Comorbidities in Primary Open Angle Glaucoma Patients Attending a Tertiary Hospital in Niger Delta, Nigeria-A 5year Review

Onua, A.A.¹ and Pepple, G.F.^{2*}

¹ Department of Ophthalmology, University of Port Harcourt, Nigeria ² Department of Surgery, Rivers State University, Nigeria *Corresponding Author: Pepple, G.F. Department of Surgery, Rivers State University, Nigeria

Abstract

Background: Glaucoma is a leading cause of irreversible blindness worldwide and primary open-angle glaucoma (POAG) is the most prevalent clinical type of glaucoma in sub-Sahara Africa. Existing comorbid status in patients influence the course and management of glaucoma. Recognizing the role and influence of the comorbidities in POAG in our environment could be important in determining the course of and effective management of POAG. Methodology: This was a 5-year retrospective study of the demographic, epidemiological, and comorbid clinical status of 500 POAG patients attending the Glaucoma unit of the Ophthalmology department of the University of Port Harcourt Teaching Hospital. Findings from clinical records and basic ophthalmic examinations were used to obtain data from the respondents. Records of basic ocular examinations (which included Visual acuity-both distant and near, evaluation of the evelids, the globe, cornea, pupil, the lens and fundoscopy) were extracted. Data were analyzed using version 25 software (SPSS) Inc; Chicago, IL, USA for statistical analysis. Relevant data were presented in tables and charts. Statistical significance was set at $p \le 0.05$. **Results:** Males were 306 (61.2%) while females constituted 38.8% (n=194). This gives a male to female ratio of 1.5:1. The age group 45-54 years had the highest population of those examined (41.6%) while participants less than 45 years (3.0%) constituted the least. Major comorbidities with adult-onset POAG were cataract, systemic hypertension and diabetes mellitus. Seventy-two percent (n=360) of the study participants had more than one comorbid state. **Conclusion:** Diabetes mellitus, systemic hypertension and cataract are major comorbidities associated with primary open angle glaucoma and cognizance of their probable co-existence with POAG would be necessary for multi-disciplinary approach in the management of patients.

Keywords: Glaucoma, Comorbidities, Port Harcourt.

Date of Submission: 11-03-2023

Date of Acceptance: 25-03-2023

I. Introduction

Glaucoma ranks the second leading cause of blindness in the world after cataract, and the most common cause of irreversible blindness [1]. Visual impairment and blindness constitute major public health and social problems worldwide with serious economic implications, often leading to social dependence, poor quality of life, lack of access to education; loss of productivity and income, lower social participation and increased mortality [2-6]. In developing countries, like Nigeria, loss of vision is worsened by the poor quality of rehabilitative and supportive services due to a dearth of both manpower and technology. The World Health Organization (WHO) estimates that 2.2 billion people in the world are visually impaired; and 90% of the world's blind population live in developing countries [6,7]. The prevalence of glaucoma is estimated at 1.2% of the population above 40 years of age in Nigeria [8].

The burden of glaucoma in the world is high and also increasing with the aging population [9]. The Africa region has the highest incidence and prevalence of glaucoma [10] and in Nigeria is responsible for 15-20% of blindness in Nigeria [8].

Primary open-angle glaucoma (POAG) is the most common type, accounting for over 51% of all cases of glaucoma [10]. It is the most prevalent variant of glaucoma in Nigeria; and the Niger Delta Region POAG has the highest number of glaucoma patients – being responsible for 20.8% of bilateral blindness [11].

Most patients with glaucoma are old and often have other non-ocular comorbidities for which they frequently visit other care givers. It is therefore vital for the practicing ophthalmologist to be acquainted with the comorbidities of glaucoma patients. In fact, POAG, with increased intraocular pressure has been associated with hypertension [12–16], and diabetes [17–19]. Yet, lower systolic blood pressure, and lower perfusion pressure, are risk factors for POAG [20]. In a study from Taiwan, patients with POAG were compared with matched subjects

regarding comorbidity, with the most important excess risks found for hypertension, hyperlipidemia, systemic lupus erythematosus, diabetes, hypothyroidism, as well as fluid and electrolyte disorders [21].

The aim of the present study is to study the coexisting non-ocular diseases with open-angle glaucoma among patients attending the glaucoma clinic in our setting (UPTH) from 2017 to 2021.

Ethical Statement:

II. Materials and Methods:

Ethical approval to conduct this study was obtained from the Ethics Committee of University of Port Harcourt. This study adhered to the tenets of the Declaration of Helsinki on study involving human subjects. All information obtained from the participants of this study was treated with utmost confidentiality. No personal identification (names, clinic number) was stored electronically.

Study Area:

This study was carried out in the Glaucoma Unit of University of Port Harcourt Teaching Hospital, Port Harcourt, Rivers State, Nigeria.

Study Design:

This was a retrospective study of 500 POAG patients attending the Glaucoma clinic of the University of Port Harcourt Teaching Hospital from 2018 to 2022.

Eligibility Criteria:

Inclusion Criteria

Patients diagnosed with primary open angle glaucoma who are indigenes of Rivers State.

Exclusion Criteria: Subjects with history of eye surgery prior to diagnosis of glaucoma, cases of secondary glaucoma, angle-closure glaucoma and history of ocular trauma.

Sampling Method:

Findings from clinical records and basic ophthalmic examinations were used to obtain data from the respondents. Records of basic ocular examinations (which included Visual acuity-both distant and near, evaluation of the eyelids, the globe, cornea, pupil, the lens and fundoscopy) were extracted.

Sample and Data Analysis

The data obtained were entered into Microsoft Excel sheet, cleansed and later exported to IBM Statistical Package for Social Sciences (SPSS) version 25 software (SPSS) Inc; Chicago, IL, USA for statistical analysis. Relevant data were presented in tables and charts. Statistical significance was performed using Chi square and statistical significance was set at $p \le 0.05$.

III. Results

Age and Sex Distribution of the study population

Out of 500 participants examined, males were 306 (61.2%) while females constituted 38.8% (n=194). This gives a male to female ratio of 1.5:1. The age group 45-54 years had the highest population of those examined (41.6%) while participants less than 45 years (3.0%) constituted the least. Age range of the study population was 40 to 92 years [Table 1].

Age Group (yrs)	Male	(%)	Female	e (%)	Total	(%)
< 45	12	(2.4)	8	(1.6)	20	(3.0)
45-54	136	(27.2)	72	(14.4)	208	(41.6)
55-64	70	(14.0)	50	(10.0)	120	(24.0)
65-74	54	(10.8)	30	(6.0)	84	(16.8)
75 -84	22	(4.4)	24	(4.8)	46	(9.2)
85 and above	12	(2.4)	10	(1.5)	22	(3.9)
Total	306	(61.2)	194	(38.8)	500	(100)

Mean age=59.4±11.2 years; M:F =1.5:1; Age range 40 to 92 years; Modal class 45-54 years

Distribution of the study Population According to Occupation

Majority of the study participants were retired civil servants (n=136; 21.8%). Unemployed subjects were 12 (2.4%) and accounted for the least among the study population. There was a statistically significant difference in the distribution of the participants of this study among the various occupational status (p=0.000) [Figure 1].

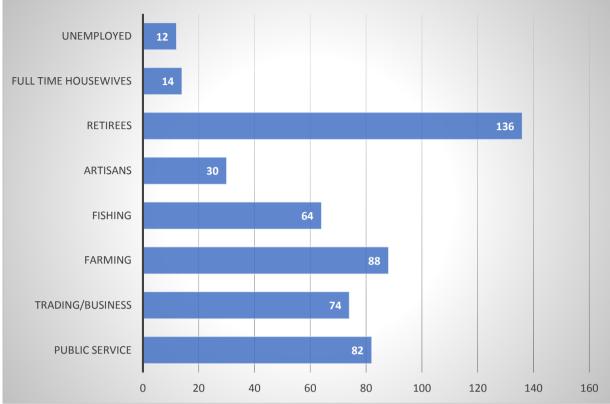


Figure 1: Distribution of the study Population According to Occupation

Major Comorbidities with adult-onset POAG in the Study Population

The major comorbidities found with adult-onset POAG in the study population were cataract; observed in 76.8% (n=302) persons, systemic hypertension in 55.5% (n=218) and diabetes mellitus in 39.7% (n=156). Some of the study participants had more than one comorbid state [Figures 2]

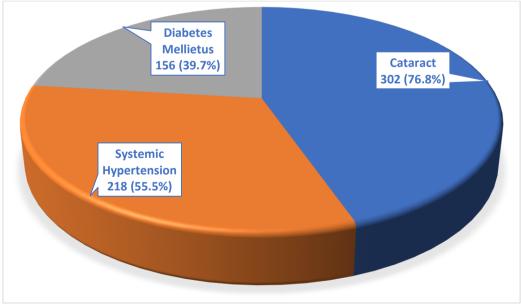


Figure 2: Comorbidities found in the study population

IV. Discussion

The major comorbidities with POAG found in this study were systemic hypertension, diabetes mellitus and cataract. This is in agreement with many authors on this subject [22, 23]. It has been postulated that there is a link between metabolic diseases such as hypertension and diabetes mellitus and primary open angle glaucoma [12–15, 17-19]. In the Beaver Dam Eye Study, Klein et al., noted that the prevalence of POAG was higher in diabetic individuals compared to none diabetics (4.2% versus 2.0%; P = 0.004); and in the Baltimore Eye Survey, persons whose POAG had been diagnosed before they enrolled in the study showed a positive association with diabetes (odds ratio, 1.7, 95% confidence interval, 1.03, 2.86). In the Blue Mountains Eye Study participants with glaucoma were more likely to have systemic hypertension than participants without glaucoma in 65.7% of cases (95% CI: 56.6–74.8) versus 45.4% (95% CI: 43.8–47.1) [24-26].

Cataract and POAG are common co-morbidities, as the conditions are prevalent in aging populations. However, a definitive correlation between these co-morbidities has not been established. The Barbados Eye Study found that cataracts were more common among POAG cases than controls [27].

Many theories have been put forward to explain the correlation between diabetes mellitus and POAG. The first theory suggests that sustained hyperglycemia and lipid dysregulation might increase the risk of damage from neuronal stress [28]. A second theory postulates that there is a compromise in the hemodynamics of diabetic eyes because of retinal vascular endothelial cell dysfunction [29]. Another explanation is that, optic neuropathy results from remodeling of the connective tissue of the optic nerve head and dysregulation at the trabecular meshwork and the lamina cribrosa, with increased IOP and greater mechanical stress on the optic nerve head. Diabetes can exacerbate connective tissue remodeling and accentuate these biomechanical changes [30]. Vascular endothelial cell dysfunction and loss of retinal pericytes have been described in diabetic retinopathy and are associated with hypoxia [31]. Furthermore, metabolic disturbances of the carbohydrate metabolism could play a role in glaucomatous damage and pathogenesis [32].

Leske and colleagues postulated that diabetes mellitus and systemic hypertension coexist with POAG among black populations [27]. Our current study, the Barbados Eye Study and some other studies in Nigeria corroborated this position [33,34].

In this work, it was observed that the mean age of the study participants was 59.4 ± 11.2 years and modal age class was 45-54 years. This finding is in tandem with many investigators. Working independently and in different periods of time, Murdoch et al., in a study among 1563 people of Hausa/Fulani ethnic extraction of Nigeria; reported that POAG was more prevalent in individuals aged 45 years and older [35] while Adeoye in South Western region of Nigeria observed that POAG was more prevalent in individuals aged 50 years and older; and that POAG accounted for 11.1% of blindness in Nigeria [36]. The commonest form of POAG in our environment is the adult-onset type which occurs from the age of 40 years [37-39].

Corroborating with the findings of this work are the works of Leske et al., in the Barbados Eye Study which observed that adult-onset POAG was predominately in populations 45 years and older and that POAG significantly increases with age in all populations [25].

In this study, we noticed that majority of the study participants (21.8%) were retired civil servants. The distribution of the proportion of retired civil servants in the study population is in tandem with the retirement age from civil service in Nigeria at 65 years [40].

V. Conclusion

Diabetes mellitus, systemic hypertension and cataract are major comorbidities associated with primary open angle glaucoma and cognizance of this would be necessary for the multi-disciplinary approach in the management of POAG patients.

Funding-Nil

Declarations of conflict of interest: The authors of this manuscript have no conflict of interest to disclose. **Ethical approval**: All procedures performed in studies involving human participants were in accordance with the ethical standards of the University of Port Harcourt Research and Ethics committee and with the 1964 Declaration of Helsinki and its later amendments.

References

- [1]. GBD (2019) Blindness and Vision Impairment Collaborators (2017) Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 390(10100):1211–1259. https://doi.org/10.1016/S0140-6736(17)32154-2. Assessed 13th July 2021.
- [2]. Jin S, Trope GE, Buys YM, Badley EM, Thavorn K, Yan P, Nithianandan H, Jin YP (2019) Reduced social participation among seniors with self-reported visual impairment and glaucoma. *PLoS ONE* 14(7):e0218540. https://doi.org/10. 1371/journal.pone.0218540
- [3]. Ramrattan RS, Wolfs RC, Panda-Jonas S, Jonas JB, Bakker D, Pols HA, Hofman A, de Jong PT (2001) Prevalence and causes of visual field loss in the elderly and associations with impairment in daily functioning: the Rotterdam study. *Arch Ophthalmol* 119(12):1788–1794. https://doi.org/10.1001/archopht.119.12.1788

- [4]. Taipale J, Mikhailova A, Ojamo M, Nattinen J, Vaatainen S, Gissler M, Koskinen S, Rissanen H, Sainio P, Uusitalo H (2019) Low vision status and declining vision decrease health-related quality of life: results from a nationwide 11-year follow-up study. *Qual Life Res* 28(12):3225–3236. https://doi.org/10.1007/s11136-019-02260-3
- [5]. McCarty CA, Nanjan MB, Taylor HR (2001) Vision impairment predicts 5-year mortality. Br J Ophthalmol 85(3):322–326. https://doi.org/10.1136/bjo.85.3.322
- [6]. World Health Organization, (2020). Magnitude and cause of visual impairment. WHO Fact Sheet No. 282. Geneva: WHO. Available from: <<u>http://www.who.int/mediacentre/factsheets/fs282/en/</u>> [accessed 2/3/ 2021].
- [7]. Kyari, F., Gudlavalleti, M.V., Sivsubramaniam, S., Gilbert, C.E., Abdull, M.M., Entekume, G., Foster, A. & Nigeria National Blindness and Visual Impairment Study Group (2009). Prevalence of blindness and visual impairment in Nigeria: The National Blindness and Visual Impairment Study. Invest Ophthalmol Vis Sci., 50(5): 2033-2039.
- [8]. Abdull, M.M., Sivasubramaniam, S., Murthy, G.V.S., Gilbert, C., Abubakar, T., & Ezelum, C.H. (2009). Causes of blindness and visual impairment in Nigeria: the Nigeria national blindness and visual impairment survey. *Invest Ophthalmol Vis Sci.* 50 (9):4114–4120.
- [9]. Ghiso JA, Doudevski I, Ritch R, Rostagno AA (2013) Alzheimer's disease and glaucoma: mechanistic similarities and differences. J Glaucoma 22(Suppl 5): S36-38. https://doi.org/10.1097/IJG.0b013e3182934af6
- [10]. Quigley, H.A. & Broman, A.T. (2006). The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol; 90:262–267.
- [11]. Pedro-Egbe, C.N., Chukwuka, I.O., Babatunde, S. & Umeh, R.E. (2006). Blindness and Visual Impairment in the Niger-Delta: A study of Ahoada-East Local Government Area of Rivers State, Nigeria. *PH Med. J*; 1(1), 56-61.
- [12]. Zhao D, Cho J, Kim MH, Guallar E (2014) The association of blood pressure and primary open-angle glaucoma: a meta-analysis. *Am J Ophthalmol* 158(3):615–627
- [13]. Caprioli J, Coleman AL (2010) Blood pressure, perfusion pressure, and glaucoma. Am J Ophthalmol 149(5):704–712. https://doi.org/10.1016/j.ajo.2010.01.018
- [14]. Costa VP, Arcieri ES, Harris A (2009) Blood pressure and glaucoma. Br J Ophthalmol 93(10):1276–1282. https://doi. org/10.1136/bjo.2008.149047
- [15]. He Z, Vingrys AJ, Armitage JA, Bui BV (2011) The role of blood pressure in glaucoma. Clin Exp Optom 94(2):133–149. https://doi.org/10.1111/j.1444-0938.2010.00564.x
- [16]. Werne A, Harris A, Moore D, BenZion I, Siesky B (2008) The circadian variations in systemic blood pressure, ocular perfusion pressure, and ocular blood flow: risk factors for glaucoma? Surv Ophthalmol 53(6):559–567. https://doi. org/10.1016/j.survophthal.2008.08.021
- [17]. Costa L, Cunha JP, Amado D, Pinto LA, Ferreira J (2015) Diabetes Mellitus as a Risk Factor in Glaucoma's Physiopathology and Surgical Survival Time: A Literature Review. J Curr Glaucoma Pract 9(3):81–85. https://doi.org/10.5005/jp-journals-10008-1190
- [18]. Gerber AL, Harris A, Siesky B, Lee E, Schaab TJ, Huck A, Amireskandari A (2015) Vascular Dysfunction in Diabetes and Glaucoma: A Complex Relationship Reviewed. J Glaucoma 24(6):474–479. https://doi.org/10.1097/IJG.00000000000137
- Wong VH, Bui BV, Vingrys AJ (2011) Clinical and experimental links between diabetes and glaucoma. Clin Exp Optom 94(1):4– 23. https://doi.org/10.1111/j.1444-0938.2010.00546.x
- [20]. Leske MC, Wu SY, Hennis A, Honkanen R, Nemesure B, Group BES (2008) Risk factors for incident open-angle glaucoma: the Barbados Eye Studies. Ophthalmology 115 (1): 85-93https://doi.org/10.1016/j.ophtha.2007.03.017
- [21]. Lin HC, Chien CW, Hu CC, Ho JD (2010) Comparison of comorbid conditions between open-angle glaucoma patients and a control cohort: a case-control study. Ophthalmology 117(11):2088–2095. <u>https://doi.org/10.1016/j.ophtha.2010.03.003</u>
- [22]. Wandell, P., Carlsson, A.C. & Ljunggren, G. (2022). Systemic diseases and their association with open-angle glaucoma in the population of Stockholm. Int Ophthalmol 42:1481–1489 <u>https://doi.org/10.1007/s10792-021-02137-w</u>
- [23]. Poh S, Mohamed Abdul RB, Lamoureux EL, Wong TY, Sabanayagam C (2016) Metabolic syndrome and eye diseases. Diabetes Res Clin Pract 113:86–100. https://doi.org/ 10.1016/j.diabres.2016.01.016
- [24]. Klein, B.E., Klein, R. & Lee, K.E. (2004). Heritability of risk factors for primary open-angle glaucoma: The Beaver Dam Eye Study. Invest Ophthalmol Vis Sci; 45: 59–62.
- [25]. Leske, M.C., Heijl, A., Hussein, M., Bengtsson, B., Hyman, L. & Komaroff, E. (2003). Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial. Arch Ophthalmol; 121:48-56.
- [26]. Lee, A.J., Wang, J.J., Kifley, A. & Mitchell, P. (2006). Open-angle glaucoma and cardiovascular mortality: the Blue Mountains Eye Study. *Ophthalmology*; 113:1069-1076.
- [27]. Leske, M.C., Wu, S.Y., Hennis, A., Honkanen, R., Nemesure, B. & Barbados Eye Studies Study Group. (2008). Risk factors for incident open-angle glaucoma: The Barbados Eye Studies. Ophthalmology, 115:85–93. [PubMed: 17629563].
- [28]. Kong, G.Y.X., Van Bergen, N.J., Trounce, I.A. & Crowston, J.G. (2009). Mitochondrial dysfunction and glaucoma. J. Glaucoma; 18: 93–100.
- [29]. Clermont, A.C. & Bursell, S. E. (2007). Retinal blood flow in diabetes. Microcirculation; 14: 49–61.
- [30]. Roberts, M.D., Grau, V., Grimm, J., Reynaud, J., Bellezza, A.J. Burgoyne, C.F. & Downs, J.C. (2009). Remodeling of the connective tissue microarchitecture of the lamina cribrosa in early experimental glaucoma. *Invest. Ophthalmol. Vis. Sci.* 2009; 50: 681–690.
- [31]. Song, B.J., Aiello, L.P. & Pasquale, L.R. (2016). Presence and Risk Factors for Glaucoma in Patients with Diabetes. Curr. Diab. Rep;16: 124.
- [32]. Elisaf, M., Kitsos, G., Bairaktari, E., Kalaitzidis, R., Kalogeropoulos, C. & Psilas, K. (2001). Metabolic abnormalities in patients with primary open-angle glaucoma. Acta Ophthalmol. Scand; 79: 129–132.
- [33]. Agbeja-Baiyeroju, A.M., Bekibele, C.O., Bamgboye, E.A., Omokhodion, F. & Oluleye, T.S. (2003). The Ibadan glaucoma study. *Afr J Med Med Sci*; 32:371–376. [PubMed: 15259920].
- [34]. Omoti, A.E., Enock, M.E., Okeigbernen, V.W., Akpe, B.A. & Fuh, U.C. (2009). Vascular risk factors for open angle glaucoma in african eyes. *Middle East Afr J Ophthalmol*; 16:146–150. [PubMed: 20142982].
- [35]. Allen, K.F., Gaier, E.D. & Wiggs, J.L. (2015). Genetics of primary inherited disorders of the optic nerve: clinical applications. ColdSpring Harb Perspect Med; 5: a017277.
- [36]. <u>Adekoya</u>, B.J., <u>Shah</u>, S.P., <u>Onakoya</u>, A.O. & <u>Ayanniyi</u>, A.A. (2014). Glaucoma in Southwest Nigeria: Clinical presentation, family history and perceptions. <u>International Ophthalmology</u>, 34: 1027–1036.
- [37]. Murdoch, I.E., Cousens, S.N., Babalola, O.E., Yang, Y.F., Abiose, A. and Jones, B.R. (2001). Glaucoma prevalence may not be uniformly high in all black population. Afr J Med Sci; 30 (4): 337-3379.
- [38]. Fan, B.J. & Wiggs, J.L. (2010). Glaucoma: Genes, Phenotypes, and New Directions for Therapy. J Clin Invest; 120: 3064–3072.

- Awoyesuku, E.A. & Ejimadu, C.S. (2012). Visual disability in newly diagnosed Primary Open angle Glaucoma (POAG) patients [39].
- in a tertiary hospital in Nigeria. Nigeria Journal of Medicine; 21:78-80. Federal Republic of Nigeria. Public Service Rules 2008. Abuja: Federal Civil Service Commission (Federal Government of Nigeria), August, 2009. Available from: https://www.nama.gov.ng/PublicServiceRules. pdf. [accessed on 12-11-2021]. [40].