GHANA COLLEGE OF PHYSICIANS AND SURGEONS

Faculty of Ophthalmology

Determination of Normative Values for Central Corneal Thickness in Ghanaian Children in the Ablekuma South Sub-Metropolitan Area

A Dissertation submitted to the Faculty of Ophthalmology, in partial fulfillment of the requirements for the conferment of a Fellow of the Ghana College of Surgeons (FGCS)

BY

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DECLARATION BY CANDIDATE

This dissertation was based on my own research, which was conducted under the supervision of my consultants at the Lions International Eye Centre, Korle Bu Teaching Hospital. I declare that except for references to other people's work which I have duly acknowledged, this dissertation is original to me. This dissertation has not been submitted in part or full for the award of any other degree.

Signed: .....

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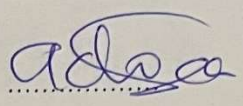
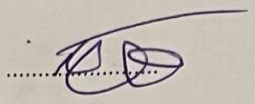
Prof. Vera Adobea Essuman (FGCPS, FWACS)		13/06/2022
Dr. Naa Naamuah Tagoe (FGCPS, FWACS)		13/6/2022

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ABSTRACT

Background

The thickness of the cornea has importance in ocular health. Several studies including the work done by the Ocular Hypertension Treatment Study (OHTS) have demonstrated the significance of Central Corneal Thickness (CCT) measurements in the accurate assessment of intraocular pressure (IOP), accurate diagnosis and prognosis of glaucoma. The variation of CCT with age, gender and race have also been confirmed in studies. CCT has been shown to increase gradually with age in children stabilizing after the age of 10 years and has been shown to be thinner in African/Americans compared to whites. In the adult population, CCT values have been shown to affect the accurate diagnosis and management of glaucoma resulting in the need for assessment of the normal CCT values for any given population.

The racial and ethnic variation in CCT values does not support extrapolation of normal population values from one geographic location to the other. In Ghana, data on normal CCT values in children is lacking, resulting in assessment of intraocular pressure based on reference values from populations with potentially different CCT values. It is therefore imperative that CCT values be assessed in healthy Ghanaian children to determine normal values for our population. This will provide baseline data for assessment of deviations from the mean values in the Ghanaian population in future studies to better correlate CCT with IOP values in Ghana.

Aim

The overall aim of this study was to measure the CCT in healthy Ghanaian children and determine the normal values of defined age-groups.

Materials and methods

A prospective cross-sectional study was conducted to measure the CCT of 420 children (840 eyes) aged 6 to 15 years. Informed written consent was obtained from parents/ guardians and assent obtained from children aged 8 years and above. An interviewer-administered questionnaire was used to obtain demographic data followed by an anterior and posterior ocular exam. One drop of 0.5% amethocaine was instilled in the eye 1 minute prior to measurement after which a hand-held pachymeter was used to take 3 measurements from the central 3mm of the cornea of the eye.

Data handling and statistical analysis plan

Statistically significant differences were assessed with the independent t-test for differences in continuous variables such as CCT, analysis of variance (ANOVA) for differences between groups such as age and gender and linear regression for differences in trends. Statistical significance was set at a *p value* of less than 0.05.

Results:

The overall mean CCT was 538.8 ± 27 µm (420 children, 840 eyes) and among children aged 6-8 years was 541.4±24.9 µm., for children aged 8-10 years 534.9±25.8 µm and those 10-15 years 538.3±28.6 µm. ANOVA (Analysis of variance with the F statistics) with the Post Hoc tests showed no significant difference in mean CCT among the age groups for both eyes. There was found to be a weak negative correlation between CCT and age. Thus, CCT decreased with age. Though CCT was higher in males, the difference was not statistically significant. Our study also demonstrated that there was a weak positive correlation between CCT and IOP. CCT was higher in hyperopes compared to emmetropes and thinnest in myopes and the difference was statistically significant.

Conclusion:

CCT in healthy Ghanaian children was found to be 538.8 ± 27 µm and did not vary significantly among age groups or sex. Results of this study provide baseline data for larger national studies that could ultimately lead to the development of national reference ranges for CCT values in the Ghanaian paediatric population. Secondary benefits of this study include improvement in the diagnosis, prognostic prediction, and management of glaucoma in children.

Keywords: Corneal thickness, age, children, Ghanaian, glaucoma

Table of Contents

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AMA	Accra Metropolitan Area
ANOVA	Analysis of variance
BES	Beijing Eye Study
CCT	Central corneal thickness
EP	Evangelical Presbyterian
IOP	Intraocular pressure
IRB	Institutional review board
KBTH	Korle Bu Teaching Hospital
NTG	Normal Tension Glaucoma
OHT	Ocular hypertension
OHTS	Ocular hypertension treatment study
PEDIG	Pediatric Eye Investigative Group
POAG	Primary Open Angle Glaucoma
RAND	Random number generator
SRS	Simple Random Sampling
SSA	Sub-Saharan Africa
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

The cornea is transparent and constitutes the anterior most part of the eyeball and its thickness plays an important role in the diagnosis and management of certain ocular pathologies. It measures about 11-12 mm horizontally and 10-11 mm vertically.[1] It plays a protective role as well as being responsible for approximately two-thirds to 75% of the optical power of the eye. [2,3] The healthy cornea is free of blood vessels and receives nutrient supply via the tear film anteriorly and aqueous humour posteriorly.

The layers of the cornea from anterior to posterior are the epithelium, Bowman layer, stroma, Descemet membrane and the endothelium. The corneal stroma accounts for 90% of the corneal thickness.

The average corneal thickness is 540 um and is thinnest in the centre with thickness increasing towards the periphery.[4,5] Corneal thickness has been reported to undergo diurnal variation, typically thickest on waking up, returning to baseline upon 2 hours of waking.[3,6] This fact needs to be taken into consideration for accurate measurement and interpretation of CCT.

The thickness of the cornea has importance in ocular health. Its measurement is useful in the accurate diagnosis of some corneal pathologies such as keratoconus, other corneal ectasias and corneal dystrophies[3]. Evaluation of the CCT is key in the diagnosis and management of glaucoma. Several studies including the work done by the Ocular Hypertension Treatment Study (OHTS) have demonstrated the significance of Central Corneal Thickness (CCT) measurements in the accurate assessment of intraocular pressure, accurate diagnosis and prognosis of glaucoma[4,7–10].

Central corneal thickness also plays a significant role in the area of refractive surgery. In the past refractive surgery was reserved for adult patients and most refractive surgeons would only perform this in adults, however paediatric refractive surgery is now an emerging field, found to be very useful for children whose refractive errors cannot be corrected with conventional means such as spectacles and contact lenses.[11,12]. These refractive errors include high anisometropia and high ametropia. In procedures such as excimer laser photoablation, precise measurement of corneal diameter, curvature and central thickness need to be ascertained to be able to determine the flap size.[12–15]

The determination of mean CCT values for children is imperative as it affects evaluation for glaucoma as well as plays a role in formulating guidelines for paediatric refractive surgery in our population.

RATIONALE FOR THE STUDY

The variation of CCT with age, gender and race has been confirmed in many studies.[4,16–19] Whilst CCT has been shown to increase gradually with age in children, stabilizing after the age of 10 years[20], it has also been shown to be thinner in African/Americans compared to whites.[16,20–22] In the adult population, CCT values have been shown to affect the accurate diagnosis and management of glaucoma resulting in the need for assessment of the normal CCT values for a given population.[7,23,24]This principle also applies in children, particularly in the case of paediatric glaucoma suspects who do not have all the overt clinical signs to establish a diagnosis of glaucoma. Corneal thickness has been found to be thinner in children with primary congenital glaucoma(PCG) and those with juvenile open angle glaucoma(JOAG) and thicker in aphakic/pseudophakic children as well those with aniridia.[25] The racial and ethnic variation in CCT values do not support extrapolation of normal population values from one geographic location to the other.[26] Studies in paediatric populations have observed similar findings with CCT mean values being thinner in children of African descent(535 µm -551 µm) compared to Caucasians(559 µm - 573 µm).[20,21,26] It is therefore essential to determine the normative CCT values for children in Ghanaian population. This study will provide initial data on CCT values in Ghanaian children and will serve as a foundation for subsequent larger studies. This will assist ophthalmologists in our setting to better correlate IOP with CCT values in Ghanaian children in the diagnosis and management of glaucoma.

Secondly, Paediatric refractive surgery is an emerging field and as we aim to provide comprehensive eye care services to our paediatric population in Ghana, it is important to establish baseline data on important parameters such as CCT in children to guide formulation of relevant national guidelines.

STATEMENT OF RESEARCH PROBLEM

The ocular hypertension study brought to attention the importance of CCT in the risk assessment, evaluation and management of glaucoma.[27] Globally, data on CCT measurement in children is limited with most published work done in the developed countries.[20] Considering the fact that CCT measurements vary depending on race and ethnicity, local studies need to be done to enable better interpretation of IOP values for the diagnosis and management of glaucoma as well as aid in the diagnosis of certain corneal pathologies. A number of studies have reported lower CCT values in children of African descent.[17,20,21,28] The sample size for children of African descent in some of these studies is small, with very few studies being conducted in Sub-Saharan Africa.

In Ghana, data on normal CCT values in children is lacking, resulting in assessment of intraocular pressure based on reference values from populations with potentially different CCT values. This makes evaluation of Ghanaian children for some childhood glaucomas such as juvenile open angle glaucoma and other corneal pathologies difficult.

Anecdotally, children with juvenile glaucoma are diagnosed late. This is partly because they present late and also because some may have their IOP at borderline values requiring prolonged follow up to establish progression. This is a situation where knowledge of CCT of such individuals may help with early diagnosis, especially in those with thin CCT.

The growing evidence of racial variation in CCT values in children discourages the extrapolation of CCT values across different races and geographic locations. This, coupled with the scanty data on CCT values for children in the West African sub-region, makes it imperative for more studies to fill this gap in knowledge. This study therefore seeks to determine the CCT values in healthy Ghanaian children in the Ablekuma sub-metropolitan area to serve as a baseline for further studies on the role of CCT in the diagnosis of paediatric glaucoma and other pathologies.

HYPOTHESIS

Null hypothesis: There is no difference in mean CCT values of Ghanaian children compared to Caucasian children.

AIM AND SPECIFIC OBJECTIVES OF THE STUDY

Aim:

The overall aim of this study is to determine the normative CCT values in healthy Ghanaian children aged 6-15 years in the Ablekuma Sub-Metropolitan area using ultrasound pachymetry.

Specific Objectives:

1. To determine the mean central corneal thickness in healthy Ghanaian children.
2. To assess the variations in mean corneal thickness with age in healthy Ghanaian children
3. To evaluate the difference in central corneal thickness between male and female Ghanaian children
4. To determine the relationship between CCT and IOP as well as refractive error.

CHAPTER 2
LITERATURE REVIEW

2.1. Background:

The thickness of the cornea has importance in ocular health. Several studies including the work done by the Ocular Hypertension Treatment Study (OHTS) have demonstrated the significance of Central Corneal Thickness (CCT) measurements in the accurate assessment of intraocular pressure (IOP), accurate diagnosis and prognosis of glaucoma.[20,27,29,30] The Ocular Hypertension Treatment Study (OHTS) was a multicenter, prospective, randomized clinical trial that evaluated the safety and efficacy of topical ocular hypotensive medications in preventing or delaying the onset of optic nerve damage as well as visual field loss, that is, primary open-angle glaucoma(POAG) in individuals with elevated IOP and no evidence of glaucomatous damage.[4,27] A part of the study investigated baseline demographic and clinical factors that predicted which participants in the OHTS developed POAG. One very significant finding was that thinner central corneal thickness measurement predicted the development of POAG in both univariate and multivariate models. Mean central corneal thickness was 553.1±38.8µm among participants who developed POAG compared with 574.3±37.8 µm among those who did not develop POAG and participants with a corneal thickness of 555µmor less had a 3-fold greater risk of developing POAG compared with participants whose CTT was more than 588 µm.[27]

These results were validated in the European Glaucoma Prevention Study (EGPS) and in the merged OHTS/ EGPS prediction model it was found that each 40 µm of central corneal thinning conferred a 2-fold increased risk for developing glaucoma over a 5 year period[8] thus indicating that patients with a thin cornea had a high risk of glaucoma development. CCT has therefore been identified as a significant predictor of glaucoma development and progression.[27,29]

Measurement of the central corneal thickness is also required for the preoperative assessment and preparation of patients going in for corneal refractive surgery.[11,31] With the development of refractive surgery, particularly photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK), the importance of CCT has again been recognized. Ophthalmologists have noted that after laser refractive surgery, IOP tends to decrease as CCT decreases.[8] Paediatric refractive surgery is an emerging field and there is growing literature about the use of various refractive

technologies in the pediatric population.[12,13] The most common indications for pediatric refractive surgery today are unilateral anisometropic amblyopia, bilateral high ametropia and refractive accommodative esotropia. [13,32] Most of these children have failed traditional treatments such as occlusion therapy, glasses and contact lenses[13,32] Both laser-assisted in situ keratomileusis(LASIK) and Photorefractive keratectomy (PRK) have been used in children as young as two years of age.[33,34] Astle et al[33] demonstrated that PRK could be done successfully in children when he conducted the procedure in 40 eyes, with mean age of 6 years.

CCT can be measured by different modalities which may either be through ultrasound or optical techniques.[35]

2.2. Corneal anatomy and topography:

The cornea and sclera constitute the outer coat of the eyeball.[36] The cornea, which is the anterior most part of the globe is an avascular and transparent structure that acts as a barrier and protects the eye against infections.[36] It also contributes to two-third of the refractive power of the eye, which corresponds to approximately 40-44 dioptres of refractive power.[36,37] The human cornea is composed of five layers: the corneal epithelium, Bowman's layer, stroma, Descemet's membrane and endothelium (figure 1).

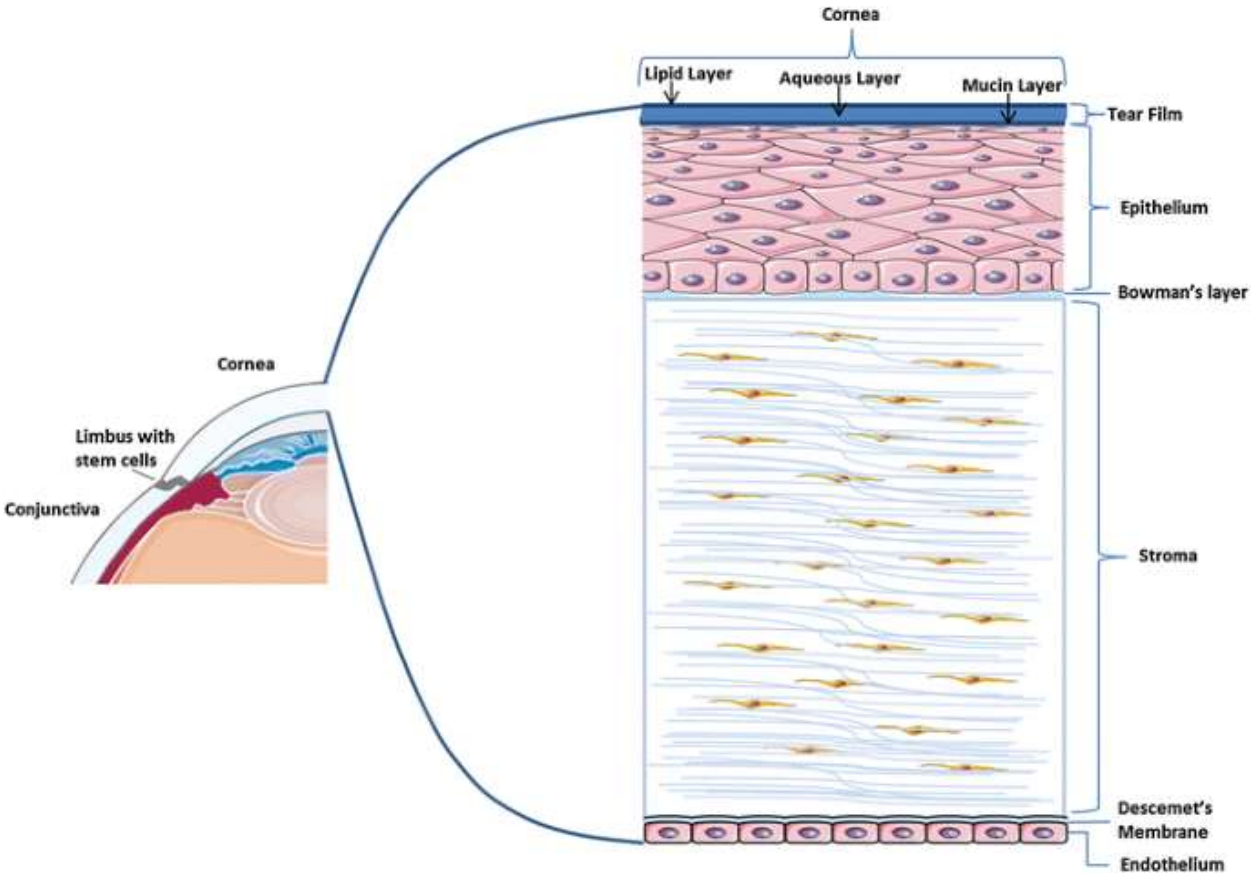

Figure 1: Image of layers of cornea[30]

- Corneal epithelium: This is the first layer of the cornea consisting of 5-7 layers of non-keratinized stratified squamous epithelial cells (figure 1) and is about 50-53 µm deep.[36,38] The deepest layer of the corneal epithelium comprises of a single layer of either cuboidal or columnar cells approximately 20 µm tall, referred to as the basal layer.[36] There are differences in the microscopic structure between the peripheral and central cornea epithelium.[36,37] In the central cornea, there are about 5–7 layers with columnar-shaped basal cells whiles in the peripheral cornea, the epithelium has 7–10 layers with cuboidal basal cells..[36]
- Bowman's layer: This is the second layer of corneal epithelium which is a fibrous meshwork beneath the corneal epithelium and most anterior portion of the stroma.[36] It is condensation of collagen and proteoglycans and has no regenerative ability.[36] Bowman's

layer is acellular and is not regarded as a true membrane.[36] The main function is to help the cornea maintains its shape.[36]

- Corneal stroma: Most of the corneal tissue is constituted by the stroma, which is a collagen-rich central layer that comprises about 90% of the total thickness of the cornea.[36,37] Keratocytes are the major cell type of stroma and they are involved in maintaining the extracellular matrix environment.[36] They synthesize collagen molecules and glycosaminoglycans(GAGs),[36] The stroma of the cornea is characteristically transparent which is the result of the precise arrangement of stromal fibers and extracellular matrix which are laid in a parallel fashion(figure 2).[36] These fibres are organized into bundles referred to as corneal fibrils which predominantly contain Type I collagen.[36] Corneal collagen fibrils are further packed into layers or lamellae(figure4) which resist the tensile forces due to intraocular pressure as well as protecting the internal ocular tissues from external trauma.[36,37] The human corneal stroma contains approximately two hundred lamellae, each layer arranged at right angles relative to fibers in adjacent lamella.[36,37] The stroma is generally responsible for the maintenance of corneal transparency, providing mechanical strength of the cornea, and is the main refracting lens.[36]

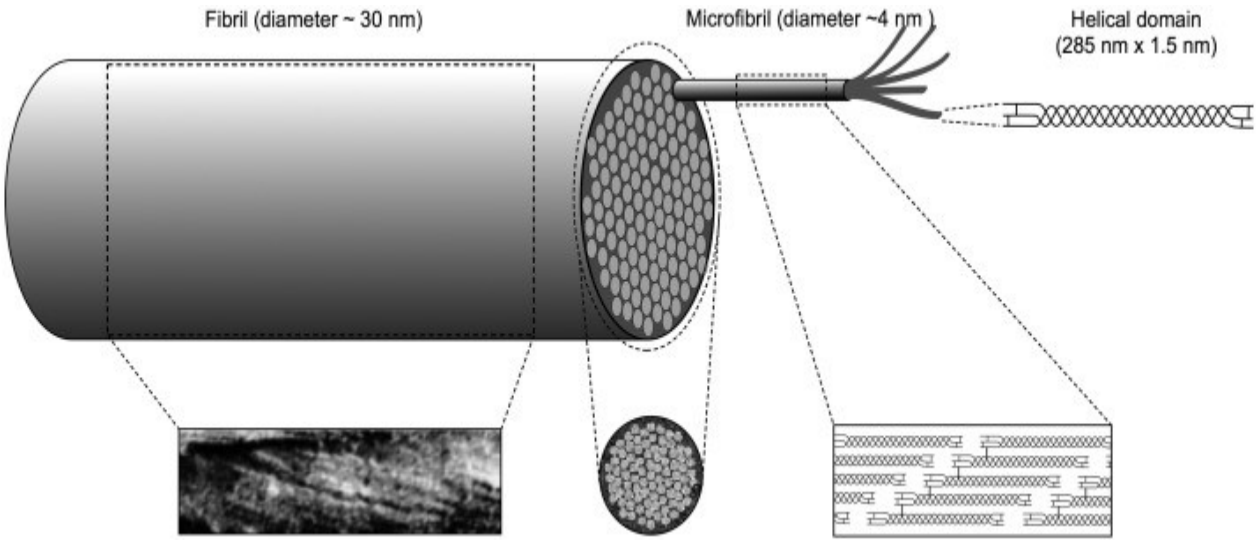

Figure 2: Arrangement of corneal fibres in parallel fashion[29]

- Descemet's membrane: It is made up of Type IV collagen and laminin and serves as the resting layer for endothelial cells.[36]
- Endothelial layer: The endothelium is the innermost layer of the cornea and is a single layer of hexagonal-shaped cells which are metabolically active (figure 3). There is an endothelial pump which regulates water content thus helps in maintaining corneal clarity. [36]

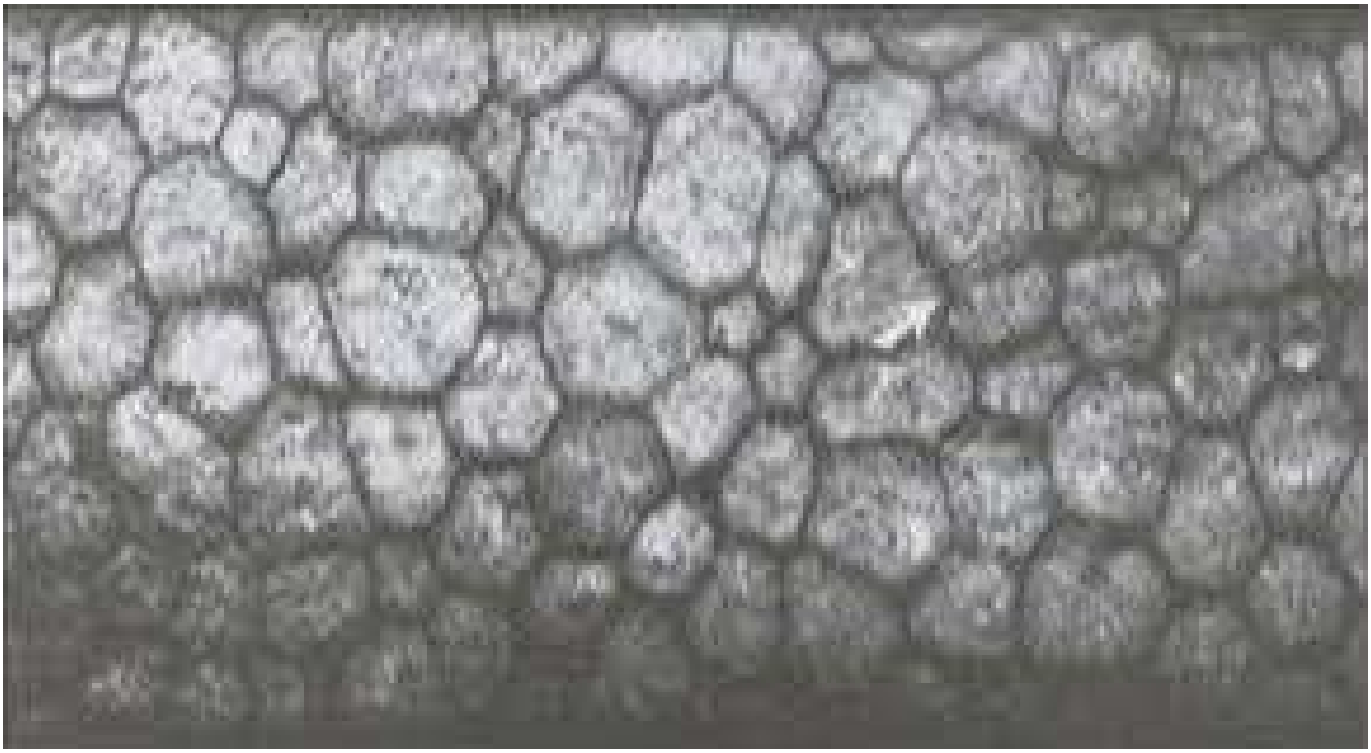

Figure 3: Corneal endothelium showing hexagonal shaped cells[28]

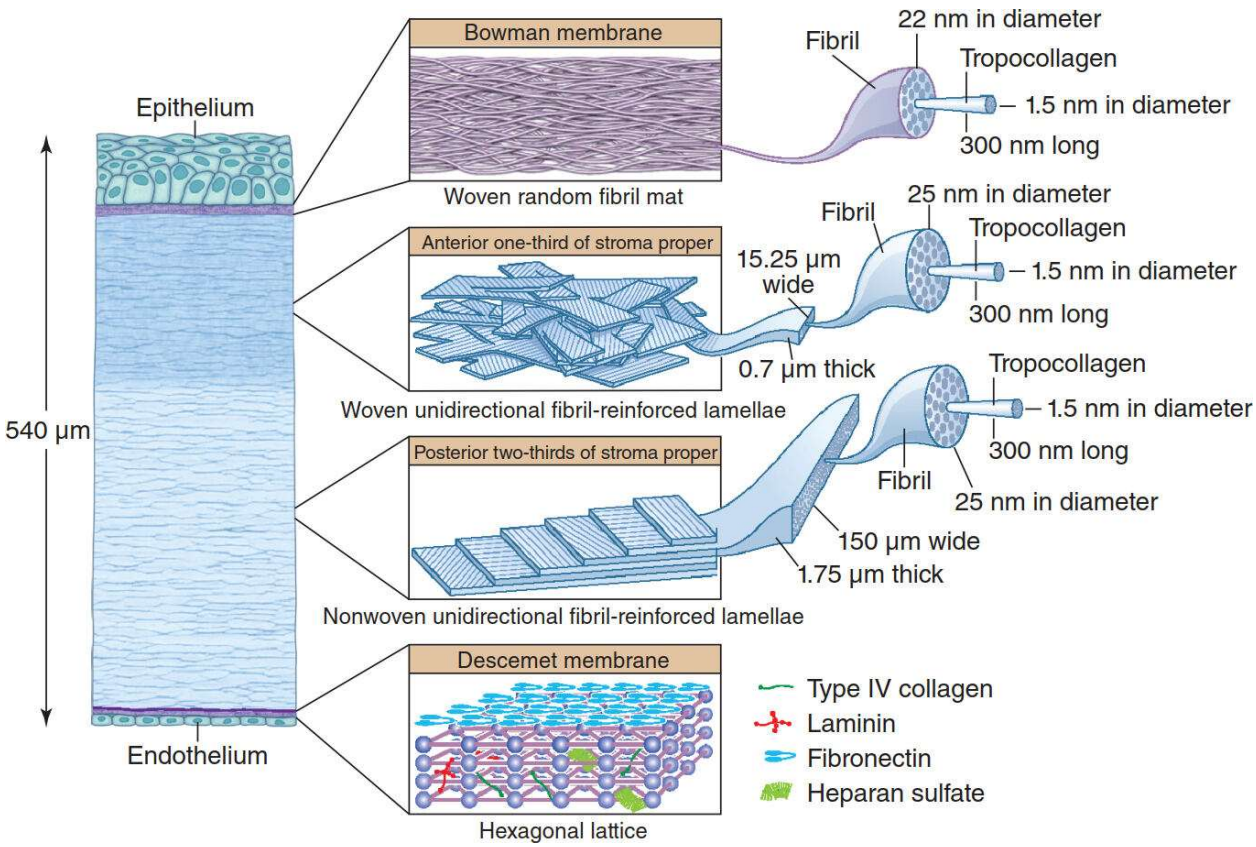

Figure 4: Detailed description of layers of cornea[32]

The dimensions of the cornea is 11–12 mm horizontally and 9–11 mm vertically.[36] The cornea has a central and peripheral portion (figure 5). The thickness of the cornea is not even in all zones and there is a gradual increase in thickness from central cornea to the periphery. The thickest part of the cornea from a study by Zheng et al[39] was at the superior region, followed by the nasal, then inferior and temporal regions. Alteration in tissue thickness is due to increase in the amount of collagen in the peripheral stroma.[36]

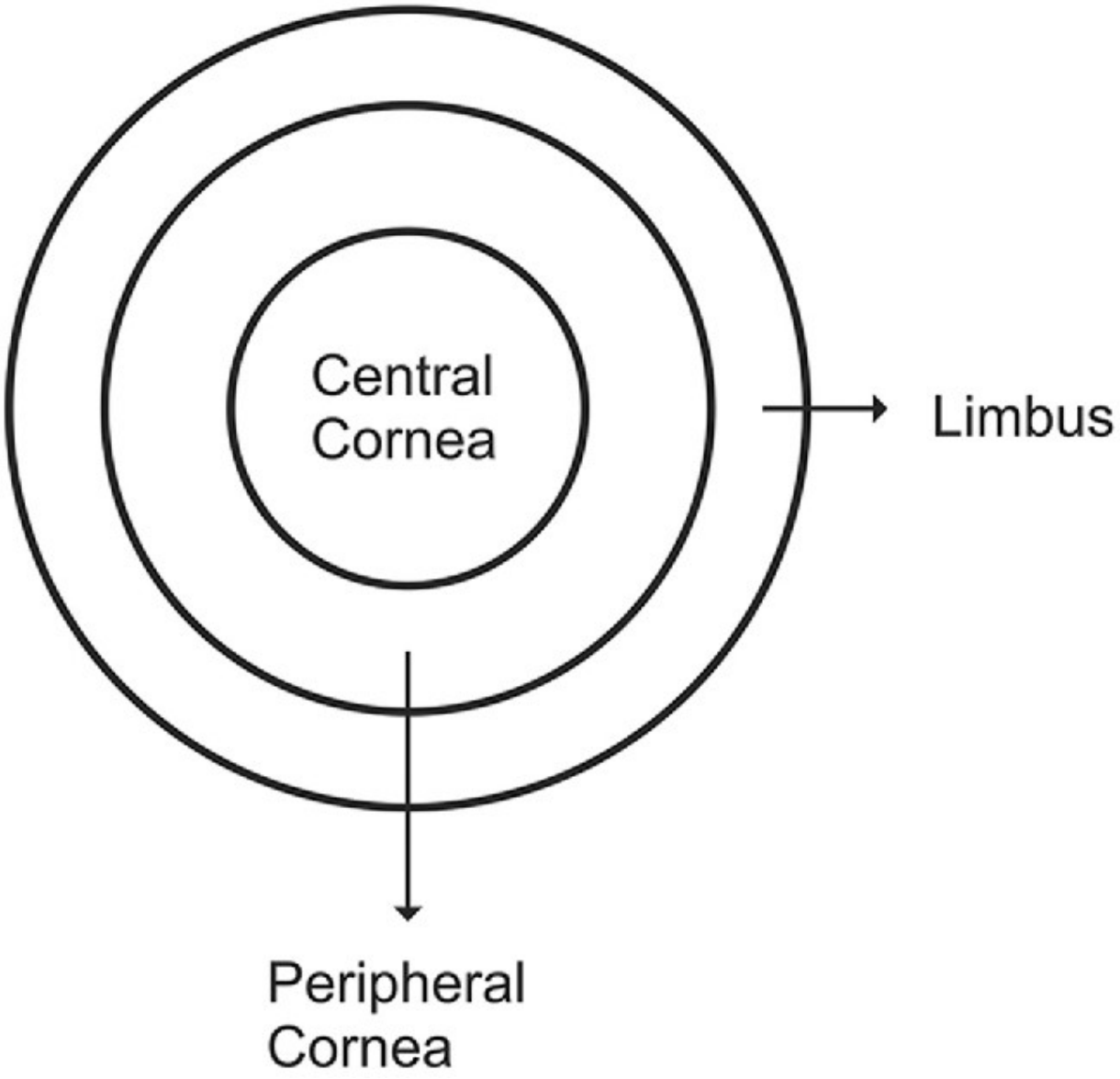

Figure 5: Picture showing central and peripheral cornea[28]

2.3. Role of CCT in IOP measurement

The cornea plays a significant role in IOP measurement and diagnosis of glaucoma.[29] Intraocular pressure is estimated by measuring the resistance of the eye to indentation or applanation by an external force and this is referred to as tonometry.[40] All tonometry techniques used in the measurement of IOP are related to the elasticity of the eye which refers to the ability of an object to resume its normal shape after being compressed or stretched.[8,41,42] This elasticity of the eye is mainly from the cornea and the sclera. Corneal elasticity mainly depends on corneal thickness and hysteresis which refers to the cornea's ability to absorb and dissipate energy.[43] Corneal hysteresis may interfere with IOP measurements and although it is not clear what it measures, it appears this variable describes the response of the cornea to rapid deformation.[8,43] Central corneal thickness on the other hand is fairly constant and is an independent factor unrelated to other ocular parameters such as corneal curvature, anterior chamber depth and axial length , hence can be used as a proxy for IOP measurement.[44,45] IOP measurement has been a matter of controversy for years due to increasing knowledge on the effect of corneal properties on its accuracy. In 1950, Goldmann introduced an approach to measure IOP, known called applanation tonometry, which became the gold standard.[46] Applanation tonometry is based on a modification of the Imbert-Fick law that relates external force directly to the internal pressure of a sphere multiplied by the area flattened by the force.[47]

The Imbert-Fick law:

$P = W/A$

Where P = pressure in sphere, W = applanating weight (force) and A = applanated area.[48]

This approach is related to the elasticity of the cornea, which indicates that it depends on corneal thickness and hysteresis.[46]

The relationship between IOP and CCT was well known by Goldmann when he introduced his tonometer in 1950. Based on the Imbert-Fick's principle, Goldmann clearly stated that this relationship holds only for an average corneal thickness of 520 μm measured by optical

pachymetry.[29] However, a review article by Robert L. Stamper stated that Goldmann had used only a few Swiss subjects in developing the calculations based upon which the Goldmann applanation tonometer was developed. Though he was aware corneal mechanical properties might influence the applanation readings because the corneal thickness measured from his subjects did not vary significantly, he considered it inconsequential. Unfortunately there were no individuals of African heritage in his cohort.[49] It has now been established by several studies that the central corneal thickness is not the same in all populations and can have a significant effect or be a source of error on applanation readings.[4,8,29] However, the Goldmann applanation tonometer despite its imperfections is still considered the gold standard for measuring intraocular pressure.[21,29]

As early as in the 1970s and 1990s, Ehlers[50] and Whitacre et al[23] found that thinner corneas lead to an underestimation of IOP whilst thicker corneas gave an overestimation of intraocular pressure. Ehlers et al[51] in human experiments found that correlation between corneal thickness and error of applanation was very significant ($P < 0.001$). These findings were brought to the attention of the general ophthalmology society in 1997 by Herndon et al.[5] Also, the ocular hypertension treatment study(OHTS) further emphasized the fact that there was a significant correlation between IOP and CCT, and there was underestimation or overestimation of IOP measurements based on whether central corneas were thinner or thicker than average normal values respectively.[4] The Beijing Eye study(BES) was conducted in 2006 to evaluate the distribution of central corneal thickness and its associations in over 3,000 adult Chinese participants. They found that intraocular pressure measurements increased for each μm increase in central corneal thickness by 0.03 mmHg.[52] See in Figure 6:

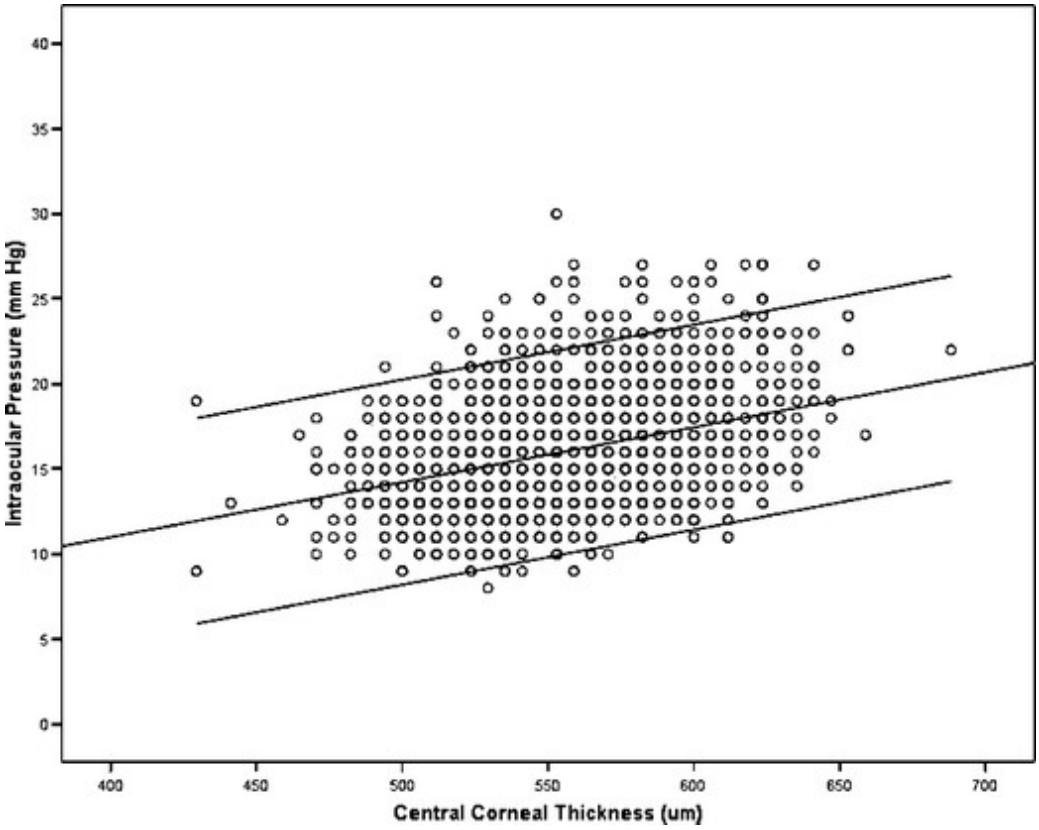

Figure 6: Scattergram showing the relationship between intraocular pressure and central corneal thickness in 3,100 subjects aged 45 years and participating in the Beijing Eye Study 2006[54]

Patwardhan et al[53] in a study to assess the impact of applying the knowledge of effect of central corneal thickness (CCT) on glaucoma management in a United Kingdom district general hospital found that CCT and adjusted IOP measurement could influence glaucoma management in a clinical context.[53]

They found that based on CCT readings, 33.9% of eyes had the IOP adjusted by greater than ±2 mmHg. 18% of eyes had the IOP reduced while 16.1% had their IOP increased. The IOP adjustment was made according to the manufacturer's logarithm(Pachmate™ DGH 55, DGH Technology Inc, PA, USA) which is based on Ehlers et al.[51,53]

See conversion table below (Table 1) showing a correction table used for adjusting IOP based on central corneal thickness (provided with Pachmate™ pachymeter and based on Ehlers et al[51,53])

Table 1: IOP Conversion table

Central Corneal Thickness (Microns)	Adjustment in IOP (mm Hg)
445	+7
455	+6
465	+6
475	+5
485	+4
495	+4
505	+3
515	+2
525	+1
535	+1
545	0
555	-1
565	-1
575	-2
585	-3
595	-4
605	-4
615	-5
625	-6
635	-6
645	-7

These IOP adjustments have implications on diagnosis and subsequent management of patients suspected to have glaucoma.

54

2.4. CCT and refractive error

There have been conflicting views on the relationship between CCT and refractive error. In a study by the paediatric eye investigative group (PEDIG) among 2079 children from age 0 to 17 years, it was found that CCT values were affected by the type and magnitude of refractive error, generally being lower in myopic eyes.[20] The spherical equivalent refractive error for the cohort ranged from −17.50 D to +13.00 D and a regression analysis done showed that mean CCT was 1 micrometer thinner for every 1.00 D of lower spherical equivalent refractive error(less hyperopia, more myopia). [20] The study demonstrated by further analysis limited to subjects with spherical equivalent of −6.00 to +8.00 D that findings were similar therefore confirming that the result observed was not due to a small number of subjects with high myopia and thin central corneas or high hyperopia and thick central corneas.[20] Another Egyptian study by Mourad et al found that CCT was generally lower in ametropes compared to emmetropes.[54] Their study comprised 84 eyes which were subdivided into three main groups: group 1 included 28 myopic eyes, group 2 included 28 hyperopic eyes, and group 3 included 28 emmetropic eyes. The study found that comparing the CCT of the myopia group with that of the hyperopia group, the difference was not statistically significant (P>0.05). However, when the myopia group CCT was compared with that of the emmetropia group statistically, it was significantly higher in the emmetropia group (P=0.031).[54] Comparing the CCT of the hyperopia group with that of the emmetropia group, it was also noted that CCT was statistically higher in the emmetropia group (P=0.015).[54]

Studies investigating the correlation between myopia and CCT have reported varied findings. Chang et al in a study among 216 young adults with an averaged refractive error of −4.17 diopters reported that CCT was thinner in eyes that were more myopic.[55] Kotb and Eissa[56] in another Egyptian study among myopes, demonstrated that the greater the myopic refractive error, the thinner the cornea. A large Japanese study by Suzuki et al showed that there was correlation between refraction and CCT but this differed between men and women. In men, refraction negatively correlated with CCT with the CCT values being thicker in myopic eyes compared to emmetropic eyes.[57] This finding however deviates from the findings of the PEDIG study[20] as well

as the Egyptian studies by Mourad et al[54] and Kotb and Eissa[56] which observed that CCT was thinner in myopes. [20]

However in a Taiwanese study involving 500 healthy participants by Chen et al no correlation was found between CCT and refractive error(p= 0.445).[44] The Beijing Eye Study also did not demonstrate any significant correlation between CCT and refractive error among adult Chinese participants. [52]

2.5. Racial variations in central corneal thickness

It has been established by several studies that mean CCT measurements vary for different racial and ethnic groups.[18,19,21,22] CCT values have been found to be lower in Africans compared to Caucasians and Hispanics.[19,20,22,58] Herndon et al found thinner mean CCT among black patients compared to their white counterparts. In their study to determine if CCT was related to the severity of glaucoma, they reported that in white patients, the mean CCT was 556±41 µm while in black patients, the mean CCT was 537±38 µm and this was a statistically significant difference.[24]

In a large study by Wang et al[58] which examined the CCT of 81,082 patients it was found that the mean CCT varied by race in a univariate analysis (P<.0001), with the thinnest corneas in Blacks (537.3 µm, SD 39.9) and the thickest corneas in Whites (558.5 µm, SD 40.3) and corneas of intermediate thickness was among Asians and Hispanics. This was similar to findings by Yo and Ariyasu who also examined the CCT among different racial groups including Caucasians, Hispanics, Asians and African Americans. They reported that African Americans had thinner corneas than Caucasians with mean central corneal thickness being 14 µm thinner in African Americans compared to Caucasians.[19] Another study conducted in Israel observed that the central corneal thickness of North African adults was thinner than other populations in their setting.[18] La Rosa et al made similar conclusions in their study where they found that CCT was lower in African Americans compared to Caucasians.[16] They also observed that a distribution analysis of CCT among the largest cluster of African American patients was between 520 to 540 µm, whiles that of the largest cluster of Caucasian patients was between 580 and 600 µm.[16] CCT values in African

American study participants was 60 µm lower than the peak frequency in Caucasian study participants.[16]

A study by Soatiana et al reviewed literature for CCT measurements in Sub-Saharan Africa (SSA), age ranging from 5-90 years for non-glaucomatous patients. The average mean CCT was found to range between 512 µm -550 µm and thus also concluded that CCT was naturally thin in SSA and was thicker in younger than older patients.[22] The ocular hypertension treatment study found that mean central corneal thickness for African American subjects was 23 µm thinner than Caucasian subjects; 555 µm compared to 579 µm and this difference was statistically significant.[4]

These findings of racial variation of CCT measurements from several studies does not support the extrapolation of CCT values from Caucasian populations for clinical application in our setting.

Several African studies on CCT in non-glaucomatous populations have reported lower mean CCT values, ranging between 500 µm and 540 µm, as shown in table 2.[22,59–61] A study done by Ntim-Amponsah et al[62], among Ghanaians aged 30-72 years found that the mean CCT was 520.4 µm for the right eye and 519.7 µm for the left eye. These figures are lower than those reported from Caucasian studies. [4,16,19] Oladigbolu, et al[63] in a study to examine the central corneal thickness of non- glaucomatous adults in Zaria, reported that the mean CCT was 531.18 µm, which is also lower than reported for Caucasian populations. In a study of 970 eyes of non-glaucomatous Cameroonian patients, the mean CCT was found to be 528.74 ± 35.89 µm.[59]

Table 2: CCT Values from selected studies in Africa

Author	Age-range (Years)	Country	Mean CCT
Ntim-Amponsah et al[62]	20 – 72	Ghana	533.3 µm (RE) 534.8 µm (LE)
Ntim-Amponsah et al[60]	21 – 90	Ghana	530µm
Oladigbolu, et al[63]		Nigeria	531.18 µm
Eballe et al[59]	5-75 years	Cameroon	528.74 µm
Sadiwalla et al[64]	18-25 years	South Africa	519.5 ± 38.6 µm
Kotb and Eissa[56]	18 -40 years	Egypt	539.23± 32.24 µm
Kelekele et al[61]	10-80 years	Congo	504.2 ± 30.7 µm
Stanislaus et al[14]	18-95 years	Tanzania	526.64±38.30 µm

2.6. Relevance of CCT in diagnosis of glaucoma

Glaucoma is the leading cause of irreversible blindness, and it is important to make diagnosis early and commence treatment to halt progression. The diagnosis of glaucoma is not always straight forward. It is uncomplicated when characteristic optic disc changes coupled with raised intraocular pressure is present. The dilemma occurs when there is only one of these parameters present. The normal intraocular pressures are stated to be between 10-21 mmHg; however, these estimations were based on the assumption that CCT was averagely 540 µm.[15,24,65] Since several studies have shown that CCT values are not constant for all racial groups, it has been suggested that a 'corrected IOP' be used instead of the measured IOP.[4] Doughty and Zaman, in a meta-analysis derived a correction factor of 2.5 mmHg for every 50 um change in CCT,[4] Thinner CCT, which has been observed in individuals of African descent[15,16,20–22], will therefore lead to erroneously low IOP values, leading to a delay in the diagnosis of glaucoma.

Central corneal thickness is believed to aid in the classification of glaucoma suspects as either Primary open angle glaucoma (POAG), ocular hypertension (OHT) and normal tension glaucoma (NTG).[29,53] Patients with normal-tension glaucoma have been found to have thinner CCT measurements compared to patients with primary open-angle glaucoma, and thus it is possible these patients may be misclassified as NTG if their IOP measurements are not adjusted based on CCT values.[29] In the Ocular Hypertension Treatment study, it was found that patients with ocular hypertension had thicker CCT. The mean CCT for Caucasians was 573 µm with almost a quarter (24%) of patients having CCT more than 600 µm.[4]

In addition, central corneal thickness is considered a significant risk factor for the severity of glaucoma.[46,60] A retrospective cohort of glaucoma progression study by De Moraes et al[30] confirmed that a thinner cornea is a risk factor for progression of glaucoma.[30] Herndon et al in a study to determine if CCT was a risk factor of advanced glaucoma found that CCT was a significant predictor of the Advanced Glaucoma Intervention Study(AGIS) score.[24] This score grades visual fields on a scale of 0 to 20 based on the degree of damage on the total deviation printout. A normal visual field is scored as zero (0), mild disease was scored 1 to 5, a score of 6 to 11 represented moderate disease, a score of 12 to 17 severe disease and 18 to 20, end-stage glaucoma.[24] They found that for every increase of CCT by 10 µm , AGIS score improved by 0.31

points. Hence they concluded that CCT was a powerful clinical factor in determining glaucoma severity at the initial examination by a specialist.[24]

It has also been postulated that thinner CCT could account for the reason why African-Americans and individuals of African origin have a higher prevalence and incidence of glaucoma, with earlier age of onset and more aggression when compared to Caucasians hence the need to measure CCT as part of glaucoma evaluation.[4,58]

There is some uncertainty about whether the effect of CCT on glaucoma is due to IOP measurement errors, leading to delayed diagnosis, or more due to the fact that individuals with thinner CCT may have some structural and biomechanical properties of the optic nerve such as deformability, which make it more susceptible to developing glaucoma. [58]

In a Ghanaian case control study in glaucomatous and non-glaucomatous eyes by Ntim-Amponsah et al, it was observed that the mean CCT was thinner in glaucoma patients compared to non-glaucomatous patients. Mean CCT was found to be 524.26 - 524.7 µm for glaucoma patients and 530 - 531.06 µm for controls.[60] Another study by Ntim-Amponsah et al determined the mean CCT of normal Ghanaians aged 30-72 years to be 521.14 µm[62]. A similar finding was observed in a Cameroonian study by Eballe et al where the mean CCT was 528.74 µm.[59] These values are lower than CCT means measured for Caucasian populations (545 µm).[9,16,18,19,22]

2.7. Relationship between CCT and age

Previous studies have reported that central corneal thickness tends to decrease with increasing age.[4,21,54] In the ocular hypertension treatment study, Brandt et al found a statistically significant negative correlation between age and central corneal thickness with the corresponding finding of 6.3 µm thinning per decade.[4] A Tanzanian study reported that compared to patients aged less than 30 years, those aged 50 years and above were 6 times more likely to have thin CCT while the odds of having thin CCT among those aged 70 years and above was 8 times higher.[61] A Cameroonian study among non-glaucomatous patients found that the cornea was thicker in the group of patients aged younger than 20 years, with an average of 537.19 ± 37.50 µm in both eyes with CCT being thinner among the group of patients aged more than 60 years. The study also reported that CCT

significantly decreased with age among women (P = 0.005, one-way ANOVA) and in the men the decrease was not statistically significant. The investigators therefore concluded that in general, central corneal thickness was negatively related to age, with CCT decreasing by 4.2 μm per 10 years.[28] Ntim-Amponsah et al[62] also concluded from their Ghanaian study on CCT that corneal thickness was thicker in individuals younger than 30 years and thinner in those above 30 years. While the mean CCT for the study population aged between 20-72 years was 534 μm, it was 523 μm in 40-49 year group and 515 μm in those aged more than 50 years.[62]

In paediatric populations CCT values have been found to be high when compared to adults. The pediatric eye disease investigator group in a study to measure the CCT in 2079 non-glaucomatous children reported mean CCT as 573 μm in Caucasian children and 551 μm in African-American children.[20] In contrast, studies like those done by La Rosa report mean CCT for Caucasians as 556 μm and for African-American adults 534 μm.[16] Eballe et al[28] in their Cameroonian study on CCT in healthy children reported mean CCT of 538 μm which is thicker than what was reported for adult non-glaucomatous patients in Cameroon. The mean CCT of non-glaucomatous adult Cameroonians was found to be 529 μm.[59]

With regards to correlation of CCT and increasing age, the pattern for children differs from adults. While in adults CCT has been found to decrease with age, in children, CCT has been found to increase with age. The pediatric eye disease investigator group (PEDIG) found that a thicker median CCT was observed with each successive year of age from 1 to 11 years but was stable thereafter.[20] Hussein et al also showed that the central cornea was significantly thicker in the group of children aged from 5 to 9 years when compared to children aged less than 5 years.[15]

Haider et al reported a positive association between age and CCT. They found that CCT remained generally stable before age 10 years and after age 10 years, the thickness of the cornea increased with age.[21] Eballe did not find any statistically significant difference in CCT between the age groups of age 5–7 years, 8–10 years, 11–13 years, and 14–16 years.[28]

2.8. Relationship between CCT and Sex

Several studies in adult populations have found no correlation between central corneal thickness and sex. Kotb and Eissa in a study to find out the correlation between myopic refractive error, corneal power and central corneal thickness (CCT) in the adult Egyptian population reported no statistical difference in CCT values for males and females.[56] This finding has been corroborated by several other studies including that by Stanislaus et al[14] who did not find any statistical difference in mean CCT between males and females in Dar-Es-Salaam. In studies among children, a similar finding has been reported. Haider et al also report no association between sex and CCT.[21] Though in the Cameroonian study by Eballe et al mean CCT was higher in boys (541.41 ± 36.45 μm) compared to girls(536.15 ± 38.91 μm), the difference was not statistically significant. [28] In the PEDIG study however, females were found to have thinner mean CCT (p=0.003). [20]

2.9. Methods of measuring central corneal thickness

There are various modalities of measuring central corneal thickness and these may be classified as contact or non-contact methods depending on whether the measuring device touches the eye.

Ultrasound pachymetry (USP), which is a commonly used for measuring CCT is a contact method which involves the use of a probe which is placed on the anterior corneal surface.[66] Acoustic pulses locate and measure the corneal layers and interfaces at the location where the speed of sound differs.[31] Ultrasound pachymetry utilizes ultrasound energy to measure corneal thickness.[67] It does this by emitting ultrasound energy from the probe tip and some of this energy is reflected back in the form of an echo. Based on velocity and time taken for reflected energy to travel back to the receiver, the measurements are obtained.[67] USP is considered the gold standard for CCT measurement and is widely utilized.[31,35]The device is battery operated and has a proven measurement algorithm which yields accurate and reproducible results.[68] The advantage of this device is that it can be used in several settings such as out-patient clinics, theatre and as a screening tool on the field. Several studies have used ultrasound pachymetry for measuring CCT in adults and children, including neonates and preterm babies.[15,19–21,28,69] The disadvantage of this method is that due to fact that it is a contact method, cooperation from some patients may be poor,

especially in the case of children. The reliability of ultrasound pachymetry can be affected by various factors such as poor patient cooperation as well as the ability for examiner to place probe perpendicularly and centrally without excessively compressing the globe.[31] In addition, the effects of topical anaesthetic drugs required for the measurements and the displacement of the tear film of the cornea caused by the probe may be additional sources of inaccuracy. [31] The procedure also carries the inherent risk of epithelial erosions, infection, and patient discomfort due to the direct placement of the ultrasound probe.[31] However due to its portability, speed and affordability, the use of USP is very popular.[31] There are different types of ultrasound pachymetry devices such as the Pachmate™ DGH 55, DGH Technology Inc, PA, USA[68], Kerasonix KSX-1000 ultrasound pachymeter (DGH Technology, Exton, PA, USA)[67] and the Pachpen.[70] The images of Pachmate and Pachpen are shown below:

Figure 7: Picture showing Pachmate Ultrasound pachymeter[70]

Figure 8: Picture of PachPen ultrasound pachymeter[72]

Anterior segment optical coherence tomography (AS-OCT) is a newer method for measuring CCT, which is non-contact. The subject is usually seated in front of the machine and with the chin and forehead on the rest and asked to fixate on a target. It employs the same technology used for imaging the posterior segment and is based on measuring the delay of infrared light reflected from the tissue to determine tissue depth and thickness.[31] Though very comfortable due to the fact that it is non-contact, it is expensive and not suitable for out-of-hospital use due to the bulky nature of the machine.

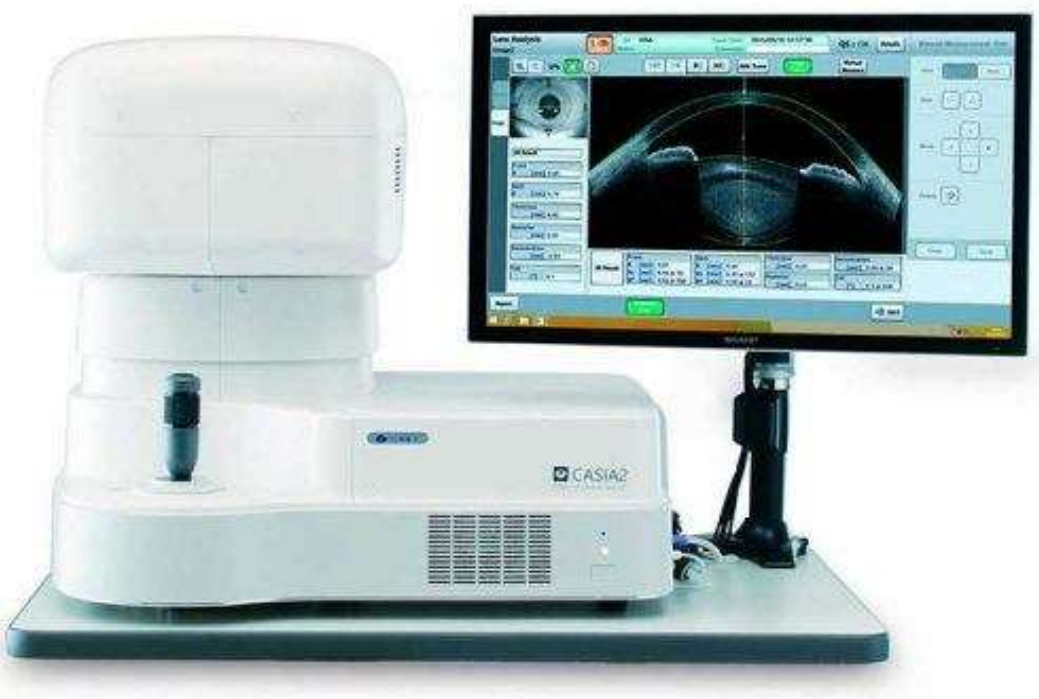

Figure 9: Picture of Anterior segment OCT[73]

Noncontact specular microscopy (NCSM): Patient sits behind the machine and fixates on a target. This method measures CCT by using the reflection of light waves from the anterior and posterior corneal surfaces by the use of a specular microscope. [31,66] The device used is quite bulky and also not suitable for out-of-hospital purposes.

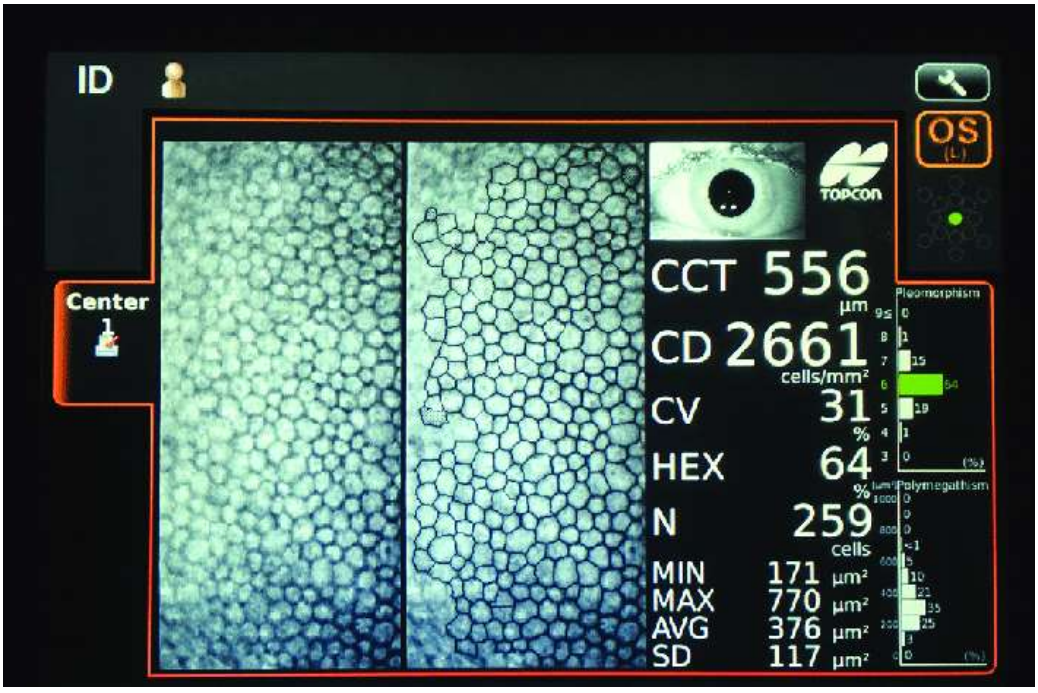

Figure 10: Picture showing Noncontact specular microscopy [74]

Figure 11: Picture showing non-contact specular microscope[75]

Orbscan II (Bausch and Lomb, Rochester, NY, USA):

The Orbscan is typically used for corneal topography but can also be employed in the measurement of CCT. It works by analyzing reflected images from multiple concentric rings projected on the anterior surface of the cornea. A high-resolution video camera then captures multiple light slits projected through the cornea similar to what is seen during slit-lamp examination. The instrument's software then analyzes multiple data points per slit and calculates the corneal thickness. A final reading is recorded following automatic adjustment using the manufacturer's recommended acoustic correction (AF) of 0.92.[67]

Figure 12: Picture showing Bausch & Lomb's Orbscan IIZ[76]

In a study by Khaja et al, comparing CCT measurements using ultrasound pachymetry versus slit-lamp optical coherence tomography, specular microscopy, and Orbscan, they reported that in subjects with healthy corneas, SL-OCT, specular microscopy, and Orbscan (with correction factor) could be used interchangeably with ultrasound pachymetry since the results showed significant linear correlations with one another.[67]

The method for CCT measurement selected for this study is ultrasound pachymetry (USP) due to its accuracy and portability. It has also been used in several paediatric studies making it easier to compare results.[15,20,21,26,69]

2.10. CCT in children

CCT has been studied in children albeit not as extensively as in adults, with very few studies in Sub-Saharan Africa.[20,28] Generally, studies suggest that CCT is thinner in children of African descent. Hussein et al in their cohort of 108 children of different age groups and racial origins, found that CCT means increased with age, reaching adult values by age 5 years.[15] They also found African-American children had thinner CCT compared to Caucasians and Hispanics.[15] The PEDIG study on 2079 children from birth to age 17 years, concluded that median CCT increased from age 1 to 11 years and then plateaued. [20]

Similar to findings among adults, CCT has been found to be thinner in children of African descent compared to their Caucasian counterparts. This observation among African-American children has been established in other studies.[17,21,28] PEDIG observed that mean CCT was approximately 20 um lower than that of Caucasian and Hispanic children.[20] Haider et al reported mean CCT in African-American children to be 535 ± 35 µm compared to 559 ± 38 µm in Caucasian children. Dai et al[26] reported even thinner CCT for African-American children compared to their Caucasian counterparts. Their study reported mean CCT of 523 ± 40 µm for African-American children while in Caucasians, it was reported as 563 ± 36 µm and in Hispanics, 568 ± 44 µm. [26] A study of 102 children aged 5-16 years from Cameroon, in SSA, also demonstrated lower mean CCT value (538.06 ± 38.03 µm)[28] compared with that in Caucasians[18]

Knowledge of CCT values in children may thus play an important role in the prompt and accurate diagnosis and subsequent management of paediatric glaucoma as in the case of adults. This is especially in the diagnosis of juvenile glaucoma, defined as glaucoma diagnosed between ages 4-40 years.[71] Unlike primary congenital glaucoma, juvenile glaucoma does not usually present with overt clinical features such as buphthalmus, megalocornea or corneal oedema, posing a challenge in diagnosis by Ophthalmologists.

Unfortunately, in Ghana, and as may be the case in other SSA settings, anecdotally, children with juvenile glaucoma are diagnosed late. This is partly because they present late and also because some may have their IOP at borderline values requiring prolonged follow up to establish progression. This is a situation where knowledge of CCT of such individuals may help with early diagnosis, especially in those with thin CCT.

CHAPTER 3

MATERIALS AND METHODS

Study design

This study was a prospective cross-sectional study which measured central corneal thickness of 420 children (840 eyes) aged 6 to 15 years.

Study duration:

This cross-sectional study was conducted from the period of July 2021 to December 2021

Study sites

The Ablekuma South (Accra metropolitan) education directorate has 54 basic schools with a total population of 20,724 pupils. This population is composed of 13, 907 pupils from 33 public and 6817 pupils from 21 private schools, thus giving a ratio of 2:1 public to private school student population. Based on this ratio 3 schools were selected: 2 public basic schools and 1 private basic school.

The schools selected through random sampling were the Martyrs of Uganda Roman Catholic(R/C) Basic School, Mamprobi South 3 Basic School, both of which are public schools and Mamprobi Evangelical Presbyterian (E.P.) Church Basic School which is a private school.

Ablekuma sub-metropolitan assembly:

The Ablekuma South Sub Metropolitan area is one of the Six (6) Sub Metropolitan District Councils of Accra Metropolitan Assembly (AMA). The Sub Metro is the largest in the Metropolis and shares its boundaries with Ablekuma Central, Ablekuma North and Ashiedu Keteke. It covers an area of 15.1 Sqkm. It hosts some business entities like supermarkets, banks, fuel stations, educational institutions, hotels and major hospitals such as the Korle bu teaching

hospital. Its cosmopolitan nature makes it suitable for this study. The Ablekuma South (Accra metropolitan) education directorate has 54 basic schools with a total population of 20,724 pupils.

Three basic schools within the Ablekuma sub metropolitan assembly with a student population spanning from primary 1 to JHS 3 were selected for this study. The schools selected through random sampling were the Martyrs of Uganda R/C Basic School (public), Mamprobi E.P. Church Basic School (private) and the Mamprobi South 3 Basic School (public). Pupils in these schools were from a varied ethnic background because of the demography of the sub metropolis. The sub metropolitan area was selected by convenience sampling due to its proximity to the Korle Bu Teaching Hospital and the varied ethnic background of the population.

Martyrs of Uganda R/C Basic School

The Martyrs of Uganda R/C basic school is located on Guggisberg avenue on the Martyrs of Uganda Catholic Church compound and opposite the Mamprobi Post office. It is a public school with an estimated total population of 924 pupils.

Mamprobi E.P. Church Basic School

The Mamprobi E.P. Church Basic School is a private school located near the Mamprobi Police station, Accra. It is a private school owned and managed by the Evangelical Presbyterian (EP) church. The school's total population is 718 pupils.

Mamprobi South 3 Basic School

The Mamprobi South 3 Basic School is located near the "Tuesday Market" in Korle Gonno-Accra. This is a public school with an estimated total population of 957 pupils.

Target population

Ghanaian children aged 6 to 15 years in the three selected schools who met the inclusion criteria.

Sample population

This included Ghanaian children aged 6 to 15 years from Martyrs of Uganda R/C Basic School, Mamprobi E.P. Church Basic School and Mamprobi South 3 Basic School who met inclusion criteria.

Inclusion criteria

1. Children within the specified age group (6- 15 years) with healthy cornea.
2. Children with parental consent or assent.

A healthy cornea was defined as a cornea that did not show any clinical signs of abnormality such as scaring, abnormal size or shape.

Exclusion criteria

1. Children with history of ocular trauma requiring ocular medications or surgical intervention
2. Children with history of prior intraocular surgery
3. Children with any known ocular pathology that could have any effect on central corneal thickness such as;
    - Glaucoma - primary congenital glaucoma, juvenile open-angle glaucoma, secondary glaucoma
    - Conjunctivitis - vernal keratoconjunctivitis, allergic conjunctivitis, bacterial or viral conjunctivitis at the time of examination
    - Corneal pathologies – keratoconus, corneal dystrophies, microcornea, megalocornea, corneal scarring
    - Anterior segment dysgenesis – Axenfeld Rieger, Rieger's syndrome, Peter's Anomaly
    - Other ocular anomalies such as ptosis, colobomas
4. Use of contact lens within the past week
5. Any documented abnormal intraocular health.

Sample size determination

The study sample size was calculated using the formula[72]:

$n = N*X / (X + N - 1)$,

where,

$X = Z_{\alpha/2}^2 *p*(1-p) / MOE^2$,

for a confidence level of 95%, α is 0.05 and $Z_{\alpha/2} = 1.96$

N =Population size (N= 20724)

MOE is the margin of error (MOE= 5%)

p is the sample proportion (Assumed to be 50%, that is 50% of participants will have normal CCT expected for the population).

Substituting the values into the above formula generates a minimum sample of 378 participants required.

To accommodate 10% missing/incomplete data the total sample size will be =416 (832 eyes). This was approximated to 420 children.

This sample was distributed over 3 age categories of 6 to less than 8; 8 to less than 10 and 10 to 15. To achieve a proportional distribution, the total number of children expected to be sampled per school was divided by the total number of classes which was 9 (class 1 to JHS 3). Thus, an equal number of participants per class were enrolled. The classes were chosen because the ages of children in these classes ranged from 6-15 years.

This age group categorization was done based on similar studies in literature, including one of the largest studies on this subject[20] and it is to facilitate easy comparison of results.

This formula was selected because no population study on CCT in Ghanaian children has been conducted before, thus our population variance is unknown. Also, an attempt to use the sample size and standard deviation of a similar study conducted among Cameroonian school children gave a small final sample size.

Sampling technique

A total of 420 Ghanaian children were selected from the three basic schools. Multistage sampling was used in the sampling procedure. This was done in two stages with simple random sampling (SRM) at each stage. At the first stage, simple random sampling was used in selecting three Basic schools from the list of schools provided by sub-metropolitan education office for the study. To achieve a representative sample, two public schools and one private school were selected, based on total population of pupils in public schools to private schools (the ratio of public: private school population is 2:1).

A sampling frame consisting of the list of schools in the catchment area of Korle Bu Teaching Hospital, in the Ablekuma South Sub Metropolitan area, was obtained from the Ghana Education Service. The names of the schools were entered into Microsoft excel worksheet. A command was given for the randomization of the list of names provided using random number generator (RAND function) in Microsoft Excel 2012 software. The first three schools which appeared were selected namely, the Martyrs of Uganda R/C Basic School (public), Mamprobi E.P. Church Basic School (private) and the Mamprobi South 3 Basic School(public) respectively.

The study participants were stratified by age to ensure fair distribution within the age categories. These grouping used was: 6 to <8 years, 8 to <10 years, and 10 to 15 years. To enroll participants in the 6 to 15 years age category, probability sampling was used as described in the second stage.

In the second stage, a sampling ratio was derived by dividing the required sample size by the total number of pupils in all the three selected schools. The outcome (sampling ratio- 420/2599) was multiplied by the number of students in each school to obtain the number to be sampled from each school.

In selecting the number to be sampled from each class; the number of children in the class was divided by the total number of children in that particular school. The outcome was multiplied by the number to be sampled from the school to obtain the number to be sampled from the class. This was done for all the schools.

Simple random sampling was then used again in selecting participants in each class for each school

All children in each class were numbered one to total class number. Numbered pieces of paper corresponding to listing on class register were then placed in a container and numbers were picked randomly by an independent person. A child was enrolled into the study if the number picked corresponded to their name. Numbers were randomly picked until the required number to be selected per class was reached. If a selected child did not meet the inclusion criteria, a new number was drawn randomly from the ballot.

The three schools with their population and the number of students to be selected from each school (proportional allocation to the size of each school) to constitute the total sample of 420 is illustrated on Table 3 below:

Table 3: Sampling distribution table for selected schools

School	**Total number of students in each school (N)**	**Sampling ratio (R)**	**Number of students sampled from each school (N*R)**
Martyrs of Uganda R/C Basic School	924	[924/2599]	149
Mamprobi E.P. Church Basic School	718	[718/2599]	117
Mamprobi South '3' Basic School	957	[957/2599]	154
Total	**2599**		**420**

Sampling process

Algorithm:

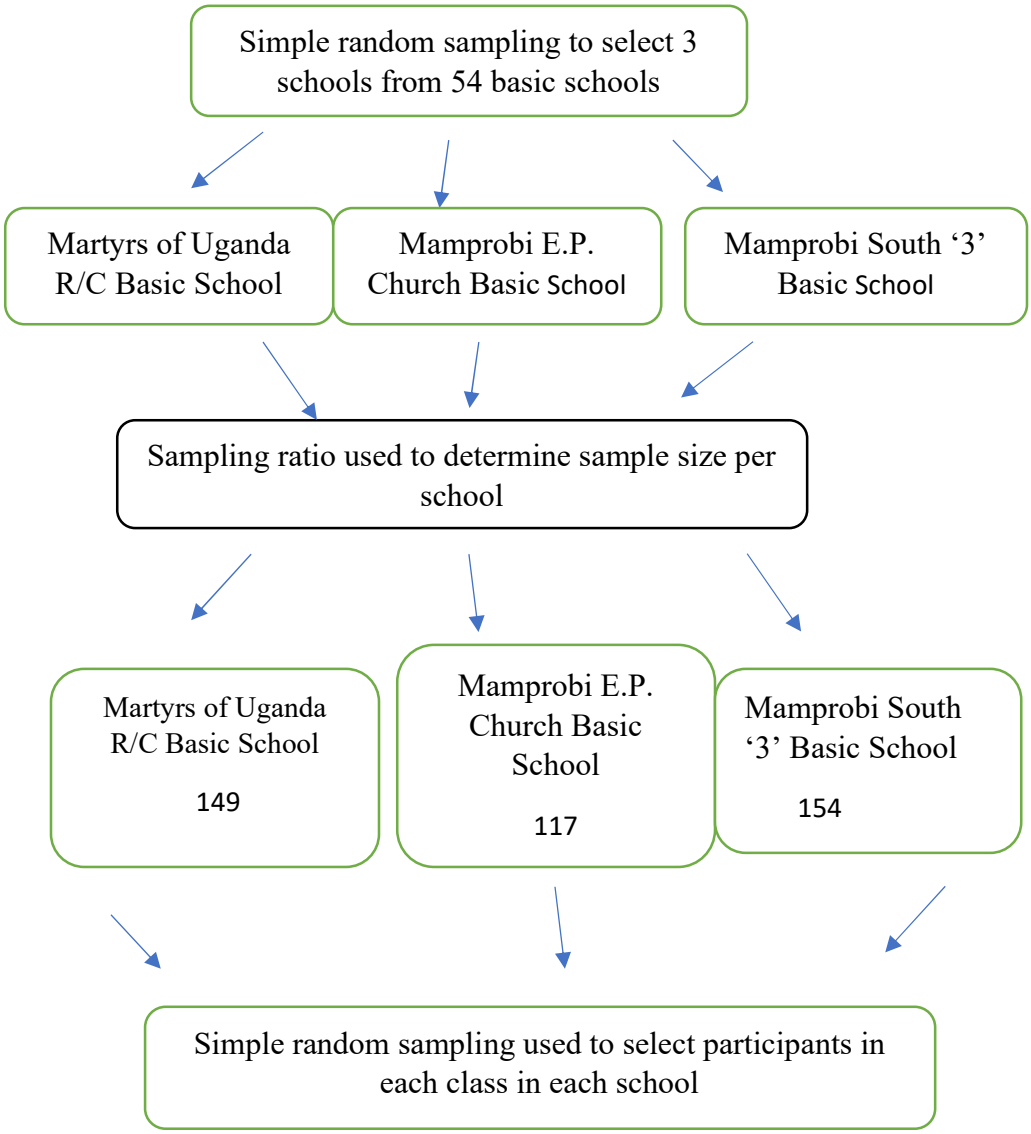

Figure 13: Algorithm of sampling process in selected schools from the Ablekuma sub-Metropolitan area

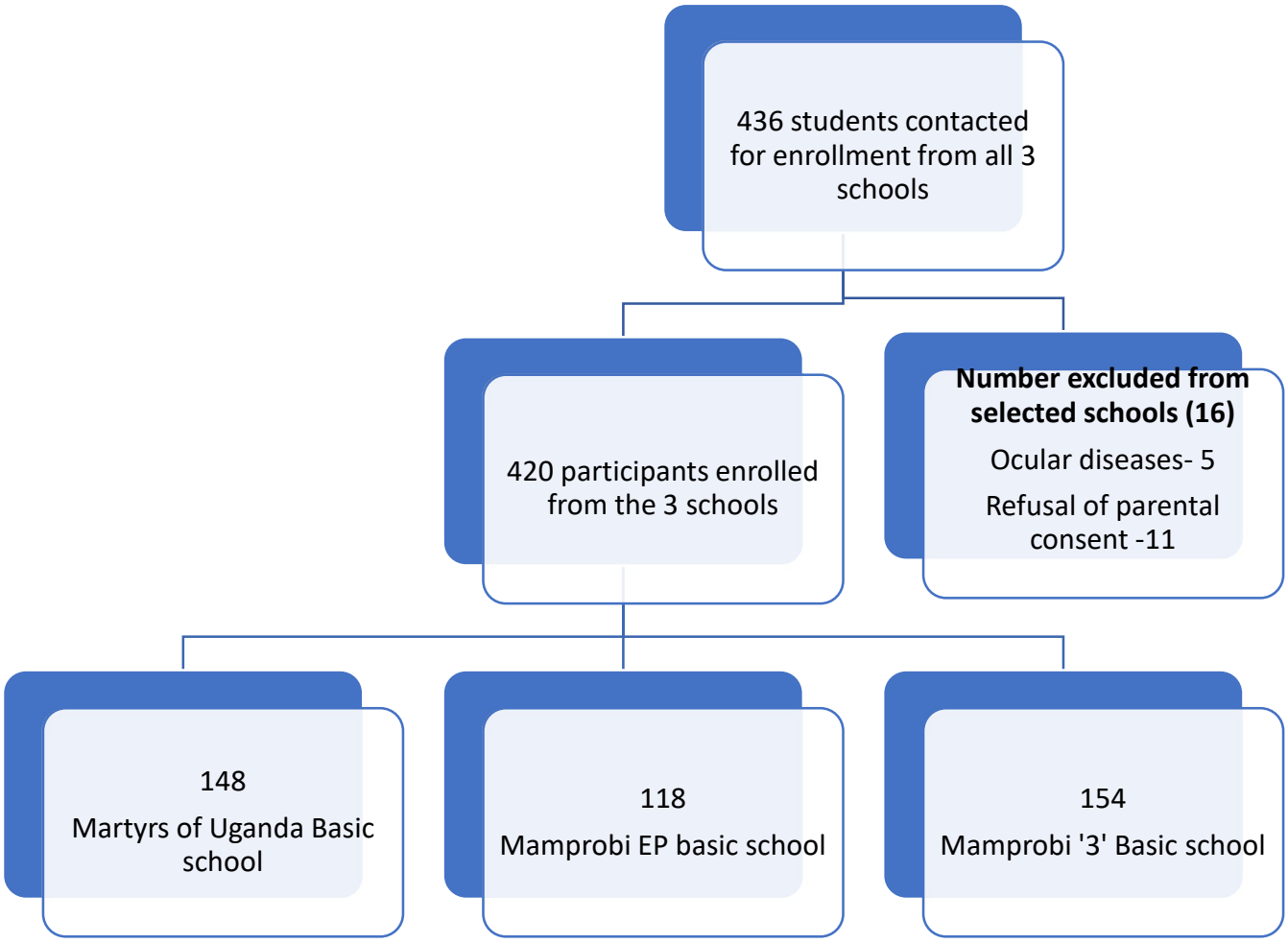

Figure 14: Participant enrollment from selected schools in the Ablekuma sub-Metropolitan area

Procedures

The study commenced after ethical approval was granted by the Scientific and Technical Committee (STC) and Institutional Review Board (IRB) of the Korle Bu Teaching Hospital and administrative approval from the Ghana College of Physicians and Surgeons. Permission was subsequently sought from the Ablekuma sub-metropolitan education office of the Ghana Education Service. The district education supervisor and all heads of the selected schools were written to from the Sub-Metropolitan office, informing them about the study and granting permission for data collection to take place.

The research team comprised of the principal investigator (PI), an ophthalmic nurse, an ophthalmology resident, a paediatric optometrist and a statistician. The ophthalmic nurse was responsible for demographic data collection and visual acuity testing, the ophthalmology resident was responsible for anterior segment examination and IOP measurement, the optometrist was in charge of cycloplegic autorefraction and the role of the PI was for posterior segment examination and measurement of CCT. Pre-research preparations were conducted by training of the entire research team on the recruitment, consenting process, data capturing documents and examination procedures and skills. The team met twice to discuss the inclusion and exclusion criteria, order of data capture and examination as well as strategies to ensure adherence to Covid-19 protocol.

At the study sites, consent forms were given to students for parental consent prior to data collection day. Sampled participants who met the inclusion criteria were then brought to a room prepared for examinations. There were 4 main stations:

1. **Demographic data and visual acuity:**

The background characteristics of participants such as age, gender and ethnicity were recorded by the ophthalmic nurse who also assessed the visual acuity of the participants using the LogMAR chart at 3 m. Visual impairment was graded according to the WHO guidelines:

Classification of distance visual impairment:

Mild –visual acuity worse than 6/12 to 6/18 (worse than LogMAR 0.3 to 0.5)[73]

Moderate –visual acuity worse than 6/18 to 6/60 (worse than LogMAR 0.5 to 1.0)[73]

Severe –visual acuity worse than 6/60 to 3/60 (worse than LogMAR 1.0 to 1.3)[73]

Blindness –visual acuity worse than 3/60 (worse than LogMAR 1.3)[73]

2. Anterior segment examination and IOP

A general eye examination, including IOP assessment was done to exclude any ocular pathology. Intraocular pressure was measured using the I-care tonometer. The participants were asked to look in primary gaze after instillation of topical 0.5% Amethocaine. To ensure accuracy, measurements were taken only when participant was relaxed and not squeezing eyes and probe of tonometer was applied to the centre of the cornea. Five measurements were taken manually per eye and the average was calculated and displayed on the screen of the tonometer. For uniformity, all IOP measurements were done by the ophthalmology resident using the I-care tonometer. Anterior segment examination was done using a torch light and 20D lens for magnification.

3. Funduscopy and CCT measurement

All funduscopies were done by the principal investigator (PI) using the direct ophthalmoscope. A cup to disc ratio of more than 0.6 was a criterion for exclusion. Those children were referred as cases of suspicious discs to the LIEC, KBTH for further investigations and follow-up. They were then replaced with another child from the same class through simple random sampling.

The measurement of the CCT was also performed solely by the principal investigator. To take CCT measurements, the study participant was made to sit comfortably in a chair in front of the PI. One drop 0.5% amethocaine was then instilled into the eye. The participant was then encouraged to visualize a fixation point with their eyes fully opened. A hand-held pachymeter, *Pachmate*® (DGH Technologies Inc, Exton PA, USA) was used to take 3 measurements from the central 3mm of the cornea of both eyes. The device was calibrated each day prior to initiation of measurements according to the manufacturers protocol.[68] The tip of the probe of the Pachymeter was positioned perpendicular to the centre of the cornea. Once proper alignment of the tip of the probe to the cornea was made, the preset series of measurements (five per cornea) were taken automatically by the pachymeter. If no measurement was obtained within 3 seconds of positioning of the probe, it

suggested poor applanation and repositioning was done. The results were displayed on the LED screen of the device and stored in its memory. The displayed results per eye were then recorded onto the data capture form. Three measurements were taken for each eye and the lowest of the 3 was recorded as the CCT as it is expected that the central cornea will have the thinnest measurement and the lowest measurement most likely represents the direct path through the central cornea.[21] This method was also chosen because it was the method used by other studies in children. [15,21] The tip of the pachymeter was then sterilized with 70% methylated spirit after every use. After confirmation of the days results from the device memory with information on the data capture form, the memory was erased to create space for the next day's recordings.

4. **Cycloplegic refraction:**

Cycloplegic autorefraction (Righton Retinomax K plus 3, handheld) was done after instillation of one drop of 1% cyclopentolate twice, 10 minutes apart. The spherical equivalent of each eye was documented and used in analysis. All refractions were done by the paediatric optometrist. Participants were classified based on the spherical equivalent (SE) as either emmetropia (+0.75D to -0.5D), myopia (>-0.5D) and hyperopia (≥+0.75D). This classification was based on groupings used by previous studies on CCT and refractive errors in children.[74–76]

The study ensured strict adherence to COVID-19 infection prevention protocols as recommended by the World Health Organization (WHO).[77]

- Medical face masks/N 95 respirators were worn by members of the research team.
- All study participants had to wear facemasks at all times during data capture.
- Social distancing was observed by calling in 5 study participants at a time. There was one child per station with one waiting at the entrance.
- A brief history was taken for symptoms of fever, cough, anosmia, loss of taste, malaise.
- Children who had any of these symptoms were referred to the school nurse.
- Hand hygiene was observed in between patients.

The study data collection was conducted over a 4-month period, from 27th July 2021 to 9th December, 2021.

Study materials and equipment:

Materials	Equipment
Cotton wool	Torch light
Methylated spirit and hand sanitizers	20D lens
I-care probes	I-care tonometer
Topical 0.5% amethocaine	Hand-held pachymeter, *Pachmate*® (DGH Technologies Inc, Exton PA, USA)
1% cyclopentolate	Autorefractometer (Righton Retinomax K plus 3, handheld)
Questionnaires	
LogMAR visual acuity chart (3m)	
Stationery	

Data management and quality assurance

Data security and confidentiality of participants' information was paramount in the study. Data collected was secured in a locked cabinet with only the researcher having access to the cabinet. Codes were given to each questionnaire. Participants' information was treated as confidential. To ensure confidentiality, the de-identified data was entered into Microsoft Excel on a password-protected computer and examined for completeness. Completed data capture forms were stored in a locked cabinet and this will be kept for 5 years after completion of the study and then destroyed.

Ethical and legal considerations

The study protocol was presented to the KBTH-IRB for review and approval prior to conducting the study. Permission was also obtained from the Municipal Directorate of Ghana Education service and the Heads of participating schools. An informed written consent was obtained from parents or guardians of participants and assent from the participants prior to inclusion in the study.

CHAPTER 4

RESULTS

4.1 Introduction

This chapter of the dissertation shows the outcome of the data analysis from the study. This study was done with the overall aim of determining the normative CCT in healthy Ghanaian children aged 6-15 years in the Ablekuma Sub-Metropolitan area using ultrasound pachymetry.

Statistical analysis was done with STATA version 11. Demographic characteristics of study participants were analysed using frequency tables, bar charts and cross-tabulation. Test for normality of the distribution of age and central corneal thickness measurements in the study population was done using the Kolmogorov-Smirnov test.

Statistically significant differences were assessed with the independent t-test for differences continuous variables such CCT, analysis of variance (ANOVA) for differences between groups such as age and gender and linear regression for differences in trends. Significance was set at a p value of less than 0.05.

4.2 Demographic characteristics of study participants

A total of 420 children aged from 6 to 15 years from selected schools in the Ablekuma Sub-Metropolitan area at the basic level of education (class 1 to JHS 3) were enrolled in the study. A descriptive statistic of the demographic characteristics of the participants are presented below.

4.2.1 Age

The age of the children in this study was analyzed descriptively. A test for normality for the age distribution using the Kolmogorov-Smirnov test revealed that the distribution of the ages of the participants was not normal (p-value = 0.001).

From the analysis, the mean age and standard deviation (SD) of the participants was 10.3±2.6 years. The ages ranged from 6 years to 15 years. The median (interquartile range) age was 10.0 (8.0-13.0) years. Almost half (212, 50.4 %) of the study participants were between 10-15 years. A descriptive statistic of the age of the study participants are presented in table 4, figures 15, 16, and 17.

Table 4: Descriptive statistics of the age of participants

Statistics	Value (Years)
Mean	10.3
Median	10.0
Mode	10.0
Standard deviation	2.6
Minimum	6.0
Maximum	15.0
Lower quartile	8.0
Upper quartile	13.0

Normality test for age of children (Kolmogorov-Smirnov test = 0.108; p-value = 0.001) showing age of children as non-normally distributed.

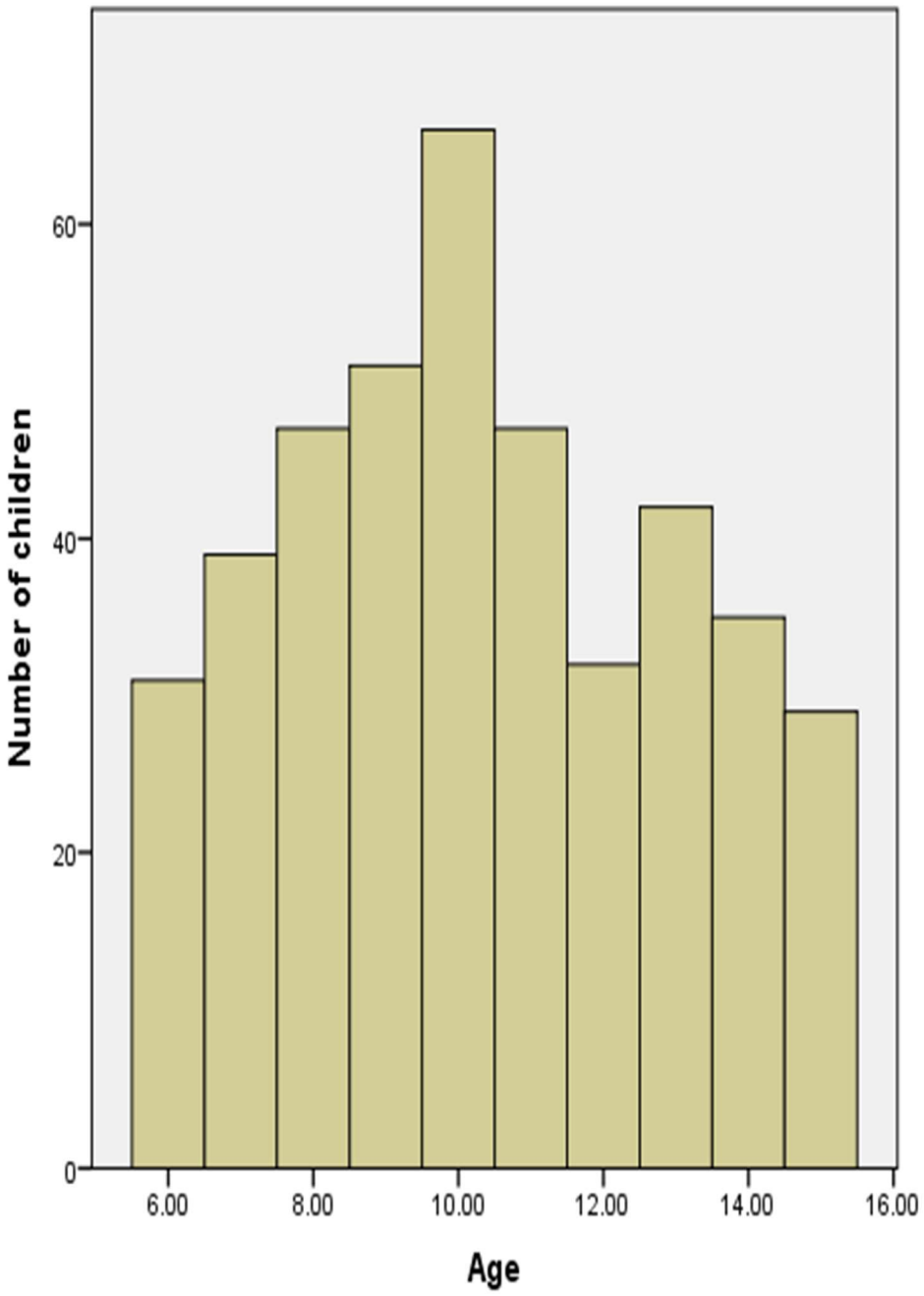

Figure 15:A histogram showing non-normal distribution of age of study participants.

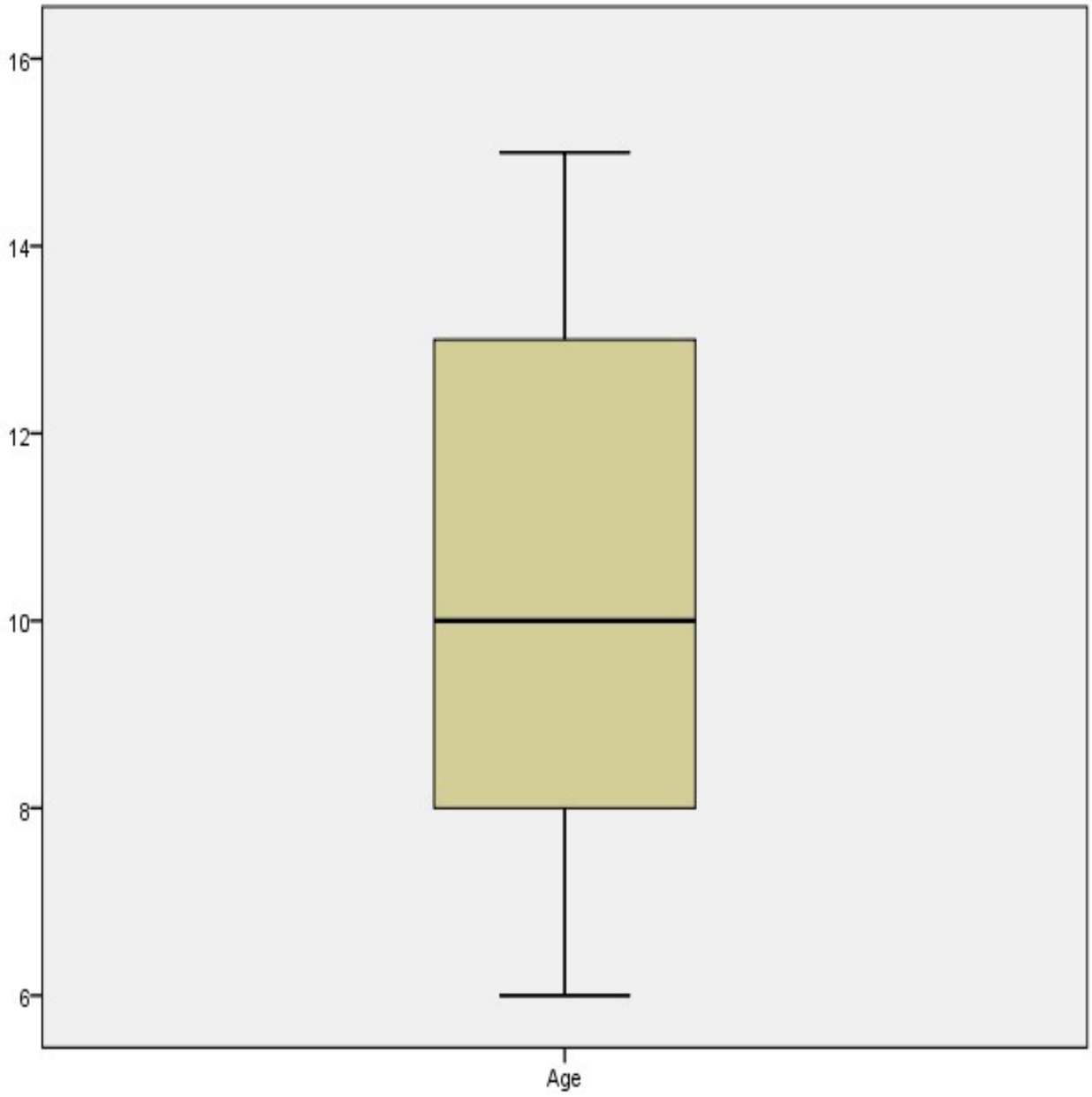

Figure 16:A box plot of the age distribution of study participants showing the median, minimum, maximum, lower and upper quartile ages respectively.

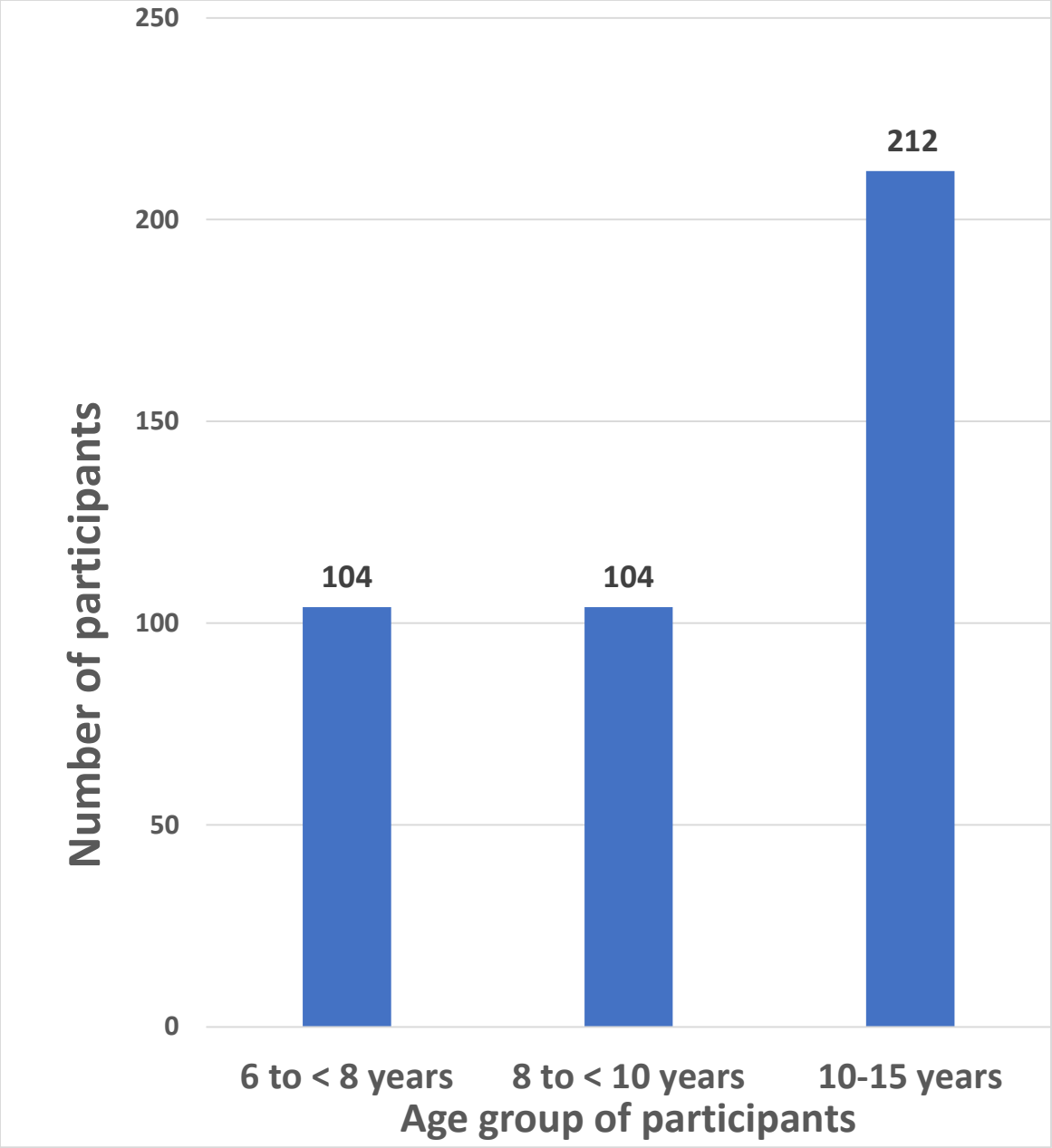

Figure 17: Distribution of study participants by age groups.

4.2.2 Sex

A little over half (214, 51.0 %) of the study participants were females. Figure 18 presents the sex distribution of the study participants.

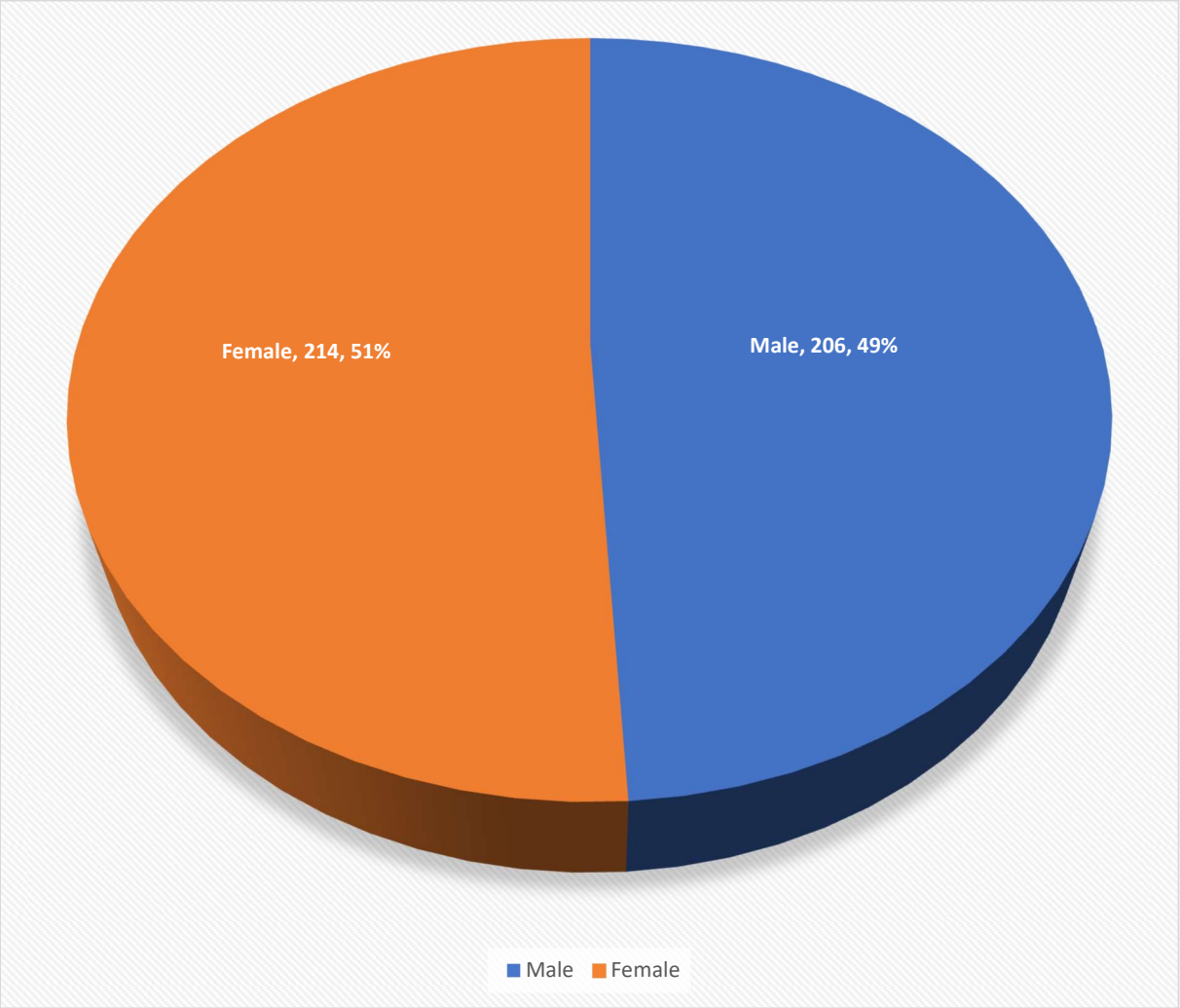

Figure 18: Sex distribution of study participants

4.2.3 Educational Status

About a third of the participants were in the lower primary level of education (143, 34.2%) and upper primary level (144, 34.3%). The educational status of participants is shown in figure 19 below.

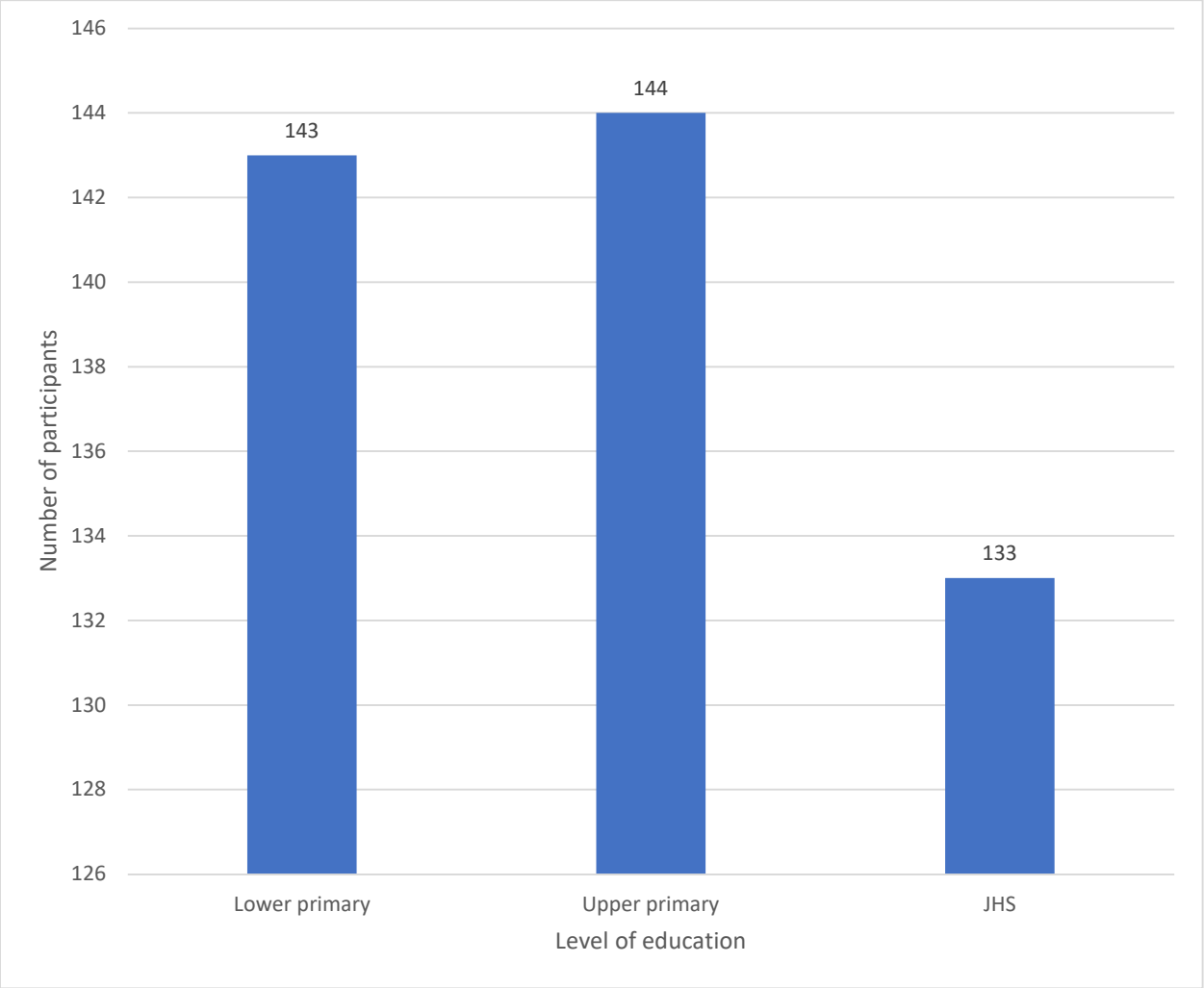

Figure 19: Educational status of participants.

Lower primary = Class 1 to Class 3

Upper primary = Class 4 to Class 6

JHS = Junior High School

4.2.4 Study sites of participants

Three basic schools namely, Martyrs of Uganda Basic School, Mamprobi Evangelical Presbyterian Church Basic School and the Mamprobi South 3 Basic School were included in the study. The highest enrollment of the participants (154, 36.7%) was from the Mamprobi South 3 Basic

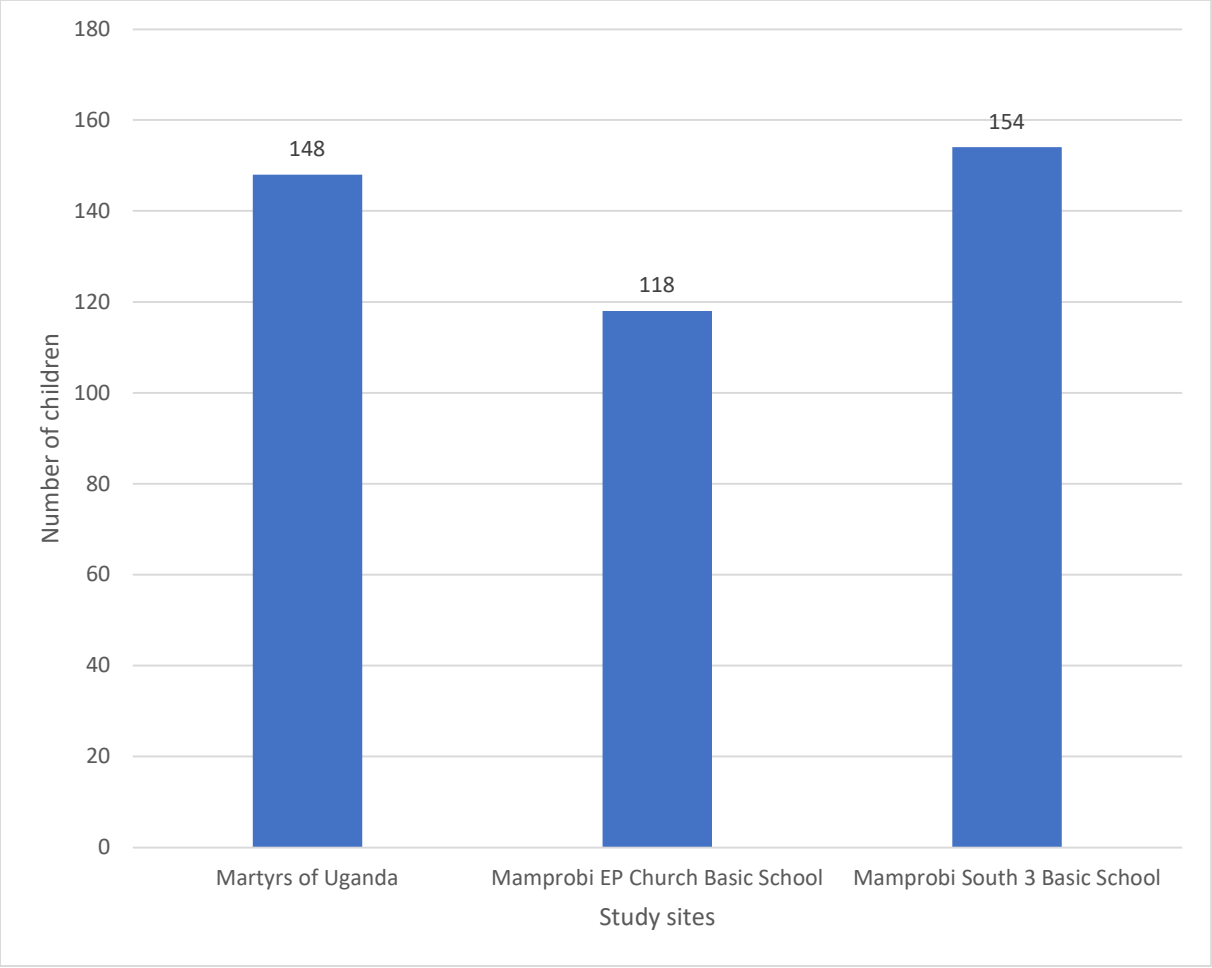

Figure 20: Study sites of participants

EP = Evangelical Presbyterian.

4.2.5 Ethnicity

The ethnic group with the highest (205, 48.8%) representation in this study cohort was the Ga ethnicity.

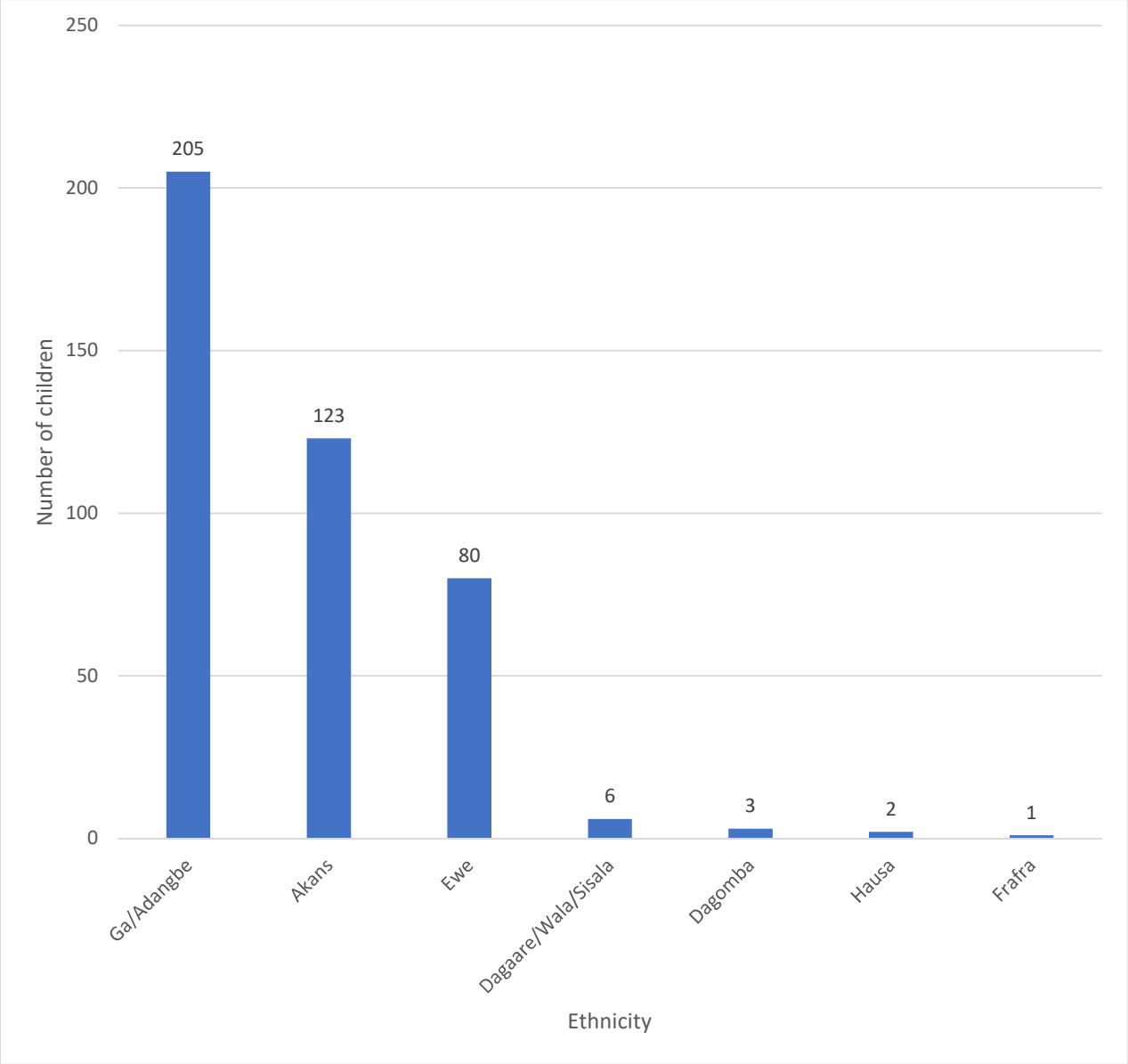

Figure 21: Ethnicity of participants.

4.3.1 Presenting distance vision (unaided) right eye of study participants

Presenting distance visual acuities (unaided) right eye of study participants were assessed. A total of 381 (90.7 %) participants had normal vision at presentation. Thirty (7.1 %) had mild visual impairment, and 9 (2.2 %) had moderate visual impairment. See figure 22 below.

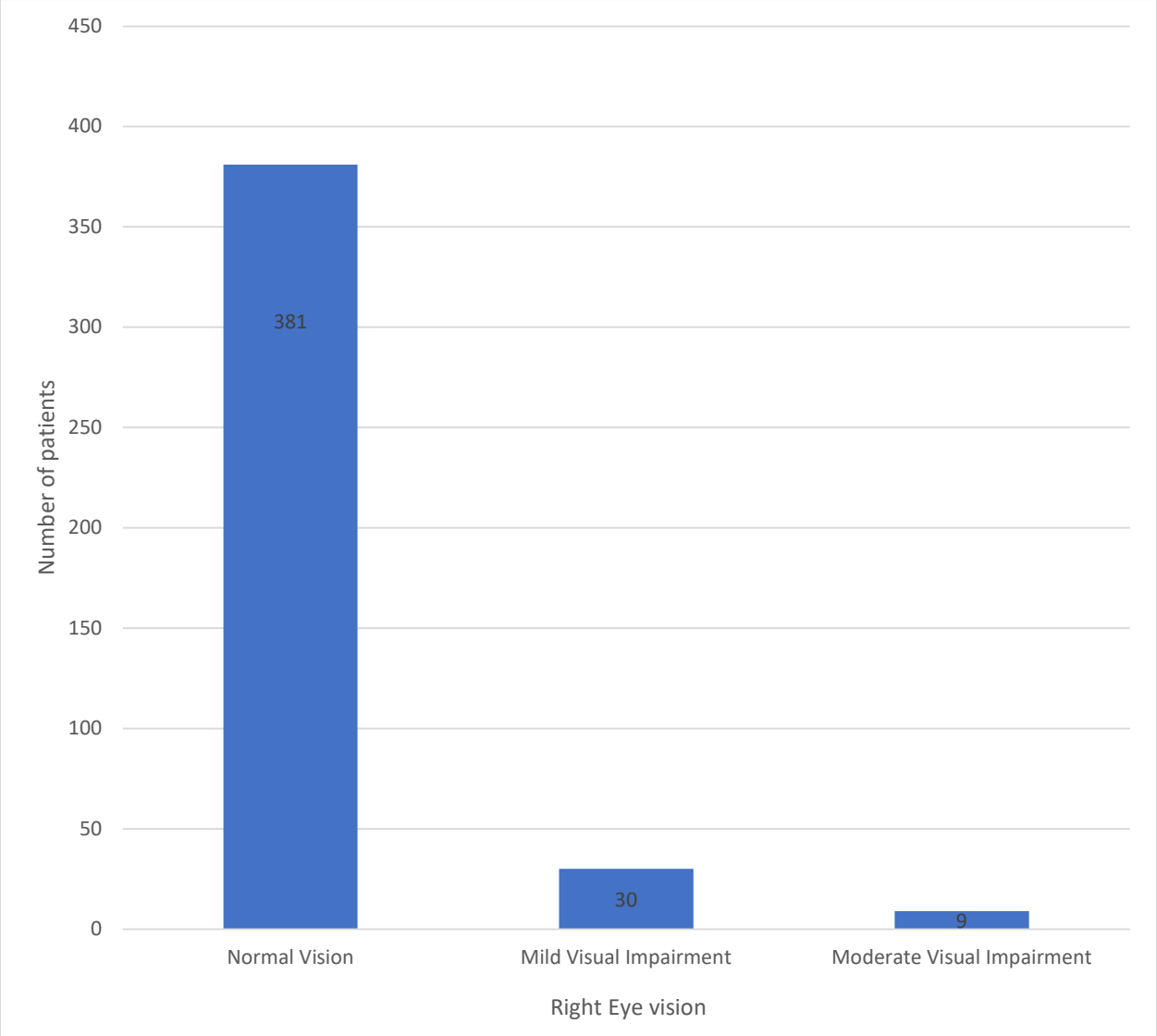

Figure 22: Presenting distance vision (unaided) right eye of study participants

4.3.2 Presenting distance vision (unaided) left eye of study participants

Presenting distance visual acuities (unaided) left eye of study participants were assessed. A total of 393 (93.6 %) participants had normal vision at presentation and 27 (6.4 %) had mild visual impairment. Details of the presenting distance vision (unaided) left eye of study participants in shown in figure 23.

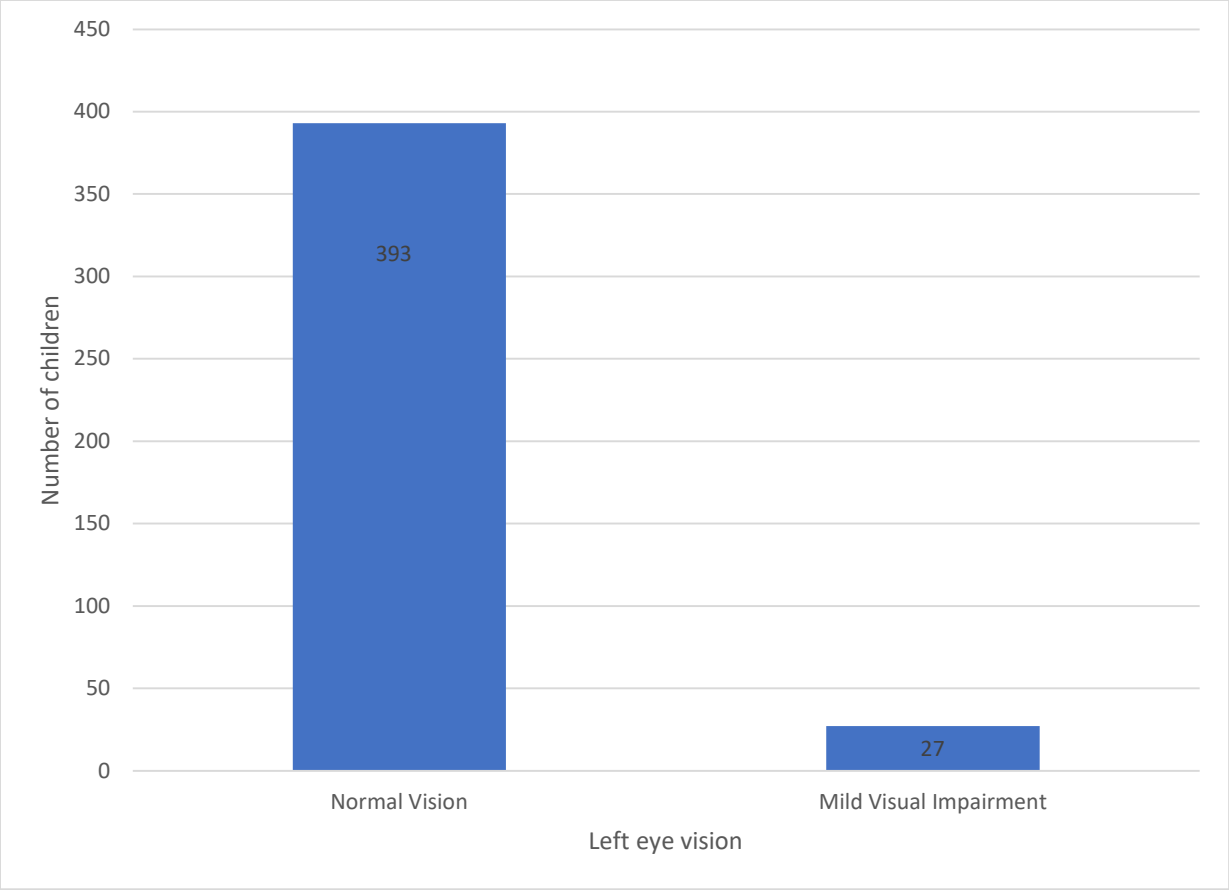

Figure 23: Presenting distance vision (unaided) left eye of study participants

4.4 The mean central corneal thickness of study participants in the Ablekuma Sub metropolitan area

Table 5 presents a descriptive summary of central cornea thickness (CCTs) of participants. From the Table 5, the Kolmogorov-Smirnov test for normality showed that the mean CCT of the right eye was not normally distributed (p-value = 0.046), with mean and median (interquartile range) CCT for the right as 538.3±27.3 µm and 536.0 (34.0) µm respectively. However, the mean CCT for the left eye was normally distributed (p-value = 0.200) with mean and median (interquartile range) CCT; 539.3±26.8 µm and 539.3 (37.0) µm respectively.

Table 5: Descriptive summary of central cornea thickness (CCTs) of participants

Statistics	**CCT**		
	Right eye CCT (µm)	**Left eye CCT (µm)**	**Both (all) eyes CCT (µm)**
Mean	538.3	539.3	538.8
Median	536.0	539.3	538.5
Mode	535.0	522.0	550.0
Standard deviation	27.3	26.8	27.0
Minimum	455.0	455.0	455.0
Maximum	625.0	625.0	624.0
Interquartile range	34.0	37.0	35
Lower quartile	522.0	522.0	522.0
Upper quartile	556.0	559.0	557.0
P-values for normality test (Kolmogorov-Smirnov test)	0.046	0.200*	0.200*

*Normally distributed.

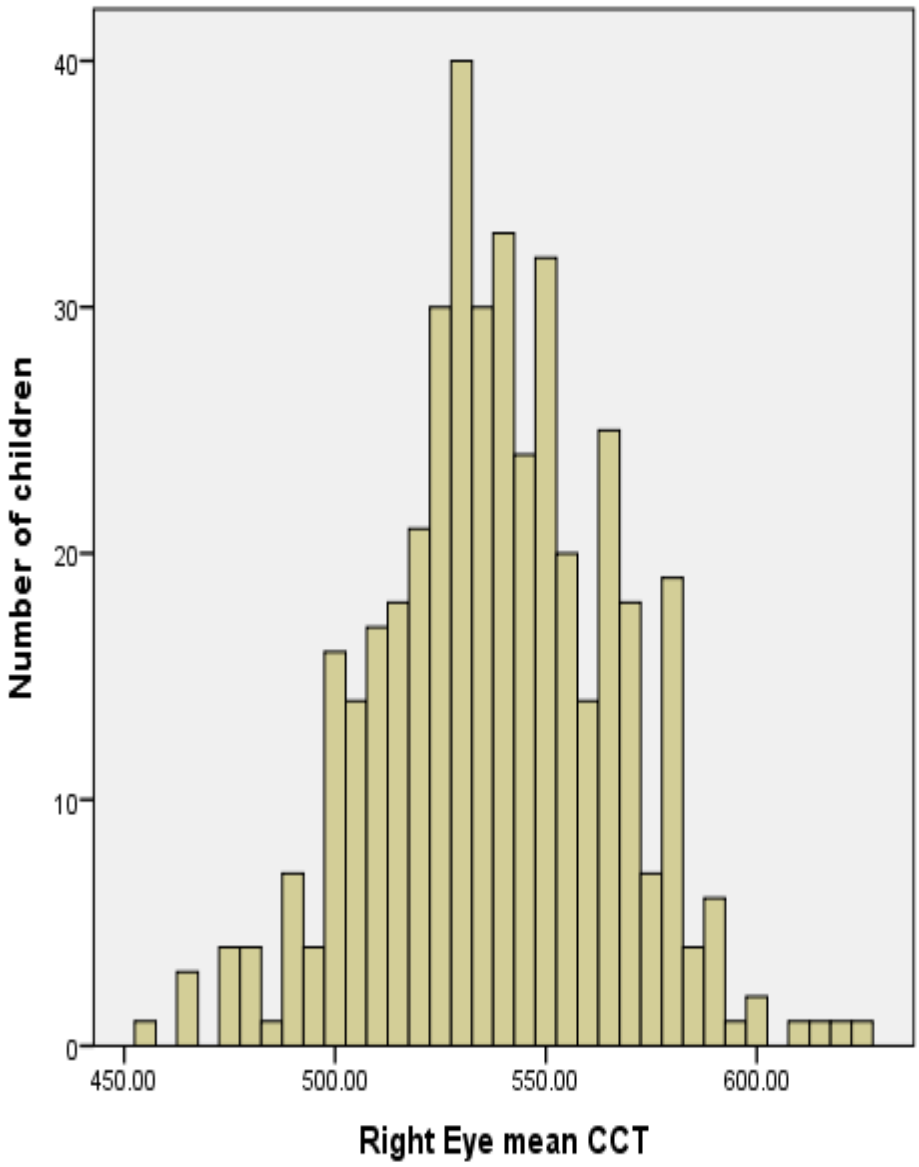

Figure 24: A histogram of the distribution of right eye CCT of study participants

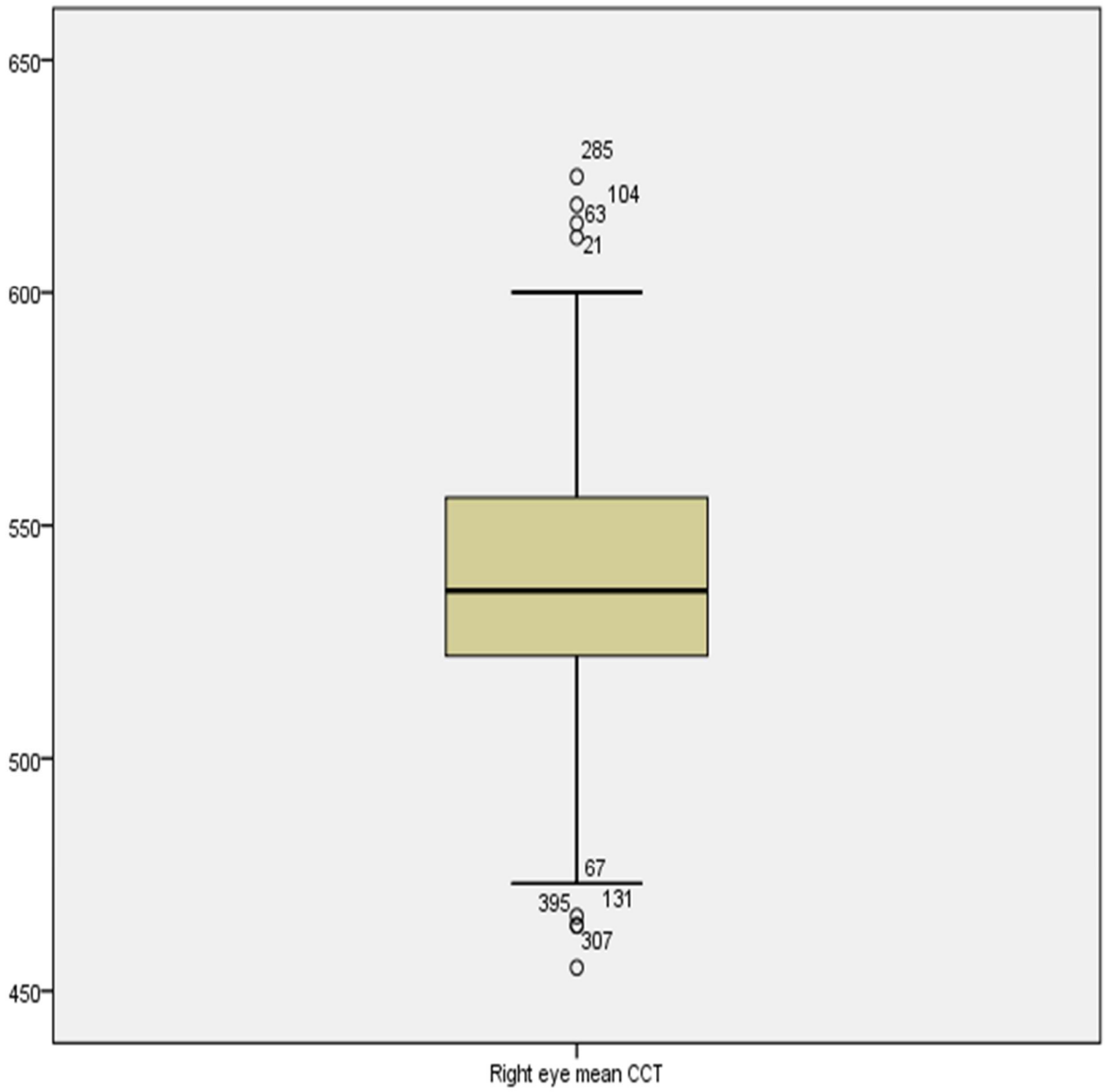

Figure 25: A box plot of Right eye mean CCT of children from selected schools in Ablekuma sub-Metropolitan area

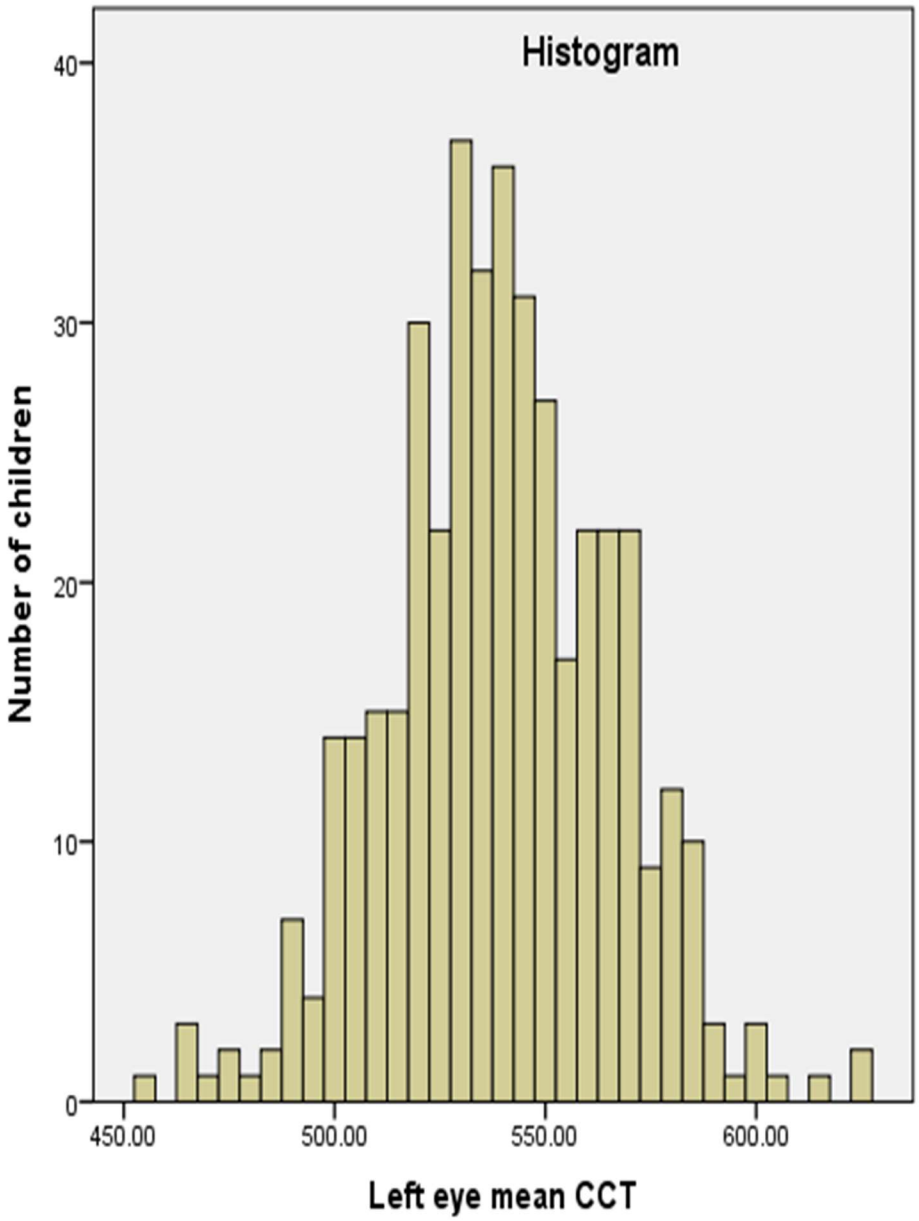

Figure 26: A histogram of the distribution of left eye CCT of children from selected schools in Ablekuma sub-Metropolitan area

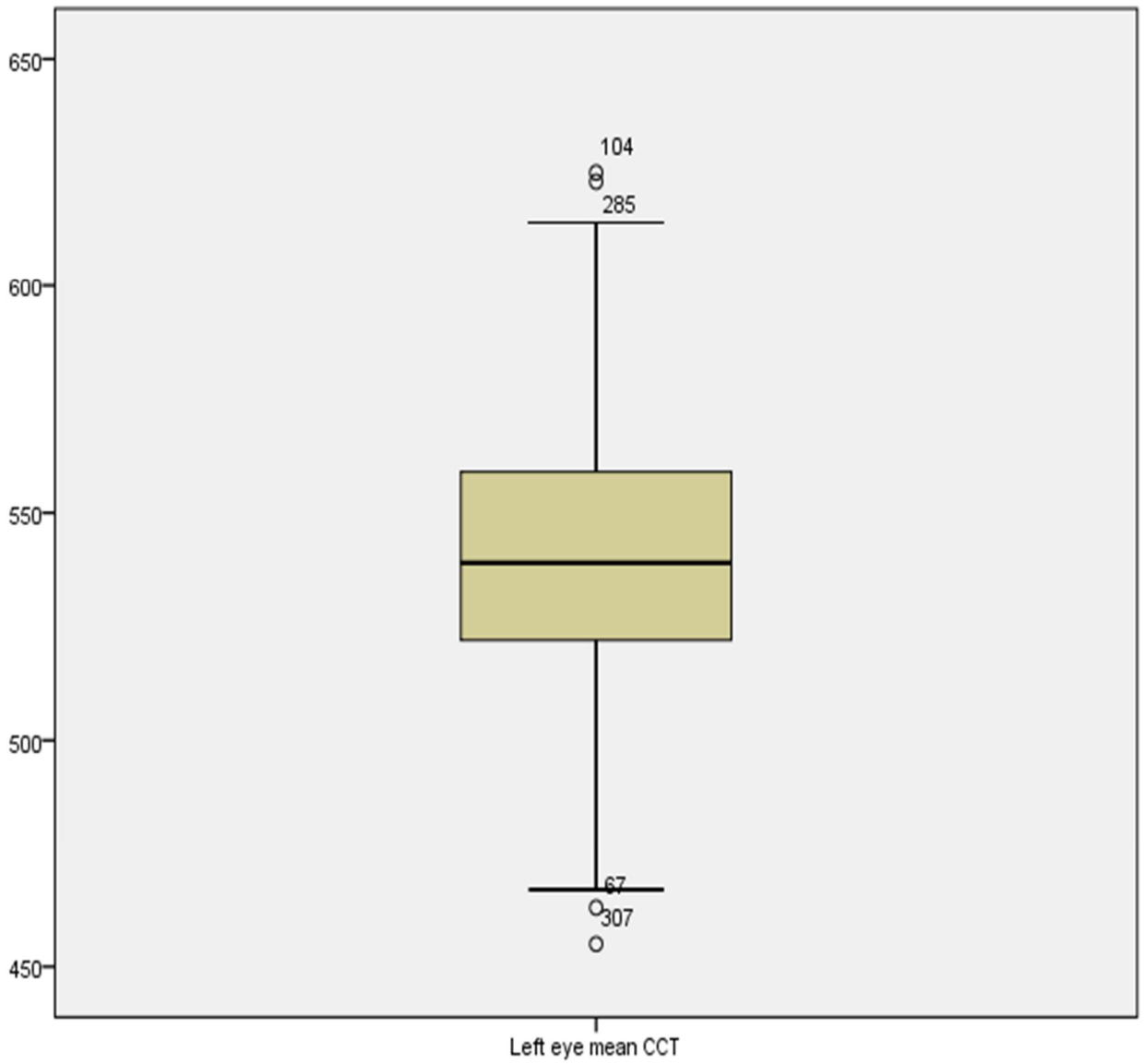

Figure 27: A box plot of left eye mean CCT of children from selected schools in Ablekuma sub-Metropolitan area

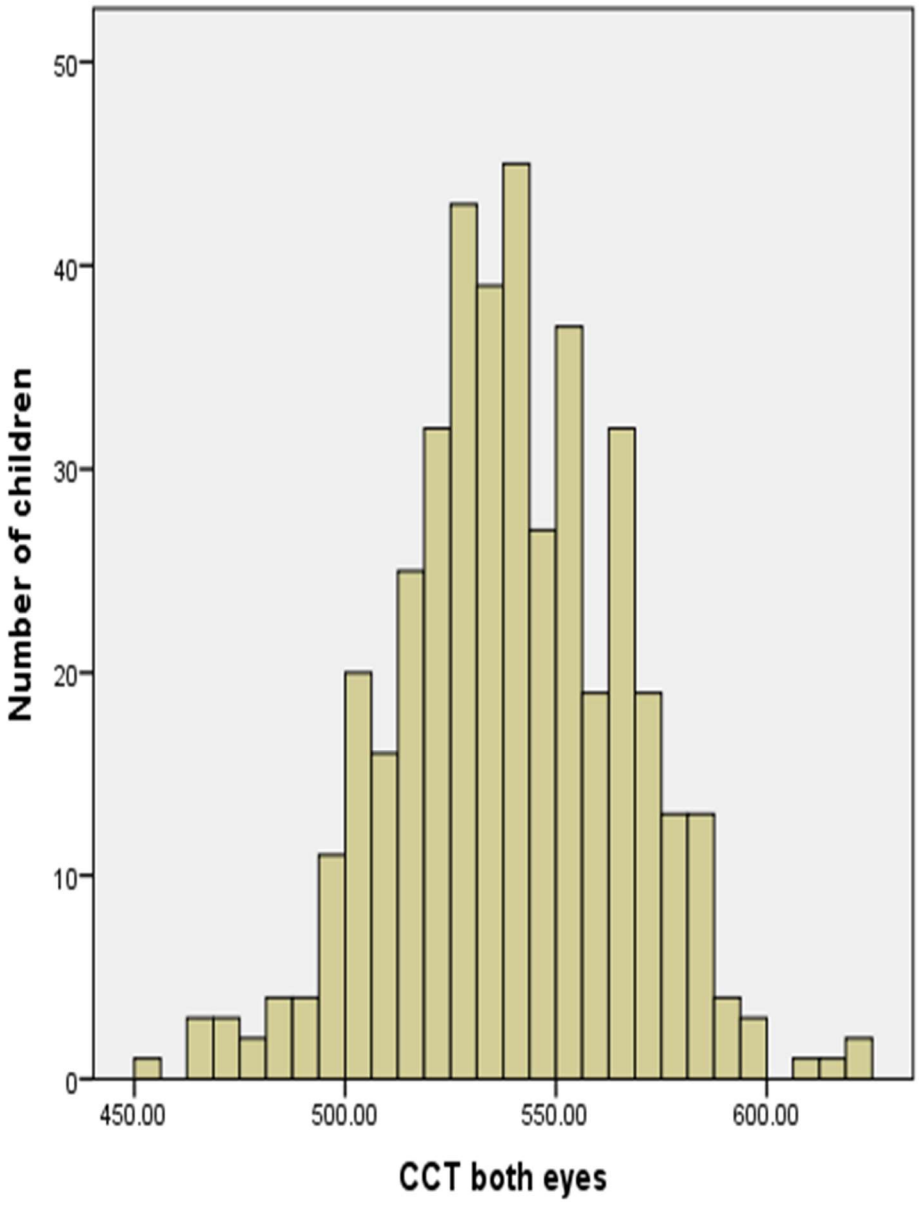

Figure 28: A histogram of the distribution of CCT in all eyes (both left and right) of children from selected schools in Ablekuma sub-Metropolitan area

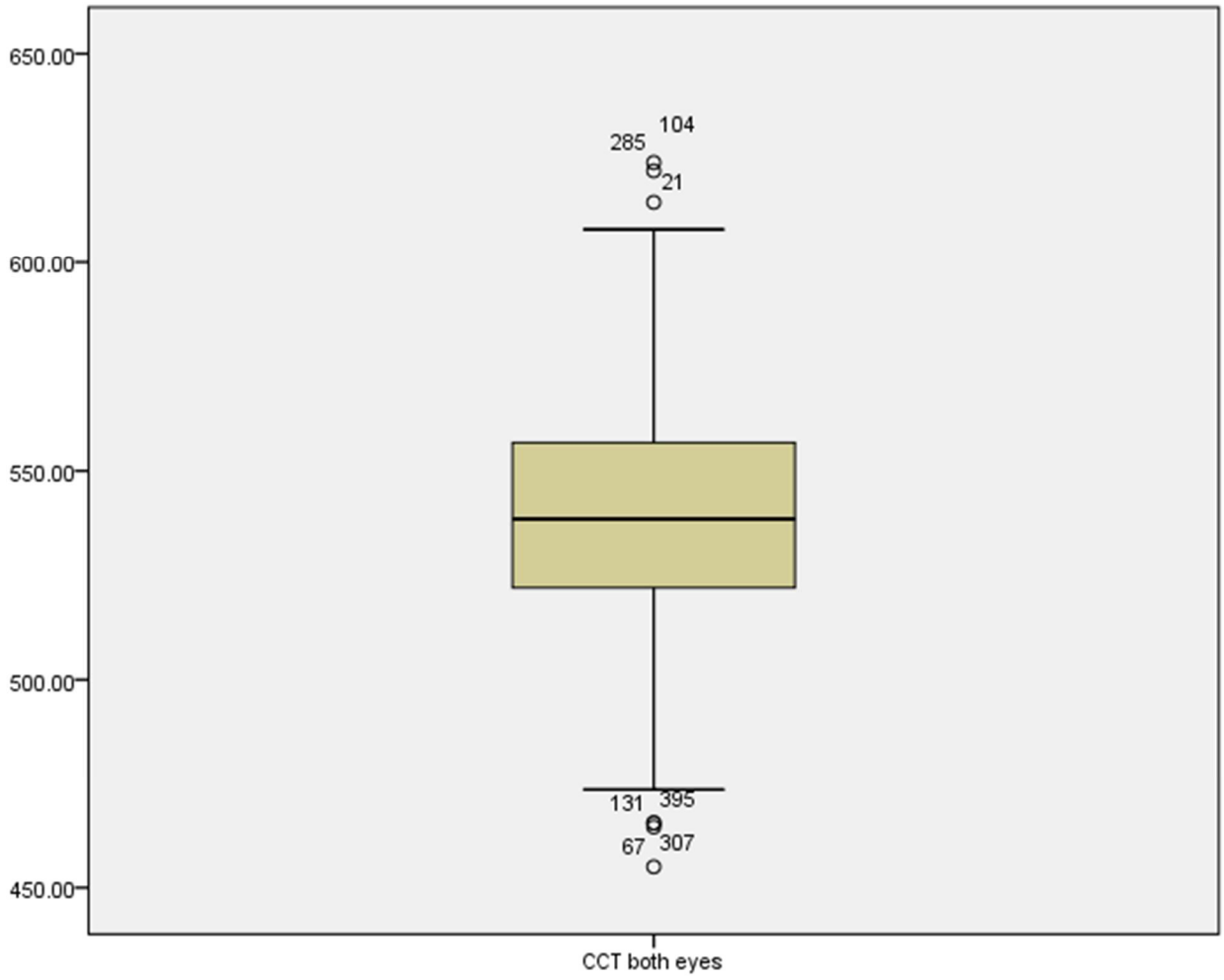

Figure 29: A boxplot of the distribution of CCT in both eyes of children from selected schools in Ablekuma sub-Metropolitan area

4.5 Variations in mean central corneal thickness with age in study participants

Variations in the mean corneal thickness with age were examined. From table 4.9 below, the mean CCT for the right eye among children aged 6-8 years was 541.2±25.6 µm. Children aged 8-10 years had a mean CCT of 534.2±26.1 µm for the right eye and those 10-15 years recorded a mean CCT of 538.3±28.6 µm for the right eye. ANOVA (Analysis of variance with the F statistics) showed no significant difference in mean CCT among the age groups for the right eye (F= 1.792; p-value = 0.168). **Table 6.**

The mean CCT for the left eye among children aged 6-8 years was 541.7±24.4 µm. Children aged 8-10 years had a mean CCT of 535.8±25.7 µm for the left eye and those 10-15 years recorded a mean CCT of 539.8±28.4 µm for the left eye. ANOVA showed no significant difference in mean CCT among the age groups for the left eye (F = 1.362; p-value = 0.257). **Table 7.**

For both eyes, the mean CCT among children aged 6-8 years was 541.4±24.9 µm. Children aged 8-10 years had a mean CCT of 534.9±25.8 µm for both eyes and those 10-15 years recorded a mean CCT of 539.4±28.3 µm for both eyes. The ANOVA (Analysis of variance with the F statistics) showed no significant difference in mean CCT among the age groups for both eyes (F = 1.585; p-value = 0.206). **Table 8.**

There was a very weak negative correlation between the CCT and age of children (r = -0.04; p-value = 0.372). A linear regression model of CCT as a function of age in years showed that: CCT = 543.4 – 0. 45Age.Thus, for every increase per year in age of a child, there is a corresponding decrease in the CCT by 0.45 µm.

Table 6: Variations in mean corneal thickness with age for the right eye in children from selected schools in Ablekuma sub-Metropolitan area

CCT statistics (µm)	Age group		
	6 to<8 years	8 to <10 years	10-15 years
Mean	541.2	534.2	538.3
Median	541.0	533.0	539.0
Mode	571.0	535.0	526.0
Standard deviation	25.6	26.1	28.6
Minimum	481.0	464.0	455.0
Maximum	615.0	589.0	625.0
Interquartile range	33.3	33.0	35.5
Lower quartile	528.3	519.0	521.3
Upper quartile	561.5	552.0	556.8
ANOVA F statistics = 1.792; p-value = 0.168			

ANOVA (Analysis of variance with the F statistics) Post Hoc tests showing no significant difference in mean CCT among the age groups for the right eye (F= 1.792; p-value = 0.168).

Table 7: Variations in mean corneal thickness with age for the left eye in healthy Ghanaian children

CCT statistics (µm)	Age group		
	6 to <8 years	8 to <10 years	10-15 years
Mean	541.7	535.8	539.8
Median	541.0	533.0	539.0
Mode	541.0	511.0	539.0
Standard deviation	24.4	25.7	28.4
Minimum	479.0	467.0	455.0
Maximum	614.0	583.0	625.0
Interquartile range	32.5	35.0	36.5
Lower quartile	528.3	522.0	521.0
Upper quartile	560.8	557.0	557.5
ANOVA F statistics = 1.362; p-value = 0.257			

ANOVA Post Hoc tests showing no significant difference in mean CCT among the age groups for the left eye (F= 1.362; p-value = 0.257).

Table 8: Variations in mean corneal thickness of both eyes with age in healthy Ghanaian children

CCT statistics (µm)	Age group		
	6 to <8 years	8 to <10 years	10-15 years
Mean	541.4	534.9	539.4
Median	540.8	533.0	539.8
Mode	550.0	539.5	550.0
Standard deviation	24.9	25.8	28.3
Minimum	480.0	465.5	455.0
Maximum	614.5	586.0	624.0
Interquartile range	32.9	35.0	35.1
Lower quartile	528.0	519.5	521.5
Upper quartile	560.9	554.5	556.6
ANOVA F statistics = 1.585; p-value = 0.206			

ANOVA Post Hoc tests showing no significant difference in the mean CCT among the age groups (F= 1.585; p-value = 0.206).

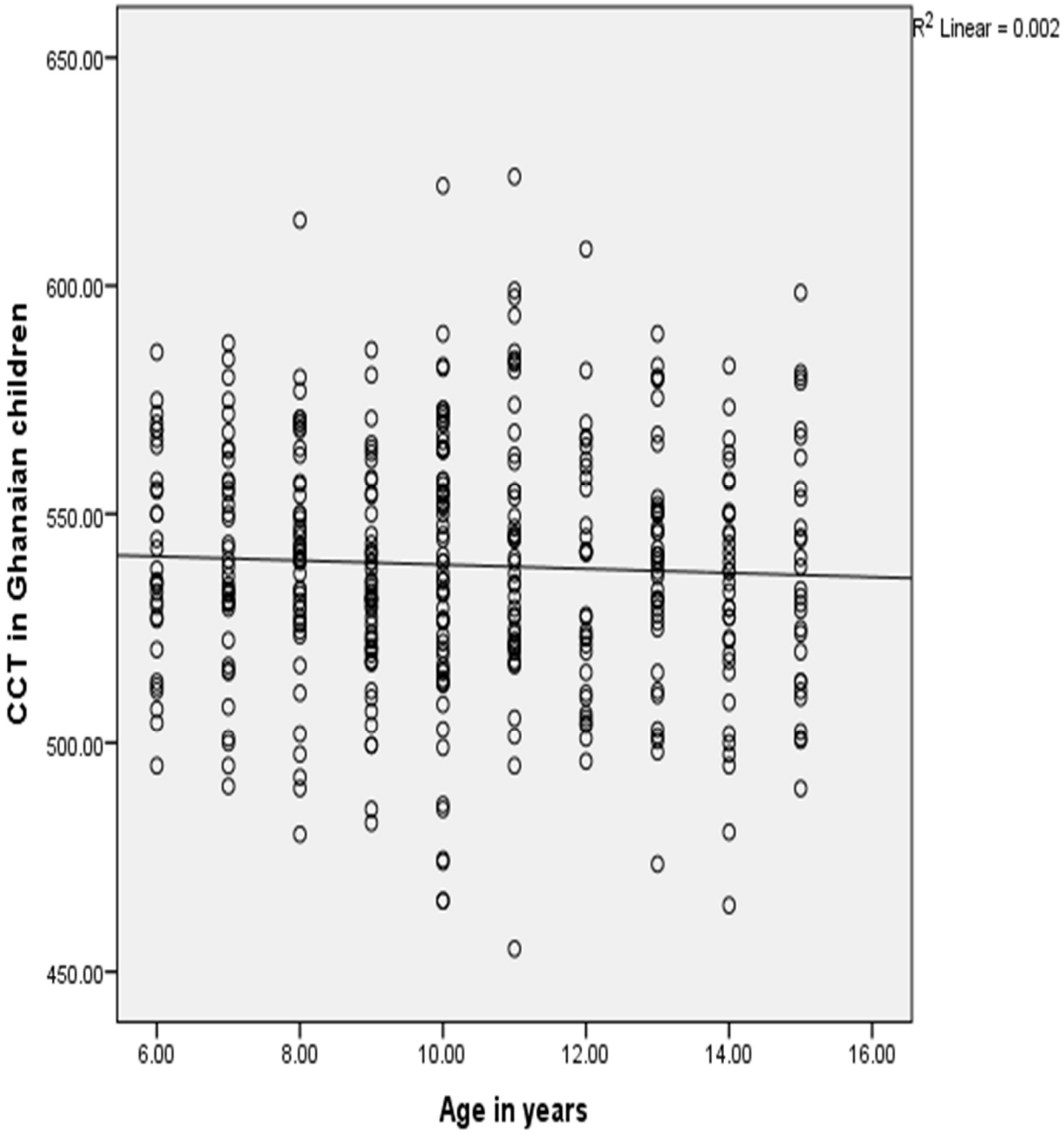

Figure 30: A scatter plot of CCT in both eyes against age in Ghanaian children

4.6 Difference in central corneal thickness between male and female study participants

Table 9 below shows the difference in central corneal thickness between male and female Ghanaian children. From the table, males had a mean CCT value of 540.4±25.5 µm and females had a mean CCT of 537.2±28.2 µm respectively. Independent t- tests showed no significant difference in the mean CCT between males and females. (p-value = 0.229).

Table 9: Difference in central corneal thickness between male and female study participants

CCT statistics (µm)	**Sex**	
	Male	**Female**
Mean	540.4	537.2
Median	541.5	533.5
Mode	550.0	550.0
Standard deviation	25.5	28.2
Minimum	465.5	455.0
Maximum	622.0	624.0
Interquartile range	30.1	36.5
Lower quartile	527.5	518.8
Upper quartile	557.6	555.3
Independent T-test (t= 1.205; p-value = 0.229; CI = -2.0 to 8.3).		

4.7 Descriptive summary of intraocular pressures (IOPs) of participants

Table 10 presents a descriptive summary of intraocular pressures (IOPs) of participants. From the, the Kolmogorov-Smirnov test for normality shows that the mean IOP of the right eye is not normally distributed (p-value = 0.0401) with mean and median (interquartile range) IOP for the right as 15.6±3.0 mmHg and 16.0 (4.0) mmHg respectively. The mean IOP for the left eye was also not normally distributed (p-value = 0.001) with mean and median (interquartile range) IOP; 15.6±3.2 mmHg and 16.0 (5.0) mmHg respectively.

Table 10:Descriptive summary of intraocular pressures (IOPs) of participants

Statistics	**IOP**	
	Right eye IOP (mmHg)	**Left eye IOP (mmHg)**
Mean	15.6	15.6
Median	16.0	16.0
Mode	17.0	14.0
Standard deviation	3.0	3.2
Minimum	8.0	8.0
Maximum	24.0	25.0
Interquartile range	4.0	5.0
Lower quartile	14.0	13.0
Upper quartile	18.0	18.0
P-values for normality test (Kolmogorov-Smirnov test)	0.0401*	0.001*

*Non-normally distributed.

4.8 Descriptive summary of the cup-to-disc ratio (CDR) of the participants

The descriptive summary of the CDR is presented on table 11 below. From the table 11, the Kolmogorov-Smirnov test for normality shows that the mean CDR of both eyes were not normally distributed (p-value = 0.001). The mean and median (interquartile range) CDR for the right was 0.3±0.1 and 0.3 (0.2) respectively. Also, the mean and median (interquartile range) CDR for the left eye was; 0.3±0.1 and 0.3 (0.2) respectively.

Table 11:Descriptive summary of cup-to-disc ratio (CDR) of the participants

Statistics of CDR	**CDR**	
	Right eye CDR	**Left eye CDR**
Mean	0.3	0.3
Median	0.3	0.3
Mode	0.3	0.3
Standard deviation	0.1	0.1
Minimum	0.1	0.1
Maximum	0.6	0.6
Interquartile range	0.2	0.2
Lower quartile	0.2	0.2
Upper quartile	0.4	0.4
P-values for normality test (Kolmogorov-Smirnov test)	0.001*	0.001*

*Non-normally distributed.

4.9. Relationship between IOP and CCT (both eyes) in study participants

Using the Carl Pearson's correlation analysis, there was a weak positive correlation between IOP and CCT in normal Ghanaian children which was also statistically significant (r = 0.4; p-value = 0.001). A linear regression model was also derived for the mean IOP as a function of CCT (x).

Where x is the CCT.

From the linear regression model fitted for both eyes;

IOP = 0.041+0.029x

Thus, for every increase in a unit μm of CCT, there is a corresponding decrease in the IOP by 0.029 mmHg.

Figure 31 presents a scatter plot of mean central corneal thickness (CCT) by IOP.

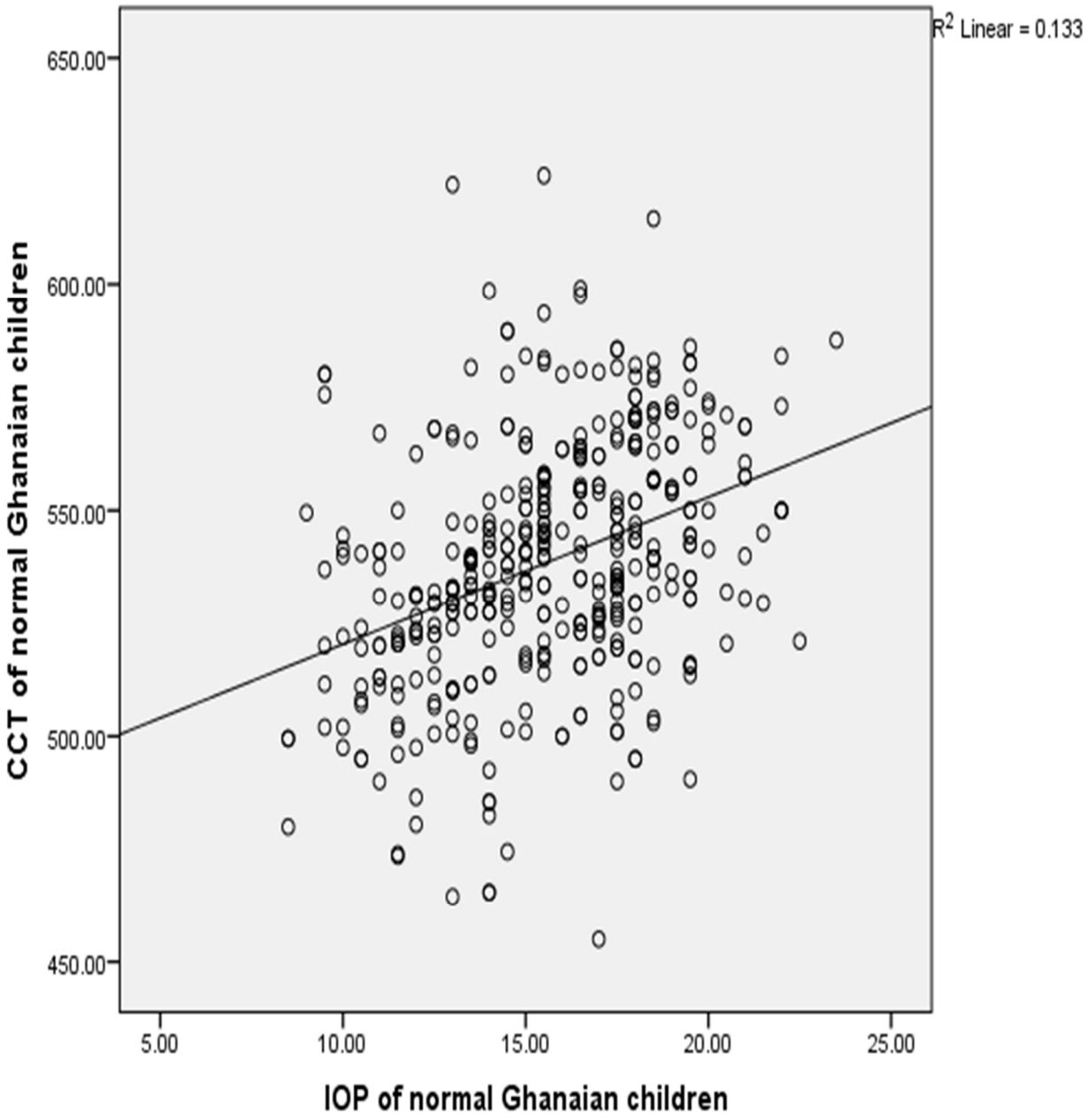

Figure 31: A scatter plot of mean central corneal thickness (CCT) by IOP in study participants

4.10 Relationship between mean central corneal thickness (CCT) and spherical equivalent of refractive error

A descriptive summary of the spherical equivalent for the right and left eyes are presented on table 12 below. Kolmogorov-Smirnov test for normality shows that the mean spherical equivalent of both eyes was not normally distributed (p-value = 0.001). The mean and median (interquartile range) spherical equivalent for the right eye is 0.2±1.2 and 0.5 (0.5) respectively. The mean and median (interquartile range) spherical equivalent for the left eye was; 0.3±1.1 and 0.5 (0.5) respectively.

Table 12:Descriptive summary of spherical equivalent of the participants

Statistics of spherical equivalent	**Spherical equivalent**	
	Right eye spherical equivalent	**Left eye spherical equivalent**
Mean	0.2	0.3
Median	0.5	0.5
Mode	-0.8	0.8
Standard deviation	1.2	1.1
Minimum	-3.3	-4.0
Maximum	6.5	3.8
Interquartile range	0.5	0.5
Lower quartile	-0.8	-0.5
Upper quartile	1.0	1.0
P-values for normality test (Kolmogorov-Smirnov test)	0.001*	0.001*

*Non-normally distributed.

Figures **32, 33** and **34** below show scatter plots of mean central corneal thickness (CCT) and spherical equivalent of refractive errors for right, left and both eyes respectively. There was a weak positive correlation between CCT and right and left eyes spherical equivalent respectively. This correlation was however, not statistically significant for the right eye but significant for the left eye (right eye: r = 0.1, p-value = 0.071; left eye r = 0.1, p-value = 0.004). There was also a weak positive correlation between CCT and combined right and left eyes' spherical equivalent which was statistically significant (r = 0.1, p-value = 0.015).

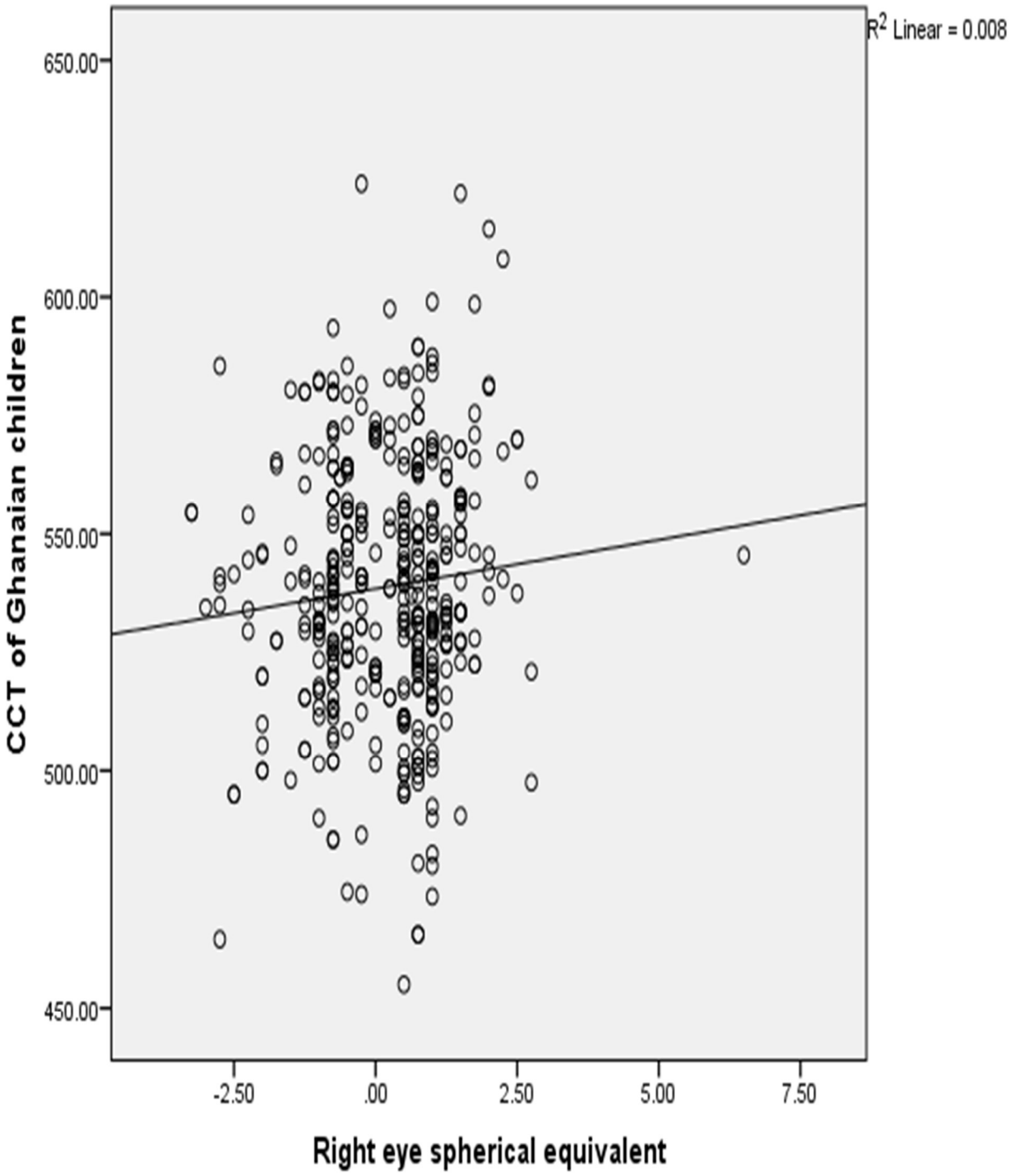

Figure 32: A scatter plot of mean central corneal thickness (CCT) by right eye spherical equivalent

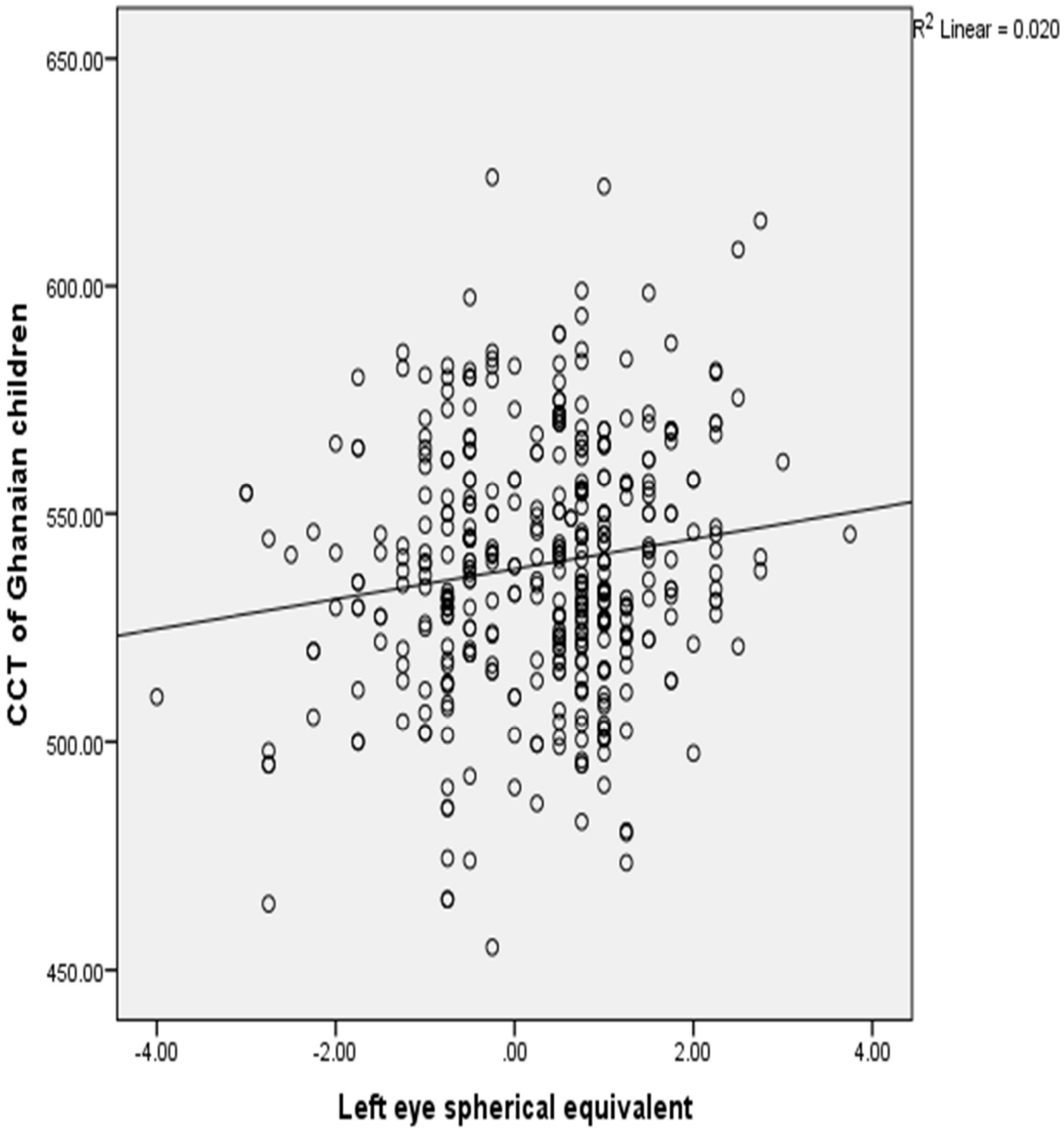

Figure 33: A scatter plot of mean central corneal thickness (CCT) by left eye spherical equivalent

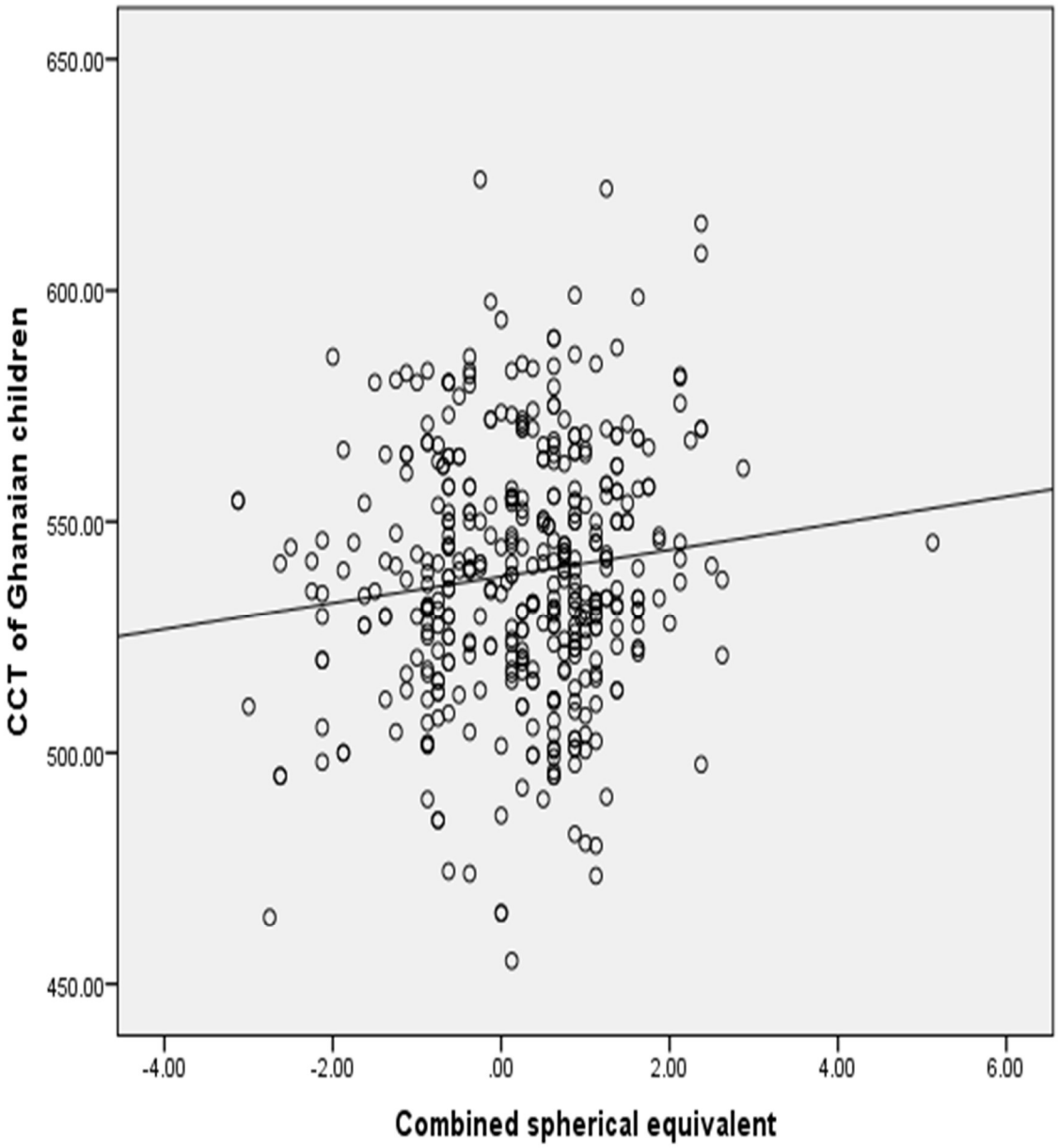

Figure 34:A scatter plot of mean central corneal thickness (CCT) by Combined spherical equivalent (both eyes)

4.11 Variations in mean corneal thickness and refractive errors in healthy Ghanaian children

Table 13 below shows the variations in mean corneal thickness and refractive errors in healthy Ghanaian children. The mean CCT for children with emmetropia, hyperopia and myopia are 539.6±27.2 µm, 542.5±26.6 µm and 530.8±25.3 µm respectively. An ANOVA Post Hoc tests for significant difference in mean CCT among the types of refractive errors shows a statistically significant difference in mean CCT and types of refractive errors (F= 4.582; p-value = 0.011).

Table 13:Variations in mean corneal thickness and refractive errors in healthy Ghanaian children

CCT Statistics (µm)	**Refractive error**		
	Emmetropia (n=230)	**Hyperopia (n = 114)**	**Myopia (n = 76)**
Mean	539.6	542.5	530.8
Median	540.8	540.0	529.5
Mode	539.5	533.5	529.5
Standard deviation	27.2	26.6	25.3
Minimum	455.0	473.5	464.5
Maximum	624.0	622.0	585.5
Interquartile range	35.0	31.0	34.0
Lower quartile	522.5	527.0	511.5
Upper quartile	557.5	558.0	545.5
ANOVA F statistics for mean CCT = 4.582; p-value = 0.011			

ANOVA Post Hoc tests showing significant difference in the mean CCT and types of refractive errors (F= 4.582; p-value = 0.011).

4.12 Association between ethnicity and CCT

The highest number of participants were from the Ga/ Adangbe ethnic group (205, 48.9%). Mean CCT in Ga/ Adangbe participants was 539.2±27.1, in Akans was 538.2±25.7, in Ewes 540.7±26.3 and in others 529.0±36.5 (Table 14). The difference was however not statistically significant (p=0.459)

Table 14:Association between ethnicity and mean CCT

Mean CCT	Ethnicity				p-value
	Akans	Ga/Adangbe	Ewes	Others	
Number (%)	123(29.4%)	205(48.9%)	75 (17.9%)	16 (3.8%)	
Mean CCT	538.2±25.7	539.2±27.1	540.7±26.3	529.0±36.5	0.459*

*ANOVA test.

Others include; Dagaare/Wala/ Sisala = 5(1.2), Dagomba = 3(0.7), Hausa = 6(1.4), Frafra = 2(0.5)

CHAPTER 5

DISCUSSION

Several studies have reported racial variation of CCT measurements, both in children and adults. Unfortunately, few studies have been done in the paediatric population, especially in Sub-Saharan Africa. The overall aim of this study was to determine the normative CCT in healthy Ghanaian children aged 6-15 years in the Ablekuma Sub-Metropolitan area using ultrasound pachymetry. A total of 420 children aged from 6 to 15 years from selected schools in the Ablekuma South Sub-Metropolitan area at the basic level of education were involved in the study

The overall mean CCT was found to be 538.8 ± 27 µm which is thinner than the mean CCT for Caucasians in studies such as the PEDIG study, which is one of the largest studies on paediatric CCT.[20] The mean CCT for Caucasians was reported to be 573 µm. In the PEDIG study, mean CCT was reported to be 551 µm in African-Americans which is still about 12 µm higher than what was found in our study.[20] The mean CCT for Ghanaian children in this study is also less than that reported by Wei et al[75] in a Chinese study among children aged 7-18 years, which was 554.19±35.46 µm as well as what was observed by Muir et al[78] who found that the mean CCT white children was 562±35 µm [75,78] It is also thinner than what was observed by Eraslan et al[79] in a Turkish study among children aged 6 to 13 years (559.3±35.3 µm). Our finding of mean CCT of 538.8 µm is however comparable to studies such as what was done by Haider et al[21] who reported mean CCT as 535± 38 µm in African American children. Their study also reported that mean CCT in African-American children was significantly was thinner compared to Caucasian children (559 ± 38 µm).[21] The mean CCT in our sample population was also comparable to what was reported in a Cameroonian study by Eballe et al, who found the mean CCT among healthy school children aged 5-16 years to be 538.06 ± 38.03 µm.[28] Hussein et al[15] also reported the mean CCT of African-American children to be 532 ± 34 µm. This is similar to the findings of this study as well as that of Haider and Eballe. In the study by Hussein et al[15], CCT in African-American children was thinner than that of Caucasian children (551 ± 48 µm) as well as Hispanic children (550 ± 48 µm). Conversely, our mean CCT was higher than what was reported by Dai et al[26] in a study comparing paediatric CCT among different ethnic groups. Their study reported a mean CCT of 523 ± 40 µm for African-American children while in Caucasians, it was reported as 563 ± 36 µm and in

Hispanics, 568 ± 44 µm.[26] A few studies have investigated the reasons accounting for the difference in CCT among different racial groups.[80,81] One study attributed these differences to genetic or hereditary factors[81]while another study suggested environmental factors such as geographic area, latitude and UV light exposure.[80] In the study by Landers et al, it was observed that members of the same nuclear family had similar CCT values, suggesting a possible hereditary element.[81] Jiaonan Ma et al[80] observed from their study that individuals who lived in high latitudes, exposed to long duration of sunlight and alternating periods of dry and wet weather conditions had thinner corneas.[80] Though this may be a plausible explanation why African populations in the tropics have thinner corneas, it does not explain why African-Americans in temperate regions also have thinner corneas compared to their Caucasian counterparts.[19] Other studies have also suggested the possible association between CCT and nutritional status.[82] Since CCT is known to be affected by the number of keratocytes, anything that affects the expression of these cells will affect corneal thickness.[76] There is the need for further studies to determine the cause of differences in CCT across racial groups.

Variations in mean CCT with age

From our analysis, the mean age and standard deviation (SD) of the participants was 10.3±2.6 years. Previous studies in adults have reported that central corneal thickness tends to decrease with increasing age.[4,21,54] In the ocular hypertension treatment study, a statistically significant negative correlation between age and central corneal thickness was found with the corresponding finding of a 6.3 µm thinning over every decade.[4] A study conducted in Tanzania reported that, study participants aged 50 years and above were 6 times more likely to have thin CCT compared to study participants aged less than 30 years while the odds of having thinner corneal thickness among those aged 70 years and above was eight times higher.[61] A Cameroonian study among non-glaucomatous patients aged 5-75 years found that the cornea was thicker in the group of patients aged younger than 20 years, with an average of 537.19 ± 37.50 µm in both eyes with CCT being thinner among the group of patients aged more than 60 years. The study also reported that CCT significantly decreased with age among women (P = 0.005, one-way ANOVA) and in the men the decrease was not statistically significant. The investigators therefore concluded that in general,

central corneal thickness was negatively related to age, with CCT decreasing by 4.2 µm per 10 years.[28] Ntim-Amponsah et al[62] also concluded from their Ghanaian study on CCT that corneal thickness was higher in individuals younger than 30 years and thinner in those above 30 years. While the mean CCT for the study population aged between 20-72 years was 534 µm, it was 523 µm in 40-49 year group and 515 µm in those aged more than 50 years.[62] The mean CCT in our study among children 6-15 years was 538.8 µm which is comparable to the mean for Ghanaian sample aged 20-72 years. For both eyes, the mean CCT among children aged 6 to <8 years was 541.4±24.9 µm., for children aged 8 to <10 years 534.9±25.8 µm for both eyes and those 10-15 years 538.3±28.6 µm. Our data probably suggests that CCT approximates adult ranges from age 8 years. Hussein et al suggested from that the pediatric corneal thickness reached at adult levels by age 5 years.[15]

The ANOVA showed no significant difference in mean CCT among the age groups for both eyes (F = 1.585; p-value = 0.206). There was a weak negative correlation between the CCT and age of children (r = -0.04; p-value = 0.372). A linear regression model of CCT as a function of age in years showed that: CCT = 543.4 – 0. 45Age.Thus, for every increase in age per year of a child, there is a corresponding decrease in the CCT by 0.45 µm. This differs from the PEDIG study where a thicker median CCT was observed with each successive year of age from 1 to 11 years and then remained stable afterwards.[20] Hussein et al[15]. also reported that mean CCT values increased with increasing age, reaching adult thickness at age 5 to 9 years. The contrast in these findings could be due to the difference in sample populations. The PEDIG study as well as Hussein et al included children below age 5 years and were predominantly Caucasian studies, whereas our study was in black children and excluded the age group below 6 years. In the Cameroonian study by Eballe et al[28] children aged 8–10 years had a higher CCT than the other age groups. Children aged 5-7years had mean CCT of. 532.33 ± 40.38 µm, those aged 8-10 years 550.96 ± 39.25 µm, those aged 11-13 years 537.39 ± 38.75 µm and 14-16 years 534.84 ± 36.75 µm. Despite this finding, Eballe did not find any statistically significant difference in CCT between the age groups of age 5–7 years, 8–10 years, 11–13 years, and 14–16 years.[28] In our study, the age 6–8-year group had the highest mean CCT of 541±24.9 µm. Haider et al[21] in their study comparing CCT in Caucasian and African-American children also reported a positive association between age and CCT. They found that CCT increased with age from 10 years, with children aged 10-18 years having the highest mean CCT.[21] They also observed that increase in CCT measurements with increasing age was slightly

greater for white children compared to African American children of the same age group. The differences observed in the relationship between CCT and age for Caucasian and children of African descent need to be investigated further. It is not clear if difference in corneal structure accounts for the different patterns. Differences in corneal structure between racial groups may also explain why individual of African descent are more prone to developing glaucoma.[21] One possible explanation could be that since CCT is found to be affected by environmental factors such as prolonged exposure to sunlight or UV light[80], the cornea in African children probably starts thinning at an earlier age compared with their Caucasian counterparts. Further studies examining the microscopic structure of the cornea across age groups and races may help explain the differences. Other studies have not shown any correlation between CCT and age. Zheng et al[39] in a Chinese study, did not report association between age and CCT. Neither did Dai et al[26] and Nejabat et al[83] in a paediatric Persian study, who also observed from their studies that CCT did not vary with age.[26]

Relationship between CCT and Sex

In this study though the mean CCT was higher in males (540.4 μm) than females (537.2 μm), the difference was not statistically significant (Table 4.13), thus this study did not find any association between sex and CCT. This finding is comparable to what Eballe et al[28] found in a paediatric CCT study where the average CCT was 541.41 ± 36.45 μm in boys and 536.15 ± 38.91 μm in girls with no statistically significant difference between the genders. In another study by Eballe et al using a sample population aged 5-75 years there was no statistically significant difference in CCT between male and female participants.[59] Haider et al also report no association between sex and CCT.[21] In addition, other studies done by Kotb and Eissa[56], Stanislaus et al [14] , Nejabat et al[83] and Dai et al[26] did not report statistically significant differences in CCT between males and females. In the PEDIG study however, females were found to have thinner mean CCT compared to males and the difference was statistically significant ($p=0.003$).[20] This is similar to an Iranian study which reported higher CCT values in males.[82] Unfortunately none of these studies investigated the possible reasons for this difference.

Relationship between CCT and IOP

In previous studies, CCT has been found to correlate with IOP.[9,20,84] Indeed, the role of CCT in IOP measurement is based on the use of the Imbert-Fick's principle as was stipulated by Goldman.[85] Thus, the thinner the CCT, the less force exerted to flatten the cornea and vice versa. Thinner CCTs are believed to result in the erroneous underestimation of IOPs while thick CCT will result in the overestimation of IOP. In this study there was a weak positive correlation between CCT and IOP in normal Ghanaian children which was also statistically significant ($r = 0.4$; p-value $= 0.001$). It was found that for every increase in a unit µm of CCT, there is a corresponding increase in IOP by 0.029mmHg. Our study finding is consistent with several studies in the literature including the Beijing Eye Study done in adults and the PEDIG study conducted in children.[20,52] In the Beijing Eye study (BES) it was found that intraocular pressure measurements increased for each µm increase in central corneal thickness by 0.03 mmHg. In respect to paediatric studies the PEDIG study also reported that for every 100 µm of thicker CCT measured, the intraocular pressure was 1.5 mmHg higher($p< 0.001$).[20] Our findings are also consistent with that of Nejabat et al[83] in a study among Persian children aged 6-13 years which reported that IOP correlated positively with CCT.[83] Their outcomes demonstrated that for every 100 µm increase in CCT, IOP measured with Goldman applanation tonometry(GAT) increased by 0.8mmHg(OD) and 3.3 mmHg(OS), and for non-contact tonometry(NCT) by 1.4mmHg(OD) and 2.9 mmHg(OS).[83] Wei et al[75]also demonstrated in their paediatric Chinese study that there were significant correlations between the CCT and IOP values and that IOP would increase by 0.32 mm Hg for every 10 µm increase in CCT.[75] Muir et al[78] in a paediatric study found that there was a positive association between CCT and measured IOP and based on a linear regression analysis model concluded that for every 100 µm increase in CCT, the measured IOP increased by 2.2±0.6mmHg. In addition, a meta-analysis by Farvardin et al[84] on IOP and CCT in healthy children analyzing 19 published articles concluded that there was a very significant relationship between IOP and CCT (P=0.00),

The mean IOP in this study was 15.6mmHg for both eyes. This is lower than the mean IOP measured by I-care tonometer in Polish children aged 5-17 years which reported mean IOP of 16.9mmHg. [86]The difference could be accounted for due to higher mean CCT among Polish children which was reported to be 563 ± 30 µm.[86] In this same study it was observed that among the cohort of children whose CCT was less than the mean 563 µm, mean IOP measured by I-care

tonometry was 15.8mmHg which is comparable to what was found in our study.[86] This also supports the theory that CCT correlates with IOP.

This underscores the need to correlate IOP measurements with CCT as there is growing evidence that IOP measurements can be affected by CCT. This is especially important in the evaluation of children with suspicious discs with no overt symptoms as is the case of primary congenital glaucoma. These children may present with borderline IOPs and the diagnosis of Juvenile open-angle glaucoma (JOAG) may be delayed or completely missed placing them at risk of irreversible vision loss from the disease.

CCT and refractive error

The relationship between CCT and refractive error has yielded different results from various studies. In this current study the mean CCT for children with emmetropia, hyperopia and myopia were 539.6±27.2 µm, 542.5±26.6 µm and 530.8±25.3 µm respectively and the difference was statistically significant (F= 4.582; p-value = 0.011). Thus, CCT was higher in hyperopes compared to emmetropes and thinnest in myopes. This finding is consistent with results of the PEDIG study on paediatric CCT which reported that the higher the degree of myopia, the thinner the CCT.[20] Chang et al in a study among 216 young adults also reported that CCT was thinner in eyes that were more myopic.[55] Our finding of thinner CCT in myopes is also comparable to the outcome of the study by Kotb and Eissa[56] in an Egyptian adult population which demonstrated that the greater the myopic refractive error, the thinner the cornea. It is thought that the relationship between CCT and refractive errors is due to corneal biomechanical properties.[44] For instance in myopic eyes with relatively longer axial lengths, the stretching of the eye wall comprising sclera and cornea may account for thinner CCT in myopes.[44]

However ,in another Egyptian study by Mourad et al, it was found that CCT was generally lower in ametropes compared to emmetropes.[54] Their study comprised 84 eyes which were subdivided

into three main groups: group 1 included 28 myopic eyes, group 2 included 28 hyperopic eyes, and group 3 included 28 emmetropic eyes. The study found that comparing the CCT of the myopia group with that of the hyperopia group, the difference was not statistically significant (P>0.05). However, when the myopia group CCT was compared with that of the emmetropia group statistically, it was significantly higher in the emmetropia group (P=0.031).[54] Comparing the CCT of the hyperopia group with that of the emmetropia group, it was also noted that CCT was statistically higher in the emmetropia group (P=0.015).[54] A large Japanese study by Suzuki et al[57] showed a that there was correlation between refraction and CCT but this differed between men and women. In men, refraction negatively correlated with CCT with the CCT values being thicker in myopic eyes compared to emmetropic eyes.[57]

Some studies have found no correlation between CCT and refractive error. These include a Taiwanese study involving 500 healthy participants by Chen et al .[44] The Beijing Eye Study also failed to demonstrate any significant correlation between CCT and refractive error among adult Chinese participants.[52] There is a dearth in literature on the relationship between CCT and refractive errors in children and thus more studies are needed in this area.

Limitations of the study

The expectation of this study was to document for the first time in Ghana, normal values for CCT in healthy Ghanaian children. In this study, the CCT of children aged 6-15 years was measured. The following limitations were encountered:

Children under age 6 years were not included in study and as a result, we do not have CCT values for that age category. This was due to the fact that it was anticipated that it would be very difficult for children under 6 years to cooperate for the full eye examination including CCT measurement without sedation. Since the study location was schools, it was not possible to do any examinations under sedation.

The study was conducted in the Greater Accra region, which may not necessarily be representative of other regions in Ghana. However, Accra is a cosmopolitan city populated by individuals from different ethnic backgrounds and thus as seen in our results, there were children from diverse ethnic backgrounds despite Gas being the predominant ethnic group.

Strengths of study:

This study was a cross-sectional observational study so there were no problems of missing data as is the case with retrospective studies. For the first time in Ghana, normal values for CCT in healthy Ghanaian children has been documented and the results of this study provide baseline data for larger national studies that could ultimately lead to the development of national reference ranges for CCT values in the Ghanaian paediatric population.

The sample size used is one of the largest on paediatric CCT in sub-Saharan Africa, involving 420 children (840 eyes) aged 6-15 years. Our study is also one of the few studies in sub-Saharan that correlates CCT with refractive error and IOP in children.

Our classification into age-defined groups enabled us to compare with similar studies to find variation of CCT with age and predict age at which CCT approximates adult CCT in our population.

All aspects of measurements were done by the same person to ensure uniformity. All IOPs were measured by the same research team member, all CCT measurements were done by the principal investigator and all refractions were done by the paediatric optometrist.

Conclusion

The overall mean CCT in healthy Ghanaian school children aged 6-15 years in the Ablekuma Sub-Metropolitan area was found to be 538.8 ± 27 µm using ultrasound pachymetry.

The mean CCT among children aged 6-8 years was 541.4±24.9 µm., for children aged 8-10 years 534.9±25.8 µm and those 10-15 years 538.3±28.6 µm for both eyes. There was no significant difference in mean CCT among the age groups for both eyes, however there was a weak negative correlation between CCT and age suggesting that CCT decreased with age.

Though CCT was higher in males, the difference was not statistically significant.

Our study demonstrated that there was a weak positive correlation between CCT and IOP in normal Ghanaian children which was also statistically significant (rho = 0.4; p-value = 0.001). A linear regression model was derived for the mean CCT as a function of IOP (x). Thus, from the linear regression model; CCT = 487.7+3.3x. Therefore, for every increase in a unit of IOP, there is a corresponding increase in the CCT.

With regards to the relationship between CCT and refractive error, mean CCT for children with emmetropia, hyperopia and myopia were 539.6±27.2 µm, 542.5±26.6 µm and 530.8±25.3 µm respectively and the difference was statistically significant (F= 4.582; p-value = 0.011). Thus, CCT was higher in hyperopes compared to emmetropes and thinnest in myopes.

Results of this study provide baseline data for larger national studies that could ultimately lead to the development of national reference ranges for CCT values in the Ghanaian paediatric population. Secondary benefits of this study include improvement in the diagnosis, prognostic prediction and management of glaucoma in children.

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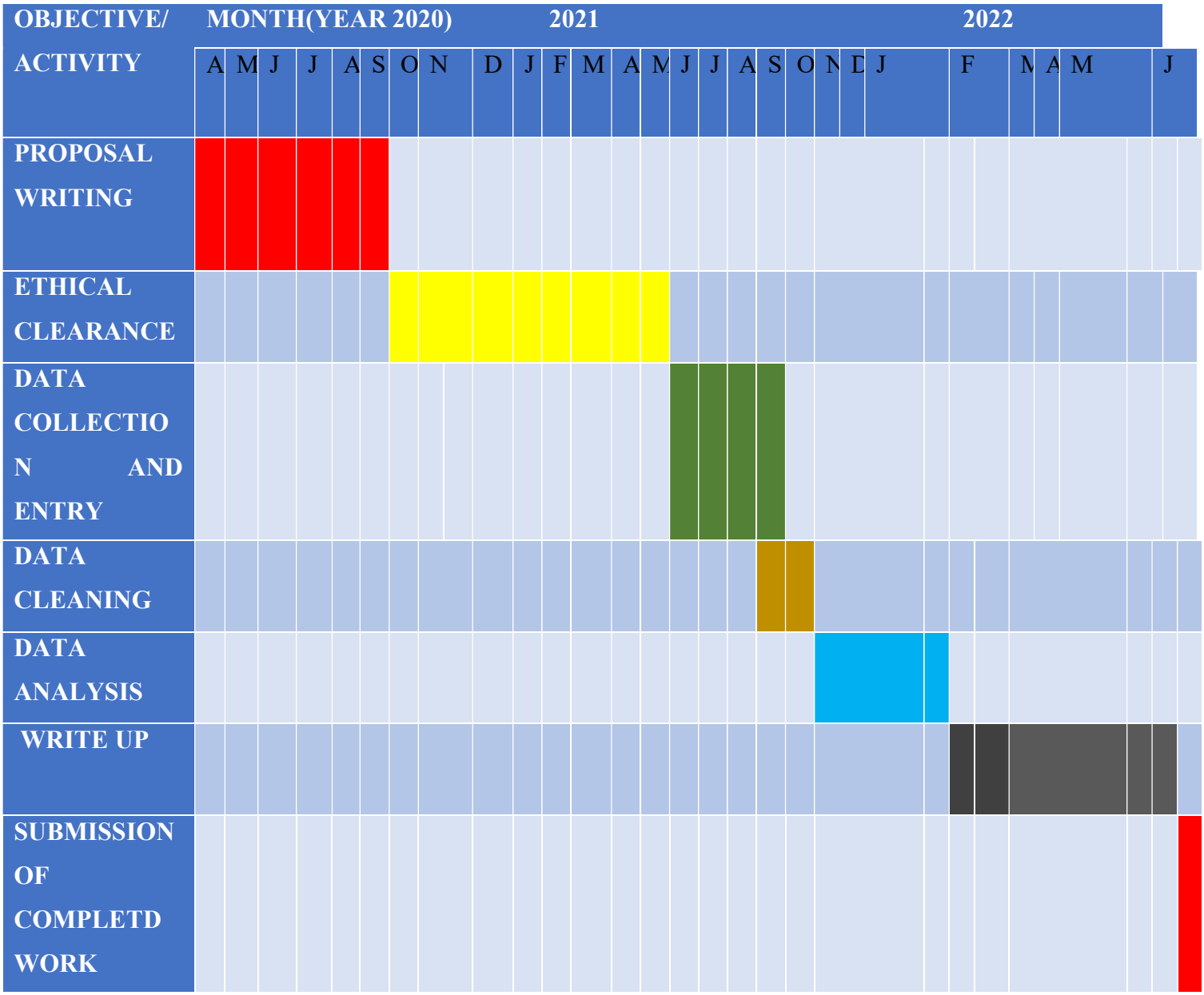
LOGISTICS AND TIME SCHEDULE



STUDY BUDGET

ITEM	QUANTITY	UNIT COST (GH ¢)	TOTAL COST (GH ¢)
Printing and binding of proposals, data capture forms and dissertation			500
Allowance for research assistants	4 for 6 months	600	2400
Amethocaine	20 bottles	30	600
Cotton	5 rolls	20	100
Gloves	4 boxes	25	100
Alcohol pads	4 boxes(100pcs/box)	10	40
Batteries (AAA)	4x 5	30	150
Transportation for study team			500
Stationery			100
IRB fees			500
TOTAL			4,990

Contingency cost	**5%**		**250**
TOTAL			**5,240.00**

Source of funding:

The research was self-funded.

APPENDICES

Appendix A: Participant's Informed Consent

Name of Principal Investigator: Dr. Vera Mawusime Beyuo

Name of Organization: Lion's International Eye Centre, Korle-Bu Teaching Hospital.

Project title: The Central Corneal Thickness in Healthy Ghanaian Children in the Ablekuma Sub-metropolitan area.

I.....have been invited to take part in the study above. It was explained to me that the study aims to measure the central corneal thickness in healthy children in Ghana and determine the values for the various age groups. of defined age-groups.

I have been told the procedures of the study will involve:

A general eye examination to detect any abnormality, instillation of an anaesthetic eye drop and using the ultrasound pachymeter to measure the central corneal thickness.

Risk or dangers and discomfort:

Risk, dangers and discomfort are mild with this study. This includes mild burning sensation when the topical amethocaine 0.5% is instilled into eyes. There is no documentation of participant name as well.

Benefits:

My child will benefit from a free eye screening and will be referred for further assessment if any eye disease is diagnosed. There are no financial benefits from this study. However, findings from the study will serve as a guide in the management of children with glaucoma and other eye conditions.

Confidentiality:

Information obtained from me would be treated as confidential and kept in a file which will not have my name on it but a code number assigned to it which will not be disclosed to anyone. Outcome of this study would be reported at meetings and in journals but my name will not be reported.

My right to refuse or withdraw:

I understand the information given me on the above-mentioned research and voluntarily consent. I understand that if I change my mind I can withdraw from the study.

Persons to contact:

I have been told that the proposal will be reviewed and approved by the Ethical and Protocol review committee at the Korle bu teaching hospital whose mandate is to protect participants from harm. If I wish to find out more about this committee, I may contact the chairperson of the Ethical and Protocol Review Committee of the Korle bu Teaching Hospital.

Contact Information:

If I have any questions, I may ask those now or later. If I wish to ask questions later, I may contact:

Dr. Vera Beyuo

Lion's International Eye Centre, Korle bu Teaching Hospital

Tel.: 0200284333

Signature (participant's parent or guardian): .....

Place: .....

Date: .....

If illiterate:

Thumbprint .....

Date: .....

Place: .....

Signature (researcher): .....

Place: .....

Date: .....

Appendix B: Participant's Informed Assent form (for child)

Name of Principal Investigator: Dr. Vera Mawusime Beyuo
Name of Organization: Lion's International Eye Centre, Korle-Bu Teaching Hospital.
Project title: The Central Corneal Thickness in Healthy Ghanaian Children

I.....have been invited to take part in the study above. It was explained to me that the study aims to measure the central corneal thickness in healthy children in Ghana and determine the values for the various age groups.

I have been told the procedures of the study will involve:

A general eye examination to detect any abnormality, instillation of an anaesthetic eye drop and using the ultrasound pachymeter to measure the central corneal thickness.

Risk or dangers and discomfort:

Risk, dangers and discomfort are mild with this study. This includes mild burning sensation when the topical amethocaine 0.5% is instilled into eyes. There is no documentation of participant name as well.

Benefits:

I will benefit from a free eye screening and will be referred for further assessment if any eye disease is diagnosed There are no financial benefits from this study. However, findings from the study will serve as a guide in the management of children with glaucoma and other eye conditions.

Confidentiality:

Information obtained from me would be treated as confidential and kept in a file which will not have my name on it but a code number assigned to it which will not be disclosed to anyone. Outcome of this study would be reported at meetings and in journals but my name will not be reported.

My right to refuse or withdraw:

I understand the information given me on the above-mentioned research and voluntarily consent. I understand that if I change my mind I can withdraw from the study.

Persons to contact:

I have been told that the proposal will be reviewed and approved by the Ethical and Protocol review committee at the Korle bu teaching hospital whose mandate is to protect participants from harm. If I wish to find out more about this committee, I may contact the chairperson of the Ethical and Protocol Review Committee of the Korle bu Teaching Hospital.

Contact Information:

If I have any questions, I may ask those now or later. If I wish to ask questions later, I may contact:

Dr. Vera Beyuo

Lion's International Eye Centre, Korle bu Teaching Hospital

Tel.: 0200284333

Signature (participant): .....

Place: .....

Date: .....

Signature (researcher): .....

Place: .....

Date: .....

Appendix C: Study Questionnaire

Date:

Study ID number:

Study site:

Demography

Age:

Class:

Sex:

Ethnicity:

Medical history:

Past history of ocular disease	: (a) YES	(b) NO
Past history of ocular trauma	: (a) YES	(b) NO
Family history of glaucoma	: (a) YES	(b) NO
Family history of blindness	: (a) YES	(b) NO

Examination:

Right eye		Left eye
	Visual acuity	
	Conjunctiva	
	Cornea	
	Anterior chamber	
	Iris	
	Pupil	
	Lens	
	Vitreous	
	Retina	
	Intraocular pressure (IOP)	
	Refraction	

Central corneal thickness measurements:

EYE	RIGHT EYE	LEFT EYE
CCT MEAN VALUE		
STANDARD DEVIATION		

Appendix D: Institutional Review Board (IRB) Approval Letter

In case of reply the number
And the date of this
Letter should be quoted
My Ref. No. KBTH/MD/G3/21
Your Ref. No.

KORLE BU TEACHING HOSPITAL
P. O. BOX KB 77,
KORLE BU, ACCRA.

Tel: +233 302 667759/673034-6
Fax: +233 302 667759
Email: info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

15th July, 2021

DR. VERA MAWUSIME BEYUO
EYE CLINIC
KORLE BU

DETERMINATION OF NORMATIVE VALUES FOR CENTRAL CORNEAL THICKNESS IN GHANAIAN CHILDREN IN THE ABLEKUMA SOUTH SUB-METROPOLITAN AREA

KBTH-IKB /00081/2021

INVESTIGATOR: Dr. Vera Mawusime Beyuo

The Korle Bu Teaching Hospital Institutional Review Board (KBTH IRB) reviewed and granted approval to the study entitled: "**Determination of Normative values for Central Corneal Thickness in Ghanaian Children in the Ablekuma South Sub-Metropolitan Area**"

Please note that the Board requires you to submit a final review report on completion of this study to the KBTH-IRB.

Kindly, note that, any modification/amendment to the approved study protocol without approval from KBTH-IRB renders this certificate invalid.

Please report all serious adverse events related to this study to KBTH-IRB within seven days verbally and fourteen days in writing.

This IRB approval is valid till 30th June, 2022. You are to submit annual report for continuing review.

Sincere regards,

DR. DANIEL ANKRAH
VICE CHAIR (KBTH-IRB)
FOR: CHAIR (KBTH-IRB

Cc: The Chief Executive Officer, KBTH
The Director of Medical Affairs, KBTH

Appendix E: Scientific and Technical Committee Approval letter

In case of reply the number
And the date of this
Letter should be quoted
My Ref. No. KBTH/MD/C3/21
Your Ref. No.....

KORLE BU TEACHING HOSPITAL
P. O. BOX KB 77,
KORLE BU, ACCRA.
Tel: +233 302 667759/673034-(
Fax: +233 302 667759
Email: Info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

4th June, 2021

DR. VERA MAWUSIME BEYUO
EYE CENTRE
KORLE BU, ACCRA

SCIENTIFIC AND TECHNICAL COMMITTEE APPROVAL
PROTOCOL IDENTIFICATION NUMBER: KBTH-STC 00081/2021

The Korle Bu Teaching Hospital Scientific and Technical Committee (KBTH-STC), on 4th June, 2021 approved your submitted study protocol.

TITLE OF PROTOCOL: "Determination of Normative values for Central Corneal Thickness in Ghanaian Children in the Ablekuma South Sub-Metropolitan Area."

PRINCIPAL INVESTIGATOR: Dr. Vera Mawusime Beyuo

This approval requires that you **forward your approved document to Korle Bu Teaching Hospital –Institutional Review Board (KBTH-IRB) for the ethical aspect of the proposal to be assessed before the project can be initiated.**

This STC approval is valid till 30th December, 2021
You may, however, request extension of the approval period, or renewal as the case may be, should the study extend beyond the stated period.

Upon completion, you are required to submit a final report on the study to the STC. This is to enable the STC ensure among others that, the project has been implemented as per the approved protocol. You are also required to inform the KBTH-STC and Research Directorate of any publications that may emanate from the research findings.

Kindly note that, should the need arise, the KBTH-STC or IRB may institute appropriate measures to satisfy itself that study is being conducted according to the highest scientific and ethical standards.

Please note that any modification to the study protocol without Scientific Technical Committee (STC) approval renders this approval invalid.

Sincere regards,

Prof. G. Obeng Adjei
Chairman, KBTH-STC

Cc: The Chairman, KBTH-IRB

Appendix F: Ghana Education Service Approval Letter

GHANA EDUCATION SERVICE

In case of reply the number and date of this letter should be quoted

My Ref. No: GES/PG 48 V13

Your Ref. No:

Republic of Ghana

METRO EDUCATION OFFICE
POST OFFICE BOX 337
ACCRA

Tel. No.: 030-2632370
030-2676199
054-0480229
Email: metroeducationoffice@gmail.com

2ND AUGUST, 2021

THE HEADTEACHERS

MARTYRS OF UGANDA R/C BASIC
MAMPROBI E. P. CHURCH BASIC
MAMPROBI SOUTH '3' BASIC
ACCRA

**LETTER OF INTRODUCTION TO CONDUCT RESEARCH
DR. VERA MAWUSIME BEYUO - UNIVERSITY OF GHANA MEDICAL SCHOOL**

I write to introduce **Dr. Vera Mawusime Beyuo**, a senior resident in paediatric ophthalmology at the Eye Department of the Korle-Bu Teaching Hospital.

Dr. Vera Mawusime Beyuo is conducting a study titled: ***"Determination of Normative Values for Central Corneal Thickness in Ghanaian Children in The Ablekuma South Sub-Metropolitan Area".***

Permission has therefore, been granted for Dr. Vera Mawusime Beyuo to collect data on Students in the Ablekuma South, Sub-Metro.

By this letter, the researcher is directed to contact you for further directives. Kindly ensure that students and teachers assist her. Meanwhile you are entreated to ensure that contact hours are not compromised.

Thank you.

STEPHEN ABAMFO (MR.)
DIRECTOR OF EDUCATION
ACCRA METRO

Cc: The Circuit Supervisor, Ojoo, AMEO, Accra
Dr. Vera Mawusime Beyuo, Korle-Bu Teaching Hospital, Accra