1.0 INTRODUCTION

1.1 Background

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 fiber atrophy occurs in glaucoma. The GDxVCC (Carl Zeiss Meditec Inc., Dublin CA, USA), is a retinal nerve fiber layer (RNFL) analyzer that uses scanning laser polarimetry to quantify nerve fiber layer thickness in order to detect early glaucomatous changes.[1]

Central corneal thickness (CCT) can influence intraocular pressure (IOP) measurements. Thin corneas underestimate IOP measurements and thick corneas overestimate IOP measurements.[2,3] An inverse relationship between CCT and optic disc size has been shown in one study, but this was not statistically significant in African-American patients.[2]

1.2 Aim of study

The objectives of this study were

1. 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.
2. To evaluate the possible relationship between optic disc size and central corneal thickness in the African population.

1.3 Literature review

1.3.1 Method of measuring disc size (slit-lamp biomicroscopy)

Diagnosing pathological changes based on cup to disc ratio alone is of limited value. It is important to take into account the disc size.[4]

There are different methods to measure disc size and each has its own strengths and limitations. It is possible to measure the size of the optic nerve head at a slit-lamp with many types of lenses.[5] By using a slit-lamp and a high magnification fundus lens (eg. Volk 60 D (diopter), 78 D, 90 D), a vertical slit is placed over the optic disc and the beam is adjusted until it approximates the vertical disc diameter. The measurement is then read off the calibrated knob on the slit-lamp. Correction factors are needed, depending on the power of the fundus lens used. Table 1.1 illustrates the corresponding correction factor that is required, depending on the lens used to examine the disc.

Table 1.1 Correction factors required for different lenses[1]

Magnification correction factors	
Type of lens used	**Correction factor**
Volk 60 D	**0.92**
Volk 78 D	**1.15**
Volk 90 D	**1.39**
Nikon 60 D	**1.02**
Nikon 90 D	**1.54**

The easiest way to measure the size of the cup is to express the size of the cup diameter as a ratio of the disc diameter. It is accepted that the cup enlarges in the vertical meridian in glaucoma and thus the estimate of the cup is also made in the vertical meridian.

Measuring the disc size with a lens at the slitlamp is a very practical, easy and cheap method of assessing disc size. Disc size evaluation is important in the complete assessment of the optic nerve head and is important in the decision making process of glaucoma. Thus, measuring disc size is no longer omitted today, as it was in the past.

1.3.2 Disc size is influenced by ethnicity

Racial differences in optic disc size exist. There are a number of studies that have shown that individuals from the Black population have large discs compared to individuals from the White population. In their studies, Chi et al[6] and Varma et al[7] showed that Blacks have larger optic discs compared to their White counterparts.

The high prevalence of glaucoma in addition to larger discs in the Black population when compared to the White population, has led to the hypothesis that individuals with larger discs are more susceptible to glaucoma than individuals with smaller optic discs. However, there are no studies to substantiate this hypothesis.

1.3.3 The relationship between disc size and vertical cup to disc ratio (CDR)

Healey and colleagues carried out a population based study – the Blue Mountains Eye Study - that showed that the CDR increased with an increase in vertical disc size.[8] They also showed that there was an increase in the cup to disc ratio of 0.27 for each millimeter increase in disc diameter. This is significant enough to warrant the measurement of disc size.

Beck et al[9] evaluated stereoscopic photographs taken from 100 Black and 100 White volunteers. They estimated the horizontal and vertical diameters and measured the CDR. They concluded that Blacks had a greater CDR than Whites. Chi and co-workers[6] compared the optic discs of 30 Black and 31 White volunteers using an optic disc analyzer. They found that Blacks have larger disc areas, larger CDRs and similar neuroretinal rims. It has been shown that the African-American subjects have a larger CDR with a larger disc size when compared to the White population in other studies.[10,11] A study done by Garway-Heath et al[12] concluded that the CDR relative to the disc size is useful in identifying glaucomatous discs.

There is an advantage to measuring disc size. A study done by Jonas et al[13] showed that large discs with large CDR have limited value in quantifying glaucomatous damage to the optic nerve. In the clinical setting, many patients are referred with large CDR and normal visual fields. By measuring disc size, ophthalmologists will be able to make certain assumptions with greater confidence. Example: If a patient with a large CDR and a large disc is evaluated and there are no nerve fiber layer defects or visual field changes, then it is likely that this is physiologic cupping in a large disc.[12] However, in a patient with a similar optic nerve head appearance as above but with risk factors, retinal nerve fiber layer changes and glaucomatous field changes, the clinician should be aware that this may be glaucomatous optic nerve damage.

Measuring CDR in relation to disc size is important in the complete assessment of the optic nerve head. Additional factors in the assessment of the optic nerve head include the

contour of the neuroretinal rim, optic disc haemorrhages, peripapillary atrophy, bared circumlinear vessels and the appearance of the retinal nerve fiber layer.[14]

1.3.4 Relationship between central corneal thickness and intraocular pressure

Central corneal thickness (CCT) measurements have recently been recognized as playing an important role in the diagnosis of glaucoma, especially in patients at high risk of developing glaucoma. CCT influences intraocular pressure (IOP) measurements. In a cross sectional study undertaken by Brandt et al,[15] 1301 patients with ocular hypertension were studied to determine if CCT influences IOP measurements and if CCT is related to race. They found that the mean CCT for the African-American group was 555.7μm and the CCT for the Caucasian group was 573μm. This demonstrated that African-Americans have thinner corneas than Caucasians. They also concluded that CCT may influence the accuracy of IOP measurements.

LaRosa et al[3] compared the CCT of African-Americans and Caucasians in non-glaucomatous and glaucomatous eyes. They found a statistically significant difference in the CCT measurements of African-Americans and Caucasians with glaucoma compared to those found in the control group. African-Americans had thinner CCT than Caucasians and this results in lower applanation IOP readings and hence an underestimation of the true IOP. This raises the possibility of taking CCT into account when measuring IOP.

Pakravan et al[2] revealed that central corneal thickness is inversely correlated with optic disc area. They found that thicker CCT caused a slight overestimation of true IOP and thinner CCT resulted in underestimation of true IOP.

Meta-analysis of CCT[16] shows that the mean CCT of normal eyes is 534µm; but the mean CCT for normal eyes differs, depending on whether it is measured with an ultrasound pachymeter or with an optical pachymeter. The mean CCT measured with an ultrasound pachymeter for normal eyes is 544µm.[16]

Figure 1.1 The Heidelberg engineering IOPac advanced pachymeter

The ultrasound pachymeter that was used in this study is illustrated in Figure 1.1. The probe is placed on the anaesthetized cornea and the mean CCT is determined for each eye. The IOP that has already been determined with the Goldmann applanation tonometer for that eye is entered into the pachymeter. The pachymeter determines the adjusted IOP (A-IOP) of the eye by taking into consideration the CCT of the eye.

1.3.5 Relationship between disc size and myopia

Jonas and co-workers carried out a study to determine the range of refractive errors on which the optic disc size depends.[17] They studied 1999 eyes. The refractive error ranged from -24.25 diopters (D) to +9.4 D. They found that the disc area increased steeply with an increase to high myopia, starting at -8 D and decreased towards high hyperopia, starting at +4 D. They concluded that optic disc size depends on refractive error. There

is an increase in disc size beyond -8 D and a decrease in disc size beyond +4 D. This is in keeping with histomorphometric findings.

The Blue Mountains Eye Study[18] and the Barbados Eye Study[19] found that there was a strong association between myopia and glaucoma.

1.3.6 Relationship between disc size and retinal nerve fiber layer

Retinal nerve fiber layer (RNLF) damage precedes visual field loss.[20] There is controversy about whether there is a positive correlation between disc size and the number of retinal nerve fibers. This may be partially explained by different methods used to measure disc size, the sample size used or the species in which the amount of nerve fibers were determined.

A cross-sectional study carried out by Budenz et al[21] showed that for every square millimeter increase in optic disc area, the mean RNFL thickness increased by approximately 3.3μm. In addition, they showed that for every decade of increased age, the RNFL thickness decreased by 2μm. In conclusion, they suggested that these variables may have to be taken into account when evaluating patients for the diagnosis and follow up of glaucoma.

1.3.7 Method of measuring retinal nerve fiber layer loss

In the 1990s Sommer et al showed that structural nerve injury preceded field loss in early glaucoma.[20] It therefore makes sense, to measure RNFL to detect glaucoma changes. Glaucoma is characterised by apoptotic ganglion cell loss related partially to intraocular pressure. When evaluating a patient with glaucoma, it is important to comment on the health of the retinal ganglion cells. It is difficult to evaluate these cells with an ophthalmoscope and thus an objective measure, which includes the aid of the scanning

laser polarimeter with variable corneal compensation (GDxVCC, Carl Zeiss Meditec Inc., Dublin CA, USA) may be helpful. The scanning laser polarimeter quantifies RNFL and is able to give an objective measure of RNFL loss. The GDxVCC has a variable corneal compensation mechanism and is therefore able to determine glaucoma better than the previous scanning laser polarimeter with fixed corneal compensation.

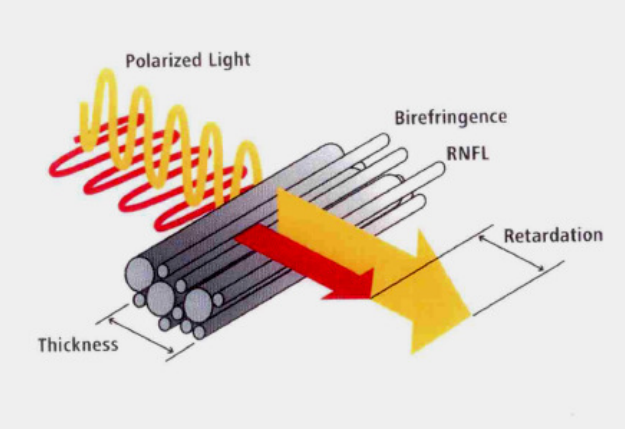

Figure 1.2 Polarization by the scanning laser polarimeter (GDxVCC)[22]
- courtesy of Carl Zeiss Meditec Inc.

Figure 1.2 illustrates how the scanning laser polarimeter works. The RNFL is a polarizing structure. When light of known polarization is shone through the RNFL, it reflects back with the state of polarization changed. The amount of change is known as retardation. Retardation is proportional to the thickness of the birefringent structure. Thicker structures cause more change to birefringence that is reflected back and vice versa. It uses a 780nm laser to scan the parapapillary area and measures birefringence of the RNLF, which is an indication of the thickness which is thought to represent relative retinal health. The birefringence of the cornea and the lens is neutralized with the variable corneal compensator.

It is rapid, reproducible and objective. Reproducibility is important in the diagnosis of glaucoma so that the user is confident that any differences in eyes are real and not due to poor instrument precision. Readings from the GDxVCC are not affected by IOP or refractive errors.

A typical printout from the scanning laser polarimeter (Figure 1.3) will contain the fundus image, the RNFL map and the deviation map for each eye. The temporal-superior-nasal-inferior-temporal (TSNIT) graph and TSNIT parameters are also included. These findings assist ophthalmologists in evaluating the RNFL objectively. There is an option to perform serial analysis (Figure 1.4) and compare multiple scans directly. It has a sensitivity of 62% and a specificity of 96% for detecting glaucomatous damage. [23]

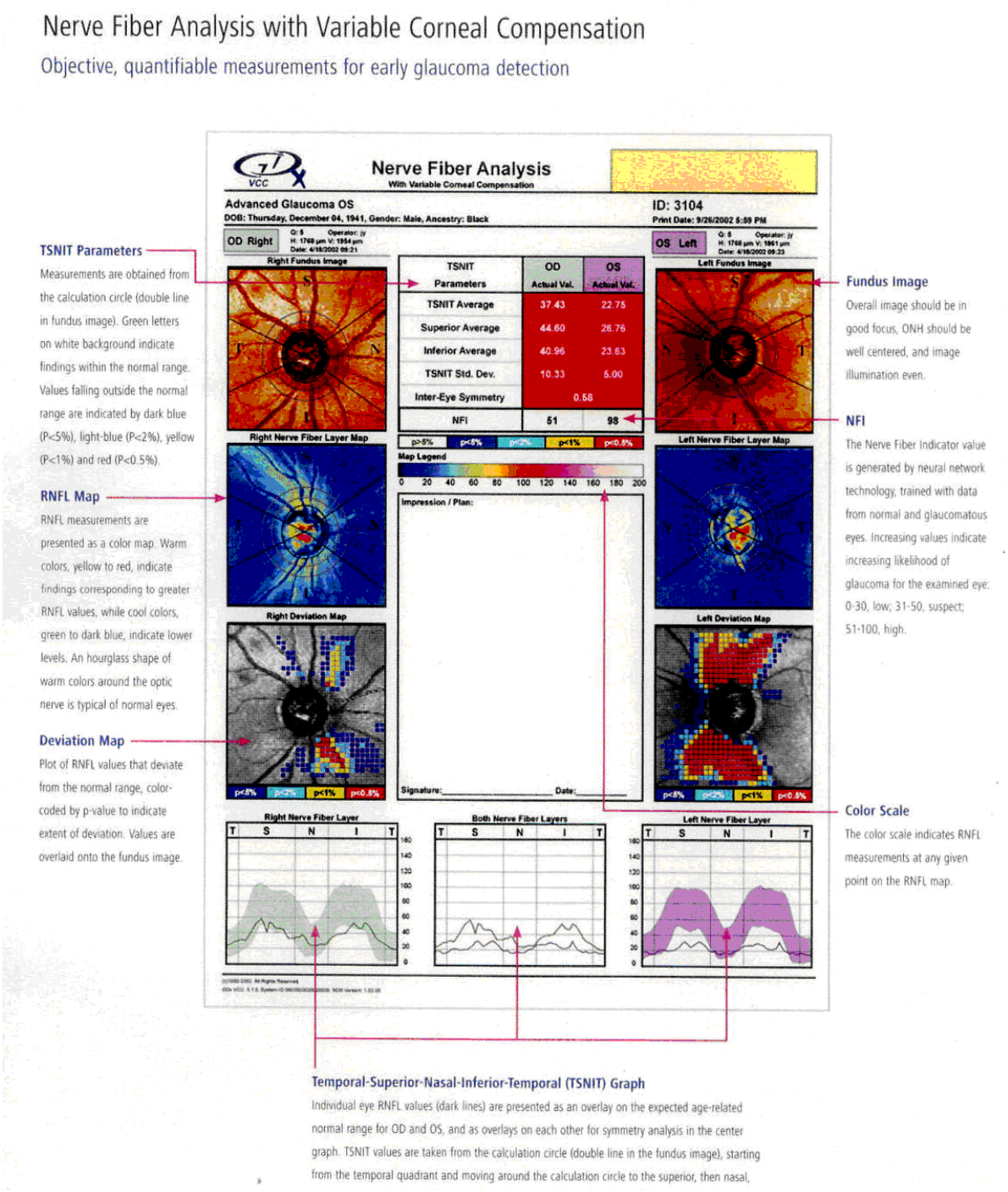

Figure 1.3 Nerve fiber analysis with variable corneal compensation (GDxVCC) - courtesy of Carl Zeiss Meditec Inc.

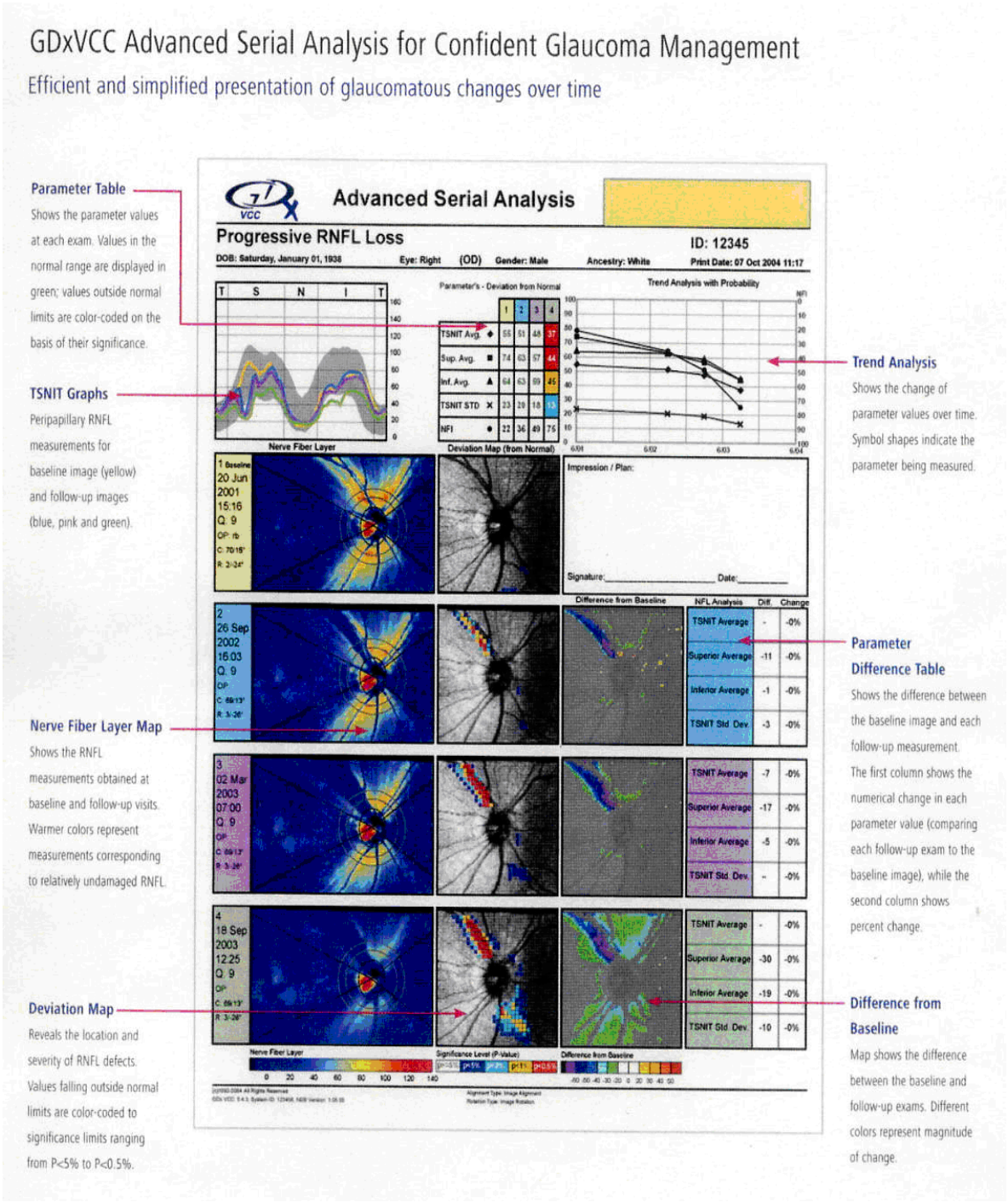

Figure 1.4 Advanced serial analysis (GDxVCC) - courtesy of Carl Zeiss Meditec Inc.

1.4 Research hypothesis

Large discs are defined as optic discs measuring 1.8mm or more.[24] The importance of assessing CDR in relation to disc size was extensively studied by Jonas and co-workers[4] as well as Garway-Heath and associates.[12] They showed that the CDR 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. Large CDR are generally misdiagnosed as glaucomatous. This can be prevented if disc size is measured because we know that large discs generally have large CDR.[8,12,13] In this way, the distinction between physiologic cupping and glaucomatous cupping can be made with greater confidence.

The primary use of the scanning laser polarimeter in this study is to detect glaucomatous RNFL damage.

It is essential to measure CCT because studies have shown that CCT influences IOP measurement.[2,3,15] Thinner corneas underestimate true intraocular pressure. This can lead to a misdiagnosis and mismanagement of glaucoma in individuals with thin corneas.

2.0 EXPERIMENTAL PROCEDURE

2.1 Design

Large discs are defined as optic discs having a corrected vertical disc height measuring 1.8mm or more. Large cups are defined as CDR $\geq$ 0.6.

A case series consisting of 69 African patients with large optic discs and large optic cups, was 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 are defined as patients who are thought to have glaucoma (glaucoma suspect, primary open angle glaucoma, normal tension glaucoma) and attend the glaucoma clinic at St John Eye Hospital.

1. A glaucoma suspect is defined as a patient with one of the following three features. A nerve or RNFL defect, or visual field abnormality consistent with glaucoma, or a consistently high IOP (>22mmHg).
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.
3. Normal tension glaucoma is defined as IOP < 21mmHg with visual field defects and RNFL defects.
4. Ocular hypertension is defined as IOP > 21 mmHg and no changes on visual fields or the RNFL analysis.

2.2 Method and materials

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. A clearance certificate was issued (M070435).

Glaucoma patients with large optic discs and large optic cups, attending the glaucoma clinic at St. John Eye Hospital, were invited to participate in the study. Patients were recruited between June 2007 and September 2007. Informed consent was obtained from those patients willing to participate in the study. (Appendix A)

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 patients.[25,26] 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 refractive errors up to -8 diopters.[14] Children were excluded from the study because disc size varies in a growing eye and children do not have a stable refraction until a much older age.[14]

All 69 patients were examined by myself and a data capture sheet was filled in for each patient. The data capture sheet (Appendix B) included :

1. History.
2. Slit-lamp biomicroscopy findings which included IOP, gonioscopy and fundus examination that concentrated on the qualitative and quantitative measurements of the optic nerve head.
3. Refraction.
4. Special investigations included central corneal thickness (CCT) measurements, visual fields and retinal nerve fiber layer analysis.

A Haag Streit biomicroscope (Figure 2.1) was used to examine the eye. A 60 D lens (Figure 2.2) 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).[1]

Figure 2.1 The Haag Streit biomicroscope

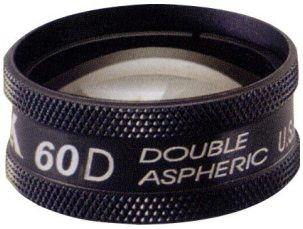

Figure 2.2 The 60 diopter lens

A calibrated Goldmann tonometer (Figure 2.3) was used to measure the intraocular pressure. This measurement was entered into the Heidelberg engineering IOPac advanced pachymeter (Figure 1.1) to obtain the A-IOP, taking CCT into account.

Figure 2.3 The calibrated Goldmann tonometer

Gonioscopy was carried out using a Volk 3-mirror-lens (Figure 2.4). The lens is used to view the angle of the eye. Many classification systems can be used to document angle anatomy. The Shaffer-Etienne classification system (Figure 2.5) was used in this study.

Figure 2.4 The Volk 3-mirror lens

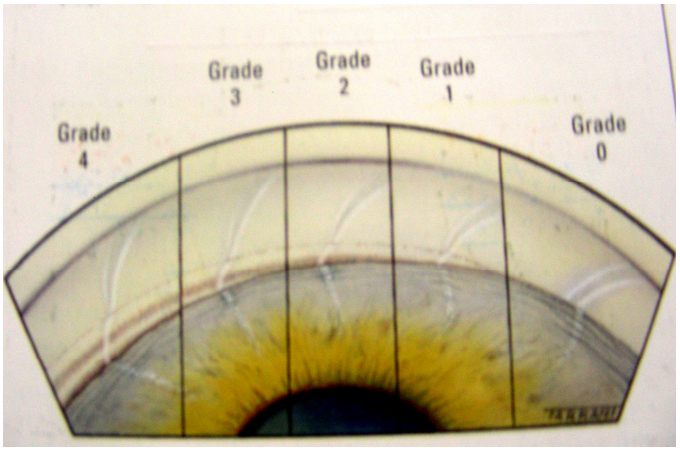

Figure 2.5 The Shaffer-Etienne classification system

According to the Shaffer-Etienne classification system:

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 line to the ciliary band.

Refraction was carried out with a Nikon handheld autorefractor (Figure 2.6) 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.

Figure 2.6 The Nikon handheld autorefractor

Visual fields were documented using the Oculus automative perimeter (Figure 2.7). This documented any functional loss or progression of function loss by the nerve over time.

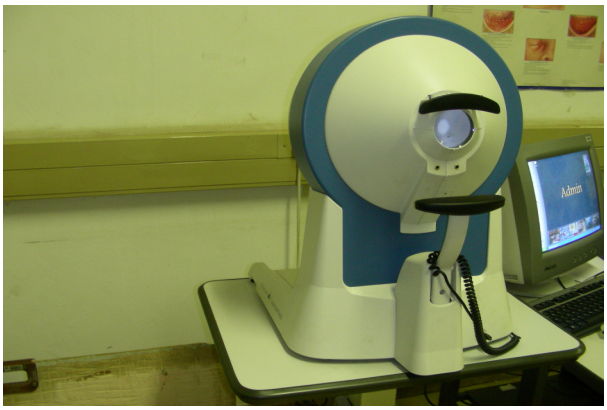

Figure 2.7 The Oculus automative perimeter – used to measure visual fields

A retinal nerve fiber analysis was done with a scanning laser polarimeter (Figure 2.8) to confirm the presence or absence of glaucomatous retinal nerve fiber layer defect. This was based on the nerve fiber index, TSNIT (temporal, superior, nasal, inferior, temporal) graph and parameters and the deviation map (Figure 1.3 and Figure 1.4).

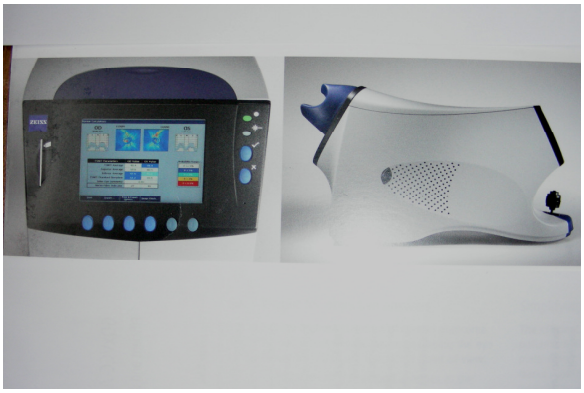

Figure 2.8 The scanning laser polarimeter (GDxVCC)

The excel data base (Figure 2.9) was used for data summary. Statistics were performed using the statistical software (Figure 2.9) Stata version 8 (Stata Corporation, College station, Texas, USA).

Figure 2.10 Excel database and Stata analysis and statistical software program

3.0 RESULTS

138 eyes of 69 African patients were evaluated. 41 (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.

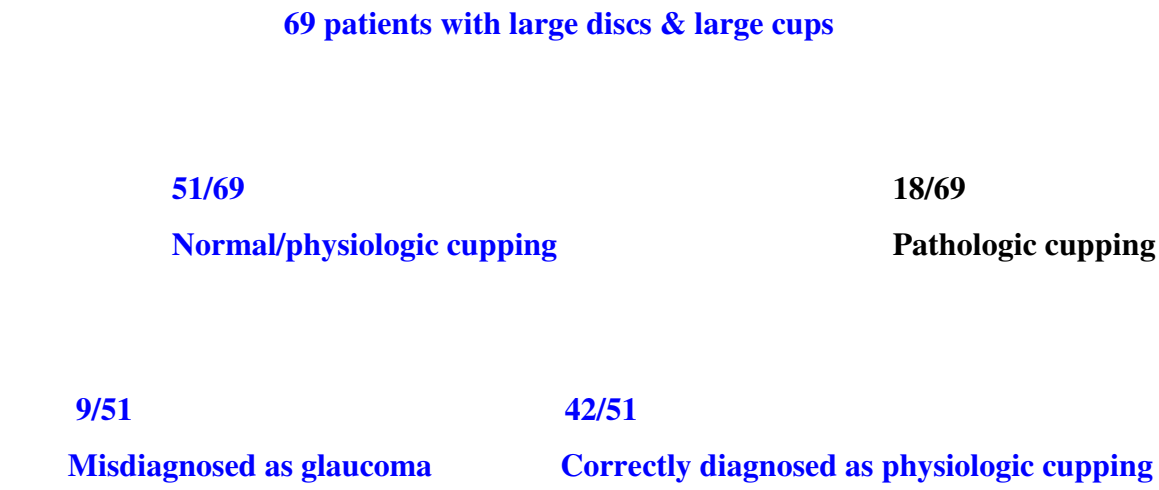

Figure 3.1 Subsections of patients in the study

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 antiglaucoma medications. The main reason for the misdiagnosis was an increased CDR in the presence of a large disc.

3.1 Outcome measures

- central corneal thickness (CCT)
- 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 fiber layer analysis
- visual fields

3.1.1 Central corneal thickness (CCT)

There were no opaque corneas. CCT was measured using the Heidelberg engineering IOPac advanced pachymeter (Figure 1.1). CCT ranged between 454µm and 618µm. The mean CCT was 516µm±37.5µm. 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.

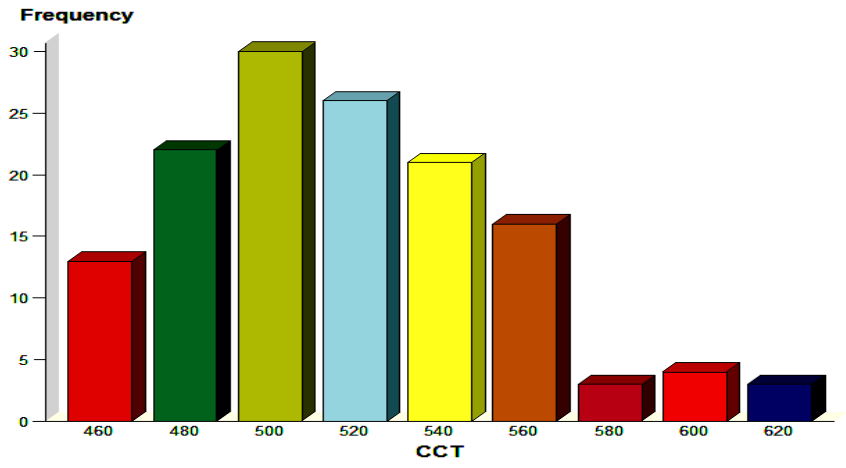

Figure 3.2 Distribution of central corneal thickness

3.1.2 Adjusted intraocular pressure (A-IOP)

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.

3.1.3 Corrected vertical disc height (VDH)

Vertical and horizontal disc diameters were measured. The VDH and the horizontal disc diameters (HDD) were measured using the beam of a Haag Streit biomicroscope and a 60D Nikon lens with a correction factor of 1.02. The VDH ranged between 1.9mm and 3.2mm (mean±SD, 2.3±0.26mm). The HDD ranged between 1.7mm and 2.9mm (mean±SD, 2.1mm±0.21mm).

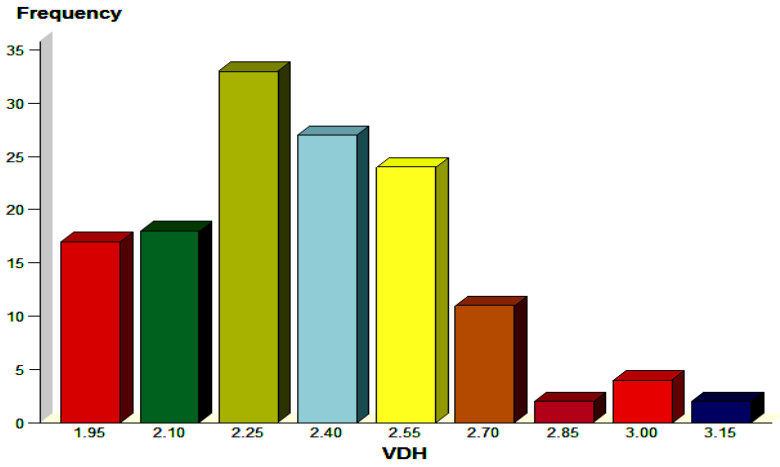

Figure 3.3 Distribution of corrected vertical disc height

3.1.4 Vertical cup to disc ratio (CDR)

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

3.1.5 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. This is in keeping with the findings of the Blue Mountains Eye Study,[24] which found that there was an increase in vertical CDR with an increase in VDH.

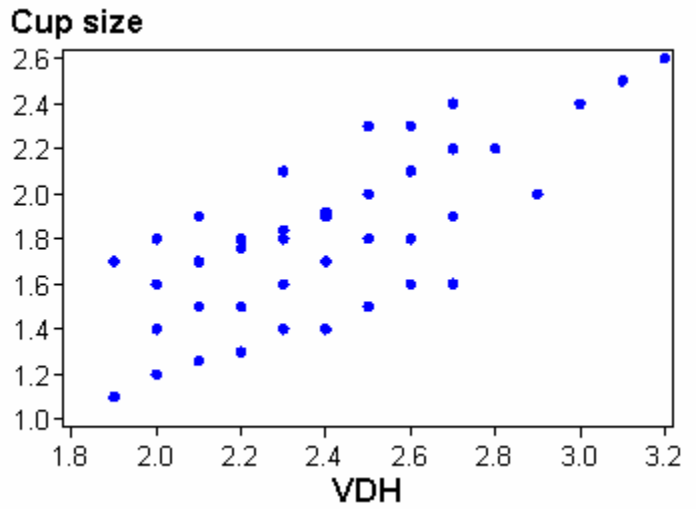

Figure 3.4 The relationship between VDH and vertical cup height

3.1.6 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.

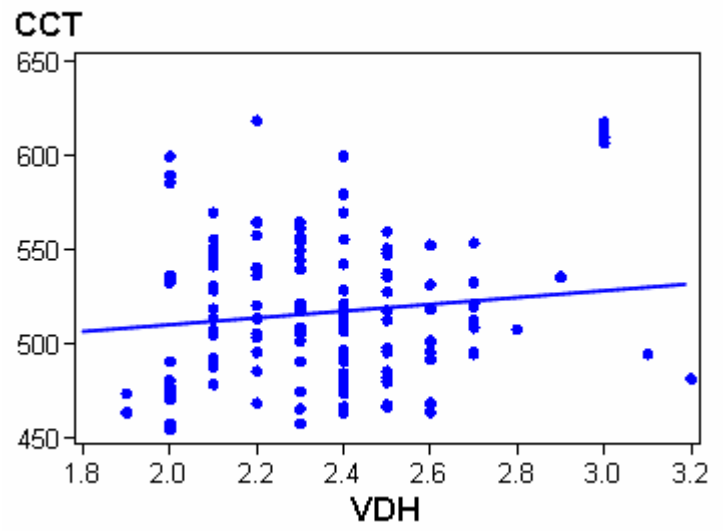

Figure 3.5 The relationship between VDH and CCT

3.1.7 Retinal nerve fiber 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 fiber index (NFI)

   This is the best parameter to differentiate glaucomatous and healthy eyes.[22] 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.
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.

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 fundus due to cataract formation.

3.1.8 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 looked at. 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 were 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. 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 were 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.

Table 3.1 Analysis of visual fields

Glaucoma status	**Total number of eyes=138 (100%)**
Undetermined	**18 (13%)**
Patients with the correct diagnosis of physiologic cupping	**84 (61%)**
Patients diagnosed with glaucoma	**36 (26%)**

4.0 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 fiber layer. However, 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.[14] 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.

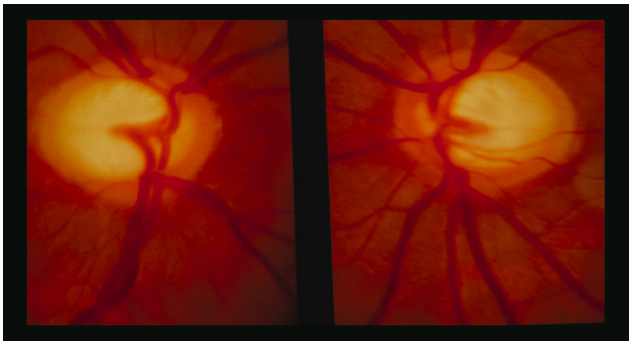

Figure 4.1 Large discs with large cups

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 Whites in the same city.[27] A study done by Rotchford et al[28] 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 White counterparts.

African patients have larger optic disc sizes when compared to their White counterparts. This was shown by Chi et al and Varma et al in their studies.[6,7] Thirdly, African patients have thin central corneal thickness when compared to their White counterparts.[2,3,15,16] By limiting the data to African patients, it was hoped that consistent results, not confounded by findings from other racial groups would be obtained.

The discussion of the results of this study will be divided into two parts:

1. Discussion of other results
2. Discussion of the results pertaining to the objectives of the study
    - The relationship between disc size and central corneal thickness
    - The proportion of patients who were misdiagnosed with glaucoma

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 fiber layer is associated with variation in disc size.

This study included 59% females and 41% males. Durukan et al[29] showed that disc sizes do not differ significantly between males and females. The Baltimore Eye Survey[27] was a population based study that included Black and White Americans. They found that the difference in disc size between males and females, was very small. In this study there was no statistically significant difference in disc size between males and females.

The Baltimore Eye Survey[27] and the Beaver Dam Eye Study[30] found no association between gender and glaucoma. However, the Barbados Eye Study[31] found that there was an increased prevalence of glaucoma in males than in females. In this study, a slight increased prevalence of glaucoma in females (19%) when compared to males (7%) was found.

The age range of patients in this study was between 18 and 87 years with a mean age of 56 years. There was no increase in disc size with age. This is in keeping with the Baltimore Eye Survey[27] that showed no association between disc size and age.

Most of the patients diagnosed with glaucoma were over the age of 50 (16 of the 18 patients). This is in keeping with the findings of the Beaver Dam Eye Study[30] that showed that the prevalence of glaucoma increases with an increase in age.

Blacks have larger discs when compared to their White counterparts.[6,7] 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.[10] 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 Blacks (1.96±0.16) compared to the VDH of Caucasians (1.82±0.15).[10] This study showed much larger disc sizes, possibly due to genetic variation. There was a normal gausian distribution for VDH (Figure 3.3).

Large cups were defined as a cup-disc ratio greater than 0.6. The Blue Mountains Eye Study showed that there was an increase in cup to disc ratio with an increase in disc size.[8,24] The researchers stated that for each millimeter increase in disc diameter there was an increase in cup to disc ratio of 0.27. Beck et al[9] also reported that large discs have proportionately large cup to disc ratios in the normal eyes of Black subjects. The data from our study showed that there was a direct linear relationship between vertical disc height and vertical cup height (Figure 3.4).

Central corneal thickness influences intraocular pressure measurements. The mean central corneal thickness in the normal human eye is 545µm.[16] 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.[2] A study conducted by LaRosa et al (2001) showed that African-Americans have thinner

corneas than Caucasians, therefore the intraocular pressures in Black patients may be underestimated.[3]

In this study, no correlation could be found between disc size and CCT. The Pearson correlation co-efficient was 0.12667. Pakravan et al[2] showed that there was an inverse relationship between disc size and CCT in African-American patients, but that this was not statistically significant.

To diagnose glaucoma, the following criteria were used: an increased intraocular pressure; structural changes of the optic nerve head; visual field changes and corresponding retinal nerve fiber 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 fiber layer analysis to assist with the diagnosis. It is important to bear in mind that during early glaucoma, there may not be visual field defects.

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.

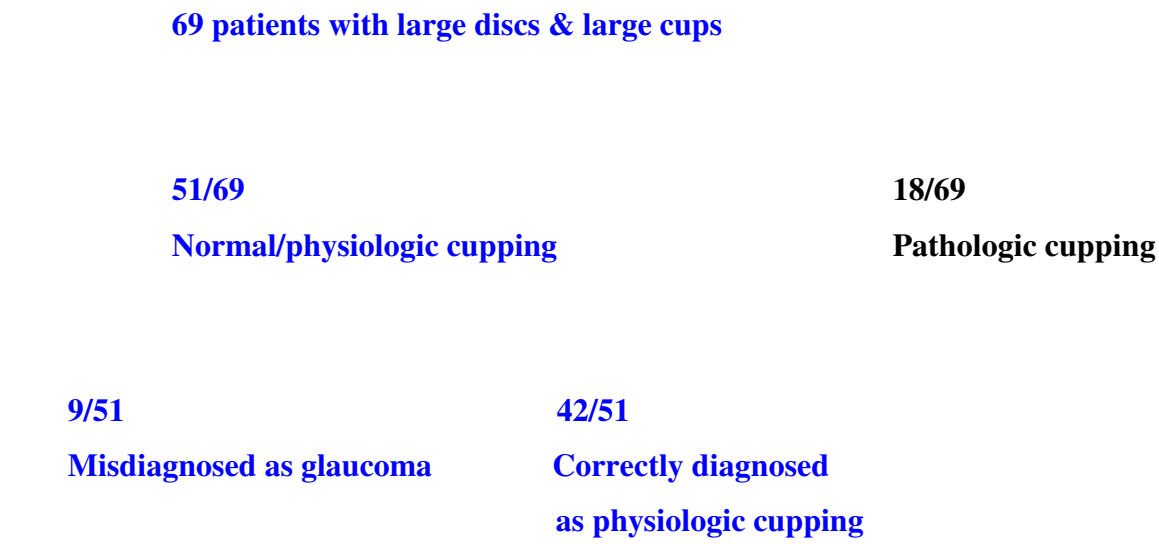

Figure 4.2 Subsections of patients in the study

A significant number of patients in the group of patients with large discs (51/69) had physiologic 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. 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[32] showed that larger discs were more likely to be misdiagnosed with glaucoma than were smaller discs. Furthermore, Healey et al,[8] Garway Heath et al,[12] Jonas et al[13] correlated cup size to disc size so that larger discs have larger cup sizes. 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 intraocular pressure 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 fiber layer of this patient showed no retinal nerve fiber layer defects.

The above illustrates how a patient may suffer morbidity through misdiagnosis.

Other morbidity issues suffered include :

a) The psychological trauma of having a potentially blinding eye condition.
b) The unnecessary cost of glaucoma medication or surgery.
c) The cost of transport for regular consultation.
d) Unnecessary costs for the hospital, the tax-payer and the patient (in addition to transport cost).
e) Side effects of medication use.
f) The extra burden on doctors in having to see vast numbers of patients regularly.
g) Patients are bound to life-long treatment.
h) The complications of surgery.

Although the literature reports an increase incidence of glaucoma in African-Americans and African patients, one has to be very careful in diagnosing a patient with glaucoma, because the possibility of physiologic cupping in African patients with large discs must be considered.

There are limitations in this study is that it is a case series with only 69 patients. Another limitation is that of observer bias especially when the disc size and the cup size is measured by a single examiner.

5.0 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. It is important to bear in mind that patients who have large discs are more likely to have large cups. Measuring these parameters will 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 intraocular pressures, 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). In the study carried out by Pakravan et al[2] an inverse correlation between CCT and disc size in African-American patients was shown but this was not statistically significant. In this study, the researchers found no correlation between CCT and disc size. The Pearson correlation co-efficient was 0.13.

APPENDIX A

PATIENT INFORMATION AND CONSENT FORM

Patient information

Good day. My name is Dr. Soma. I am a registrar in the department of ophthalmology. I am doing a study on glaucoma, to see whether a measurement on the eye (the disc) that has traditionally been used to assess glaucoma, can be used to make certain assumptions. The study will include patients from the glaucoma clinic who have large discs. From these patients, the study will allow me to determine how many patients have normally large cups and how many have glaucomatous large cups. I would also like to find a relationship between disc size and corneal thickness. There will be no difference in the treatment you receive and no experiment will be performed.

Consent form :

Hospital :_____
Clinical department :_____

I, _____, the undersigned, hereby consent to voluntarily participate in the study . I understand the aim of the study which has been explained to me. I further also consent to allow information to be used from my file, without my name being mentioned.

I am aware that I do have the right not to participate or to discontinue participation at any time without prejudicing any treatment that is required for existing or future medical conditions.

Signature of the patient:

_____

Witness 1 :_____
Witness 2 :_____

Date :_____ Time :_____

APPENDIX B

DATA CAPTURE SHEET

Date :
Patient number :
Age :
Race :
Gender :
Address :
Telephone number :

History :

Duration of symptoms
Previous treatment with antiglaucoma medications & duration of use
Previous history of eye surgery
Family history of glaucoma
Medical history (diabetes, hypertension and vascular disease)

Examination :

VA
BCVA/Refraction
Anterior segment
Cornea
Pupil
Lens
Intraocular pressure
Gonioscopy
Fundus examination
Disc size(vertical and horizontal)
Vertical cup to disc ratio
ISNT rule
Disc haemorrhages
Scleral rim/Peripapillary atrophy

ISNT rule is a pattern of relative thickness of the inferior, superior, nasal and temporal rim of optic disc.

Special investigations :
VF (Oculus)
Retinal nerve fiber analyser (GDxVCC)
Refraction (Autorefractor)
Pachymetry (Measures central corneal thickness)

Management :
Medical or surgical

REFERENCES

1. Hitchings RA, Migdal C, Bechetoille A, et al. Terminology and guidelines for glaucoma. 2nd ed. Italy: Editrice DOGMA s.r.l, 2003:1-13,1-19,1-20.

2. Pakravan M, Parsa A, Sanagou M, et al. Central corneal thickness and correlation to optic disc size: A potential link for susceptibility to glaucoma. *Br J Ophthalmol* 2007;**91**:26-8.

3. LaRosa F, Gross R, Orengo-Nania S. Central corneal thickness of Caucasians and African-Americans in glaucomatous and non-glaucomatous populations. *Arch Ophthalmol* 2001;**119**:23-7.

4. Jonas JB, Bergua A, Schmitz-Valckenberg P, et al. Ranking of optic disc variables for detection of glaucomatous optic nerve damage. *Invest Ophthalmol Vis Sci* 2000;**41**:1764-73.

5. Ansari-Shahrezaei S, Maar N, Biowski R, et al. Biomicroscopic measurement of the optic disc with a high-power positive lens. *Invest Ophthalmol Vis Sci* 2001;**42**:153-7.

6. Chi T, Ritch R, Stickler D, et al. Racial differences in optic nerve head parameters. *Arch Ophthalmol* 1989;**107**:836-9.

7. Varma R, Tielsch JM, Quigley HA, et al. Race, age, gender and refractive error-related differences in the normal optic disc. *Arch Ophthalmol* 1994;**112**:1068-76.

8. Healey PR, Mitchell P, Smith W, et al. Relationship between cup-disc ratio and optic disc diameter: The Blue Mountains Eye Study. *Aust N Z J Ophthalmol* 1997;**25**:S99-101.

9. Beck RW, Messner DK, Musch DC, et al. Is there a racial difference in physiologic cup size? *Ophthalmology* 1985;**92**:873-6.

10. Quigley HA, Brown AE, Morrison JD, et al. The size and shape of the optic disc in normal human eyes. *Arch Ophthalmol* 1990;**108**:51-7.

11. Girkin CA, McGwin G Jr, Long C, et al. Subjective and objective optic nerve assessment in African-Americans and Whites. *Invest Ophthalmol Vis Sci* 2004;**45**:2272-8.

12. Garway-Heath DF, Ruben ST, Viswanathan A, et al. Vertical cup/disc ratio in relation to optic disc size: Its value in the assessment of the glaucoma suspect. *Br J Ophthalmol* 1998;**82**:1118-24.

13. Jonas JB, Zach FM, Gusek GC, et al. Pseudoglaucomatous physiologic large cups. *Am J Ophthalmol* 1989;**107**:137-44.

14. Susanna R Jr, Vessani RM. New findings in the evaluation of the optic disc in glaucoma diagnosis. *Curr Opin Ophthalmol* 2007;**18**:122-8.

15. Brandt JD, Beisser JA, Kass MA, et al. Central corneal thickness in Ocular Hypertension Treatment Study (OHTS). *Ophthalmology* 2001;**108**:1779-88.

16. Doughty MJ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. *Surv Ophthalmol* 2000;**44**:367-408.

17. Jonas JB. Optic disc size correlated with refractive error. *Am J Ophthalmol* 2005;**139**:346-8.

18. Mitchell P, Hourihan F, Sandbach J, et al. The relationship between glaucoma and myopia: The Blue Mountains Eye Study. *Ophthalmology* 1999;**106**:2010-15.

19. Wu SY, Nemesure B, Leske MC. Refractive errors in a Black adult population: The Barbados Eye Study. *Invest ophthalmol Vis Sci* 1999;**40**:2179-84.

20. Sommer A, Katz J, Quigley HA, et al. Clinically detectable nerve fiber atrophy precedes the onset of glaucomatous field loss. *Arch Ophthalmol* 1991;**109**:77-84.

21. Budenz DL, Anderson DR, Varma R, et al. Determinants of normal retinal nerve fiber layer thickness measured by stratus OCT. *Ophthalmology* 2007;**5**:1-5.

22. Lester M, Garway-Heath D, Leimj H. Optic nerve head and retinal nerve fiber analysis. Italy: Editrice DOGMA s.r.l, 2003:101-2.

23. Paczka JA, Friedman DS, Quigley HA, et al. Diagnostic capabilities of frequency-doubling technology, scanning laser polarimetry, and nerve fiber layer photographs to distinguish glaucomatous damage. *Acta Ophthalmol Scand* 2001;**131**:188-97.

24. Crowston JG, Hopley CR, Healey PR, et al. The effect of optic disc diameter on vertical cup to disc ratio percentiles in a population based cohort: The Blue Mountains Eye Study. *Br J Ophthalmol* 2004;**88**:766-70.

25. Jonas JB, Gusek GC, Naumann GOH. Optic disc morphology in high myopia. *Graefes Arch Clin Exp Ophthalmol* 1988;**226**:587-90.

26. Jonas JB, Dichtl A. Optic disc morphology in myopic primary open-angle glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1997;**235**:627-33.

27. Tielsch JM, Sommer A, Katz J, et al. Racial variations in the prevalence of primary open angle glaucoma: Baltimore Eye Survey. *JAMA* 1991;**266**:369-74.

28. Rotchford AP, Johnson GJ. Glaucoma in Zulus: A population-based cross-sectional survey in a rural district in South Africa. *Arch Ophthalmol* 2002;**120**:471-8.

29. Durukan AH, Yucel I, Akar Y, et al. Assessment of optic nerve head topographic parameters with a confocal scanning laser ophthalmoscope. *Clin Experiment Ophthalmol* 2004;**32**:259-64.

30. Klein BEK, Klein R, Sponsel WE, et al. Prevalence of glaucoma: The Beaver Dam Eye Study. *Ophthalmology* 1992;**99**:1499-1504.

31. Leske MC, Connell AM, Schachat AP, et al. The Barbados Eye Study. Prevalence of open angle glaucoma. *Arch Ophthalmol* 1994;**112**:821-9.

32. Heijl A, Mölder H. Optic disc diameter influences the ability to detect glaucomatous disc damage. *Acta Ophthalmol* 1993;**71**:122-9.