lifestyle groups may be opening opportunities to re-adjust and re-align primary eye care programs so that they are integrated with other programs.

More specifically this may be calling a policy consideration to commence glaucoma screening in an integrated manner with other primary care programs like cervical cancer. In addition finding that the burden was most pronounced in the groups with limited education, may further suggest re-packaging such screening programs to target these most at risk groups. If this is done, complimented with the addition of appropriate and continued health awareness messages but to younger groups in school as well as politicians, this has the potential to diffuse to the most at risk communities too. Such health promotion messages should include informing the communities the consequences of delayed diagnosis and treatment. In this study finding that 11.7% of patients diagnosed with POAG became blind as a result reminds all of us that early diagnosis and treatment for glaucoma in all adults may significantly delay blindness, and what an outcome.

Furthermore, and using the WHO "Vision 2020: right to sight" programme as a framework for policy and programming, the need for community sensitisation regarding the disease and its dangers is not just mandatory, but we also conclude that outreach and ad hoc screening and eye check-ups for all those aged 15 years and above is recommended so that POAG can be diagnosed early. The structured screening and surveillance program so instituted will also help to examine additional factors that could be associated with glaucoma especially to examine if POAG can also be explained by heritability.

This study does not only call for additional observational studies to further the understanding of factors at play, but on the basis of available knowledge, it also calls for immediate policy actions and uptake of generated information into action frameworks so as to strengthen primary eye care services in Zambia.

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