MORPHOMETRIC STUDY OF THE OPTIC NERVE HEAD IN NORMAL HAUSA NIGERIAN ADULTS, USING OPTICAL COHERENCE TOMOGRAPHY

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DECLARATION

I hereby declare that this research work titled "**Morphormetric study of the Optic Nerve Head in Normal Hausa Nigerian Adults, Using Optical Coherence Tomography"** was conducted by me under the supervision of DR M.H. Modibbo and it has not been submitted anywhere partly or in full for academic or examination purpose. In circumstances where I mentioned someone else's work, I have given acknowledgement by way of references.

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CERTIFICATION

This is to certify that this research work and the subsequent write up by Nuraddeen Jaafar were carried out under my supervision

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APPROVAL

This dissertation has been examined and approved for the award of MASTERS DEGREE IN ANATOMY.

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DEDICATION

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TABLE OF CONTENTS

CHAPTER ONE

CHAPTER TWO

CHAPTER THREE

CHAPTER FOUR

CHAPTER FIVE

LIST OF TABLES

LIST OF FIGURES

LIST OF PLATES

LISTS OF APPENDICES

ABSTRACT

The optic nerve is the neural tract of the human body that is responsible for special sensation of sight. Glaucoma and other degenerative retinal conditions specifically target and damage the optic nerve. These progressive irreversible conditions are recognised by changes on the optic nerve head. Early diagnosis of these conditions is therefore key to overall prognostic outcome in managing these diseases. Subjective assessments of the optic nerve head is mostly employed in our environment in making diagnosis of glaucoma and other progressive optic neuropathies. The aim of this study was to evaluate the optic nerve head parameters with objective measurements among our population using Optical coherence tomography. This would provide a reference value for our community and help for early diagnosis and management of optic neuropathies. Six hundred and eighty four eyes of 342 healthy Hausa adults were examined using OCT. The mean optic disc area, rim area and cup disc ratio (CDR) found in the study were 2.35mm^2, 1.76mm^2 and 0.44 respectively. There was a positive correlation observed between all the disc parameters with the disc area (which is of clinical and statistical significance). It was observed that most of the optic disc parameters in the subjects were larger in the left than the right eyes. This difference was however not statistically significant in all the analysed parameters. After correction for gender, still no statistically significant difference was observed. Most of the disc parameters showed a statistically significant difference between male and female. Males were found to have larger (2.38mm^2) than the female subjects (2.29mm^2) and significantly larger CDRs. Significant age difference was observed among various disc parameters. Older subjects had larger disc area. However, this difference was not statistically significant. There was a significant decline of the neuroretinal rim area observed in the older subjects against the young ones. In

conclusion, this study has provided a reference data of the optic nerve head parameters in Hausa adults for use as a baseline tool for the diagnosis and management of optic nerve head disorders.

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND

The eye is the organ responsible for the special sense of vision. Impulses are received and coordinated by the structures of the eye ball (globe), integrated in the complex neural system of the retina and transmitted to the visual cortex by the optic nerve (Dacey, 2000). The retina is the innermost layer of the eye wall and is composed of light sensitive nerve tissue. It is a thin delicate layer with surface area of 266mm^2 and has about 200million neurons (Duane, 2003).

The retina is composed of the following layers; pigmented epithelium, rods and cones photoreceptor layer, external limiting membrane, outer nuclear layer, outer plexiform layer, inner nuclear layer, inner plexiform layer, ganglion cell layer, nerve fibre layer and internal limiting membrane. The ganglion cell neurons converge as the nerve fibre layer to exit the eye through the sclera as the optic nerve (Duane, 2003). Being a transparent structure, the major landmarks are the optic nerve head (ONH), retinal vessels, the macula area and the peripheral retina (Chen *et al.*,2000).

Optic nerve head is also termed the optic disc, papilla or simply the *disc* (Duane, 2003). It is the very beginning of the optic nerve, the 2nd cranial nerve that is visible on retinal examination (Plate I). Axons of the retinal ganglion cells form nerve bundles that converge on the ONH in four zones (superior, inferior, medial and lateral) and exit the eye posterioly through the lamina cribrosa of the sclera to become the optic nerve. There is a central pale depression of the disc termed the optic cup. This contains no retinal tissue and bares the central retinal vessels (artery and vein). The area between the central cup and margins of the disc is the neuroretinal rim

(NRR). It looks pinkish red ophthalmoscopically as it contains the nerve fibres with fine capillary network (Hoyt *et al.*, 1972).

Morphormetry of the ONH parameters is used to correlate normal from pathologic conditions of the optic nerve. Such parameters are disc size, NRR area, NRR thickness per quadrant, cup area, cup to disc ratio (CDR), and peripapillary nerve fibre layer thickness. Primary retinal lesions, neuroophthalmic conditions or primary optic nerve disorders present with characteristic ONH findings that enable making diagnoses and monitoring progression of these disorders (Paunescu *et al.*, 2004).

Different studies have shown variations in the topography of the ONH parameters among sexes (Zangwill *et al.*, 2004) and races (Hermann *et al.*, 2004; Hsu *et al.*, 2012). Samarawickrama *et al.*, (2012) observed that neuroretinal rim thickness per quadrant shows significant variation among different populations. Also, normal ocular parameters like ocular axial length (Oliveira, *et al.*, 2007 ; Knight *et al.*, 2012) and refractive power of the eye (Migliors *et al.*, 1994) are shown to affect some ONH parameters.

Evaluation of the ONH can be done using qualitative techniques which are clinical ophthalmoscopy and stereophotography (Hermann *et al.*, 2004).These methods are subjective with high interobserver variability. Quantitative evaluation using imaging techniques like optical coherence tomography gives accurate and more objective measurements. This helps in early detection of optic disc and retinal disorders, providing means of early diagnosis and objective monitoring of abnormalities like glaucoma (Lawan *et al*., 2014).

Optical coherence tomography (OCT) is a non contact, non invasive imagine technique which provides in vivo cross-sectional image of the various parts of the retina including the ONH that are reproducible, quantitative and objective (Michael., *et al.,* 2000). This technique was introduced in 1991 and was later employed in the field of ophthalmology as a diagnostic means in objective evaluation of ocular tissues in various eye conditions (Optical Coherence Tomography Wikipedia). The OCT machine is a computer assisted optical instrument that uses the principle of low coherence interferometry to measure the echo time delay and intensity of backscattered and back reflected light form internal microstructure in biological tissues (Michael *et al*., 2000). In the eye, it provides cross sectional images of the optic nerve head and the retina with high resolution tomographic sections with $\leq$ 10 μm axial resolution (Michael *et al*., 2000).

Imaging in OCT is analogous to ultrasound but light is used instead of sound. A near infrared light beam is projected to the retina and an optical interferometer inside the machine detects reflection time delay and back scattering of light. Each retinal layer and the optic nerve head have different optical reflectivity which allows construction of high resolution B-scan images (Savini *et al*., 2005).

1.2 Uses of Optical Coherance Tomography

Commonest indication of optic nerve head analysis of OCT technology is in the diagnosis and management of glaucoma (Chen *et al.,* 2000). It shows objective measurements of the changes of various parameters of optic disc including the area, cup the neuroretinal rim and the cup disc ratio (Cheung *et al.,* 2008). It also gives objective measurement of the retinal thickness in the peri-papillary area which is key in evaluation of glaucoma (Zangwill *et al.,* 2004; Hess *et al.,* 2005).

Optical coherence tomography is also useful in evaluation of retinal structures in various disease conditions like age related macular degeneration, macula hole, diabetic retinopathy, retinal edema, retinal detachment amongst others (Hee *et al.,* 1996 ; Gasterland *et al.,* 2001).

1.3 Statement of Research Problem

Accurate and reliable measurement of ONH parameters is important in early detection and monitoring treatment of certain eye diseases like glaucoma. It also helps in identifying retinal degenerating conditions, neuroophthalmic conditions like compressive optic neuropathy and congenital defects of the optic nerve (Borboni *et al.,* 2009). As each individual parameter of the ONH is crucial in disease diagnosis, objective methods of measurements are necessary to obtain accuracy in evaluation (Sihota *et al.,* 2006).

1.4 Justification of the Study

Glaucoma and other slow progressive retinal disorders are common problems in our society (Lawan, 2006). Analysis of the parameters of the ONH using objective measurement techniques in normal Nigerian adults is therefore crucial in establishing a normative data for our population. This is because ONH changes are the hallmark of glaucoma progression. This will help in better appreciation of changes that occur in disease process involving the optic nerve and in distinguishing normal from a suspicious appearance of the optic nerve head (ONH), due to the background knowledge of the clinicians of the normal reference value of its parameters among the population of our community.

To the best of my knowledge, no study was conducted in Nigeria to provide a normative database on the ONH parameters of normal Nigerian adults using OCT scanning.

1.5 Aim

To evaluate the topographic parameters of the optic nerve head of normal Hausa Nigerian adults, using optical coherence tomography.

1.5.1 Objectives

1. To measure the optic nerve head indices in normal Hausa adults.
2. To assess bilateral asymmetry of the optic nerve head parameters among the study population
3. To evaluate the relation of age and gender of the study population on the optic nerve head parameters
4. To provide reference value of optic nerve head parameters among Hausa adults

CHAPTER TWO

LITERATURE REVIEW

2.1 OVERVIEW

The ability to correctly diagnose and treat various acquired pathologies of the optic nerve and retina is largely dependent on our understanding of the normal retinal nerve fibre layer (RNFL) and optic nerve head (ONH) with its variations (Lawan *et al*., 2014). With the advent of computerized image analysis instrumentation, more recent information about the optic nerve head has been determined. Assessment of the optic disc parameters is of utmost importance not only for the diagnosis of optic nerve anomalies, glaucoma and neuro-ophthalmologic diseases but also for the follow-up of the management of these conditions (Tariq *et al*., 2012). Quantitative stereometric and volumetric information of the optic disc are a superior means of assessing these parameters (Tariq *et al*., 2012). Several imaging methods are currently employed in clinical practice to obtain reproducible data of the optic disc parameters.

A change in the appearance of the optic nerve is a hallmark of glaucoma (Khurana, 2007). The observed changes in the optic nerve are associated with the loss of retinal ganglion cell axons (which constitute the nerve fiber layer of the retina) (Khurana, 2007). As the axons of the retinal ganglion cells degenerate, there is a decrease in the volume of neural tissue in the optic nerve, resulting in an enlarged optic cup and a change in topographic configuration. Detecting and diagnosing progressive damage from glaucoma depends on identifying these changes and the corresponding loss of visual function (Lawan *et al*., 2014). Clinical examination of the optic nerve has been possible since the development of the direct ophthalmoscope by Helmholz in 1851 (Kirsch & Anderson, 1973). Assessment of the appearance of the optic nerve head

(ONH) is an important part of the glaucoma examination. Before the development of advanced technologies, careful comparison of simultaneous stereo-optic nerve photographs was, perhaps, the clinician's best tool for detecting progressive optic nerve damage (Andrew & Felipe, 2014). The photographs can be stored for subsequent study and review. Unavoidably, however, this technique is qualitative and subjective because it involves the interpretation of subtle findings by the clinician (Duane, 2003).

The need for accurate, reproducible, and cost-effective quantitative techniques of assessing the optic disc, along with appreciation of the limitations of subjective clinical observation, stimulated the development of new technologies (Hoyt *et al*., 1972). Many of the early innovative techniques developed for quantitative analysis of the ONH were not clinically practical. They suffered from problems with reproducibility, were cumbersome or too costly for clinical use, and did not become widely available (Tariq *et al*., 2012).

Recent technological advances have stimulated the development of a new generation of instruments; Optical Coherence Tomography (OCT) and the confocal scanning laser ophthalmoscopes (cSLOs) for quantitative examination of the ONH (Michael *et al*., 2000). The progresses in microcomputers, diode lasers and digital image acquisition have allowed improved capture, storage, retrieval, and analysis of optic nerve topography (Michael *et al*., 2000). It appears that accurate and reproducible optic nerve topographic data are now obtainable with OCT and cSLO systems. These methods do not only give quantitative measurements of disc parameters but also provide accurate means of early detection of subtle changes in the disc (Shaun *et al*., 2008)). These new knowledge should allow us to better understand interindividual and intraindividual variations of retinal and disc topography and to make prompt intervention even in early stages of diseases (Jonas *et al*., 2003).

Optical coherence tomography (OCT; Zeiss-Humphrey Instruments, San Leandro, CA) provides high-resolution direct measurements and cross-sectional imaging of the retina, the Optic Nerve Head (ONH) and the RNFL (Michael *et al*., 2000). The operation of the OCT is analogous to ultrasound B-scan imaging, except that light is used rather than sound waves (Michael *et al*., 2000).

Measurements are performed with a fiber optically integrated Michelson interferometer with a short coherence length superlumanescent 850nm diode source (Hee *et al*., 1996). Light is directed onto a partially reflecting mirror and is split into reference and measurement beam which is then reflected from the eye with minutely different time delays depending on its internal microstructure (Michael *et al*., 2000). The light in the reference beam is reflected from the mirror at a variable distance that produces a variable but known time delay (Michael *et al*., 2000).

The light from the eye, consisting of multiple echoes, and the light from the reference mirror, consisting of a single echo with a known delay are combined and detected (Michael *et al*., 2000). The echo structure of the reflected measurement beam, representing the layers of the retina, is then determined by electronic processing (Hee *et al*., 1996).

2.2 THEORETICAL CONSIDERATIONS AND EMBRYOGENESIS OF THE OPTIC DISC

The optic nerve head is formed late in the embryonic period as the optic stalk encloses the hyaloid artery in the eighth week, 20-mm stage (Orgul & Cioffi, 1996). At this stage, the hyaloid artery is inside the hyaloid canal, which communicates with the primary vitreous (Orgul & Cioffi, 1996). Bergmeister's papilla consists of a cone-shaped mass of glial cells at the mouth of the hyaloid canal (23- to 32-mm stage), where the hyaloid artery exits from the disc (Tam *et al*., 2000). From the hyaloid artery, the vascular buds develop (the 13th week, 96-mm stage) within the Bergmeister's papilla and through it into the nerve fiber layer of the retina (Chen *et al*., 2000). The glial cells form the sheaths of these vessels (Tam *et al*., 2000). Eventually, the hyaloid artery disappears before birth, Bergmeister's papilla becomes atrophic, and the physiologic cup of the optic disc develops at the 15th week of gestation (Anderson *et al*., 1969).

Although there are many different theories, it is still unclear which factors determine the ultimate individual optic nerve dimensions (Orgul & Cioffi, 1996). Studies have provided many different postulates that were considered as possible mechanisms (Provis *et al*., 1985; Jonas *et al.*, 1991.) These include: different number and variable caliber of optic nerve fibers (Jonas *et al.*, 1991), different number and volume of neuroglial cells, different number of ganglion cells and/or varying percentages of ganglion cells lost during embryogenesis (Sefton & Lam, 1984; Provis *et al*., 1985). A study on development of retinal vasculature emphasised the effect of different times in embryogenesis when final fixation of the scleral lamina cribrosa occurs (Jonas *et al.*, 1991). The study also highlighted that final ONH dimensions are dependent on alignment between the lamina cribrosa fixation and growth of the optic nerve fibers. This factor was also highlighted by Dandona *et al*. (1990). Embryogenesis therefore account for high interindividual variation in normal optic disc size as yet with more optic nerve fibers are usually associated with larger optic discs (Dandona *et al*., 1990). This is due to sequence of events that occurs during embryologic development and continues postnatally after birth (Quigley *et al.*, 1991).

Rakic and Riley (1983) studied embryologic development of the fetal rhesus monkey. They observed that the cross-sectional area of the optic nerve increased steadily whereas the total number of axons showed a rapid initial increase followed by a biphasic decrease (Rakic and Riley 1983). The number of axons increased rapidly during the first 10 wk of embryonic life with the peak number doubled that of the average adult (Mikelberg *et al*., 1989). This was found to be followed by a 3-wk period in which the number of optic nerve axons remained approximately constant after which a rapid decrease in the number of axons occurred (Dolman *et al*., 1980). This reduction in optic nerve fibers then continued at a much slower rate in the initial months after birth until the average adult number of approximately 1.2 million was reached (Tam *et al*., 2000). It was proposed that this check in the rate of growth of the fibres resulted to a substantial loss of retinal ganglion cells and their axons (Quigley *et al.*, 1987). This is presumably caused by the death of fibers (apoptosis) that failed to synapse with appropriate connections in the brain (Quigley *et al.*, 1987).

It is thought that the total number of axons formed early in development may determine the optic disc size, whereas the cup size may be related to the empty space left after loss of axons in later developmental stages (Tam *et al.*, 2000). The slit like pores in the sclera lamina at the bottom of the optic cup are believed to provide indirect evidence for this hypothesis (Dandona *et al.,* 1990). Axon or axon-like structures must have been in place during the formation of the lamina cribrosa meshwork for the pores to exist (Jonas *et al.*, 1991).

2.3 NORMAL OPTIC DISC DIMENSIONS

Optic disc parameters that are of most clinical significance are the size (disc size), nueroretinal rim (NRR), optic cup area, cup to disc ratio (CDR) and peripapillary nerve fibre layer (Duane, 2003). Peripapillary nerve fibre layer thickness (RNFL) is most studied separately in most studies as it gives independent information on the degenerative optic disc conditions like glaucoma (Kanski, 2011).

2.3.1 Optic Disc Area

This is the surface area bounded by the optic disc outline; the optic disc outline is identified by marking the end of the retinal pigment epithelial (RPE) layer at the disc margin on either side at the scleral canal and calculating the disc diameter in each individual linear scan; the optic disc outline represents an ellipse that is generated by connecting the RPE markers at each clock hour of the disc (Barbara *et al*., 2010).

Optic disc area is highly variable from one person to another as well as between the two eyes of the same person (Tam *et al.,* 2000). Disc area observed in individuals may reflect ethnic or racial variation (Girkin *et al*., 2005). There are individuals with large optic nerve heads and those with small optic nerve heads, both of which are normal (Jonas *et al.*, 1989[c]; Jonas *et al.*, 1999). Relative hypoplasia (small disc) is clinically detectable in at least 10% of the population (Townsend & Comer, 1987 ; Townsend, 1991). The mean optic disc diameter has been found to be between 1.47 mm^2 and 1.89 mm^2, depending on the method of measurement and diversity of patient population used (Jonas *et al.*, 1999).

Optic discs that are very large or very small may be referred to as macrodiscs or microdiscs, respectively (Tam *et al*., 2000). Considering the Gaussian distribution curve, only 2.28% of optic discs fall into these categories. Optic discs which are larger than 4.09mm^2 with mean of 2.69mm^2, +2 standard deviations (SD), are defined as macrodiscs (Jonas *et al.*,1999). Macrodiscs can further be classified as primary macrodiscs or secondary acquired macrodiscs (Jonas *et al.*,1999). Primary macrodiscs may be "asymptomatic," without any morphologic or functional defects, or "symptomatic," with morphologic and functional defects such as optic pits or morning-glory syndrome and may be associated with colobomatous defects (Townsend, 1991). Secondary acquired macrodiscs are usually associated with high myopia and may continue to increase in size after birth. Microdiscs are discs which have an optic disc area that is smaller than 1.29 mm^2 (Jonas *et al.*,1989[a]).

Studies conducted on different populations have described ranges of optic disc sizes, expressed as disc area in mm^2. The Sydney Adolescent Vascular Eye (SAVE) study by Tariq *et al.,* (2012) in Australia conducted on young adult volunteers obtained a disc area of 1.98mm^2. The researchers observed that disc area was significantly larger among the Asians than that of the white subjects. Another study by Gherghel *et al.,* (2000) in a study in Switzerland on evaluation of optic nerve head among adults, found a mean optic disc area of 1.92mm^2. They used Heildenberg Retinal Tomography (HRT) protocol for optic disc examination. Hermann *et al.,* (2004) on the other hand found a mean optic disc area of 1.82mm^2 in study also conducted on white population using Confocal Scanning Laser Ophthalmoscopy (cSLO) to evaluate the ONH parameters in 882 adult volunteers. This value is lower than that reported by Nakamura *et al.,* 1999 in Japan (mean disc area of 2.15mm^2) and that by Bartz-Schmidt *et al*., 1996 (mean disc area of 2.14mm^2).

This difference may reflect significant ethnic variations as these workers used similar examination technique of a same cSLO with HRT protocol.

Varma *et al*., (1994) in a study to evaluate stereoscopic optic disc photographs of adult subjects observed a mean disc area of 2.92mm^2 among blacks significantly higher than that found in the(2.63mm^2). Similarly, a large series in Rotterdam, Netherland (Rotterdam Eye study), by Ramrattan *et al.,* (1999) where adult subjects were examined using stereoscopic methods reported larger disc area than the above studies. They found a mean optic disc area of 2.42mm^2 using stereoscopic simultaneous disc image analyser. This technique of fundus evaluation may result in slight disc magnification hence the high value.

The Vellory Eye Study by Jonas *et al.*, (2003) in India reported a slightly higher value of the optic disc area than the above studies. Using Stratus OCT, the study found a mean disc area of 2.58mm^2 which correlated positively with most of the disc parameters vis, rim area, CDR and cup volume (Jonas *et al.,* 2003). Similarly, Shaun *et al.,* (2008) in a study using stratus OCT with fast optic disc protocol reported disc area of 2.63mm^2. No statistical correlation of the disc area with refractive error among the subjects was observed (Shaun *et* al., 2008) as against what was popularised by Jonas *et al*., (1989[b]). A study by Tarannum *et al.,* (2011) also in India reported a larger value of disc area of 3.36mm^2. As the study protocol is same as that by Shaun *et al*., (2008) using stratus OCT, effect of disc magnification may be an explanation for this high value as most of the subjects had myopic refractive error.

In African population must of the published data on the optic disc parameters were on the cup disc ratio and retinal nerve fibre and only few on disc or rim area (Tharwat *et al.,* 2013 ; Lawan *et al.,* 2014). Mean disc area of 2.50mm^2 was reported by Tharwat *et al.,* (2013) in Egypt using confocal scanning ophthalmoscopy (cSLO).

The optic disc diameter can further be broken down into horizontal and vertical dimensions. A study by Jonas *et al.,* (1988[a]) in Germany showed that the average optic disc was slightly oval in form; the vertical axis was longer than the horizontal axis by approximately 7 to 10%. The mean horizontal disc diameter was found to be 1.76mm^2 (0.91–2.61 mm^2) and the mean vertical disc diameter to be 1.92 mm^2 (Jonas *et al.,* (1988[a]). This finding is also famous for many studies carried out on different populations (Kee *et al*., 1997; Gherghel *et al*., 2000; Paunescu *et al*., 2004). Shaun *et al*., (2008) in India observed that the vertical disc diameter is longer (2.04mm^2) than the horizontal (1.66mm^2) diameter. These findings are also clinically significant in predicting the refractive of the eye (Jonas *et al*., 1988[a])

2.3.2 Optic Cup

The optic cup is the central physiological excavation of the optic nerve head (Khurana, 2007). It represents the area through the sclera canal that is devoid of nerve fibres (Tam *et al.,* 2000). The shape of the physiologic cup is affected by the obliquity of the wall of the canal through the choroid and sclera (Tam *et al.,* 2000). The wall of the cup is steep where the wall of the canal is angled outward and where the canal has a wall perpendicular to the ocular coats, the cup has a sloping wall (Armaly & Sayegh, 1969). The slope of the cup may vary from one sector to another, and there is considerable individual variation in the size and shape of the chorioscleral canal and therefore of the optic cup (Kergoat *et al*., 2001). In many eyes, the optic nerve exits through a canal the passes nasally and upward into the orbit, so that the upper nasal neuroretinal rim is bounded by a steep wall when viewed from the ophthalmoscopic viewpoint, while the lower temporal wall of the cup is sloped, so that ophthalmoscopically the cup wall is, in essence, being viewed from within the cup rather than from above. In other discs, particularly those with a large cup, the walls are perpendicular to the scleral wall in all meridians (Jonas *et al*., (1999). There is also typically no evident slope of the exit canal in eyes with only a small dimple of a cup, resulting from a near-perfect match between the size of the chorioscleral canal and the amount of neuroretinal tissue (axons and glia) that comprise the optic disc (Tam *et al*., 2000).

Jonas *et al.*, (1999) reported a mean optic cup area of 0.72mm^2. A proposed division of the cup diameter into horizontal and vertical components was also evaluated for clinical assessment of configuration of the optic nerve (Jonas *et al*., 1999). The mean horizontal and vertical diameters were reported as 0.8mm and 0.77mm respectively (Jonas et al., 1999). This finding was however opposite to what is usually observed with optic disc cup in which the vertical diameter is often longer than the horizontal (Tarannum *et al.*, 2011 ; Andrew & Felipe, 2014).

Studies in India (Shaun *et al*., 2008) and in Turkey (Hakan *et al*., 2004) reported almost similar values of the optic cup of 0.87mm^2 and 0.88mm^2 respectively. The later study used cSLO with HRT protocol while the former used Stratus OCT probably explaining the similarities of the same Asian background of the subjects. Tarannum *et al*., (2011) also in India reported an optic cup area of 1.26mm^2. It is one of few studies that reported such a large cup area with use of OCT. It could be explained that the study reported large disc area (3.36mm^2) which was found to be statistically significantly correlated with the cup area.

A study in Mansoura, Egypt by Tharwat *et al*., (2013) evaluated the ONH and retinal nerve fibres (RNFL) of about 150 eyes of subjects using SD-OCT. The study reported optic cup area of 1.1mm^2 in the normal subjects which statistically and pathologically significant, smaller than that of the glaucomatous eyes of 1.8mm^2 (Tharwat *et al.*, 2013).

2.3.3 Neuroretinal Rim (NRR)

Perhaps the most important optic nerve head parameter is the neuroretinal rim (Duane, 2003). It is the nerve fibre layer tissue within the disc that surrounds the cup and bounded externally by the disc rim (peripapillary margin) (Tam *et al*., 2000). The neuroretinal rim is an important indicator of pathology and the target of ophthalmoscopic evaluation because it is the intrapapillary sum of retinal and optic nerve fibers (Airaksinen *et al.*, 1985[b]). It has been positively correlated to optic disc area; larger optic discs have larger rim areas and smaller optic discs have smaller rim areas (Britton *et al.*, 1987; Varma *et al.*, 1994).

In india, the Vellory Eye study (Jonas *et al.*, 2003) reported a mean rim area of 1.60mm^2. Shaun *et al.,* (2008) observed a slightly higher value of 1.78mm^2. In the Vellory Eye Study, optic disc evaluation was done using stereoscopic slide analysis while the later study employed OCT in optic disc assessment. Tarannum *et al.,* (2011), in a study also in India reported much larger value of mean rim area of 2.49mm2. A combined OCT and scanning Laser Ophthalmoscopy (cSLO) in examining the ONH was used in that study (Tarannum *et al*., 2011). Another study using Fundus photography among Hispanics reported a mean rim area of 2.23mm^2. This is not too far from the values given by Tsai *et al.,* (1995) of 2.13mm^2.

The configuration of the NRR is of clinical significant (Jonas *et al*., 1991). It is usually widest at the inferior optic disc rim followed by the superior, nasal, and then the temporal rim (ISNT) (Jonas *et al.*, 1991). This is proposed to be caused by a number of factors, which may include the following: (1) the diameter of the retinal arterioles, which are significantly wider in the inferotemporal arcade than the superiotemporal arcade (Townsend & Comer, 1987; Jonas *et al.*, 1993;Marsh- Tootle *et al.*, 1994) (2) the greater visibility and detectability of the nerve fiber bundles in the inferotemporal arcade (Dandona *et al.*, 1990; Jonas *et al.*, 1993). (3) location of the foveola 0.53 $\pm$ 0.34 mm^2 inferior to the optic disc centre (Jonas *et al.*, 1993). (4) the morphology of the lamina cribrosa with the largest pores and least amount of interpore connective tissue in the inferior and superior regions compared with the temporal and nasal regions (Oghden *et al.*,1988 ; Dandona *et al.*, 1990) and (5) the diameter and distribution of nerve fibers within the optic disc (Mikelberg *et al.*,1989).

Using a computerized image analysis to determine axon diameter distribution in normal human eyes the mean diameter was found to be 0.72 $\pm$ 0.07 mm^2, with the mean diameter of fibers in the infero-temporal portion of the optic nerve being smaller than those in the superior-nasal portion (Jonas *et al*., 1993). Compared with other sectors of the optic nerve, it was also found that the inferior temporal segment had a higher axonal density. This is consistent with the fact that the major portion of the papillomacular bundle enters the optic nerve head within this area. Violation of the famous Jonas ISNT rule configuration is considered by many clinicians as a feature of glaucomatous optic nerve damage (Kanski, 2011)

A mean rim area of 1.85mm^2 was reported in the Rotterdam Eye study (Ramrattan *et al.*, 1999). Much lower value was reported in a study in Egypt ; a rim area of 1.40mm^2 in the normal eyes with a mean peripapillary thickness of 111.2um. The neuroretinal rim was also found to thickest in the inferior disc quadrant (Tharwat *et al.*, 2013). However a study in Nigeria by Lawan *et al.*, (2014) reported a mean rim peripapillary thickness of 104um which was thickest superioly than inferioly. Ethnic differences may be an explanation for the variation but the study protocol may also explain this difference. In the former study, the researchers used a spectral domain OCT (SD-OCT) while the Nigerian study employed a Time domain OCT with far less resolution than SD-OCT.

2.2.4 Cup to Disc Ratio (CDR)

This part of the optic disc is considered as the portion (percentage) of the cup in relation to the overall disc area (Rudnicka *et al*., 2001). Glaucoma and other optic neuropathies are recognised by characteristic structural changes of the ONH involving the neural rim and the CDR (Beck *et al.*, 1987; Healey *et al.*, 1997). Most glaucoma screening protocols especially in population based studies employed the evaluation of the CDR as a tool. Because the average optic disc diameter is slightly vertically oval and the average cup is more horizontally oval, the average cup-to disc ratio in normal eyes should be slightly larger in the horizontal than vertical dimension (Jonas *et al.*, 1991).The horizontal cup-to disc ratio was found to be smaller than the vertical one in 7% of studied eyes in normal subjects (Jonas *et al*., 1991). This is important when evaluating for glaucomatous optic nerve change in which the vertical cup-to-disc ratio typically enlarges more rapidly than the horizontal (Quigley *et al*., 1990).

A high cup-to-disc ratio is considered to be physiologic in a large optic nerve head, whereas an average cup-to-disc ratio may be considered pathologic in a small optic nerve head (Quigley *et al.*, 1990). The cup-to-disc ratio also may vary between the right and left eye of the same person with corresponding size differences between the two optic nerves (Girkin *et al.*, 2006). The larger nerve will normally have a larger

CDR and the smaller nerve will tend to have a smaller cup-to-disc ratio physiologically (Gundersen *et al*., 1998). A direct correlation between the size of the vertical disc and vertical cup diameters was also observed to be frequent among most adults. The Blue Mountain Eye Study found a mean CDR of 0.42 which was found to be statistically associated with disc area (Ong *et al*., 1999). An increase in disc asymmetry of 1.0 mm associated with an increase in cup diameter asymmetry of approximately 0.7 mm in the same direction was described and was clinically significant (Ong *et al*., 1999). This same association between optic disc diameter and optic cup diameter has also been clearly demonstrated in several previous studies (Bengtsson, 1979; Britton *et al.*, 1987).

In normal human optic nerve heads, the differences between the right and left eyes in the horizontal cup-to-disc ratio of 0.3 in only 1% of individuals, 0.2 in 4%, and.0.1 in 26% (Jonas *et al*., 1999). This is an important finding because when evaluating for the possibility of glaucoma a CDR difference of 0.2 or more is often considered to be pathologic (Fatima *et al.,* 2013). In fact, many of these glaucoma suspects may actually just be normal subjects with optic nerve relative hypoplasia variations. Significantly, eyes with large optic discs have larger neuroretinal rim areas, larger cup-to-disc ratios, more optic nerve fibers, less nerve fiber crowding per square millimetre of disc area (Jonas *et al.*, 1991; Papastathopoulos *et al.*, 1995).

Shaun *et al.*, (2008) found a mean cup to disc ratio (CDR) of 0.53 among adults. The CDR was found to be statistically significantly associated with the disc size: larger discs having larger CDR. This association was also demonstrated by a study in India which also observed a CDR of 0.56 and a positive correlation with the disc area (Tarannum *et al.,* 2011). A study in Turkey found a mean CDR of 0.48 using confocal ophthalmoscopy (Hakan *et al.,* 2004). A positive association between the observed

CDR and the disc area was reported to be statistically significant but not with observed refractive error (Hakan *et al.,* 2004).

Studies in Africa found a larger mean Cup to Disc Ratio. Tharwat *et al.,* (2013) in Egypt found a mean CDR of 0.62 using a high resolution Forrier OCT. This finding is slightly different from that in Nigeria by Kyari *et al.,* (2015). The Nigerian study however evaluated the CDR using slit lamp 75D condensing lens and found a mean CDR of 0.7 as a cut-off value as abnormal for diagnosis of glaucomatous optic disc changes (Kyari *et al*., 2015). No report of other disc parameters was available though in the study. Similarly, a study in Ibadan Nigeria, CDR of 0.7 was found to be the demarcation between normal and glaucomatous eyes (Olusola & Sarimiye, 2014). Other disc parameters were not evaluated to come up with a standardised correlation for full glaucoma evaluation.

With increasing optic disc size and neuroretinal rim area, there is also an increase in the total number of optic nerve fibers and retinal photoreceptors (Jonas *et al.,* 1992 ; Panda –Jonas *et al.,* 1994). Jonas found a mean optic nerve count of 1,158,000 ± 222,000 fibers, with a normal range between 777,000 and 1,679,000 fibers. In another study, (Jonas *et al*., 1990) determined the mean optic nerve fiber count to be 1,159,000 ± 196,000. Many other studies have confirmed similar total optic nerve fiber calculations (Sanchez *et al*., 1986; Mikelberg *et al*., 1991).

Optic pits and the morning glory syndrome are associated with a reduced amount of nerve fibers and abnormal neuroglial tissue. Nerve fiber density per disc area has been shown to be higher in small optic discs compared with large ones (Townsend & Comer, 1987). This indicates a crowding of optic nerve fibers in small optic discs compared with larger optic discs (Kee *et al*., 1997). However, because large nerves usually have more nerve fibers compared with small nerves, CDR is especially important when evaluating patients for glaucoma (Jonas 1988[b]).

More importantly, in patients with smaller than average optic nerves the diagnosis of glaucoma has often been overlooked. Furthermore, because larger nerves have been demonstrated to have more optic nerve fibers, they may be less at risk for glaucomatous nerve fiber loss compared with smaller nerves, which congenitally have fewer optic nerve fibers. The larger optic nerves have a greater anatomical reserve from which fibers may be lost (Funk *et al*., 1989).

2.4 GENDER DIFFERENCES IN OPTIC DISC

Although it has been known that women have slightly smaller eyes, or shorter axial lengths than men (Betz *et al.*,1982; Ong *et al.*,1999), the issue of optic nerve size has been widely disputed. Most studies in the literature have shown that women to have slightly smaller optic nerves than men. However, some researchers (Jonas *et al.*, 1991) have found this difference to be insignificant, and others (Tsai *et al.*, 1992) have found no correlation at all. Many proposed that the 'smaller looking' disc in females is actually as a result of axial magnification not an absolute significant value (Rudnicka *et al*.,; 1998; Rudnicka *et al*., 2001). Individual's general physical status was also demonstrated to have positive correlation with some ONH parameters (Bourne *et al*., 2008).

It was proposed that the optic nerve fiber count did not vary significantly between men and women, supporting the argument for a lack of difference in optic disc size between the two sexes (Jonas *et al.,* 1991). Similarly, previous studies on histomorphometry and histochemistry did not show a significant variation in neural axons between males and females (Oghden *et al*.,1988). A study assessing the planimetric measurements of the ONH on Caucasians by Garway-Heath *et al*., (1998), the Vellory Eye Study in India (Jonas *et al.,* 2003) and a Japanese study (Kashiwagi *et al*., 2000) have all reported that optic rim and disc area were unrelated to gender in their respective studies. Similarly, a population study by Shaun *et al.,* 2008 using OCT, no any significant correlation between disc parameters and gender was demonstrated. It was observed that disc area and rim area were significantly greater in men than in women (Bourne *et al.,* 2008). This difference was proposed to be due the possible difference in statue between male and female and also to the effect of ocular axial length and keratometry (wider radius of curvature). Similar gender significance of keratometry and axial length on ONH topography had been reported by other studies (Ramrattan *et al*., 1997; Gundersen *et al*., 1998).

Many other published clinical data also described a significant gender difference in optic disc topography. Tarannum *et al.,* (2011) showed that disc area among the population studied was significantly larger in males than in females. Even after correcting for refractive errors and magnification gender based difference was statistically significant. Moreover, the Baltimore Eye Survey (Varma *et al*., 1994) and The Rotterdam Study (Ramrattan *et al*., 1999) reported the disc area to be smaller in women than men. Axial length was not measured in either study with the result that no adjustment was made for this in calculations of ocular magnification. Quigley *et al*., (1990) similarly found a significantly shorter horizontal disc diameter in women than in men. Similarly, Mansour (1991) demonstrated a similar finding of significantly shorter horizontal disc diameter and disc area in women. The Framingham Eye Study (Leibowitz *et al*., 1991) revealed that women tend to have a significantly smaller mean cup-to-disc ratio, than men. Lawal *et al.,* (2014) in a study conducted on adult volunteers in Kano, Nigeria to also showed significant gender variation in rim thickness of the neuroretinal rim quadrants.

2.5 AGING CHANGES OF THE OPTIC DISC

In normal individuals, ageing process may result in decrease retinal sensitivity which may be attributed to cataracts, miotic pupils, and/or retinal changes (Tsai *et al*., 1992). This can also be explained by a progressive autolysis of the retinal ganglion cells with resultant loss in the total number of optic nerve fibers (Heijl *et al.*, 1987).

Histomorphometry of human optic nerves proposed that the approximate loss of nerve fibers annually was about 3000 axons per year (Jonas *et al*., 1990). It was also observed that a decline of the neuroretinal rim was very obvious in elderly subject as compared to younger ones (Tsai *et al*., 1992). Actually, linear annual nerve fibre loss was estimated to be about 4,000 fibers, having started with approximately 1,400,000 axons at birth (Dacey, 2000). This hypothesis may support the findings of decline in rim area of the optic disc by many studies (Townsend, 1991; Garwy-Heath *et al*., 1997). Normal aging changes could therefore account for the loss of about 25% of the optic nerve fibers by 60–69 years of age, assuming that one started life with approximately 1,100,000 initially (Dolman *et al.*, 1980).

Another important difference between normal aging changes and glaucomatous changes may be the size of the optic nerve fibers involved. Mikelberg *et al.*, (1989) have demonstrated an increase in the mean axon diameter with age, which suggests a preferential loss of smaller diameter axons with age. Disease conditions like glaucoma may in contrast have non-selective damage involving both large and small diameter axons (Alvarez *et al*., 1997 ; Sample *et al*., 1997).

Clinically, the loss of nerve fibers with age may account for the observation of generalized enlargement of the CDR without glaucomatous involvement (Colenbrander, 1960; Kyari *et al.*, 2015). These nerve changes may also be substantiated by a decline in disc rim area with advancing age (Armaly & Sayegh, 1969 ; Carpel & Engstrom, 1981). An age-related decline in disc rim area consistent with histologic evidence of an age-related decline of ganglion cell axons was clearly demonstrated (Tsai *et al*., 1992).

The Tanjong Pagar Study in Singapore evaluated the optic disc parameters using optic disc photography (Bourne *et al*., 2008). The mean disc area of 2.09mm^2 which was significantly correlated with age was observed (Bourne *et al*., 2008). The study also found that the CDR (mean= 0.55) showed statistically significant increase with age (r=0.154, p=0.0001). In Indian population, no statistical significant difference was observed with age changes (Jonas *et al*., 2003). This similar association was also demonstrated in the Rotterdam Eye study in the United States (Ramrattan *et al.*, 1999). Similarly, Varma *et al.*, (1994) in a comparative optic disc study among different races did not show any significant correlation of any ONH parameter with age. The minimal difference found was in rim area which was found to be thinner among elderly but this association was however observed to have no statistical significance (Varma *et al.,* 1994).

Optic disc topographic change with age was also demonstrated in some African population-based studies. Using stratus Optical Coherence Tomography, Lawan *et al.*, (2014) in Kano, Nigeria found that peripapillary rim area declined steadily with advancing age. Kyari *et al.,* (2015) also in Nigeria observed a significant decline in rim thickness and larger cup disc ratio (CDR) in older subjects. The Cameroon Glaucoma screening Protocol, a study among a rural southern Cameroon, also observed that the CDR showed a significant increase with age. Using fundus photography, they observed an average CDR of 0.15 in the youngest and 0.45 in the oldest subjects (Paul-Rolf *et al*., 2009).

2.6 EFFECTS OF AMETROPIA

It has also been suggested that ametropia (refractive error) may be correlated with optic nerve size. Studies have shown that low to moderate amounts (25.00 D to 15.00 D) of myopia (short-sightedness) and hyperopia (long-sightedness) do not seem to correlate significantly with optic disc size (Jonas *et al*., 1988[b] & Varma *et al*., 1994). However, outside that range, higher degree of myopia are usually associated with significantly larger optic discs and higher hyperopia is typically associated with significantly smaller optic discs (Varma *et al*., 1994). Results of the Rotterdam Study have demonstrated that disc area linearly increased by 1.2%6 0.15% for each diopter of myopia (Ramrattan *et al*., 1999).

Currently, glaucoma is diagnosed by considering the clinical appearance of the optic disc and retinal nerve fiber layer and by digital imaging of standard achromatic perimetry (American Academy of Ophthalmology, 2000). However, myopic individuals often have enlarged optic discs with a more oval configuration and larger areas of peripapillary atrophy (Barbara *et al*., 2010). Because of these features, glaucomatous changes cannot be easily interpreted in myopic discs, possibly leading to a misdiagnosis of glaucoma. In early glaucoma, structural change is known to precede functional damage of the optic nerve that would be detected clinically by perimetry (Quigley *et al*, 1992 ; Tay *et al*., 2005). The optic disc and retinal nerve fibre layer are sensitive indicators for predicting early glaucomatous changes and the extent of RNFL damage correlates with the severity of functional deficit in the visual field (Lueng *et al*., 2005). Thus, RNFL assessment may be more valuable than optic disc assessment in the case of myopic subjects. However, whether RNFL thickness could vary with the refractive status of the eye remains unclear. It is therefore important to investigate whether there is any correlation between RNFL measurements and the axial length/refractive error in myopic patients with correction for ONH changes considering that the risk of developing glaucoma increases with the severity of myopia (Sommer *et al*., 1991). Considering different approaches of various studies to the connection between myopia and glaucoma, examining the morphological characteristics of optical discs of patients diagnosed with primary open-angle glaucoma and high and low refractive errors in order that the results obtained will help ophthalmologists in routine examinations of the HRT/OCT findings, to help to avoid errors in diagnosis of glaucomatous or myopic damage to the optic disk and its surroundings (Oliveira *et al*., 2007). The damage size of neuroretinal rim was found to be higher in the people with high ametropia (>5 D) (Ranko *et al*., 2013). Researchers have concluded that glaucomatous eyes with high myopia (> 5 D) have larger diameters of optic disc, also larger cup and thinner layer of retinal nerve fibers, compared with the glaucomatous patients with < 5D myopia (Ranko *et al*., 2013).

2.7 RACIAL VARIATION ON THE OPTIC DISC

Glaucoma, a progressive optic neuropathy remains the leading course of irreversible blindness among Asians and blacks, while it is the third leading cause among Whites (Barbara *et al*., 2010; Lawan, 2006). The burden from glaucoma disproportionately affects individuals of Asian and African ancestry who are at much greater risk of developing glaucoma and blindness from glaucoma (Bourne *et al*., 2008).The reason for this differential burden is multifactorial and incompletely understood (Resnikoff *et al*., 2004). Socioeconomic disparity, differences in healthcare access, and differences in both systemic co morbidities and ocular parameters such as corneal thickness all play some role, yet variation in the structure of the optic nerve remains an important and critical factor in the more aggressive disease seen in this at-risk underserved population. (Tielsch *et al.*, 1991).

Several clinical and histological studies have characterized racial differences in optic disc structure between blacks and whites (Varma *et al*., 1994 ; Girkin *et al*., 2010). Quantitative evaluation of conventional optic disc photography from the Baltimore Eye Survey demonstrated that mean optic disc area was 12% larger in Blacks compared to Whites (Varma *et al.,* 1994). The mean cup area was larger as well. While the mean global rim area was similar in both racial groups, due to the relatively larger optic disc in blacks, there was a decrease in rim/disc area, indicating that there may be a decrease in rim thickness and nerve fibers relative to disc size in this population. In a smaller study including 200 normal subjects, also using disc photography, Beck and colleagues also demonstrated that there was an increase in cup-to-disc ratio in Blacks relative to Whites (Beck *et al.*, 1985)

Over the years, most of the researches attempting to quantify these differences have compared African-Americans with whites. Chi *et al.,* (1989) used a Rodenstock Optic Disc Analyzer (RODA) to measure various optic nerve head parameters on subjects between the ages of 18 and 35. They found the optic disc area, cup-to-disc ratio, and cup volume to be significantly larger in African-Americans than in whites. Varma *et al.,* (1994) with the use of the Topcon Imagenet, a digitalized image analyzer system, studied a much larger sample size of patients age 40 and older with similar results. African-Americans had significantly larger optic disc areas, cup areas, and CDR than whites (Varma *et al.*, 1994).

Mansour, (1991) measured horizontal and vertical disc diameters and compared resulting optic disc areas in white, Hispanic (Central American), non-American Indian, Asian (Chinese, Korean, and Vietnamese) and African-Americans. Whites and Hispanics were found to have significantly smaller optic disc areas than non-American Indians and Asians, with African-Americans having the largest disc dimensions. Tsai *et al*., (1995) used the HRT- cSLO device to evaluate ethnic differences in optic disc topography of subjects aged 18 to 40 years. The results showed optic disc area, cup volume, maximal cup depth, and vertical CDR to be largest in African-Americans, followed by Asians (75% Chinese, 9% Japanese, 9% Korean,, and 7% Vietnamese) and Hispanics (77% Mexican, 7% Columbian, 4% Salvadorian, and 2% each of Ecuadorian, Cuban, Chilean, Nicaraguan, Brazilian, and Puerto Rican), and smallest in whites (Tsai *et al*., (1995) .

Barbara *et al*., 2010 in a study involving African American, Hispanics and whites have found a larger disc area of 2.49mm^2, 2.32mm^2 in Hispanics and 2.11mm^2 among whites. A published clinical data regarding the racial variations in CDR have estimated the average young adult CDR to be about 0.4 for whites, 0.55 for Asians and Hispanics, and about 0.6 for African-Americans (Townsend, 1991).

2.8 OPTIC DISC MORPHOLOGY AND DISEASE DETECTION

Progressive optic neuropathy is the hallmark of glaucoma (Tam *et al*., 2000). Detecting change in optic nerve topography with an OCT would be a most meaningful application in glaucoma diagnosis and follow up (Shaun *et al*., 2008). As explained above, this quantitative technique may exceed the sensitivity of any available clinical tool for optic nerve examination (Michael *et al*., 2000). When evaluating a technology that may be more sensitive than accepted standards, it often is difficult to confirm the finding of the new technology until changes are observed with the less-sensitive standards (Michael *et al*., 2000). This may be the case with Optical Coherence tomography as c hanges in optic nerve topography may precede visual field changes (Bourne *et al*., 2008). Several investigators have used other strategies to look for evidence of the ability to detect change (Michael *et al*., 2000). Indeed, it is not clear what represents clinically significant change, although it is possible to define statistical change (Shaun *et al*., 2008).

Several investigators have used models of change such as pre- and post-trabeculectomy and animal models to predict the possibility to detect subtle topographic changes of disease process affecting the optic disc (Irak *et al*., 1996 & Burgoyne *et al*., 1996). There remains the problem of confirming such changes when other standard tests may be far less sensitive (Irak *et al*., 1996). Prospective longitudinal studies will be needed to answer these questions (Tam *et al.*, 2000).

Optic disc and nerve fiber layer imaging techniques have evolved out of an attempt to acquire quantitative objective topographic information regarding optic disc structure and in-vivo measurements of retinal nerve fiber layer thickness in order to improve the ability to detect glaucoma and progressive glaucomatous damage. Other studies evaluating these instruments have previously been performed in predominantly white study populations and have not included adequate numbers of black subjects to evaluate the role of quantitative optic disc analysis, the parameters that are most predictive of glaucoma, and optimum analysis strategies for detection of glaucoma in this at risk population (Varma *et al*., 1994).

Differences in optic disc structure between blacks and whites may have an effect on the ability of optic disc imaging techniques to detect glaucoma. Broadway demonstrated that the discriminating ability of cSLO varied depending on the phenotype of optic disc damage present (Broadway *et al.,* 1998). This is an important consideration in that one of the primary reported differences in optic disc structure between blacks and whites is disc area (Varma *et al.*, 1994). Compared results of cSLO between 146 eyes from black subjects and 97 eyes from white subjects found that blacks had significantly greater optic disc area, cup area and volume, and similar rim area and volume (Girkin *et al.,* 2005). Additionally, black subjects were observed to have had a deeper optic disc cup than Whites (Zangwill *et al.,* 2004). Following adjustment for racial variation in disc area, there was no significant difference between racial groups other than cup depth (Tsai *et al.*, 1995). This finding indicates that most of the normal variation in optic disc topography between Blacks and Whites seen with the cSLO is due to differences in disc area except for differences in cup depth (Tsai *et al.*, 1995).

A study conducted to determine the structural characteristics of the optic disc that are associated with early glaucoma in Blacks and Whites and whether these characteristics differ between these races (Girkin *et al.*, 2003), parameters of optic disc topography from 260 eyes from black participants and 193 eyes from white participants were included in the analysis. A staged multivariable logistic regression model was used to calculate the association between cup, rim and disc margin parameters (Girkin *et al.*, 2003). To account for the effect of differences in optic disc area, this parameter was included in the multivariable model at each level of interaction in constructing the final model (Girkin *et al.*, 2003).

The study by Girkin *et al.*, (2003) found similar racial differences in glaucoma detection between normal control subjects with CSLO than prior studies using disc photography. These differences included a larger disc area, CDR, rim area and cup area in Blacks. Additionally other studies (Jonas *et al.*, 1999; Girkin *et al.*, 2003) demonstrated racial differences exist in the optic disc structural parameters that are independently predictive of early glaucoma between Blacks and Whites even when accounting for differences in optic disc area. While the most predictive parameter, rim area, was the same for each racial group, the magnitude of association was higher in Whites. Differences in disc area do account for some of these racial differences; however, residual differences still persist (Girkin *et al.*, 2003).

Racial variation on optic nerve structure may have a significant impact on the ability to detect glaucoma by subjective and objective techniques (Muanza *et al.*, 2011). Larger optic nerves have a larger scleral canal and consequently larger optic cups for the same rim volume and number of retinal nerve fibers (Mansour *et al.*, 1991). Thus, a larger nerve is more likely to be misconstrued as glaucomatous on casual observations, whereas a smaller nerve with a small degree of glaucomatous cupping may be overlooked as normal (Mansour *et al.*,1991). Differences in optic disc structure between blacks and whites may have an effect on the ability of optic disc and nerve fiber layer imaging techniques to detect disease process like glaucoma (Kee *et al.*, 1997). Broadway demonstrated that the discriminating ability of the cSLO varied depending on the phenotype of optic disc damage present (Broadway *et al.*, 1998). This is an important consideration in that one of the primary reported differences in optic disc structure between blacks and whites is disc area (Varma *et al.*, 1994).

Prior studies using the OCT and cSLO have also demonstrated that racial variations in optic disc structure had little impact on the ability of structural parameters and discriminating functions to detect glaucomatous visual field defects (Beck *et al*., 1985). However, differences in normative values required race-specific cut-off values to optimize specific detection strategies (Deleon-Ortega *et al.*, 2006). The widely used Moorefield's regression analysis (MRA) popularised by Wollstein *et al.*, (2000) which takes in to account disc area, performed similarly across racial groups, but optic disc area had a significant impact on the diagnostic efficacy of this technique with more patients incorrectly diagnosed as glaucomatous who had larger optic nerves, probably reflecting the normative database used to develop this technique (Girkin *et al.*, 2006).

Clinicians have long recognized that it can be a particularly challenging problem to distinguish between normal and abnormal optic nerves, considering the wide range of biologic variation (Jonas *et al*., 1999). Several investigators have approached this challenge with innovative strategies (Varma *et al*., 2003). In a study of normal, ocular-hypertensive, ocular-hypertensive with clinically abnormal retinal nerve fiber layer, and glaucomatous eyes, Airaksinen and associates found that rim volume was able to discriminate among the four groups, although there was considerable overlap between these groups (Airaksinen *et al*., 1985[a]). Similarly, others have found that although there were group differences among normal, ocular-hypertensive, and glaucomatous eyes, there was considerable overlap between groups (Quigley *et al*., 1992 ; Wollstein *et al*., 2000 ; Tay *et al*., 2005).

Using discriminant analysis, researchers were able to differentiate normal from early glaucoma with a sensitivity of 87% and a specificity of 84% using various parameters (Muanza *et al*., 2011). It was also observed that for small crowded discs, it is difficult to make such determinations using simple discriminant analysis (Asawaphureekorn *et al*., 1996). There are other novel approaches to analyzing data from OCT and cSLO topography, but all of these analysis strategies remain to be validated in large cohorts (Bartz- Smitdz *et al*., 1996). It is likely that, similar to the progress in automated perimetry, new analysis strategies will continue to evolve (Bartz- Smitdz *et al*., 1996). Although group means have been found to differ among normal, suspect, and glaucomatous eyes, most of the studies have demonstrated considerable overlap between diagnostic groups (Tay *et al*., 2005). This has been a challenge with all glaucoma diagnostic technologies (Sihota *et al*., 2006). Even when it is possible to find differences in group averages, it is often difficult to categorize an individual accurately when there is a wide range of biologic variability (Jonas *et al*., 1991; Wollstein *et al*., 2000). From the foregoing studies, it can be conclude that OCT topographic parameters are able to differentiate the normal from the glaucomatous optic disc in a precise manner when looking at groups (Zangwill *et al*., 2004).

CHAPTER THREE

MATERIALS AND METHOD

3.1 STUDY AREA

Kano state is located on latitude 12 ^{0} 00’N, longitude 08^{o}30^{1}E in the north-western region of Nigeria (Kano encyclopaedia). The state has a land mass of 20,131km^2, and ranked the most populous state in Nigeria with a population of over 9 million at 2006 estimate (Nigerian National Population Commission, 2006). It is considered the commercial and political capital of northern Nigeria. The principal inhabitants are of Hausa/Fulani ethnic origin with minority representing virtually all tribes in Nigeria and a minute fraction of non citizens (Gazzet, 2007).

3.2 STUDY DESIGN

This was a descriptive cross sectional study to assess the optic nerve head parameters in healthy Hausa adults using Optical coherence tomogram.

3.3 STUDY POPULATION

The study population was made of normal Hausa adult volunteers from patients’ relatives (that attend the eye clinic AKTH) who met the criteria for inclusion.

3.4 INCLUSION CRITERIA

- Age 18 – 65 years
- Belonging to Hausa ethnic origin
- Unaided visual acuity (VA) of 6/6 or better
- Normal intraocular pressure(IOP) 10-21mmHg

- No history of eye injury or surgery
- No ocular pathology found on eye examination

3.5 EXCLUSION CRITERIA

- History of glaucoma
- History or evidence of intraocular surgery
- History of systemic illness with possible ocular involvement such as diabetes mellitus, hypertension or sickle cell disease.

3.6 SAMPLE SIZE ESTIMATION AND SAMPLING TECHNIQUE

The sample size was determined using the formula for determining minimum sample size (Lwanga & Lemeshow, 1991)

$$N = \frac{Z^2 pq}{d^2}$$

Where:

N = minimum sample size

Z = standard normal deviation which as 1.96 to 95% CI

P = prevalence of visual impairment among glaucoma patients = 0.7 (Lawan, 2006)

q = 1-p (1-0.7)= 0.3

d = degree of precision and is taken here as 0.05

$$n = \frac{z^2 pq}{d^2}$$

$$= \frac{(1.96)^2 \times 0.7 \times 0.3}{0.05^2}$$

$$= 321$$

The minimum sample size for the study was 321 which were rounded up to 350.

The study was conducted in the eye clinic of AKTH for a period of six months. A systematic random technique was employed in selecting the subjects for this study. From the clinic records, number of clients that attend each of the four daily clinics of the week has been at least fifty (50) patients. Traditionally each patient has a relation that accompanies him/her to the hospital. A sampling interval of 5 was used to select 10 patients per day. This interval was obtained by using the formula which states that sampling interval is equal to sample frame divide by sample size**.** Sample interval = sample_frame /sample size**.** Hence the sample interval of 5 was obtained by dividing 50 (sample frame) by 10 (daily sample size). If a client had no relation or a subject did not meet the selection criteria, the next subject who fulfilled the criteria was recruited. The starting point was selected from the first patient that registered in the clinic. Consenting volunteers who met the inclusion criteria were selected until the required sample size of 350 was met.

3.7 MATERIALS

1. Consent form (Appendix I)

2. Data recording form (Appendix II)

3. Illuminated Snellen's chart

4. Pen torch

5. Direct ophthalmoscope (Keeler, UK)

6. Slit lamp biomicroscope (Keeler, UK)

7. Flourescein strips

8. Propracaine chloride 0.5% (Alcaine, Alcone)

9. Stationeries and ink for OCT printout

10. Carl Zeiss Stratus OCT machine (Model 3000 software version 4.0)

11. Airpuff aplanation tonometre (Keeler 10", model 04, UK)

3.8 METHOD

Patients and their relations were informed about the aim of the study. The nature of the procedures was fully explained to the volunteers.

3.8.1 Filling Data Sheet and Examination

The procedure began with filling of consent form. Demographic data (ID number, age, gender, occupation, marital status, ethnic origin) of the volunteers were recorded in the data record form. Grand parentage was used to identify Hausa origin. Clinical past and present ocular history, family history of glaucoma, systemic history of HPT or DM were all obtained. If criteria is met, subject then proceeds to examination stage. Visual acuity (VA) was tested indoors in the clinic. The subject was made to stand six meters away from an illuminated Snellen's visual acuity chart (Khurana, 2007). Each eye was tested separately. Only those with uncorrected VA of 6/6 proceeded with the next stage.

3.8.2 Slit Lamp Examination (Khurana, 2007)

Anterior segment of the eye was examined using the slit lamp biomicroscope (Keeler, 2000 model). Posterior segment examination was done using +78D condensing lens with the slit lamp and/or Keeler direct ophthalmoscope as shown in Plate III. Intraocular pressure (IOP) was measured by a Goldmann applanation tonometre which is mounted on the slit lamp machine. Topical 0.5% proparacaine chloride was instilled in the eye as a surface anaesthetic agent. In subjects that were not cooperative, IOP was measured with the Keeler air puff non-contact applanation tonometre (Plate IV). To proceed, subjects must have a clear ocular media, intra ocular pressure $\leq$21mmHg, normal anterior segment findings and normal looking pink optic disc. They were then scheduled to proceed with OCT examination.

Plate III: Examination of the eye using slit lamp biomicroscope

Plate IV: Measuring intraocular pressure with puff air

3.8.3 OCT Procedure (Kanski, 2007)

Optical coherence tomography procedure was carried out using Stratus OCT model 3000, version 4.0. The procedure was fully explained to the subject. Both the subject and the examiner were seated on the machine as appropriate. The subject was instructed to place his/her chin on the chin rest and forehead against the forehead rest. One eye was scanned at a time while the other eye was occluded by the occluder. The subject would be instructed to fixate a target point inside the viewing port.

The optic nerve head was scanned using the fastscan ONH protocol by clicking on the 'ONH' icon which would be highlighted. Locating the ONH is by centring the spoke wheel light pattern on ONH shadow (Plate III). The disc margin was detected automatically by the computer with plane parallel to the retinal pigment epithelium (RPE).Then the 'scan' icon would be clicked to begin the scanning. This system has a 7-10um axial resolution and acquired about 600 scans per second. The computer would project a circular pattern of 3.4mm diameter on the optic nerve head and series of scans would be taken. Signal strength of 8 and above was accepted to be of acceptable quality (Tarannum *et al.*, 2011) and printed out. Otherwise, a signal of < 7 was discarded and ONH re- scanned.

The OCT software provides calculation of optic nerve parameters. It then analysed these measurements and created a numeric and pictorial report as disc area, cup area, rim area cup volume vertical and horizontal cup to disc ratio head parameters. The neuroretinal rim width and area is determined by measuring the amount of neuroretinal tissue within the boundaries of the optic nerve. The software thus calculates optic disc rim and optic cup area. The total area of the optic disc is the sum of the rim and cup areas. The average cup/disc ratio (CDR) is the square root of the ratio of the area of the cup to the area of the disc. The vertical CDR is the ratio of vertical cup diameter to vertical disc diameter. Cup volume is the volume between the plane created by the cup outline at the vitreous interface and the posterior surface of the optic nerve head. This data is then printed out.

3.9 LIMITATIONS

1. Strike action by various cadres of hospital workers affected the patients’ clinic visits and subjects selection, thereby prolonging the period of the study.

2. The OCT machine had some mechanical problems that had to be repaired and this interrupted the study for some time**.**

3.10 DATA ANALYSIS

Data obtained were entered and analysed using the Statistical Software for Social Sciences (SPSS) version 20.0. Mean, ranges and standard deviations (SD) of ONH parameters were calculated and tabulated. Comparison of the means of disc parameters between gender and between right and left eyes was calculated using independent “t” test. The mean values of the disc parameters were compared among different age groups using the one-way analysis of variance, followed by post- hoc test for multiple comparisons. A p-value of 0.05 or less was considered statistically significant.

CHAPTER FOUR

4.1 RESULTS

Three hundred and forty two (342) volunteers participated through to the end of the study.

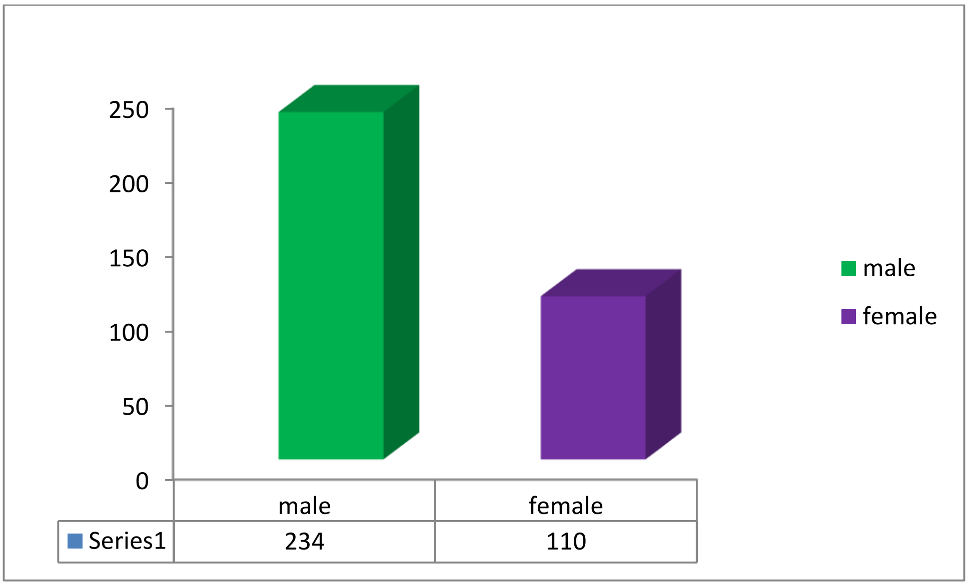
There were 232 males and 110 females participants. Male to female ratio was 2.1:1. The age range of the subjects was between 18 and 56 years with a mean age of 41.4 $\pm$8 years.

TABLE 4.1: Age and sex distribution of participants

Age (years)	Males	Females
18-27	82	57
28-37	78	30
38-47	62	19
48-57	10	4
Total	232	110

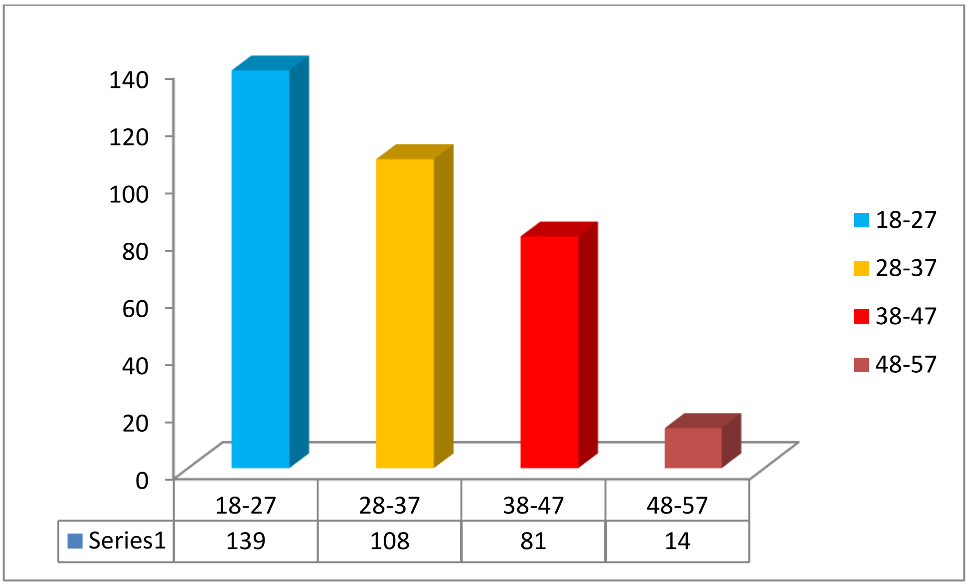
Majority (232) were male and 110 were females.

FIGURE 4.1: Male and female distribution



Majority (68%) were male and 32% were females.

FIGURE 4.2: Age categories of subjects



Subjects were grouped into four. Those of ages from 18-27 years were 139, 28-37 years were 108, those of 38-47 years of age were 81 and those subjects aged 48- 57 were 14. There were 82 males and 57 females in the first group, 78 males and 30 females in the second group, 62 males and 19 females in the third and 10 males and 4 females in the last group. Subjects of age within18 to 37 comprised about 72% of the study population while those within age 38-57 were 28%.

TABLE 4.2: Descriptive statistics of disc parameters in all subjects

Disc parameter	Minimum	Maximum	Mean	S. D
Disc area	1.20	3.58	2.35	0.3796
Rim area	1.00	3.03	1.76	0.4040
Cup area	0.21	1.50	0.59	0.2043
Cup disc ratio	0.24	0.75	0.44	0.199

The minimum disc area was 1.20mm^2 and the maximum was 3.58mm^2. The mean disc area was found to be 2.35mm^2 $\pm$ 0.38 standard deviation (SD). The mean rim area found was 1.76mm^2 $\pm$ 0.40 SD. The range was found to be from 1.00mm^2 to 3.03mm^2. The vertical cup to disc ratio was analysed and the mean value observed was found to be 0.44 $\pm$ 0.19 SD with a range of 0.24 to 0.75.The mean value obtained for cup area was 0.59mm^2 $\pm$ 0.20 SD. The minimum was 0.20mm^2 and the maximum was 1.50mm^2.

TABLE 4.3: Independent t test of disc parameters between right and left eye in all subjects

Disc parameter	Right (n=342)	Left (n=342)	t-test	p-value
Disc area	2.34	2.36	-0.61	0.54
Rim area	1.76	1.76	-0.46	0.96
Cup area	0.58	0.59	-0.56	0.61
Cup disc ratio	0.44	0.44	-0.21	0.84

The left eyes' mean disc area was found to be slightly larger ($2.36mm^2$) than that of the right eyes ($2.34mm^2$). This difference was however statistically insignificant, p= 0.54, t= -0.61. Similarly, the left eyes showed slightly larger ($1.758mm^2$) rim area than that of the right eyes ($1.754mm^2$) with p= 0.96 and t= -0.46 indicating statistically insignificant difference. Cup to disc ratio (CDR) was found to be similar (mean= 0.44) in both eyes (p=0.84, t= -0.21).

Table 4.4: Independent t test of disc parameters between right and left eye in males

Disc parameter	Right (n=232)	Left (n=232)	t-test	p-value
Disc area	2.37	2.38	-0.451	0.65
Rim area	1.78	1.78	-0.12	0.91
Cup area	0.58	0.59	-0.25	0.80
Cup disc ratio	0.44	0.45	-0.16	0.87

In male subjects, the mean difference between right and left sides of all the disc parameters showed that the left eyes had higher disc area (like in all subjects), but the difference was not statistically significant in all. The mean difference between right eye (mean=2.37mm^2) and left eye (mean=2.38mm^2) disc area was not statistically significant (p=0.65). Left eye mean rim area was slightly larger (1.784mm^2) than the right (1.780mm^2). This difference was however not statistically significant (p=0.90). Mean difference between right eye (mean=0.588) and left eye (mean=0.593) cup area was not statistically significant in male subjects (p=0.80). The mean difference of cup disc ratio obtained between right (0.445) and left (0.450) was not statistically significant (p=0.87).

Table 4.5: Independent t test of disc parameters between right and left eye in females

Disc parameter	Right (n=110)	Left (n=110)	t-test	p-value
Disc area	2.28	2.30	-0.43	0.67
Rim area	1.70	1.70	0.10	0.92
Cup area	0.56	0.58	-0.56	0.57
Cup disc ratio	0.427	0.429	-0.12	0.90

In the females, the mean disc area of the left eyes was higher than that of the left eye. The difference was not statistically significant (p=0.67). The mean rim area in the right is found to be higher than the left with no statistical significance (p= 0.92). There is no statistically significant difference between the right and the left cup area (p=0.57). Similarly, the difference in mean CDR of the right (0.427) and that of the left (0.429) was not statistically significant (p=0.90).

TABLE 4.6: Descriptive statistics of disc parameters in males and females

Disc parameter	Sex	Minimum	Maximum	Mean	SD
Disc area	Male	1.40	3.53	2.38	0.39
	Female	1.20	3.58	2.29	0.35
Rim area	Male	1.00	3.01	1.78	0.41
	Female	1.00	3.03	1.71	0.38
Cup area	Male	0.21	1.50	0.60	0.21
	Female	0.20	1.20	0.58	0.19
Cup disc ratio	Male	0.24	0.70	0.45	0.09
	Female	0.24	0.75	0.43	0.10

The lowest disc area obtained among male subjects was 1.4mm^2 and the highest was 3.53mm^2. The mean value observed was 2.38mm^2 + 0.388 SD. The mean rim area in the male subjects was found to be 1.78mm^2 $\pm$ 0.41SD. The range was from 1.00 – 3.01mm^2.The mean cup area obtained among males was 0.59mm^2 $\pm$ 0.207SD and the range was 0.21mm^2 to 1.50mm^2. The mean cup disc ratio in male subjects was 0.45 $\pm$ 0.096 SD with a range of 0.24 to 0.70.

The lowest disc area obtained among the female subjects was 1.20mm^2 with the highest being 3.58mm^2. The mean value was 2.29mm^2 + 0.354 SD. The mean rim area in the female subjects was found to be 1.71mm^2 $\pm$ 0.38SD. The range was 1.00 – 3.03mm^2. The mean cup area in female subjects was 0.58mm^2 $\pm$ 0.197 SD with a range of 0.20mm^2 to 1.20mm^2. The lowest cup disc ratio obtained in females was 0.24 and the highest 0.75. The mean cup disc ratio was 0.43 $\pm$ 0.10SD.

Table 4.7: Independent t-test of disc parameters between male and female subjects

Disc parameter	Male (n=232)	Female (n=110)	t-test	p-value
Disc area	2.38	2.29	2.80	0.005
Rim area	1.78	1.71	2.33	0.021
Cup area	0.59	0.58	0.90	0.362
Cup disc ratio	0.45	0.43	2.18	0.033

Male subjects were found to have larger (2.38mm^2) disc area than the female subjects (2.29mm^2). The independent t-test shows a difference of t=2.80. This is difference is shown to be statistically significant (p= 0.005). The mean rim area observed was larger (1.78mm^2) in males than in females (1.71mm^2). This difference statistically significant (p= 0.02, t= 2.33). Mean difference of cup area between the males and the females was not statistically significant p= 0.36, t= 0.91.Male subjects were also observed to have larger cup disc ratio (0.45) than the females (0.43) and this difference was shown to be of statistical significance (p=0.03, t=2.18).

TABLE 4.8: ANOVA Comparison of Disc Area Among the Age Groups

Age	N	Minimum	Maximum	Mean	F	P-value
18-27	139	1.20	3.58	2.3874[a,b]	8.541	0.0001
28-37	108	1.50	3.17	2.2944[a]		
38-47	81	1.60	3.48	2.3132[c]		
48-57	14	2.00	3.21	2.6364 [a,b, c]		

Superscript signs indicate p-value <0.05

Similar superscript indicate significant difference

Mean disc area was found to be highest (2.63mm^2) among the more elderly subjects. ANOVA test shows a significant difference within the age groups (f=8.54, p= 0.0001). The post- hoc multi-comparison test shows that difference of the mean disc area was statistically significant (p<0.05) between the age groups of 18-27, 28-37 and those of age 48- 57. No significant difference was observed between those aged 28-37 and 38-47.

TABLE 4.9: ANOVA Comparison of Rim Area Between Age Groups

Age	N	Minimum	Maximum	Mean	F	P
18-27	139	1.00	3.03	1.80[a]	5.645	0.001
28-37	108	1.00	2.66	1.74		
38-47	81	1.00	3.01	1.71		
48-57	14	1.20	2.30	1.69[a]		

Superscript signs indicate p-value <0.05

Similar superscript indicate significant difference

There was a steady decline observed in the neuroretinal rim thickness with highest mean (1.80mm^2) obtained among the youngest subjects and lowest among the older subjects (1.69mm^2). The ANOVA test shows a significant difference within the age groups (F=5.64, p= 0.0001). The post- hoc multi-comparison test shows that that difference of the mean rim area was statistically significant ($p<0.05$) between the age groups of 18-27 and those of age 48- 57.

TABLE 4.10: ANOVA Comparison of Cup Disc Ratio Among Age Groups

Age	N	Minimum	Maximum	Mean	F	P
18-27	139	0.24	0.75	0.44	5.901	0.001
28-37	108	0.26	0.68	0.43[a]		
38-47	81	0.26	0.70	0.45		
48-57	14	0.33	0.61	0.50[a]		

Superscript signs indicate p-value <0.05

Similar superscript indicate significant difference

The mean cup disc ratio observed was highest among oldest subjects (0.50). Analysis of variance indicates a statistical significant difference in the group. Statistically significant difference was shown between those in age group 18-27 and age group 48-57 ($p<0.05$).

4.2 DISCUSSION

Various studies evaluated the optic nerve head (ONH) topography using different examination methods, providing values of the ONH indices based on the ethnicity and the method used in the analysis (Varma *et al*., 1994 ; Shaun *et al*., 2008 ; Tharwat *et al*., 2013). This was an observational cross-sectional study conducted on 342 adults of Hausa ethnicity to evaluate the various parameters of the Optic nerve head (ONH) using optical coherence tomography (OCT) scan.

The subjects that participated in this study were mostly in the young and middle age group. This was in comparison to many other similar studies where subjects were mostly young and middle age (Ramrattan *et al*., 1999 ; Tarannum *et al*., 2011). The study protocol, as in many other studies, restricted the age to adult of a specific age range (Shaun *et al*., 2008). Also the study participants in this research were relations of patients of eye clinic, which were in most cases of young age group. Other larger studies recruited mostly young adults, like the SAVE study (Tariq *et al*., 2012). In contrast to this study, subjects of a study by Varma *et al*., 1994 consisted of Whites and East Asians of about 1571 participants cut across wider range of ages including young and the very elderly.

The number of male subjects in this study was more than twice the number of the female subjects. The reason could be that more males possibly make most of the population the patient relatives that accompany them to the hospital. Other studies showed wide variations in the ratio of male to female depending on the socio-demographic characteristics of their respective populations (Samaravickrama *et al*., 2012). In the Vellory eye study (Jonas *et al*., 2003) female subjects were twice the number of males. That was similar to study by

Shaun *et al*., 2008 also in India were majority of their subjects were females. Studies in Egypt and Nigeria showed higher number of male subjects than males (Tharwat *et al*., 2013 & Lawan *et al*., 2014).

The mean optic disc area found in this study (2.35mm^2) was higher than that reported in many studies over the world. For example, a study in the Netherlands (Hermann *et al*., 2004) observed a disc area of 1.89mm^2 among the white studied population. Similarly, Muanza *et al*., 2011 and Knight *et al*., 2012 observed disc areas lower than that found in this study of 1.83mm^2 and 1.82mm^2 respectively. This difference may be due to the fact that these studies used spectral domain OCT machine while in this study we used the stratus OCT type.

In Switzerland, Gherghel *et al*., (2000) reported a mean disc area lower than that obtained in this study. Their values is almost similar to that reported in the SAVE study of 1.98mm^2 (Tariq *et al*., 2013). Both above studies had much larger samples and more importantly they used Heildeberg Retina Tomography (HRT) scanning laser ophthalmoscopy (cSLO) for optic disc evaluation so their figures may not be entirely comparable to our finding.

Similarly, a study conducted in Japan by Nakamura *et al*., (1999) among Hispanics reported lower disc areas (2.15mm^2) than that reported in this study. Racial difference may account for this difference but yet a different OCT protocol (combined ONH/RNFL) was used in the above study as against stratus OCT used in this study. Hakan *et al*., 2004 in Turkey also reported lower values of mean disc area that that obtained in this study. In the study by Hakan *et al*., (2004), adjustment for measured refractive error of the eyes was done and that could have resulted in the difference observed.

Mean disc area obtained in this study ($2.35mm^2$) is closer to what was obtained by Barbara *et al*., 2010 among Hispanics ($2.32mm^2$) using a stratus fast ONH protocol. Additionally, they found larger discs in their African Americans subjects ($2.40mm^2$) than what they obtained among the white subjects ($2.29mm^2$). However, the difference observed between our finding and that of Barbara *et al*., (2010) could have resulted from the fact that most of their black subjects were associated with myopic refractive error.

The value obtained for disc area in this study ($2.35mm^2$) was lower than that reported ($2.42mm^2$) in the Rotterdam Eye Study (Ramrattan *et al*., 1999) that was conducted on white population. The Rotterdam Study used stereo-disc analyser in evaluating the ONH rather than OCT. This method may be affected by image magnification and possibly resulting in obtaining a larger value than that of OCT. The study also had a much larger population sample and might have resulted in the difference.

In most population studies among Indians, the mean optic disc areas reported were higher than values obtained from this study. For example, a study on ONH on 150 healthy adults using OCT reported higher value ($2.64mm^2$) than what was found in this study (Shaun *et al*., 2008). Tarannum *et al*., (2011) also in India obtained a higher mean disc area ($3.36mm^2$) than our finding. As these above studies used stratus OCT machine like the one used in this study and obtained larger disc areas, ethnic diversity and/or genetic makeup may therefore be a possible explanation for this difference. Similarly, Tharwat *et al*., 2013 in Egypt reported larger mean disc area $2.51mm^2$ using HRT in Egyptian population. In this later study however, categories of subjects recruited were both with normal and those with ‘suspicious’ discs and they had much smaller sample size (100 subjects) than our study of 342 subjects.

The mean neuroretinal rim area obtained in this study (1.76mm^2) was higher that reported by Girkin *et al*., (2010) in the African Descent and Glaucoma Evaluation Study (ADAGES). They evaluated disc parameters using OCT on samples of African descents and compared to those of European descents. They found a mean rim area of 1.53mm^2 among the normal subjects. The rim area was also found to be statistically significantly thicker among the African descent (1.58mm^2) than that among European descent (1.38mm^2).

This study also obtained higher (1.76mm^2) mean rim area than that reported in the Vellory Eye study by Jonas *et al*., (2003) in southeast India. They found a rim area of 1.60mm^2 using stratus OCT. They however had just about 70 subjects as their sample, much smaller than that of this study (342). The finding of this study also showed thicker rim area than that reported by Chi *et al*., 1989 among whites (1.27mm^2) and in African Americans (1.18mm^2). They used Rodenstock disc analyser (RODA) for optic nerve head examination and this might have affected the acquired images so their result may not be entirely comparable to our findings.

The rim area observed in this study (1.76mm^2) was lower than that reported by Mansour, (1991) in the Mexico and Colombia. The study (Mansour, 1991) examined whites, African Americans and Hispanics and non American Indians using Fundus camera imaging. All values were higher than what was found in this study. Similarly, Tsai *et al*. (1995) reported higher mean rim area among Asians, Hispanics and Chinese population than in this study. Although different examination technique (fundus imaging) was used in that study, genetic makeup of those populations might have resulted in these variations.

The value obtained of the mean neuroretinal rim area in this study ($1.76mm^2$) was much closer to what was reported by Shaun *et al*., (2008) in India ($1.77mm^2$). However, in this study a wide range of the rim area was observed among the subjects ($1.00mm^2$ to $3.03mm^2$) against $0.68mm^2$ to $0.83mm^2$ reported by the Indian study. The sample size in this study (342) was more than twice of the above study (150) and might have recruited subjects with wider variation of the rim area.

This study obtained a mean vertical cup disc ratio (CDR) of 0.44 in all subjects. The value obtained was higher than that reported among whites, Hispanics and Asians (0.27, 0.33 and 0.29 respectively) by Tsai *et al*., (1995). Their findings among African- American was still lower (0.41) than the finding in this study (0.44). This difference may be due to ethnic variation. Additionally, they examined fewer subjects than this study (44 whites, 48 Hispanics, 43 Asians and 40 Africans) and their values may well be placed within the range of CDR observed in this study (0.24 – 0.75).

Our finding of mean vertical CDR was also higher than that reported by Girkin *et al*., (2010). Using similar OCT technique as that of this study, they obtained a mean vertical CDR of 0.39 and among Africans and 0.30 among Europeans. In their cohort of 634 participants, they did linear regression adjustment for axial length and retinal nerve fibre layer (RNFL). Uncorrected however, they obtained just slightly higher mean value (0.48) of CDR than that found in this study.

Mean CDR obtained in this study (0.44) is in agreement of what was obtained by Knight *et al*., (2012) of 0.44 using similar OCT type and procedure. The latter study had 271 participants of different ethnicity (Knight *et al*., 2012). When corrected for race, the CDR observed among Africans was slightly higher than our finding (0.50). Our finding (0.44) is also similar to that reported (0.44) in the Blue Mountain Eye

Study conducted among white population (Ong *et al*., 1999). The mode of disc examination employed was by subjective fundus indirect ophthalmoscopy as against a more objective measurement employed in this study.

Cup to disc ratio finding of this study (0.44) was lower than what was reported by many studies from India (Jonas *et al*., 2003 ; Tarannum *et al*., 2011). These studies reported large disc areas among their subjects which was found to be statistically positively correlation with the CDR. As established by many clinical studies, CDR was found to be statistically correlated with the disc area (Jonas *et al*., 1991; Jonas *et al*., 2003 ; Girkin *et al*., 2010). Shaun and associates (2008), Tarrannum *et al*. (2011) and Jonas *et al*. (2003) all reported larger CDR than what was obtained in this study. All these studies examined the optic disc with a stratus OCT and did similar ONH scan protocol like our study. The difference may therefore be due to difference in ethnic influence or smaller sample sizes of these studies.

Some studies in Africa also reported higher CDR values than that observed in this study. For example in Egypt, a mean CDR value of 0.62 was reported by Tharwat *et al*. (2013). The study used HRT cSLO machine in their study and obtained a higher mean CDR. They concluded that their findings may be due effect of refractive error magnification as many of their subjects were observed to be myopics.

This study found a statistically significant difference (p=0.005) between the disc area of the male and female subjects with male disc area (2.34mm^2) being larger than that of the females (2.29mm^2) (Table 4.6). Mean rim area was also found to be larger in males than in females and the difference was also statistically significant. There was also significant difference in the cup disc ratio (p=0.03). Difference in hormonal influence might have resulted in this difference. However, ocular axial length may cause image magnification and hence the significant difference. Similar significant gender differences were reported by Bourne *et al*., (2008) in the Tanjong Pagar study in Singapore where disc parameters were observed to be significantly higher in males than in female. In India and the United States of America, similar larger discs area among males was reported (Ong *et al*., 1999 ; Jonas *et al*., 2003). The Indian study however did not find the difference to be of statistical significance.

In agreement with the findings of gender difference in this study, Varma *et al*., (1994) in South-eastern Baltimore reported that males had 3% larger disc areas than the females of the study. In their study, no correction for axial magnification was done as in this study. Also similar to our finding, Tarrannum, *et al*., (2011) in Indian population observed that disc area among males was significantly larger than that of females in their study. As females in their study had shorter axial length, they concluded that the gender based difference observed was likely due to axial magnification. Our study also conforms to the findings of Rankor, who also observed similar gender relationship (Rankor *et al*., 2013). They found that disc area and CDR were significantly higher in males than in the female subjects. Even after correction for refractive error and axial length, statistically significant gender association was apparent.

The differences observed in this of the disc parameters in relations with gender were different from observation by Shaun *et al*., (2008) among Indian population. They found no gender association with all the optic nerve head (ONH) parameters. Females, however, who comprised majority of their subjects, were more associated with refractive error than the male subjects and this could have influenced the findings of their study. Similarly, as against what was observed in this study, Tharwat in Egypt did not show any significant gender difference with ONH parameters. They found more of RNFL association with gender than ONH findings (Tharwat *et al*., 2013).

This study observed a statistical significant (p=0.01) decline in neuroretinal rim area among the more elderly subjects against the younger subjects (Figure 4.8). The highest value of disc rim area was observed among the youngest age group while the lowest was among the oldest group. No significant association was observed for disc area. Cup to disc ratio was also found to be significantly larger in the older subjects with however weak association. After adjusting for sex, rim area was still statistically associated with age.

Reduction in the rim area among the older subjects observed in this study was not demonstrated in the study by Varma *et al*., (1994). They did not find any significant rim decline in all age groups. That could be due the fact that their subjects' ages were clustered around 40 years and therefore no significant different was observed. Many other studies did not show any significant age related difference in optic nerve head (ONH) parameters. For example the Vellory eye study in India did not show any significant age relationship with ONH parameters after correction for gender (Jonas *et al*., 2003). The smaller sample size (70 subjects) than this study might have resulted in having no significant difference.

Similar age related difference observed in this study was demonstrated by other studies. Tsai *et al*., (1992) in the Baltimore, USA observed that there was a steady decline of neuroretinal rim from the youngest to the oldest subjects. They used Rodenstock disc analyser (RODA) for ONH evaluating the subjects whose ages ranged from 15 to 55 years.

Our finding was also in support of what was observed in Cameroon in a study among a rural southern Cameroon (Paul-Rolf *et al*., 2009). Using fundus photography, they observed an average CDR of 0.15 in the youngest and 0.45 in the oldest subjects. This positive correlation they observed was not very far from the finding of this study despite the fact that they used a different examination procedure. Similarly, a study in in Kano, Nigeria found that peripapillary rim area declined steadily with advancing age. The study employed the stratus type OCT similar to that used in this study to examine Hausa adult volunteers. Although they had fewer sample size (110) than this study, similar negative correlation of neuroretinal rim with age was observed as in the study (Lawan *et al*., 2014).

CHAPTER FIVE

SUMMARY, CONCLUSION AND RECOMMENDATIONS

5.1 SUMMARY

This was a descriptive cross-sectional study conducted on 342 adult Hausa volunteers at the eye clinic of the Aminu Kano Teaching Hospital. Subjects underwent complete eye examination and then optical coherence tomographic (OCT) scan of the optic nerve heads (ONH) was performed.

The mean optic disc area, rim area and cup disc ratio (CDR) found in the study were $2.35mm^2$, $1.76mm^2$ and 0.44. It was observed that most of the optic disc parameters in the subjects were larger in the left than the right eyes, but this was not found to be of statistical significance. After correction for gender, still no statistically significant difference was observed between the right and the left. No significant bilateral variation between the right and left eyes was observed among the study population.

Male subjects were found to have statistically significant larger ($2.38mm^2$) disc area than the female subjects ($2.29mm^2$). Males also had statistically significant larger CDRs. The rim area obtained in the study population showed a steady decline with increasing age and the mean vertical cup to disc ratio (CDR) was observed to be positively correlated with age.

5.2 CONCLUSION

The study has provided a normative data and reference values on the parameters of the optic nerve head among Hausa adults. This can be used as a baseline tool in evaluation and management of patients with glaucoma and other optic neuropathies.

5.3 RECOMMENDATIOS

1. There is need to conduct similar study on other ethnic groups in the country to provide a national reference value.
2. There is need to incorporating other ocular parameters like axial length measurements and refraction in a similar study to provide a more reliable reference value of the optic nerve head indices.
3. There is need for ophthalmologists to employ the use of optical coherence tomography as a tool for disease assessment and monitoring as the technology is available in our environment.

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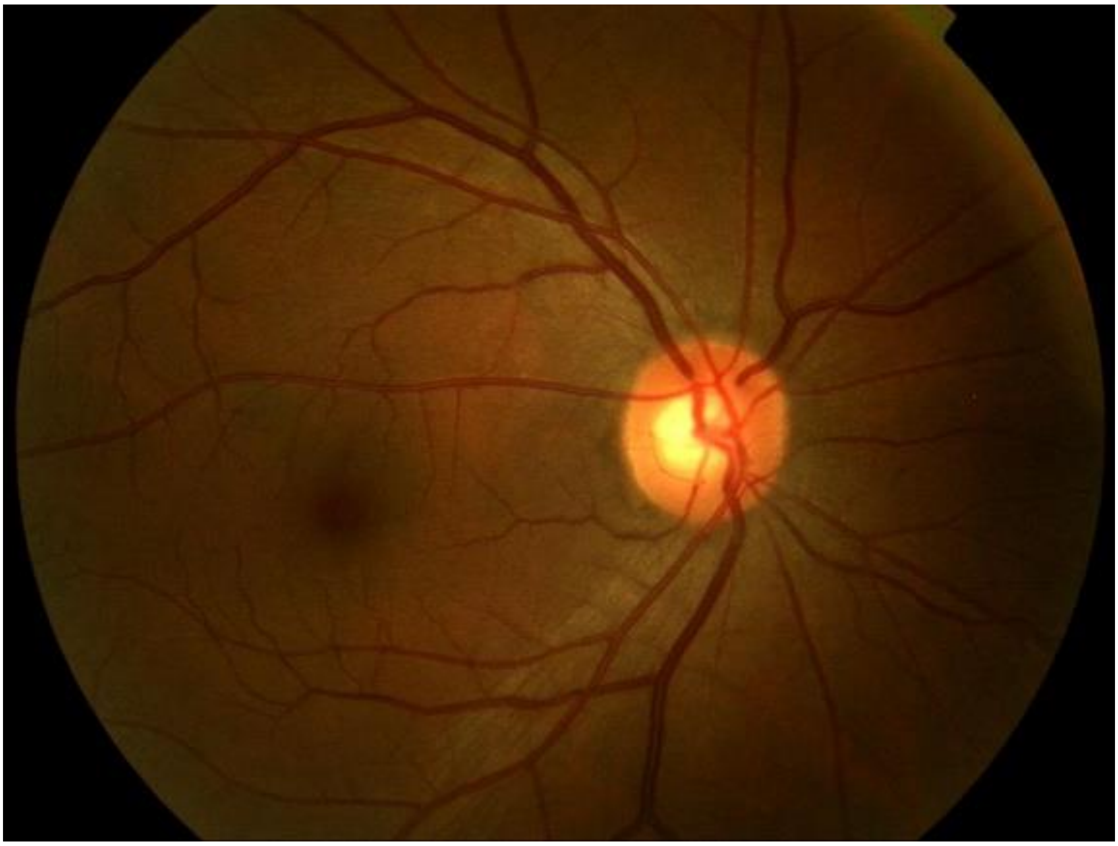

PLATE I: Ophthalmoscopic appearance of the normal optic disc (ONH)

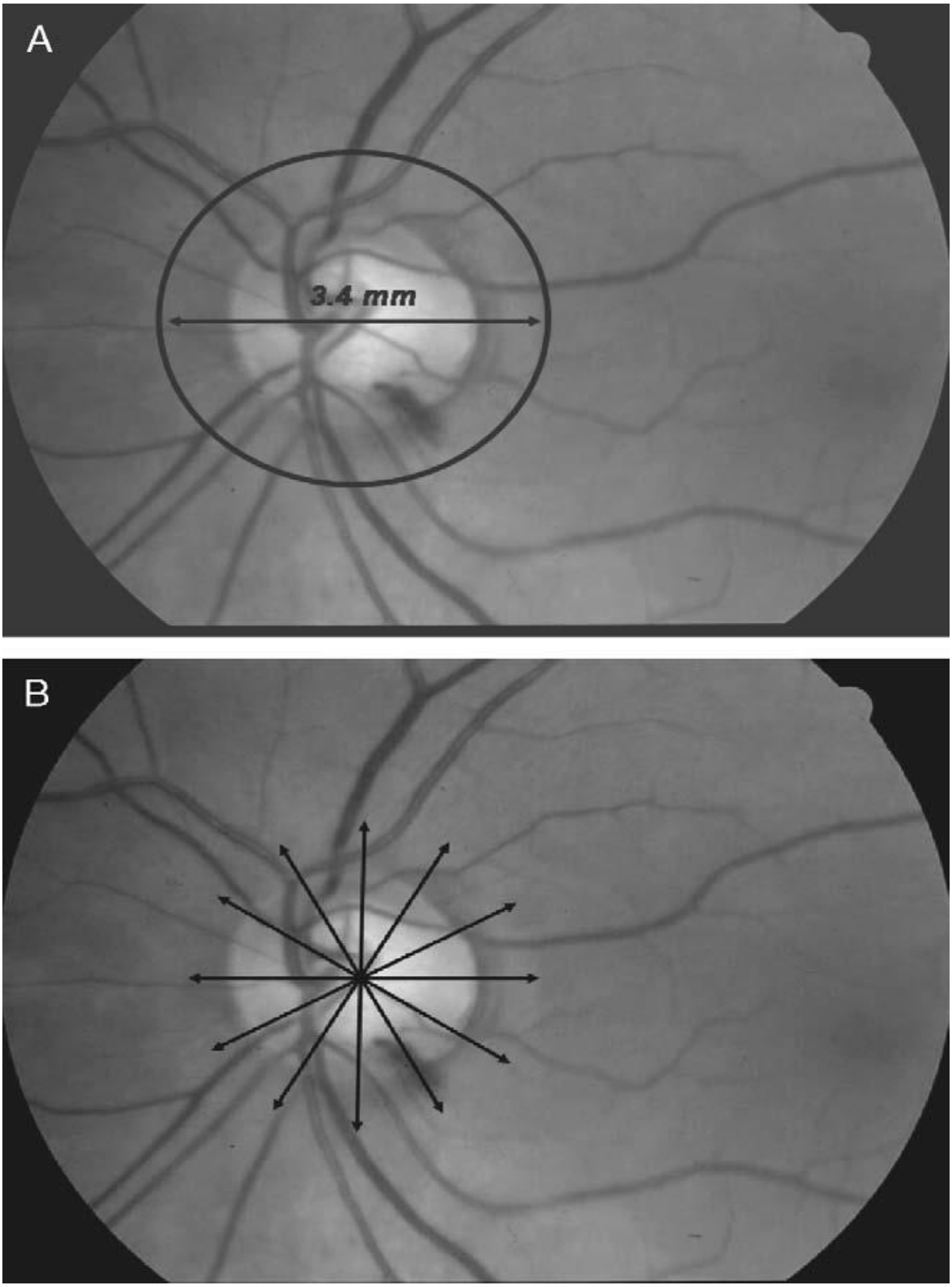

PLATE II: OCT Scan Protocol. A, Retinal nerve fibre. B, Optic nerve head

Appendix I

CONSENT FORM

I am Nuraddeen Jaafar, a masters student in Bayero University, Kano. I am conducting a research titled '**Morphormetric study of the Optic Nerve Head in Normal Hausa Nigerian Adults, Using Optical Coherence Tomography"**.

The procedure will involve examining the eye and if found suitable, scan photographs will be taken with a machine. The procedure is entirely harmless. Examinations and the scanning will be carried out at the eye clinic of Aminu Kano Teaching hospital.

Please note that:

1. Participation is voluntary
2. You have the right to withdraw from the study at any time you so wish
3. The information provided will be treated with confidence
4. The result of the study will be explained to you
5. All aspects involved in the study are at no cost to you (FREE).

I ---

give my consent to participate in this study.

Researcher :

Nuraddeen Jaafar
Signature and date ---------------------------
Phone 08069393937
E mail: nuraddeen75@yahoo.com

Appendix II

DATA SHEET

1. ID………..

2. Sex ………………

3.Age ……………………………

4. Ethnicity

father……………..paternal grand father…………… paternal grand mother………..

mother………….. maternal grand father…………… maternal grand mother…………

5. Occupation ……………………………………

6. Level of Education

Primary	Secondary	Tertiary	None

7. Ocular findings

Variable	**Measurement**	
	RT	**LT**
V A		
IOP		
Anterior segment		
Posterior segment		

8. OCT ONH parameters

Variable	**Measurement**	
	RT	**LT**
DISC AREA		
RIM AREA		
CUP AREA		
CUP DISC RATIO		