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Cupping of large optic discs - a diagnostic challenge in African patients

Dr. D Soma, MBChB, FC Ophth(SA), MMed(Ophth)(SA)[1*], Prof. GD McLaren, MBBCh, FCS(SA)Ophth, FRCOphth(UK)[2], TR Carmichael MBBCh(Wits), FC Ophth(SA), PhD(Med), MSc(med)[3]

[1]Senior Lecturer and Clinical Unit Head of Ophthalmology at Steve Biko Academic Hospital, Division of Ophthalmology, Department of Health Sciences, University of Pretoria, Pretoria, South Africa.
[2]Emeritus Professor, Division of Ophthalmology, Department of Neurosciences, University of Witwatersrand, Johannesburg, South Africa.
[3]Professor, Division of Ophthalmoogy, Department of Neurosciences, University of Witwatersrand, Johannesburg, South Africa.

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ABSTRACT

Purpose: To determine in a cohort of 69 African patients with large optic discs and large optic cups, that proportion of patients with physiologic cupping (normal eyes) misdiagnosed as glaucomatous. To evaluate the possible relationship between optic disc size and central corneal thickness.

Method and design: A case series of 69 African patients with large optic discs (vertical disc height measuring >1.8mm) and large optic cups (vertical cup to disc ratio ≥0.6) was evaluated to determine what proportion had glaucoma and what proportion was normal. Patients categorized as normal were further evaluated to determine what proportion were previously misdiagnosed and treated for glaucoma. Patients with a suspected diagnosis of glaucoma, normal tension glaucoma or primary open angle glaucoma were recruited from the glaucoma clinic at St John Eye Hospital in South Africa.

Outcome measures included corrected vertical disc height, vertical cup to disc ratio, intraocular pressure, central corneal thickness, retinal nerve fibre layer analysis and visual fields.

Results: Sixty-nine African patients (138 eyes) with large optic discs and large optic cups were evaluated. 41 patients (59%) were females and 28 (41%) were males. The mean age was 56 years. Of the 69 patients, 51 (74%) had physiologic cupping (normal eyes) and 18 (26%) patients had glaucoma. Of the group of 51 patients with physiologic cupping, there were 9 patients who were previously misdiagnosed with glaucoma and who had received treatment.

Vertical disc height ranged between 1.9 and 3.2 mm (mean±SD, 2.3±0.26mm). The distribution analysis of the vertical disc height measurements noted the largest cluster around 2.3mm. The central corneal thickness ranged between 454µm and 618µm (mean±SD, 516±37um). 107 (77.5%) of the 138 eyes had central corneal thickness less than 544µm.

Conclusion: Large optic cup to disc ratio in relation to large disc size can be normal. It can be misdiagnosed as glaucomatous if objective retinal nerve fibre layer analysis is not carried out. In this study, 9(18%) patients from a group of 51 patients with physiologic cupping were misdiagnosed as glaucomatous. There was no linear correlation between central corneal thickness and vertical disc height in this study. Pearson's correlation coefficient was 0.13. The majority (77.5%) of eyes had thin corneas. Central corneal thickness less than or equal to 544µm.

Key words: large optic discs, large optic cups, physiologic cupping, central corneal thickness, glaucoma, African.

Introduction

Glaucoma is an eye condition that results in optic nerve damage. This manifests as increased cupping of the disc. Cupping of the optic disc is a typical feature of glaucomatous optic nerve damage. Thus the vertical cup to disc ratio (CDR) has been used in the evaluation of glaucoma. The cup size is related physiologically to the disc size and pathologically to glaucomatous damage. A glaucomatous optic nerve gives rise to visual field changes. In addition, retinal nerve fibre layer atrophy occurs in glaucoma.

Diagnosing pathological changes based on the vertical cup to disc ratio alone is of limited value. It is important to take into account the disc size[1]. There are different methods to measure disc size and each with its own strength and limitations. It is possible to measure the optic nerve head at the slitlamp with different types of lenses[2]. By using a slitlamp and a high magnification fundus lens (Volk 60 diopter lens) a vertical slit is placed over the optic disc to measure the vertical disc diameter. Correction factors may be needed depending on the power of the lens used.[3] A 60 diopter Volk lens has a correction factor of 0.92[3].

Racial differences in optic disc size exists. A number of studies have shown that Africans have larger optic discs compared to Europeans[4,5].

Healey et al showed in the Blue Mountain Eye Study that there is an increase in the cup to disc ratio with an increase in the vertical disc size[6]. This is significant enough to warrant measurement of the optic disc size. Large optic discs are defined as optic discs measuring 1.8mm or more[7]. The importance of assessing the vertical cup to disc ratio in relation to disc size was extensively studied by Jonas and co-workers[8] as well as Garway-Heath and associates[9]. They showed that the vertical cup to disc ratio for disc size has the highest diagnostic power compared to other optic disc parameters for separating normal subjects from pre-perimetric glaucoma patients.

It is clinically difficult to distinguish physiologic cupping from glaucomatous changes. Patients with large vertical cup to disc ratios are generally misdiagnosed as glaucomatous. This can be prevented if disc size is measured because we know that large discs generally have large vertical cup to disc ratios[6,8,9]. In this way, the distinction between physiologic cupping and glaucomatous cupping can be made with greater confidence.

There is controversy whether there is a positive correlation between disc size and retinal nerve fibre layer thickness. Cross section study by Budenz et al.[10] showed that for every square millimeter increase in cup disc area, the mean retinal nerve fibre layer increased by 3.3um.

Central corneal thickness (CCT) plays an important role in the diagnosis of glaucoma. And it influences the intraocular pressure. In a cross section study by Brandt et al.[11] 1301 patients with ocular hypertension were studied to determine if CCT influences intraocular pressure (IOP) measurements and if CCT is related to race. They found that CCT for Africans was 555.7um and CCT for Europeans was 573um. They showed that Africans had thinner corneas than Europeans and concluded that CCT may influence the accuracy of IOP measurements. Thin corneas underestimate IOP measurements and thick corneas overestimate IOP measurements[1,12].

Objectives

The objectives of this study was to determine in a cohort of 69 African patients with large optic discs and large optic cups, that proportion of patients with physiologic cupping misdiagnosed as glaucomatous. Also, to evaluate the possible relationship between optic disc size and central corneal thickness in the African population.

Study design

A case series consisting of 69 African patients with large optic discs and large optic cups, were evaluated, to determine what proportion had glaucoma and what proportion was normal. Patients categorized as normal were further evaluated to determine what proportion was

misdiagnosed and treated as glaucoma. The relationship between disc size and central corneal thickness was also evaluated.

Glaucoma patients in this project is defined as patients who are glaucoma suspects, who are diagnosed with primary open angle glaucoma or normal tension glaucoma and attend the glaucoma clinic at St John Eye Hospital. This hospital is situated in Johannesburg, South Africa.

Method

Prior to this research project being carried out, a protocol was submitted to the human research ethics committee (medical) at the University of the Witwatersrand in Johannesburg. A clearance certificate was issued (M070435).

Large discs are defined as optic discs having a corrected vertical disc height measuring more than 1.8mm. Large cups are defined as cup to disc ratios of 0.6 or more.

This was a convenience sampling of glaucoma patients with large optic discs and large optic cups, attending the glaucoma clinic at St John Eye Hospital. Patients were invited to participate in the study and informed consent was obtained from those patients willing to participate in the study.

1. A glaucoma suspect is defined as a patient with one of the following three features. An optic nerve or retinal nerve fiber layer (RNFL) defect, or visual field abnormality consistent with glaucoma, or a consistently high IOP (>22mmHg)[13].

2. Primary open angle glaucoma is defined as a triad of increased IOP, optic nerve head changes and changes on the visual field or RNFL analysis[13].

3. Normal tension glaucoma is defined as IOP<21mmHg with visual field defects and RNFL defects[13].

4. Ocular hypertension is defined as IOP>21mmHg and no changes on visual fields or the RNFL analysis[13].

High myopes (more myopic than -8 diopters) and children were excluded from the study. High myopes were excluded because they have markedly different appearances of the optic nerve head, in normal and glaucomatous eyes[14,15]. Also, the vertical disc height is influenced by axial length (high myopia) and not by the distance of the lens from the cornea or by the refractive errors less than -8 diopters[16].

Clinical examination included history, slit-lamp biomicroscopy findings which included IOP, gonioscopy and fundus examination that concentrated on the qualitative and quantitative measurements of the optic nerve head. Special investigations included refraction, CCT measurements, visual fields and retinal nerve fibre layer analysis.

A Haag Streit biomicroscope was used to examine the eye. A 60 diopter lens was used to examine and measure the optic disc head. A vertical slit-beam was placed over the optic disc and the beam was adjusted to measure the vertical disc diameter. The measurement was read off the calibrated knob on the biomicroscope. A correction factor was needed for the lens (x1.02 for the Nikon 60 D lens)[3].

A calibrated Goldmann tonometer was used to measure the intraocular pressure (IOP). This measurement was entered into the Heidelberg engineering IOPac advanced pachymeter to obtain the Adjusted-IOP (A-IOP), taking the central corneal thickness into account.

Gonioscopy was performed using a Volk 3-mirror-lens.The Shaffer-Etienne classification system was used in this study which defines:

Grade 0 - No structures are visible and represents a closed angle.

Grade 1 - Schwalbe line is visible and represents possible angle closure.

Grade 2 - Schwalbe line and trabecular meshwork are visible but scleral spur not visible in a narrow angle.

Grade 3 - Scleral spur is visible and angle closure is impossible.

Grade 4 - All structures are visible from Schwalbe's line to the ciliary band.

Refraction was carried out with a Nikon handheld autorefractor and refined subjectively. In this way, patients who were more myopic than -8 diopters, or more hyperopic than +4 diopters, were excluded from the study.

Visual fields were performed using the Oculus automotive perimeter. This documented any functional loss or progression of functional loss by the nerve over time. This was followed up for at least 5 years in order to exclude any progression to glaucoma in patients who were classified as having physiologic cupping.

The GDxVCC (Carl Zeiss meditec Inc., Dublin CA, USA), is a retinal nerve fibre layer (RNFL) analyzer that uses scanning laser polarimetry to quantify the nerve fibre layer thickness in order to detect early glaucomatous changes[3]. A retinal nerve fibre analysis was done with a scanning laser polarimeter to confirm the presence or absence of glaucomatous retinal nerve fibre layer defects. This was based on the nerve fibre index, TSNIT (temporal, superior, nasal, inferior, temporal) graph and parameters and the deviation map[17].

The excel data base was used for data summary. Statistics were performed using the statistical software Stata version 8 (Stata Corporation, College station, Texas, USA).

Results

Hundred and thirty eight eyes of 69 African patients were evaluated. Forty one patients (59%) were females and 28 (41%) were males. Patient age ranged between 18 to 87 years with a mean age of 56 years. Visual acuity ranged from 6/6 to light perception. Refraction ranged from myopia of -6.5 D to hyperopia of +4 D.

From a cohort of 69 patients with large discs and large cups, 51/69 (74%) had normal eyes and 18/69 (26%) had pathologic cupping. The group of 51 patients with normal eyes was further evaluated and 9/51(18%) were previously misdiagnosed and treated with anti-glaucoma medications. The main reason for the misdiagnosis was an increased cup to disc ratio in the presence of a large disc.

OUTCOME MEASURES

- central corneal thickness (CCT)
- intraocular pressure (IOP) and adjusted intraocular pressure (A-IOP)
- corrected vertical disc height (VDH)
- vertical cup to disc ratio (CDR)
- relationship between VDH and vertical cup height
- relationship between VDH and central corneal thickness
- retinal nerve fibre layer analysis
- visual fields

CENTRAL CORNEAL THICKNESS

This was measured using the Heidelberg engineering IOPac advanced pachymeter. It ranged between 454µm and 618µm. The mean CCT was 516µm±37.5µm. (Figure 1) In this study, CCT<544µm was regarded as a thin cornea. Out of a total of 138 eyes, 107 eyes (77.5%) had CCT<544µm.

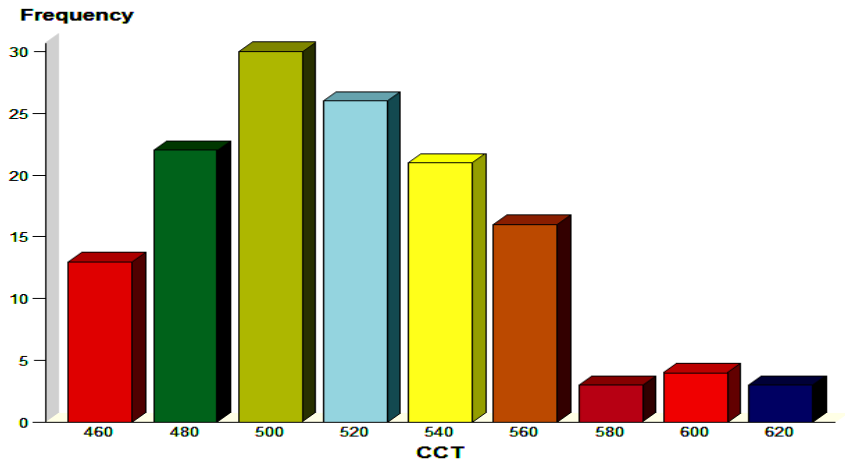

Figure 1. Distribution of central corneal thickness

INTRAOCULAR PRESSURE AND ADJUSTED INTRAOCULAR PRESSURE

The intraocular pressures ranged between 6mmHg and 23mmHg and the mean IOP was 13±3.5mmHg. Taking the central corneal thickness into account, the A-IOP ranged between 6.4mmHg and 26mmHg. The mean A-IOP was 14.7±3.5mmHg.

CORRECTED VERTICAL DISC HEIGHT

Vertical and horizontal disc diameters were measured. The VDH ranged between 1.9mm and 3.2mm (mean±SD, 2.3±0.26mm). The horizontal disc diameter ranged between 1.7mm and 2.9mm (mean±SD, 2.1mm±0.21mm) (Figure 2)

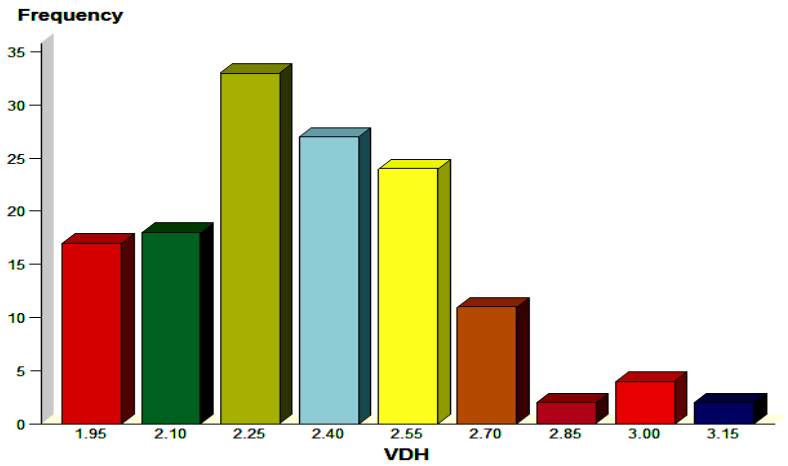

Figure 2. Distribution of corrected vertical disc height

VERTICAL CUP TO DISC RATIO

The vertical cup to disc ratio was measured relative to VDH. The verical cup to disc ratio ranged from 0.6 to 1 (mean±SD, 0.7±0.08).

RELATIONSHIP BETWEEN VDH AND VERTICAL CUP HEIGHT

The vertical cup height was calculated by taking the CDR and multiplying it with the VDH. The vertical cup height increased with an increase in VDH. There was a positive linear relationship between the vertical cup height and the VDH. (Figure 3)

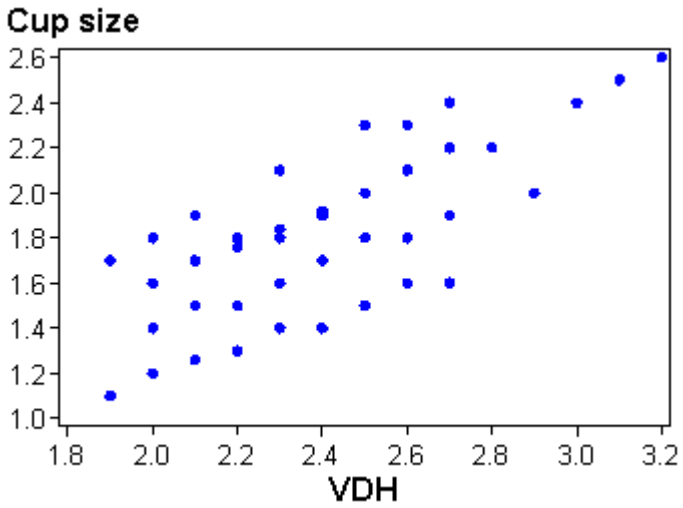

Figure 3. The relationship between VDH and vertical cup height

RELATIONSHIP BETWEEN VDH AND CCT

Vertical disc height ranged between 1.9mm and 3.2mm. The central corneal thickness ranged from 454µm to 618µm. There was no linear correlation between VDH and CCT. The Pearson correlation co-efficient was 0.13.

RETINAL NERVE FIBRE LAYER ANALYSIS

This was carried out for each eye. The findings were interpreted as normal, having RNFL changes indicative of glaucoma or as unsuccessful. The parameters that were considered for the above were based on

1. The nerve fibre index (NFI). This is the best parameter to differentiate glaucomatous and healthy eyes[17]. The NFI ranges from zero to one hundred. The more advanced the glaucoma, the higher the NFI. Glaucoma eyes have NFI values of 35 and above and healthy eyes have NFI values of 44 and below. A NFI value between 35 and 44 is considered borderline and therefore other data in the GDxVCC printout may be used to make the diagnosis of glaucoma.

2. The TSNIT graph - This shows RNFL values of each of the eyes on the expected age related normal range[17].

3. The deviation map - This map plots the RNFL values that deviate from the normal range. The colour coded p-values indicate the extent of the deviation[17].

In this study the NFI for normal eyes ranged between 3 and 44. The mean NFI for all normal eyes was 38. The NFI for glaucoma eyes ranged between 35 and 98. The mean NFI for glaucoma eyes was 49.6. In eyes that had borderline NFI values ie. NFI values between 35 and 44, other parameters on the GDxVCC together with the visual fields were used to determine if the eye had glaucoma or not.

The reason for an unsuccessful GDxVCC evaluation, which occurred in 8 eyes, was due to poor visualization of the fundii due to cataract formation.

VISUAL FIELDS

The Oculus automotive perimeter was used to measure and document visual fields in all 138 eyes. Although the study was carried out over 4 months, visual fields done before the 4 months were also assessed and followed up for 5 years to ensure the absence of glaucomatous progression in patients diagnosed with physiologic cupping. The visual fields were compared to ascertain if there were glaucomatous field losses or if there was any progression of field loss. Fields were categorized as having glaucomatous change, normal, unreliable or unsuccessful. In this study, fields with glaucomatous change was defined as one of the following: A glaucoma hemifield test outside normal limits on at least two consecutive occasions or a cluster of three or more non-edge points in a location typical for glaucoma or a corrected pattern standard deviation in less than 5% of normal individuals on two consecutive fields[13]. Normal fields were defined as visual fields with no glaucomatous changes. Unreliable fields were defined as visual fields where glaucomatous changes were difficult to assess. Unsuccessful visual fields were due to profound visual loss.

In this study, there was a total of 138 eyes. 18/138 (13%) visual fields could not be determined as normal or having glaucomatous defects because the visual fields were unreliable. 84/138 (61%) eyes were correctly diagnosed as having physiologic cupping of the optic discs and had normal visual fields. In the subsection of 36/138 (26%) eyes diagnosed with glaucoma, 30 eyes showed glaucomatous visual field defects, 5 visual fields were unreliable and 1 visual field was unsuccessful. Glaucoma was diagnosed in the latter two groups with the aid of the GDxVCC.

Discussion

Examination of the optic nerve head in glaucoma commonly involves the evaluation of the optic cup, the neuroretinal rim contour and the retinal nerve fibre layer. An important but overlooked component of the optic nerve head evaluation is measurement of the optic disc size.

In healthy subjects, small discs can have small cups and large discs can have large cups[16]. Large discs with large cups can therefore be misdiagnosed as glaucoma. Sometimes the visual fields obtained may be unreliable and therefore the diagnosis of glaucoma becomes a challenge to the ophthalmologist.

This study was limited to African patients. There were several reasons for this. Firstly, there is an

increased prevalence of glaucoma in African patients. This was shown in the Baltimore Eye Study which showed that African-Americans have a higher prevalence of glaucoma across all age groups when compared to Europeans in the same city[18,19]. A study done by Rotchford et al.[20] also showed that glaucoma was one of the leading causes of blindness in people of African origin in rural Zululand (South Africa). Secondly, the optic disc head characteristics in African patients differ from their European counterparts[4,5,20]. African patients have larger optic disc sizes when compared to their European counterparts[4,5]. Thirdly, African patients have thin central corneal thickness when compared to their European counterparts[1,11,12,21,22]. By limiting the data to African patients, it was hoped that consistent results, not confounded by findings from other racial groups would be obtained.

Optic disc size is influenced by a number of demographic factors that include race, age and gender. In addition, variation in anatomical structures of the optic nerve head and the retinal nerve fibre layer is associated with variation in disc size. Due to the smallnumber of cases, a limitation of this study is that no comparisons could be drawn about disc size related to age and gender.

Africans have larger discs when compared to their European counterparts[12,13]. The mean vertical and horizontal disc diameters as measured by Quigley for the disc of a normal human eye is a vertical disc diameter of 1.88mm and a horizontal diameter of 1.77mm[23]. In this study, large discs were defined as discs with a vertical height measuring more than 1.8mm. The vertical disc height (VDH) ranged between 1.9 and 3.2mm (mean±SD,2.3±0.26) and the horizontal disc diameter (HDD) ranged between 1.7 to 2.9mm (mean±SD, 2.1±0.22). Studies conducted by Quigley et al (1990) also demonstrated large vertical disc height in Africans (1.96±0.16) compared to the VDH of Caucasians (1.82±0.15)[23]. This study showed much larger disc sizes, possibly due to genetic variation. There was a normal gausian distribution for VDH (Figure 2). Large cups were defined as a cup-disc ratio greater than 0.6. The Blue Mountains Eye Study showed that that for each 0.1 millimeter increase in disc diameter there was an increase in cup to disc ratio of 0.27[6,7]. Beck et al reported that large discs have proportionately large cup to disc ratios in the normal eyes of African subjects[24]. The data from our study showed that there was a direct linear relationship between vertical disc height and vertical cup height (Figure 3).

Central corneal thickness influences intraocular pressure measurements. The mean central corneal thickness in the normal human eye is 545µm[22]. In this study, the CCT ranged from 457µm to 616µm (mean±SD,516±37µm) and 77,5% of patients had thin corneas (CCT<544µm). Thick corneas overestimate actual intraocular pressure measurements and thin corneas underestimate intraocular pressure measurements[12]. In this study, no correlation could be found between disc size and CCT. The Pearson correlation co-efficient was 0.12667. Pakravan et al showed that there was an inverse relationship between disc size and CCT in African-American patients, but that this was not statistically significant[12].

To diagnose glaucoma, the following criteria was used: an increased intraocular pressure; structural changes of the optic nerve head; visual field changes and corresponding retinal nerve fibre layer damage on the scanning laser polarimeter (GDxVCC). In this study, unreliable visual fields sometimes made it difficult to make a diagnosis of glaucoma and the researchers therefore had to rely on the retinal nerve fibre layer analysis to assist with the diagnosis. It is important to bear in mind that during arly glaucoma, there may not be visual field defects and patients therefore needed to be followed up for at least 5 years to ensure that patients in the physiologic cupping group did not progress to glaucoma.

Of the 69 patients studied, 51 patients (74%) had physiologic cupping and 18 patients (26%) had pathologic cupping. Of the 51 patients with physiologic cupping, 9 (18%) were previously

misdiagnosed as glaucoma and had received unnecessary treatment while the other 42 (82%) patients were correctly diagnosed as physiologic cupping.

A significant number of patients in the group of patients with large discs (51/69) had physiological cupping. The researchers concluded that although Africans are more susceptible to glaucoma and have large discs, large discs is not on its own a risk factor for the development of glaucoma. The researchers further concluded that large discs that have proportionately larger cups are more likely to be misdiagnosed as glaucoma than be diagnosed as physiologic cupping. Nine of the 51 patients were erroneously misdiagnosed and treated for glaucoma. The reason for the misdiagnosis was a large cup size in a large disc. Studies conducted by Heijl and Mölder showed that larger discs were more likely to be misdiagnosed with glaucoma than were smaller discs[25]. It is logical therefore that disc size may affect the diagnosis.

Of the nine patients misdiagnosed and treated for glaucoma, one patient had undergone surgery unnecessarily. The patient who had undergone surgery did not disclose that she had been taking allergy medication (comprising topical steroids). On examination, she was found to have large cups, an increased intraocular pressure and unreliable visual fields. This trend continued for a period of time. At that point in time ophthalmologists at the hospital did not have access to a scanning laser polarimeter such as the GDxVCC. A trabeculectomy was carried out. Post-trabeculectomy, her IOP increased and it was then discovered that she was a steroid responder. She was found to have large discs with large cups. Years later when the scanning laser polarimeter (GDxVCC) became available, the retinal nerve fibre layer of this patient showed no retinal nerve fibre layer defects.

Although the literature reports an increase incidence of glaucoma in African patients, one has to be very careful in diagnosing a patient with glaucoma, because the possibility of physiological cupping in African patients with large discs must be considered. On the other hand a recent article Kim et al mentioned risk factors on fundus photography that can predict the conversion of cupping in large discs to glaucoma. This falls out of the scope of this study[26].

Conclusion

Africans have large discs and patients with large discs have corresponding large cups. Large cups do not necessarily imply that the patient has glaucoma. In this study, the majority - 51 of the 69 patients (74%) - with large discs and large cups had physiologic cupping. Nine of the 51 patients were misdiagnosed as having glaucoma. The main reason for misdiagnosis was a large cup in relation to a large disc. Measuring these parameters may aid in preventing the misdiagnosis of glaucoma, unnecessary treatment and morbidity to these patients.

Africans have thin corneas and large discs. The central corneal thickness influences intraocular pressure, i.e. thin corneas underestimate IOP, and this has to be taken into account in the diagnosis of glaucoma. In this study, 77.5% of patients had thin corneas (CCT<544µm) but the researchers found no inverse correlation between CCT and disc size.

Conflict of Interest:

The authors have no conflict of interest to disclose.

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