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The Ibadan glaucoma study

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Summary

To obtain epidemiological data on the prevalence and risk factors for open angle glaucoma in hospital workers of African origin, and investigate appropriate methods of a rapid, cost-effective screening procedure for glaucoma. A cross-sectional study of workers in the University College Hospital (UCH) Ibadan, using a structured questionnaire for data collection. The variables available for data analysis include workers demographic characteristics, visual acuity, pupil status, intraocular pressure, cup-disk ratio, central visual fields, family history of glaucoma, chronic diseases such as hypertension and diabetes. The data was analysed with EPI-INFO version 6.02 for simple analysis, while the SPSS package was used for multivariate analysis. A total of two thousand, one hundred and nine (2,109) UCH workers participated in the screening exercise for glaucoma. A high majority of the workers 1794 (85.1%) were negative to the diagnosis of glaucoma, while the remaining 315 (14.9%) were suspected to have glaucoma out of which 57 (2.7%) were confirmed as definite glaucoma cases. The prevalence of glaucoma among UCH workers was 27 per 1000, 95% confidence interval = 20 per 1000, 35 per 1000. Factors associated with glaucoma were relative afferent pupillary defect, cup-disk ratio greater than 0.7, intraocular pressure, family history of glaucoma and the presence of chronic diseases such as diabetes. The left eye appears to have a higher probability of ocular problems compared with the right eye. The prevalence of glaucoma among hospital workers was 2.7%. The cup-disk ratio appears to be a better diagnostic tool for glaucoma since it gives the best positive predictive value (with a cut-off point of 0.7) than all other variables.

Keywords: *Glaucoma, intraocular pressure, cup-disk ratio, perimetry, African*

Résumé

Cette étude croisée avait pour objectif de repectorier les données épidémiologiques sur la prevalence et les facteurs a risque au glaucume a angle ouvert des yeux chez les employés au Centre Hospitalier Universitaire(CHU) d'origine africain et d'investiguer correctement les méthodes rapide et moins chère pour examiner le glaucume. les données collectées a l'aide d'un questionnaire structuré ont été analysés utilisant Epifo 6.02 et SPSS. Deux mille cent neuf(2109) employés étaient recrutés, 1994(85.1%) était négative au diagnostic du glaucume et 315 (14.9%) était suspecte parmi lesquelles 57(2.7%) était confirmés positive au glaucume. La prevalence de cette maladie au CHU était de 27/1000, 95% confidence égale a 20 par 1000, et 35 par 1000. Les facteurs associés au glaucume étaient le defect relatif de la pupille .la proportion du disque en verre plus de 0.7, la pression intraocculaire, l'histoire de la famille et la presence des maladies

chroniques comme le diabetes. La proportion du disque en verre apparait le plus meilleur instrument pour diagnostiquer le glaucume car ceci donne le plus meilleur prediction positive que les autres variables.

Introduction

Glaucoma is an optic neuropathy involving loss of neurones within the optic disc leading to cupping of the optic disc. It is associated with visual field deficit and has as risk factors, elevated intraocular pressure, age, race, positive family history, refractive error >4D and systemic diseases like hypertension and diabetes mellitus. Open angle glaucoma is a major cause of visual impairment and blindness worldwide [1-3] but it is more common in black populations [3-7]. According to WHO statistics, over 100 million people are glaucoma suspects, while over 20 million suffer from glaucoma, and over 5 million people are blind as a result of glaucoma worldwide⁴. Approximately 70% of global glaucoma is found in developing countries [8].

Previous data have also shown a younger age of blindness registration for blacks than-whites and a more advanced stage of visual impairment, suggesting an earlier age at onset and a more severe course of disease [4-7]. The available epidemiological data on risk factors are extremely limited [9-10] and so the reasons for the high susceptibility of black populations of glaucoma remain unknown [11]. However, the prevalence of open angle glaucoma (OAG) has been found to be much higher in blacks (7%) [12] (8.8%) [13] than in whites (0.43%) [14] (0.1%) [15].

This study was initiated to obtain epidemiological data on the prevalence and risk factors for open angle glaucoma in an African setting as well as investigating appropriate rapid and cost-effective screening procedure for glaucoma in the Nigerian environment.

Materials and methods

The University College Hospital, Ibadan, is the largest teaching hospital in Nigeria with a staff of 2,696 covering various cadres. All members of staff served as the study population. An invitation for attendance in the eye clinic of the hospital for the glaucoma screening was sent out to all staff through the departments in the hospital.

Data collected included age, sex, level of education, visual acuity (unaided and corrected), type of refractive error, cause of decreased vision (other than refractive error), intraocular pressures (with Goldman applanation tonometer), pupillary reactions, funduscopy for cup-disk ratio, other ocular lesions, visual field analysis and other potential risk factors for glaucoma. These included positive family history, refractive error, hypertension and diabetes, age and intraocular pressure. The visual field analysis was performed with the Damato dedicated glaucoma screener (30-point campimeter) [16].

All participants who had an intraocular pressure of 22mmHg and above, a cup-disk ratio of 0.5 and above and/or field loss from the campimeter were further subjected to full central visual field analysis with the Friedman field analyser. To

assess possible false-positive results, every participant with field loss had repeat funduscopy by the same consultant.

To be categorized as definite open angle glaucoma the participant must have visual field loss in the presence of cupping of the disc in at least one eye. All those who did not meet these criteria were classified as glaucoma suspects and are currently being followed up. The intraocular pressure (IOP) was not considered as one of the criteria for diagnosis, rather it was as a risk factor. All workers who were diagnosed as having glaucoma had gonioscopy done, to confirm the type of glaucoma.

Statistical analysis

The data was entered into a microcomputer using the statistical package EPI-INFO version 6.02. The package was also used for simple statistical analysis, while the SPSS package was used for multi-variate analysis. The data base files were adequately checked for consistency and completeness of the records to ensure the correct data have been analysed. Frequency distributions of all variables were produced and relevant cross tabulations of variables were carried out in accordance with study objectives. The significance of associations between any two categorical variables was examined using the Chi-square (χ^2) tests. One-way Analysis of variance (ANOVA) was used to compare the mean values of numerical variables between the four categories of UCH workers identified and, the students t-test was used for the comparison of two mean values. The estimate of prevalence of glaucoma and its 95% confidence intervals were obtained from those with open angle glaucoma as numerator. The validity of Intra-ocular Pressure (IOP), visual field loss, cup-disc ratio and CVF as diagnostic tools were evaluated by calculating their sensitivity and specificity. The definite diagnosis of Glaucoma serves as the Gold standard. The logistic regression approach was used to model the probability of Glaucoma and potential associated risk factors. The model identified the risk factors of glaucoma as well as their estimated risk ratios and 95% confidence intervals was also calculated. All statistical tests were two tailed and carried out at the 5% level of significance.

Results

Of the 2,696 members of staff in 61 departments of the University College Hospital, Ibadan, 2,109 participated in the screening exercise giving a 78.5% response rate. The non-responders (21.5%) were found to be evenly distributed throughout the various departments except for the high cadre doctors (Consultants) whose response rate was only 37%.

There were 1,079 males with a male to female ratio of 1.04:1. The mean age of the workers was 42.7 years (SD= 8.7) ranging from 22 - 65 years with a high proportion (65%) being 40 years and above (Fig.1). A sizeable majority (85.1%) of the

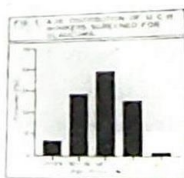


Fig. 1:

workers did not have glaucoma, 315 were glaucoma suspects, and only 57 (2.7%) were confirmed as definite glaucoma cases. This gave an estimated prevalence of glaucoma among hospital workers as 27 per 1000 with a 95% confidence interval of 20 per 1000 to 33.4 per 1000.

Demographic characteristics and glaucoma status

The highest proportion of workers (38.9%) were aged 40-49 years followed by workers in age bracket 30-39 years (28.6%). The proportion of elderly workers of age 50 years and above was 25.7% while only 6.8% of the workers were aged below 30 years. The distribution of workers' age by their glaucoma status shows that there was no statistically significant association between glaucoma and age ($P>0.05$). However, the highest proportion (3.9%) of patients with glaucoma were among those aged 50 years and above and the least 0.7% was recorded among those less than 30 years of age. A slight majority of the workers were males (51.2%) of whom about 3.2% were confirmed glaucoma cases, slightly higher than 2.1% of the females. The proportion of suspected cases of glaucoma was also higher among males but the differences were not statistically significant ($P>0.05$) Table 1.

Almost half of the workers (46.0%) had university education or equivalent including 11.5% with postgraduate education while 26.8% and 26.6% respectively. Only 12 (0.6%) of the workers had no formal education. The distribution of glaucoma cases shows that the proportion of workers with definite glaucoma increases with increase in educational status. The majority of workers with glaucoma were those with post-graduate education (3.3%) but the association between education and glaucoma status was not statistically significant ($P>0.05$).

The majority of the workers were Christians (79.7%) and 19.3% were Moslems. The distribution of glaucoma cases by workers' religion shows that while 1.7% of the Christian were confirmed to have glaucoma, a slightly higher proportion of Moslem (2.9%) had definite glaucoma. However, the distribution was also not statistically significant ($P>0.05$).

Ocular characteristics of the workers

Visual Acuity

The average visual acuity for the workers right eye and left eyes seem similar. However workers with definite glaucoma appeared to have lower visual acuity as well as corrected visual acuity. But the difference in visual acuity between the categories of glaucoma status was only statistically significant in the left eye ($P<0.05$).

Refractive errors

Refractive errors among the workers were presbyopia (17.1%), myopia (6.1%), hypermetropia (1.8%), astigmatism (0.6%) and the remaining 74.3% had no refractive error. The workers with presbyopia had the highest proportion of cases with glaucoma (0.7%) followed by myopia (0.3%). None of the workers with hypermetropia had confirmed glaucoma while only 10 (0.5%) were suspected to have glaucoma. The distribution of glaucoma was statistically significantly different among the categories of refractive errors identified during this screening exercise ($P<0.05$) Table 2.

Table 1: Demographic characteristics of UCH workers by glaucoma status

Demographic characteristics	Glaucoma status				Definite		All subjects		X ²	P.Value
	Normal		Suspected		Freq.	%	Freq.	%		
	Freq.	%	Freq.	%						
Age (yrs)										
<30	122	84.7	21	14.6	1	0.7	144	6.8	7.92	0.24
30-39	515	85.3	72	11.9	17	2.8	604	28.6		
40-49	695	84.8	107	13.0	18	2.2	820	38.9		
50-	462	85.4	58	10.7	21	3.9	541	25.7		
Total	1794	85.1	258	12.2	57	2.7	2109	100.0		
Sex									2.71	0.25
Male	909	84.2	135	12.5	35	3.2	107	51.2		
Female	885	85.9	123	11.9	22	2.1	103	48.8		
Level of Education									11.00	0.20
None	9	75.0	2	25.0	0	0.0	12	0.6		
Pry.	483	85.5	69	12.2	13	2.3	565	26.8		
Secondary	491	87.4	57	10.1	14	2.5	562	26.6		
University or equivalent	599	82.4	106	14.6	22	3.0	727	34.5		
Postgraduate	212	87.2	23	9.5	8	3.3	243	11.5		
Religion									0.54	0.76
Christian	1432	85.5	199	11.8	45	2.7	1680	79.7		
Moslem	342	84.0	53	13.0	12	2.9	407	19.3		
No Response	16	72.7	6	27.3	0	0.0	22	1.0		

Table 2: Refractive errors in UCH workers by their glaucoma status

Ocular Characteristic	Normal Glaucoma		Glaucoma States Suspected		Definite		All subjects		X ²	P value
	Freq.	%	Freq.	%	Freq.	%	Freq.	%		
Type of refractive error										
Myopia	109	5.1	14	0.7	6	0.3	129	6.1	53.65	0.0001
Hypermetopia	29	1.4	10	0.5	9	0.0	39	1.8		
Presbyopia	317	15.0	29	1.4	15	0.7	361	17.1		
Astigmatism	8	0.4	1	0.05	1	0.1	12	0.6		
No refractive error	1331	63.1	204	9.6	31	1.6	1508	74.3		

Intraocular pressure

The mean intraocular pressure for the right eye of normal individuals was 13.1mmHg, the left being 13.12mmHg while that of glaucoma suspects was 15.26mmHg (right eye) and 15.16mmHg (left eye). Workers who were found to have glaucoma had a mean IOP of 18.11mmHg (right eye) and 18.83mmHg (left eye).

Therefore, the intra-ocular pressure was higher among the workers with definite glaucoma compared to those without glaucoma (18.11mmHg vs. 13.11mmHg in the right eye and 18.8mmHg vs. 13.1mmHg in the left eye respectively, $P < 0.01$).

Pupils

The right and left pupils were found to be normal in 98.7% and 98.1% of the study population respectively. Only 0.5% and 1.1% had relative afferent pupillary defect (RAPD) for right and left eye respectively. Although the highest proportion of the work-

ers in each of the glaucoma status had a normal pupil for both right and left eyes, a higher proportion of workers with RAPD (45.5%) were glaucomatous and another 3 workers (27.3%) were suspected to have glaucoma. This distribution was statistically significantly different from the 2.5% with definite glaucoma and 12.2% suspected glaucoma reported among patients with normal pupil in the right eye respectively ($P < 0.001$). The same pattern was observed for the left eye, where 45.8% of workers with RAPD were definitely glaucomatous compared to 2.2% of workers with normal pupil.

Visual field loss

Most of the workers had no visual field loss in both right (93.9%) and left (93.4%) eyes. This was the situation in all the three categories of glaucoma status. The visual field loss in the right eye was mild (<30% loss) in 4.5% of patients and severe (>60%

loss) in 0.7% compared to 4.9% and 0.9% in the left eye respectively. Higher proportions of workers with definite Glaucoma had severe visual loss compared to those workers without Glaucoma (10.2% vs. 0.6% in the left eye and 5.3% vs. 0.6% in the right eye respectively). There was a statistically significant association between severity of visual field loss and glaucoma status in the right and left eyes ($P < 0.001$). The severity of visual field loss was also slightly higher in the left eye. The proportion of definite or suspected glaucoma was high among workers with moderate to severe visual field loss.

Cup-disc ratio

The majority of the workers had their cup disc ratio for both right (71.3%) and left eye (72.5%) lying between 0.0 - 0.3. Workers who were not glaucomatous were common in this category unlike the higher cup disc ratios where there were definite glaucoma cases. The proportion of workers with cup-disc ratio 0.7-1.0 was statistically significantly higher among workers with definite glaucoma than those without (32.8% vs. 0.2% in the right eye and 38.6% vs. 0.2% in the left eye).

Again, the frequency of workers with cup-disc ratio 0.7-1.0 were slightly higher for the left eye than the right eye ($P < 0.01$).

Gonioscopy

Gonioscopy was performed on all workers diagnosed as having glaucoma, all had open angles.

Family history

Ninety six subjects (16.6%) reported a family history of glaucoma. However, a statistically significantly higher proportion of workers with definite glaucoma reported family history of glaucoma or were known glaucoma patients ($P < 0.001$). The proportion of workers with family history of glaucoma among those currently not having glaucoma was statistically significantly lower than among workers with current definite glaucoma (3.8% vs. 21.1%) ($P < 0.01$).

Chronic diseases

Two hundred and twenty one workers were known hypertensives, seventeen were diabetics and eighty four had other chronic diseases like asthma, sickle cell anaemia and arthritis. There was a statistically higher proportion of hypertensives among those with definite glaucoma compared to workers without glaucoma (26.3% vs. 10.4%) ($P < 0.05$) but there was no statistically significant association between glaucoma status and receiving treatment for hypertension. Also, 3.5% of workers with definite glaucoma were diabetics compared to 0.7% of those without glaucoma. Although the overall frequency of workers with diabetes was low (0.8%) there was a statistically significant relationship with glaucoma status ($P < 0.001$). Neither current treatment for diabetes nor the presence of other chronic diseases was statistically significantly associated with current glaucoma status ($P > 0.1$).

Validity of diagnostic tools

The sensitivity and specificity of some ophthalmic variables for the diagnosis of glaucoma are presented in Table 3.

Visual field loss

All workers with a visual field loss assessed as mild to severe were considered as glaucomatous and this was related to those with true diagnosis of glaucoma. The sensitivity of visual field

Table 3: Sensitivity and specificity of clinical measures for the diagnosis of glaucoma

Clinical measures	Sensitivity	Specificity	Positive pred.	Neg. Pred Value
<i>Visual field loss</i>				
Right eye				
mild-severe	17.5%	94.6%	8.3%	97.6%
Mod-severe	10.5%	99.0%	23.1%	97.5%
Left eye				
mild-severe	19.2%	80.7%	8.0%	97.3%
mod-severe	14.0%	98.8%	24.2%	97.6%
<i>Cup-disk ratio</i>				
Right eye				
(0.4-1.0)	94.7%	73.5%	9.1%	96.8%
(0.7-1.0)	33.3%	99.5%	65.5%	98.2%
Left eye				
(0.4-1.0)	94.7%	74.6%	9.4%	99.8%
(0.7-1.0)	38.6%	99.2%	56.4%	98.3%
<i>CVF</i>				
Right=eye				
(Trace-severe)	98.2%	92.5%	26.7%	98.9%
Left eye				
(Trace-severe)	98.2%	92.5%	26.7%	99.9%
IOP < 15 mmHg cut off point				
Right eye	70.2%	67.8%	5.7%	98.8%
Left eye	71.9%	66.5%	5.6%	98.8%
IOP < 21 mmHg cut off point				
Right eye	24.6%	98.1%	25.9%	97.9%
Left eye	26.3%	97.9%	26.3%	97.9%

loss for a glaucoma based on this assessment was low (17.5%) but with a high specificity of 94.6%. The positive predictive value was equally low (8.3%) with a high negative predictive value (97.6%). However, when patients with moderate to severe visual field loss were defined as cases, the sensitivity reduced to 10.5% for the right eye while the specificity increased to 99.0% and the positive predictive value also increased to 23.1%. The pattern is similar when the left eye was considered, except that the sensitivity, increased to 14.0% using moderate to severe visual field loss as cut-off point.

Cup-disc ratio

Another measurement considered was the cup-disc ratio. At a cut-off point of 0.4, the sensitivity was 94.7%, specificity and 73.5%, but a very low positive predictive value of 9.1%. However, when the cut-off point was increased to 0.7, the sensitivity decreased to 33.3% while the specificity and positive predictive value increased to 99.5% and 65.5% respectively. The same pattern is expressed with the cup-disc ratio of the left eye, but the sensitivity was slightly increased to 38.6% while the positive predictive value reduced to 56.4%.

Central visual field

The use of central visual field (CVF) as a diagnostic tool for glaucoma gave a high sensitivity of 98.2% and specificity of 92.5%. But the positive predictive value was only 26.7% while

the negative predictive value was very high 99.9%. Then was no difference between the right and left eyes.

Intraocular pressure (IOP)

Using the cut-off point of 21mmHg for the intra ocular pressure in the diagnosis of glaucoma, the result showed that the intra ocular pressure has a low sensitivity for both right and left eye (24.6% and 26.3%) respectively. However, the specificity was high in both eyes (98.1%) and (97.95%) for right and left eye respectively. The positive predictive value was 25.9% and 26.3% while the negative predictive value was high for both eyes. If a cut-off point of 15mmHg was used for intra ocular pressure in the diagnosis of glaucoma, the result showed a much higher sensitivity of 70.2% and a specificity of 67.8% in the right eye while the positive predictive value was as low as 5.7%. The positive predictive value was also as low as 5.6% in the left eye. However, the negative predictive value was very high in both right and left eyes.

The IOP is therefore not always sensitive to predicting glaucoma as the low positive predictive value suggests high false positive rate. All the indices gave very high negative predictive values.

Multi-variate analysis

The significance of all variables that were found statistically significantly associated with glaucoma in a univariate analysis was included in a binary logistic model. The workers were categorised into definite glaucoma and non-glaucoma groups. This glaucoma classification serves as the dependent variable and all other variables as independent. The step-wise regression procedure was used to assess the significance of the variables as predictors of glaucoma adjusted for others.

Table 4: Estimate of logistic regression co-efficients for predicting glaucoma

Variable	Regression co-efficient (S)	SF (S)	Wald statistics	Odds ratio	95% CI (OR) (OR)
Constant	-9.4578	0.9121			
Pupils *	4.22	1.2108	12.14	68.03	6.34, 729.96
Intraocular pressure *	0.2007	0.0428	21.95	7.22	1.12, 1.38
Cup-disc Ratio (L)					
0.4 - 0.6	3.3807	0.6875	28.12	29.39	8.42, 102.53
0.7 - 1.0	6.1314	0.7211	72.29	460.09	111.95, 1890.93
Family history					
Yes	1.4460	0.4669	9.60	4.25	1.70, 10.61
Diabetes					
Yes	2.2066	1.018	4.70	9.08	1.23, 66.84

Table 4 shows the estimates of logistic regression probability model for the prediction of glaucoma from patients' ocular and clinical characteristics. The results revealed abnormal pupil (RAPD), intra-ocular pressure (IOP), cup-disc-ratio, family history of glaucoma and presence of diabetes as significant predictors of glaucoma. Workers whose cup-disc-ratio exceed 0.7 are over 400 times as likely to have glaucoma compared to those with a disc-cup-ratio below 0.4. This is followed by RAPD in the right pupils with an odds ratio of nearly 70. An increase in IOP also suggests an increase in the probability of developing glaucoma. Diabetic patients are also nine times more likely to develop glaucoma, while patients with family history of glaucoma are at least 4 times as likely to also develop glaucoma.

Discussion

The prevalence of open angle glaucoma in this study was found to be 2.7%, which is not as high as the 7% [12] in the Barbados Eye study and 8.8% [13] in the St. Lucia study in the West Indies. This could be due to differences in study design as our study was on hospital workers while theirs were stratified random sampling in the adult population (>40 years). However, this is still much higher than figures obtained in Caucasians, 0.43% [14], 0.1% [15]. The risk factors for glaucoma remain the same, namely, advanced age, black race, elevated intraocular pressure, positive family history, refractive error and systemic hypertension [1,17].

Intraocular pressure in this study was found not to be a reliable method of rapid screening procedure for glaucoma even though it remained a risk factor once elevated. This has been confirmed by other authors [18]. Sensitivity for CVF was high but the positive predictive value was only 26.7% while the negative predictive value was very high at 99.9%.

From the present study, the cup-disc ratio appears to be the best diagnostic tool for glaucoma, over and above the intraocular pressure and rapid central visual field analysis by the 30 point campimeter, since it gives the best positive predictive value than all other variables considered. It is therefore obvious that the cup-disc ratio is the best screening test, 94.7% of patients will be correctly diagnosed at cut-off of 0.4. The sensitivity of a test is very important where one needs to pick cases of glaucoma as early as possible for treatment, as glaucoma causes irreversible blindness. There is however need to note that cup disc ratio alone should not be used for the diagnosis of glaucoma.

The major reason for this has to do with the problem of its being subject to intra and inter observer error [19]. We tried to reduce this error by using very few expert examiners for the fundus examination during the screening exercise. The best method available for examining the disc changes in glaucoma and for reducing inter and intra observer error is by stereoscopic examination of the fundus [20]. This can be done with contact lens at the slit lamp or using an indirect ophthalmoscope. The use of stereoscopic fundus photographs further reduces the subjectivity of the examination [21]. Cost and capital intensive nature of these equipment could however be limiting factors in many developing countries with depressed economies. Thus the less expensive direct ophthalmoscope in the hand of an experienced investigator still has a place in screening.

Although cup disc ratio has been found in this study to be the best diagnostic tool for the detection of glaucoma, in our environment it may be better combined with a rapid assessment of the central visual field in suspected cases to improve its predictive value.

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