RELIABILITY OF GREULICH AND PYLE METHOD OF AGE DETERMINATION AMONG CHILDREN UNDERGOING LEFT WRIST X-RAYS AT MOI TEACHING AND REFERRAL HOSPITAL

BY

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DECLARATION

DECLARATION BY CANDIDATE

This thesis is my original work and has not been presented in any other university or institution for an award of a degree or any academic credit. No part of this work may be reproduced or transmitted in any form without prior written permission from the author and/or Moi University.

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DEDICATION

I would like to dedicate this work to God Almighty for the gift of life and for giving me strength to carry out this research project to its fruitful conclusion. I would also like to dedicate this work to my family who are a source of joy and motivation to me, without which this thesis would never have seen the light of day.

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LIST OF ABBREVIATIONS

BA	Bone age
CA	Chronological age
GP	Greulich and Pyle
M.T.R.H.	Moi Teaching and Referral Hospital
OPG	Orthopantomography
PACS	Picture Archiving and Communication System
SD	Standard Deviation
UNICEF	United Nations Children's Fund.

OPERATIONAL DEFINITION OF TERMS

RELIABILITY: How dependable/consistently a test (GP chart) measures a characteristic (Age)

BONE AGE: This is the degree of maturation of a child's bones as described by Greulich and Pyle.

CHRONOLOGICAL AGE: The actual duration that a person has been alive from the day he/she was born, expressed in days, months or years

RADIOGRAPHIC PARAMETERS: Measurements on the left wrist radiograph used to assess the skeletal age of an individual. This includes the appearance and ossification of the ossification centers in the carpal bones, distal radius and ulna and the metacarpal bones

WRIST X-RAY: Radiographs of the left wrist taken to assess the osseous components of the wrist.

AGE DETERMINATION: The process of estimating the age of an individual using various clinical, physical and radiological parameters e.g patterns of teeth eruption and development, ossification of bones and development of secondary sexual characteristics e.g pubic hair, axillary hair e.t.c.

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ABSTRACT

Background: Age determination is crucial in people who want to be recognized as adults to access government services such as driving licenses, employment and to be issued with marriage certificates. In the judicial system, there is an established age of legal importance, below which a person cannot be handled as an adult if they have been accused of a criminal offence. There are many people worldwide who do not have official birth notification documents so their chronological age cannot be verified. Several methods can be used to do age determination. The most commonly used radiological method is the Greulich and Pyle (GP) method. This method has been shown to be unreliable when applied to certain populations. GP method is said to be reliable when the difference between the mean GP age and the chronological age is not statistically significant. The purpose of this study was to statistically compare the chronological age with the GP age in children undergoing left wrist and hand x-ray at MTRH, with an aim of determining the reliability of GP method of age determination when applied to the local population.

Objective: To compare the chronological age with GP age in order to determine the reliability of Greulich and Pyle method of age determination.

Methods: This was a cross-sectional study carried out at the Moi Teaching and Referral Hospital (MTRH) between April 2019 and March 2020. 139 patients aged below 18 years scheduled to undergo left wrist and hand x-rays were recruited. Imaging was done by the principal researcher and/or a trained radiographer and radiographs stored in the PACS system. Age determination by the GP method was done by the principal investigator and findings verified by two consultant radiologists. Chronological age was calculated from the date of birth as recorded in the birth certificate/notification by a trained research assistant. Data was analyzed using STATA version 23. Descriptive statistics were done and presented in tables and graphs. Comparison between the mean GP age and chronological age was done using paired T-test and Bland-Altman test done to test the agreement between GP age and CA. Mean difference between GP age and chronological age was compared among male and females grouped into one year cohorts.

Results: The chronological age of the participants ranged from 1 month to 18 years. The mean age as determined by the GP method was 8.7 years, 10.5 years in males and 6.1 years in females. The mean difference between chronological age and GP age was 0.15 years (1.8 months) in males which was statistically significant with a p value of 0.015. The mean difference between chronological age and GP age was 0.08 years (1 month) in females with a p value of 0.159, which was not statistically significant.

Conclusions: There is a statistically significant difference between chronological age and GP age in males. There is no statistically significant difference between the chronological age and GP age in females.

Recommendations: Greulich and Pyle method of age determination should be used with caution in boys, where high accuracy is required. Further studies on bone development in children should be done and a customized bone age chart developed for the local population.

CHAPTER ONE: INTRODUCTION

1.1 Background

Age determination is the process used to establish, ascertain or estimate the chronological age of an individual, and most importantly to classify them as a child or an adult. Chronological age refers to the actual age of an individual in days, weeks, months or years since they were born. Determination of age is crucial especially in people who want to be recognized as adults, i.e, have attained a certain minimum age so as to be able to access government services such as being issued with driving licenses, employment in the public service and to be issued with marriage certificates. There is also a need for properly classifying asylum seekers into children or adults to avoid situations where children are treated as adults and hence end up suffering unnecessarily e.g being denied basic needs guaranteed to any child worldwide, being denied citizenship, education, etc.

In the judicial system in many jurisdictions, there is an established age of legal importance(Tsehay et al., 2017b). This is the age at which one can be handled as an adult by the judicial system if they have been charged with a criminal offense. In many jurisdictions, this is normally 18 years. Punishment for various offences is meted on individuals depending on their age. A child is likely to be referred to a children's remand home or upon conviction, to a probation program rather than being imprisoned for their offences. A child is also entitled to compulsory legal representation at the expense of the state. No matter the offence committed, capital punishment, including death sentence cannot be meted on a child, i.e one who is below the age of 18.

Perpetrators of sexual offences against children are punished according to the age of the victim. When the age of the victim of a sexual offence cannot be ascertained, age

determination is done so as to punish the perpetrator appropriately, according to the age of the victim.

In the sports arena, there are various sports confederations who organize sports according to the age of the participants, e.g under 18 years, under 21 years, under 23 years e.t.c. It is therefore crucial to determine the age of the participants when the same cannot be verified from the birth certificates/ notifications so as not to give undue advantage to some teams when they field older individuals to compete against younger participants.

There are many people worldwide who do not have official birth registration documents so their chronological age cannot be verified. According to UNICEF, 1 in 3 children under the age of five years do not have their births registered. In the Eastern Africa region, 1 in every 7 children born is not registered (Tsehay et al., 2017b). There are several countries where civil unrest and civil wars make it impossible for children to be born in the hospital and hence do not have their births captured in the birth registers. These children are not issued with birth notifications and eventually birth certificates hence their chronological age cannot be ascertained from the records. This has many social, medical and legal implications for the unregistered child. The child may not be able to assess free medical care where it is mandatory for proof of age before treatment.

There are several methods which can be used to establish the age of a child. The gold standard is to calculate the age of the child from the birth date as recorded in the birth registers, for children with proper birth registration documents. In the absence of birth certificates or notification, several other methods can be used for age determination. Both radiological and non-radiological methods can be used for age determination. There are various methods which have been used traditionally for age determination.

This includes eruption of the milk teeth, when the teeth fall off and when permanent teeth erupt.

Clinically, physical examination and measurement of various parameters can be done to estimate the age of an individual. This includes observing the patterns of development of secondary sexual characteristics such as eruption of axillary hair, presence or absence of the pubic hair and the developmental stage of the pubic hair, development of the breast tissue, morphology of the nipple areola complex and discoloration of the areola, morphology of the hips especially in girls and measurement of the testicular volume in boys. These methods have however been shown to be grossly inaccurate as there are many determinants of when the above changes will occur, including genetic makeup of the individual, differences in diet and other environmental factors. This makes radiological methods for age determination to be paramount as they have been shown to be reproducible and relatively reliable and valid.

There are various radiological methods of doing age determination. These includes the Greulich and Pyle method, Tanner-Whitehouse method, dental age assessment, determining ossification of the pelvic bones, determining the fusion/ lack of fusion of the basisphenoid basiocciput synchondrosis, visualization of the primary and secondary ossification centers of the clavicle, establishing the presence/ absence of the primary and secondary ossification centers of the femoral head and fusion of the ossification centers, etc (Manzoor Mughal et al., 2014a).

The most commonly used radiological method of age determination is the Greulich and Pyle (Tsehay et al., 2017a). In the GP method, an Atlas which contains radiographs of the left wrist is used. Antero-posterior wrist radiographs are used. The

x-rays are taken with the child seated alongside the x-ray table with the left arm next to the table. The forearm is pronated and placed on the table with the palmar surface of the hand in contact with the table. The fingers are separated and extended but relaxed to ensure they remain in contact with the table. The wrist is adjusted to bring the radial and ulnar styloid processes to be equidistant from the table. A sandbag is placed over the distal aspect of the forearm to aid in mobilization. X-ray beam is centered over the head of the third metacarpal and collimation done to include the distal radius and ulnar and the soft tissues over the tips of the fingers. Exposure factors used are 50 kilovolts and 3.2 milli-ampere-seconds with a focal film distance of 100cm. The left wrist is used because majority of people are right handed and so the right wrist is more likely to suffer from injuries as compared to the left. Also, in a conference of physical arthropologists held in the early 1900s, it was agreed unanimously that for standardization purposes, all physical measurements in the body should be done on the left side of the body (Satoh, 2015b).

In the x-rays of the hand and wrist, the distal radius and ulna bones, eight carpal bones, five metacarpals and 14 phalanges are seen. This bones fuse at different predictable ages and this makes age determination possible. The carpal bones are formed by intra-membranous ossification and the tubular bones by endochondral ossification. The carpal bones mature earlier than the long and short bones (Satoh, 2015a).

The radiographs contained in this atlas are a representation of the bone ages of the various age groups, from 0 to 19 years in boys and 0 to 18 years in girls. Various ossification centers in the distal radius, ulna and the carpal bones are reviewed. The ossification centers appear and fuse in a specific predictable order and their presence and degree of mineralization is determined. Radiographs are examined in a sequential

manner starting with the eight carpal bones. Their presence or absence is determined as the bones appear in a specified sequence. Then, the epiphyses of the distal radius and ulna bones are examined. Their degree of mineralization and fusion are determined. Finally, the proximal phalanges and metacarpals are examined to determine their degree of ossification. Bone age is then determined by comparing the radiograph under review to the radiographs in the GP chart. The radiograph with the highest degree of similarity in the GP chart to the one under review is taken as being a representative of the bone age (Alcina et al., 2018). This method has been shown to be unreliable when applied to some populations (Tsehay et al., 2017a).

Clinical examination methods can also be done to establish the age of a child. Tanner staging can be used to classify individuals into various age groups, depending on presence/absence of features of secondary sexual characteristics. OPG can also be used to determine the age of an individual from their teeth eruption (Gandhi, 2006).

The purpose of this study was to compare the age of children undergoing left wrist and hand x-rays at MTRH as determined by the GP method to the chronological age as recorded in the birth register with an aim of determining the reliability of GP method of age determination when applied to the local population.

1.2 Problem Statement

Various methods are used to do age determination in children including Tanners staging, dental age determination using OPG images and use of GP method. The most commonly used method is the GP (Manzoor Mughal et al., 2014b). The widespread use of this method is due to its ease of use as compared to Tanner's staging, easy availability of x-rays especially in resource poor settings, ease of doing wrist and hand x-rays and reduced ionizing radiation to vital organs such as the thyroid gland, parotid

gland and the lens of the eyes as compared to OPG (Manzoor Mughal et al., 2014c).GP method of age determination is reliable when used in some populations. However, due to differences in genetics, diet and other environmental factors that influence the rate of bone development and maturation, this method has been found to be unreliable when applied to some non-reference populations (Dembetembe & Morris, 2012). Inaccurate age assignment can have dire consequences in the legal, social, medical and sports circles. In our jurisdiction, the most common reason for doing age determination is for legal purposes. Inaccurate age determination using one method may warrant use of a second method, like OPG. This will increase ionizing radiation exposure to vital organs like the thyroid gland, parotid gland and the lens of the eye.GP method of age determination is said to be reliable when there is no statistically significant difference between the mean GP age and the CA. Owing to these reasons, there is need to determine the reliability of GP method of age determination in the local population. This study aims to do that by statistically comparing the difference between the mean GP age and the CA in the local population.

1.3 Justification

Age determination is a commonly requested procedure especially for medico-legal purposes. In Kenya, according to the sexual offences act, No 3 of 2006, the punishment meted on a sexual offender is determined by the age of the victim and the age of the offender. The Kenyan law also provides for lenient punishments for children convicted of criminal offences e.g. no child can be sentenced to death despite the offence committed. This makes age determination critical to correctly identify the age of individuals whose age is in doubt.

In the radiology department, imaging of the hand and wrist form the basis of age determination. Greulich and Pyle method is the most commonly used method for age determination (Tsehay et al 2017) hence there is a need to determine its reliability. In addition, there is paucity of data on Greulich and Pyle method in our region, despite its widespread use. This study aims to statistically compare the mean GP age to the chronological age. This will not only help to build on the body of knowledge on GP method of age determination, but will also be of value in the management of children whose chronological age cannot be ascertained.

1.4 Research Question

What is the reliability of GP method of age determination among children at MTRH?

1.5 Objectives

1.5.1 Broad objective

To determine the reliability of Greulich and Pyle method of age determination among children undergoing left wrist x-rays at Moi Teaching and Referral Hospital.

1.5.2 Specific objectives

1. To compare the chronological age to the GP age in males
2. To compare the chronological age to the GP age in females
3. To determine the reliability of GP method of age determination among children undergoing left wrist x-rays at MTRH.

CHAPTER TWO: LITERATURE REVIEW

Age determination is the process used to establish or ascertain the age of an individual, and most importantly to classify them as a child or an adult. Chronological age refers to the actual age of the patient in days, weeks or months calculated from the birth date.

2.1 Anatomy of the wrist

The wrist joint (radiocarpal joint) is a joint in the upper limb which has a joint capsule and within the capsule, synovial fluid hence classifies as a synovial joint. The wrist joinf forms an articulation between the hand and the forearm. The joint has a proximal and distal component each composed of various bones and articular surfaces. The proximal part of the wrist joint is made up of the distal end of the radius and the articular disc. The distal component is made up of the proximal row of the carpal bones i.e scaphoid, lunate and triquetrum bone. The pisiform does not articulate with the radius hence not part of the wrist joint articular bones.

The ulna bone does not articulate with the proximal carpal bones hence not part of the wrist joint. It however articulates with the distal radius just proximal to the wrist joint to form the distal radio-ulnar joint. A dense fibrocartilaginous complex called the triangular fibrocartilaginous complex lies between the ulnar and the carpal bones hence preventing the articulation between the ulna and the triquetral and lunate bones.

Together, the proximal row of the carpal bones forms a convex surface, which articulates with the concave surface of the radius and the articular disk.

The wrist joint has a joint capsule just like any other synovial joint. The capsule has two layers, an outer and an inner layer. The outer layer is fibrous and attaches to the

radius, ulna and the scaphoid, lunate, triquetrum and pisiform bones. The inner layer is smooth and is comprised of a synovial membrane which secrets synovial fluid that lubricates the joint.

The various osseous components of the wrist joint are anchored together by various ligaments. There are four main ligaments in the wrist joint, one for each side of the joint. The palmar radiocarpal ligament is found on the palmar/ anterior side of the wrist and passes from the radius to both proximal and distal rows of carpal bones. It increases the stability of the wrist joint and ensures that the hand follows the forearm during supination. The second ligament is the dorsal radiocarpal ligament**.** This is located on the dorsum/posterior side of the hand and passes from the radius to both the proximal and distal rows of the carpal bones. It contributes to the stability of the wrist joint and ensures that the hand follows the forearm during pronation. The third ligament is the ulnar collateral ligament. This runs from the ulnar styloid process to the triquetrum and pisiform. It acts to prevent excessive radial/lateral deviation of the hand. The fourth ligament is the radial collateral ligament. It runs from the radial styloid process to the scaphoid and trapezium and acts to prevent excessive ulnar /medial deviation of the hand.

The wrist joint receives blood supply from branches of the dorsal and palmar carpal arches, which are derived from the ulnar and radial arteries. The vessels form an arterial arcade which gives rise to the various digital branches which supply blood distally. The two arterial arcades also form an anastomosis which act as collateral pathway for blood flow in case one arterial is occluded or there is reduced blood flow.

The wrist joint receives nervous innervations from branches of three nerves ie the median nerve which gives the anterior interosseous branch, the **r**adial nerve which gives the posterior interosseous branch and the ulnar nerve which gives the deep and dorsal branches.

The wrist joint being an ellipsoidal/ condyloid type of synovial joint allows movement various axes. Flexion, extension, adduction and abduction can all occur at the wrist joint. All the movements of the wrist are performed by the muscles of the forearm.

Flexion movement is produced mainly by the flexor carpi ulnaris, flexor carpi radialis, with assistance from the flexor digitorum superficialis.

Extension movement is produced mainly by the extensor carpi radialis longus and brevis, and extensor carpi ulnaris, with assistance from the extensor digitorum.

Adduction movement is *p*roduced by the extensor carpi ulnaris and flexor carpi ulnaris

Abduction movement is produced by the abductor pollicis longus, flexor carpi radialis, extensor carpi radialis longus and brevis.

Wrist radiographs demonstrate the distal radius and ulnar bones, the carpal bones, the metacarpal bones and the phalanges. The various joint spaces and articular surfaces are also demonstrated on a wrist radiograph. The soft tissue components are not seen on plain radiographs but are imaged using other imaging modalities like ultrasound and magnetic resonance imaging.

Figure 1: Anteroposterior radiograph of the left wrist.

2.2 Epidemiology

According to UNICEF (2014), there are about 2.2 billion children world-wide. About half a billion children live in sub-Saharan Africa. This population is projected to rise to about 661 million by the year 2030. According to a study done by Society for International Development in 2014, 43 % of 48.46 million total populations in Kenya were children under the age of 18 years.

In 2013, UNICEF released data which showed that globally, 230 million, about 33 percent of children under the age of five years globally had not had their births registered.

In 2012, according to UNICEF, only around 6 in every 10 babies had their births registered at birth globally. Sub-Saharan Africa and Asian countries had the lowest number of babies registered at birth with Somalia having the lowest percentage of children registered at birth, at 3 %, Ethiopia at 7 % Tanzania at 16 % and Democratic Republic of Congo at 28%. According to the World Bank in 2014, Kenya was leading in birth registration at 66.9% among the Eastern African nations.

Globally in 2012, only around 60 per cent of all babies born were registered at birth. The rates vary significantly across regions, with the lowest levels of birth registration found in Asia and sub-Saharan Africa.

According to UNICEF, 14 % of children worldwide do not have any document showing that their births were registered. In sub-Saharan Africa, even in children whose births were registered, about 50% do not have any registration documents, i.e. birth certificates or birth notification.

2.3 Reasons for Doing Age Determination

Age determination is done mainly for legal purposes. This includes age determination for unaccompanied asylum seekers who are fleeing from conflict zones. According to guidelines in the U.K, all asylum seekers whose chronological age cannot be verified should undergo age determination. This is to ensure that they are not treated as adults and therefore denied certain rights which children who are asylum seekers are entitled to. This includes right to education appropriate to their age, right not to be unlawfully detained which would have a negative impact on their mental health. (Busler, Cowell, Johnson, Kane, 2015)

In the justice system in many jurisdictions, people who have been charged with a criminal offence and there is a doubt about their age must undergo age determination to avoid children being handled by the legal system as adults. This also prevents adults being set free for criminal offences they were convicted for as they were treated as children by the legal system.

In Kenya, according to the sexual offences act No 3 of 2006, sexual offenders are punished according to the age of the victim and the age of the offender. Kenyan laws also prohibit children from being sentenced to death despite the offence committed.

Children accused of criminal offences are also entitled to legal representation at the expense of the state in many jurisdictions and are remanded at the children's remand centers pending determination of their cases.

2.4 Methods of Age Determination

There are various methods which can be used to do age determination in people whose ages cannot be verified from records. These includes both radiological and non- radiological methods like Greulich and Pyle method, dental age determination, fusion of the medial end of the clavicle, etc.

2.4.1 Greulich and Pyle method

In the Greulich and Pyle method, wrist and hand x-ray of the left upper arm are taken. Ossification centers of the various bones in the wrist and hand are checked and their presence/ absence and the degree of development is also determined. These radiographs are then matched to the radiographs in the GP charts.

The method was developed from a study done in the USA in 1931. This was a longitudinal study which involved study of wrist and hand radiographs of 1000 children picked from a population of immigrants from Northern Europe (Tsehay et al., 2017b). In the 1950s, an atlas, known as the GP atlas was developed which is used as a reference for age determination (García Valdez, 2017).

The GP method of age determination uses an Atlas which contains radiographs of the left wrist. These radiographs are a representation of the bone ages of the various ages in boys and in girls. The atlas contains radiographs representing boys of ages 0 to 19 years and girls aged between 0 and 18 years.

Age is determined by considering the ossification centers in the distal radius and ulna and the carpal bones. This is made possible by the fact that the ossification centers appear in a specific order which can be established. The degree of development of these bones is determined and this will guide in assigning a particular bone age to a radiograph. Radiographs are reviewed sequentially from the carpal bones to the distal

radius and ulna bones and then the proximal phalanges and metacarpals. Their degree of development and mineralization is checked. Bone age is then determined by comparing the radiograph under review to the ones in the GP chart. The radiograph with the highest degree of similarity in the GP chart to the one under review is taken as being the bone age (Alcina et al., 2018).

GP method of age determination is the most preferred method in the radiology department. This is due to its ease of use as compared to other methods like the Tanner's staging, availability of x-ray facilities even in resource poor settings, ease of doing wrist and hand x-rays and reduced radiation dose to the patient due to low exposure factors required in acquiring the x-rays and reduction in the scatter radiation to vital organs such as the thyroid gland and the lens of the eyes as compared to some methods e.g. OPG (Manzoor Mughal et al., 2014c).

Excerpts from the GP chart are shown below:

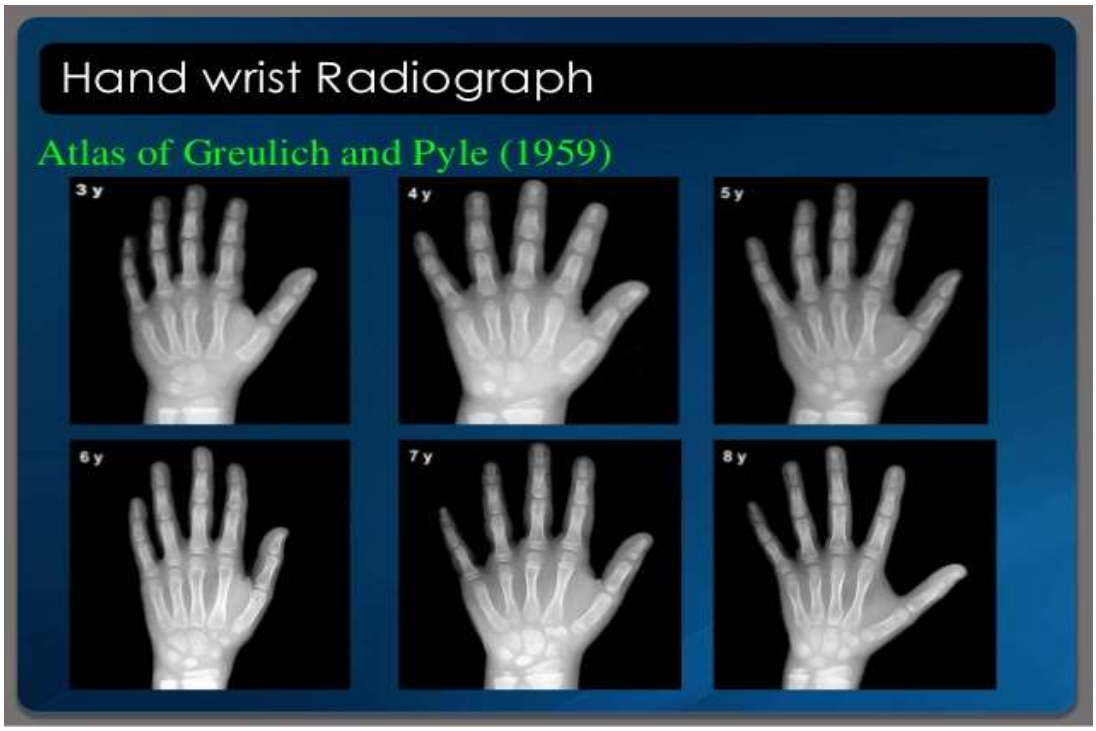

Figure 2: Excerpt from the GP chart, showing left wrist radiographs at various stages of development.

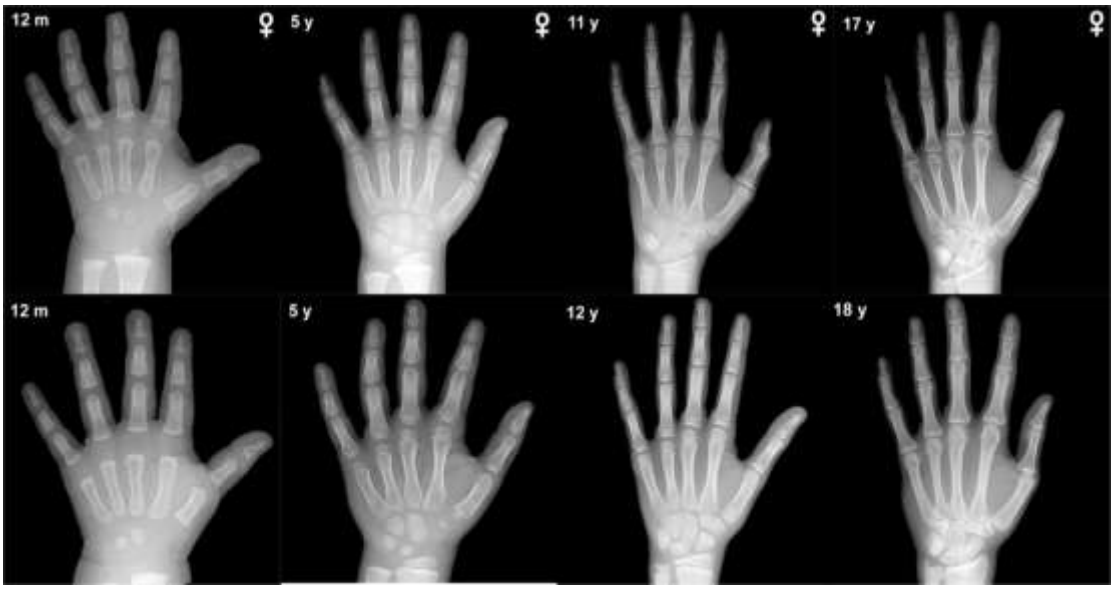

Figure 3: Excerpt from GP chart showing left wrist x-ray at various stages of development.

2.4.2 Tanner staging

This is a method that was developed by a British paediatric endocrinologist named James M Tanner in 1962. He developed a 5 point scale for staging sexual development separately for both boys and girls, called the Tanner scale. The scale was developed by charting the growth and development of children in the United Kingdom in a study called the Herpenden study. Children were photographed and measurements taken every 3 and 6 months and this information combined with data from previous studies was used to come up with the Tanner scale. The scale uses parameters such as the development of secondary sexual characteristics such as pubic hair, axillary hair, sizes of the breasts and level of pigmentation of peri-areolar breast tissues. Testicular volume is as also measured in males and these parameters are graded to give Tanner stage I to V.

Both boys and girls undergo various physical and morphological changes from Tanner's stage 1 to 5 as shown below.

Pubic Hair Scale (both males and females)

Stage 1: No hair

Stage 2: Downy hair

Stage 3: Scant terminal hair

Stage 4: Terminal hair that fills the entire triangle overlying the pubic region

Stage 5: Terminal hair that extends beyond the inguinal crease onto the thigh

Female Breast Development Scale

Stage 1: No glandular breast tissue palpable

Stage 2: Breast bud palpable under the areola (1st pubertal sign in females)

Stage 3: Breast tissue palpable outside areola; no areolar development

Stage 4: Areola elevated above the contour of the breast, forming a "double scoop" appearance

Stage 5: Areolar mound recedes into single breast contour with areolar hyperpigmentation, papillae development and nipple protrusion

Male External Genitalia Scale

Stage 1: Testicular volume < 4 ml or long axis < 2.5 cm

Stage 2: 4 ml-8 ml (or 2.5 to 3.3 cm long), 1st pubertal sign in males

Stage 3: 9 ml-12 ml (or 3.4 to 4.0 cm long)

Stage 4: 15-20 ml (or 4.1 to 4.5 cm long)

Stage 5: > 20 ml (or > 4.5 cm long).

Tanner staging should however be used with caution due to the differences in the rate of maturation in different populations (Emmanuel & Bokor, 2018). There may be delay in maturation due to malnutrition, genetic disorders and disorders of the hypothalamo-pituitary-gonadal axis. Some adolescents may show precocious puberty

with development of the secondary sexual characteristics happening earlier than expected. In addition, Tanner staging was developed using studies in white population and therefore may be unreliable when used in either the black population or other races apart from the original population which was studied to come up with the Tanner's scale. (Espeland et al., 1990)

2.4.3Tanner Whitehouse (TW)

This is a scoring method of age determination which can be done in three different ways. This includes Radius-Ulna-Short bones (RUS) method. This refers to radiological evaluation of ossification stage of the radius bone, ulna bone and the phalanges of the first, third and fifth fingers. The second method of doing the Tanner Whitehouse age determination is by using the carpal method, which involves radiological evaluation of the eight carpal bones, ie the scaphoid, lunate, triquetrum, pisiform, trapezium, trapezoid, capitates and hamate. The third way of doing TW2 age determination is by using the 20 bones method. This is done by doing radiological evaluation of seven carpal bones and 13 long bones or short bones (Satoh, 2015a)

Each of the bones that is being evaluated is compared to a standard set of bones at different stages of maturation. A score is assigned to each bone based on maturation and the gender of the patient.

Once all the bones have been scored, a total score is generated by adding all bone scores together and then plotted on a graph to determine how the bone age relates to the chronological age.

The TW2 method was developed using radiographs from average-class children in the UK between 1950 and 1960. There is a Tanner Whitehouse 3 method which is a modified TW2, developed in 2001.

Tanner Whitehouse staging has been shown to be reliable in some populations but should be used with cautions in other populations (Büken et al., 2010).

In TW method, developmental stage of the various bones is done and each stage converted to a score. Then the total score is calculated and transformed to a bone age.

2.4.4 Dental age assessment

Tooth formation and development is recognized as a useful body system to assess maturity of a child and predict the chronological age of a child. Teeth mineralization is predictable and is much less affected by the endocrine and different nutritional status than mineralization of the rest of the osseous system. Therefore, teeth formation provides a more reliable indication of chronological age compared to other methods. Demirjian et al. in 1973 presented a scoring system and method for dental age estimation on a sample of French-Canadian children.

In the Demirjan method, seven teeth present on the left side of the mandible are assessed. Eight stages of development (A to H), from calcification of the tip of the cusp to the closure of the apex, is determined for each tooth by precisely following the written and pictorial criteria set out by Demirjian. The developmental stage of each tooth is converted into a score using the conversion table given by Demirjian separately for boys and girls. The scores of all the seven teeth are added together to give the total maturity score. After the maturity score is calculated, it is converted to the dental age by referring to the table given by Demirjian, to obtain the dental age.

Another method used for dental age assessment is the Nolla's method. Seven teeth present on the left side of the mandible are taken into consideration. In Nolla method, the stages of dental development are divided into ten stages through which every tooth passes. These stages have been determined for all the teeth. Each stage also has a numerical score. The scores are totaled to give a combined 'sum of stages' score, that is then divided by the number of teeth taken into consideration to give the dental age.

Another method of doing dental age assessment is the Atlas method. This method was developed initially by Schour in 1944 but later modified by Moorres. This method involves doing an OPG and comparing the extent of teeth mineralization to standard images which are already established. In this method, dental development is studied in fourteen stages of mineralization for development of single rooted and multi-rooted teeth.these stages are identified and age assigned to each tooth as per a pre-established table (Smith’s table) (Manzoor Mughal et al., 2014c).

Chaillet et al. and Willems et al. modified original Demirjian method. In this method, dental development is divided into eight stages which are assessed to do dental age determination.

In stage A of tooth development, beginning of calcification is seen at the superior level of crypt in the form of cones. There is however no fusion of these calcified points.

In stage B of tooth development, there is fusion of the calcified points to form one or several cusps, giving a regularly outlined occlusal surface.

In stage C of tooth development, Enamel and dentin formation is complete at the occlusal surface and converge at cervical region. Dentin deposition is seen and the outline of the pulp chamber has a curved shape at the occlusal border

In stage D of tooth development, crown formation is completed down to the cementoenamel junction. The superior border of pulp chamber in uniradicular teeth has a definite curved form. Projection of pulp horns gives an umbrella top. In molars, pulp chamber has a trapezoidal form. Beginning of root formation is seen in the form of a spicule.

In stage E of tooth development, the walls of the pulp chambers form straight lines, whose continuity is broken by the pulp horn in uniradicular teeth. The root length is also less than the crown height.

In the molars, initiation of radicular bifurcation is seen as a calcified point or a semi-lunar shape. The root length is less than crown height.

In stage F of tooth development, the walls of pulp chamber form isosceles triangle. The apices end in a funnel shape. The root length is equal to or greater than the crown height.

In the molars, the bifurcation has developed down to give the roots a
distinct outline with funnel shaped endings. The root length is equal to or greater than the crown height.
In stage G of tooth development, the walls of root canal are now parallel and its apical end is partially open (distal root in molars)

In stage H of tooth development, the apical end of the root canal is completely closed. The periodontal membrane has a uniform width around the root and the apex.

2.4.5 Bone age by visualization of the clavicle

The clavicle is a long with a medullary cavity and two growth plates, one at the medial end and the second one at the lateral end. It is the first fetal bone to undergo primary ossification, and its medial epiphysis is the last to fuse. Unlike other long bones which undergo endochondral ossification initially, the clavicle ossifies via intramembranous ossification with no prior endochondral ossification. The medial and lateral primary ossification centers appear by 6th week in-utero and fuse together by the 7^{th} week of in-utero. Osteoid matrix is initially laid down and consequently, cartilage appears at the acromial and sternal ends of the bone. After the cartilage appears, growth becomes a combination of endochondral and membranous ossification. About 80% of clavicular growth in length is from the sternal cartilaginous mass and the remaining 20% contribution in bone length growth comes from the acromial end. By 8-9 weeks of in-utero life, the clavicle has acquired its characteristic S-shape. This occurs as a result of the combination of the spatial location of the two ossification centers at either end of the bone and endochondral ossification at these sites. By 11 weeks of life in-utero, the clavicle has attained its characteristic adult form. Growth then slows after birth until there is a second growth spurt between 5 and 7 years. Growth then slows again from mid childhood to pubertal stage, where there is another growth spurt. Secondary ossification centers appear during adolescence at the sternal and acromial ends of the clavicle. The lateral epiphysis may appear as a separate flake of bone. In other cases, the epiphysis simply glazes over to assume a quiescent appearance and this typically occurs during the 20th year. The medial epiphyseal ossification begins at the onset of puberty, but complete fusion to the shaft occurs about 10 years after its initial appearance. The medial clavicular epiphyseal fusion has consequently proven to be useful in estimating

skeletal age in young adults (Bhise et al., n.d.). The epiphysis appears initially as a small speck of bone in the center area of the sternal end and spreads until it nearly covers the entire medial surface. There is a well-developed timeline for clavicular development and maturation. A well-defined medial flake appears between 16 and 21 years; the flake covers the majority of the medial surface between 24 and 29 years. Complete fusion occurs between 22 and 30 years. A study in Austria offered a similar age summary, but without overlapping ages: commencement of fusion between 18 and 20 years, active fusion between 21 and 25 years, and complete fusion between 26 and 30 years(Kreitner et al., 1998).

Differential growth has however been documented in the literature and use of the above timelines have been questioned when applied to different populations.

2.4.6 Bone age determination by visualization of the iliac bone

This method uses radiographs of the iliac bone to visualize fusion of iliac bones. Also, the iliac crest apophyseal fusion is used in addition to the fusion of iliac bones. This method is rarely used as the ossification of iliac is very variable (Singh, Gorea, Oberoi, & Kapila, 2011.).

According to khaled et al , ultrasound can also be done to visualize the ossification of the iliac crest and determine the age of an individual (El-Gerby et al., 2012).

2.4.7 Bone age determination by visualization of the femoral head

This is a method which is used to estimate the age of an individual by assessing the radiographs of the femoral head. The cartilage of the epiphysis is measured and its depth determined (Walker & Lovejoy, 1985).

CHAPTER THREE: METHODOLOGY

3.1 Study Design

This was a cross-sectional study.

3.2 Study Site

The study was conducted at the Radiology and Imaging department of Moi Teaching and Referral Hospital, Eldoret.

The hospital is a level 6 hospital located in Eldoret town, Uasin-Gishu County, which is 310 Kilometers North West of Nairobi, the capital city of Kenya. The hospital is a teaching and referral hospital and serves as a teaching hospital for Moi University School of Medicine, Nursing, Public Health and Dentistry. Other institutions that use this hospital for teaching purposes include University of Eastern Africa, Baraton School of Nursing and Kenya Medical Training Center (KMTC) Eldoret. MTRH is also a training center for medical, clinical and nursing officer interns. It serves as the main referral hospital for the western part of Kenya and North Rift region and has a catchment population of 20 million people. The hospital has a capacity of 1600 beds. Apart from Radiology and Imaging, the facility has several other departments including Internal Medicine, Surgery, Pediatrics, Obstetrics and Gynecology, Psychiatry, orthopedic surgery among others.

3.3 Study Population

The study population was patients aged below 18 years, who had been scheduled to undergo wrist x-rays at Moi Teaching and Referral Hospital.

3.4 Eligibility Criteria

3.4.1 Inclusion criteria

1. Patients below 18 years who had been scheduled to undergo left wrist x-ray and had a birth certificate or birth notification.

   Cut off age of 18 years was chosen because the age of fusion of distal radius and ulnar epiphysis, the last ossification centers in the wrist to fuse is 18 years(Hassan et al., 2016).
2. Written informed consent and assent.

3.4.2 Exclusion criteria

1. Children with congenital anomaly involving the wrist region and other medical conditions which would affect normal ossification.
2. Children with severe fractures involving the distal radius, ulna and carpal bones which would make assessment of ossification centers impossible.

3.5 Sampling Procedure

3.5.1 Sample size

The main aim of the study is to compare Skeletal Age (SA) against Chronological age (CA) of children aged below 18 years. Taking Chronological age as the gold standard for the child's age, we expect a perfect fit between GP age and chronological age for us to say GP method is reliable in age determination. Past study (Gungor et al., 2015) found the mean age difference to have a standard variance of 6,therefore a minimum sample size of 139 will be needed to see a difference of 1 month at 5% level of significance (α=0.05).

$$n \geq \left[\frac{Z_{1-\propto} \times SD}{d}\right]^2$$

Where:

n= required sample size

Z_α = standard normal deviate for $\alpha = Z_\alpha = 1.96$

d = effect size (we use 1month)

SD = standard deviation from past studies (6months)

Using α of 0.05, effect size of 1 month, and standard deviation from a study by **Gungor et al. (2015)** of SD=6 months:

$$\mathbf{n} = (1.96 \times 6/1)^2$$

$$\mathbf{n = 139}$$

Gungor OE,CelikogluM, Kale B, Gungor AY ,Sari Z. The reliability of the Greulich and Pyle atlas when applied to a Southern Turkish population.EurJDent2015;9:251-4

3.5.2 Sampling Technique

Consecutive sampling was used whereby the parent and/or guardian of every child undergoing wrist x-rays and have a birth certificate/notification was approached and written informed consent sought. Assent was sought from children above the age of 7 years.

3.6 Study Procedure

All children scheduled to undergo wrist x-ray and who met the inclusion criteria were identified by a trained research assistant at the radiology department. Written informed consent was sought from their parents and/or guardians. Assent was also sought from children above the age of seven years. Data on the demographic

characteristics of the patients was recorded using a data collection form whose details are in the appendix. Wrist x-rays were performed by the principal researcher and/or a trained radiographer at the patients' cost. The x-rays were reviewed and age determination done using the Greulich and Pyle method. The determination was done by the principal investigator and verified by two consultant radiologists.

Patients were then followed up by the research assistant to confirm their date of birth from birth certificates/notifications. Chronological age was then computed from the date of birth, in years and months.

The results obtained were recorded appropriately. All data collected was kept confidential and locked in a safe place by the principal investigator to ensure that access was only to authorized persons

A chart showing the flow of patients during the study is as follows:

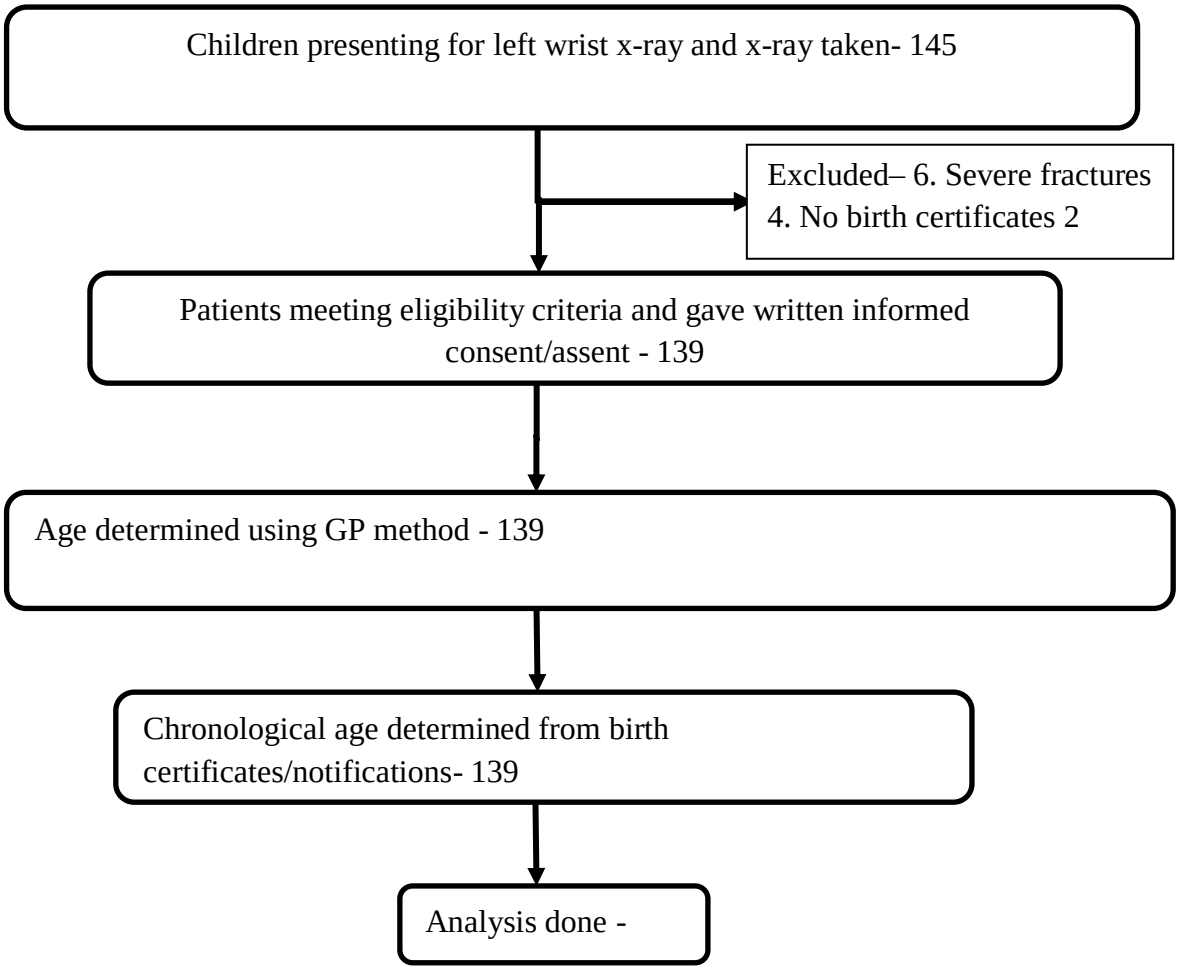

Figure 4: Enrolment Flow Chart

3.7 Bone Age Determination Using the GP Method

Bone age determination using the GP method was done by the principal researcher and findings verified by two consultant radiologists. The wrist radiograph was first mounted to an x-ray viewer. Ossification of the carpal bones, phalanges and the distal radius and ulna was determined. This was then compared to a gender specific GP chart containing wrist radiographs at various ages, up-to 18 years. The radiograph in the GP chart with similar ossification features to the one under review was chosen and assigning of bone age done. This was recorded in the data collection tool.

Wrist X-ray Imaging Protocol

All wrist x-rays were taken at the radiology department, MTRH using a GE Definium 6000 digital x-ray machine. The x-rays were taken with the child seated alongside the x-ray table with the arm to be examined next to the table. The forearm was pronated and placed on the table with the palmar surface of the hand in contact with the table. The fingers were separated and extended but relaxed to ensure they remain in contact with the table. The wrist was adjusted to bring the radial and ulnar styloid processes to be equidistant from the table. A sandbag was placed over the distal aspect of the forearm to aid in mobilization. X-ray beam was centered over the head of the third metacarpal and collimation done to include the distal radius and ulnar and the soft tissues over the tips of the fingers. Exposure factors used were 50 kilovolts and 3.2 milli-ampere-seconds with a focal film distance of 100cm. Digital images were used to avoid errors due to magnification. Images were stored on the picture archiving and communication system (PACS) workstations and saved on compact disks.

3.7 Data Collection and Management

Data was collected between April 2019 and March 2020. Entry was made in the questionnaires and later transferred to a computer database. Double data entry was done to ensure accuracy. Serial numbers were used to conceal the patients' identity and ensure privacy. The completed questionnaires were kept under lock and key in a cabinet by the principal investigator. The x-ray images were stored as DICOM files in a computer. All images were coded to conceal the patients' identity. All patients' details were kept confidential. The computers used were password-protected and access was only granted to the principal investigator and supervisors.

3.7 Data Analysis

Data was analyzed using STATA version 23.The demographic and clinical characteristics of the study participants were summarized using frequencies and percentages and presented using charts and tables. Continuous variables including bone age and chronological age were summarized using tables and graphs. Descriptive statistics were carried out for continuous variables using mean, median, standard deviation and inter-quartile range. Frequency tables were generated for categorical variables. The variation in age estimated using GP was calculated (GP age – CA age) and summarized using the measures of central tendency and dispersion. Paired sample T-test and Bland Altman plots were done to determine whether the mean difference between GP age and CA was statistically significant. Level of significance (α) was set at 0.05 thus a p-value of less than 0.05 was considered to be statistically significant.

3.8 Study Limitations

Age determination was done by the principal researcher and confirmed by two consultant radiologists, hence there was a likelihood of inter-observer error. This was minimized because the same chart (GP chart) was used in all instances.

3.9 Ethical Considerations

Approval to carry out the study was sought and granted, by the Institutional Research and Ethics Committee (IREC). Permission to conduct the study was obtained from the CEO, Moi Teaching and Referral Hospital. Parents/guardians were informed about the study and reassured that their willingness/unwillingness to participate in the study would not in any way prevent their children from receiving appropriate treatment. Assent was obtained from children above 7 years of age after carefully explaining the study procedure. All patients received medical attention regardless of whether they

did or did not consent to take part in the study. No incentives or inducements were used to convince patients to participate in the study. Utmost confidentiality was maintained throughout the study. The questionnaires used did not contain the names of the patients. The questionnaires used to collect the data were kept in a locked cabinet by the principal investigator and access was only granted to authorized persons.

CHAPTER FOUR: RESULTS

4.1 Introduction

The findings are based on 139 children who had left wrist x-ray done at Moi Teaching and Referral Hospital during the study period.

4.2Demographic Characteristics

A total of 139 participants were enrolled into the study. Seventy-six percent (n=105) were residents of UasinGishu county, six percent (n=8) came from Elgeyo-Marakwet, four percent (n=6) from Bungoma, four percent(n=6) from Busia, four percent(n=6) from Trans Nzoia. The remaining eight study participants came from West Pokot (n=5), Nandi(n=2) and Kakamega (n=1) counties. This is illustrated in the figure below.

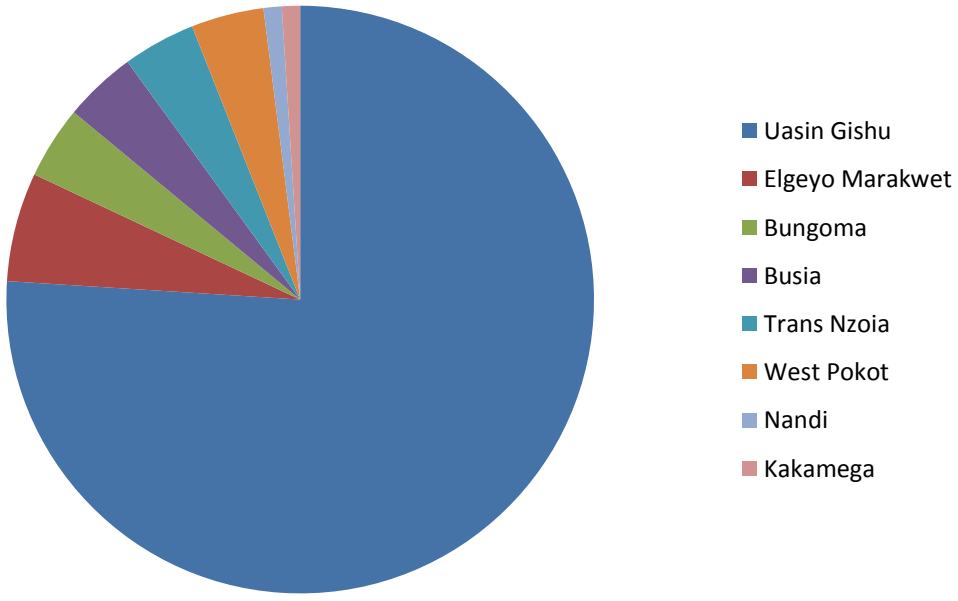

Figure 5: Pie chart showing residence of study participants

4.3 Gender of the study participants

The gender of the study participants was as follows: 59.7% Males (n=83) and 40.3%

Females (n=56). This is illustrated in the graph below

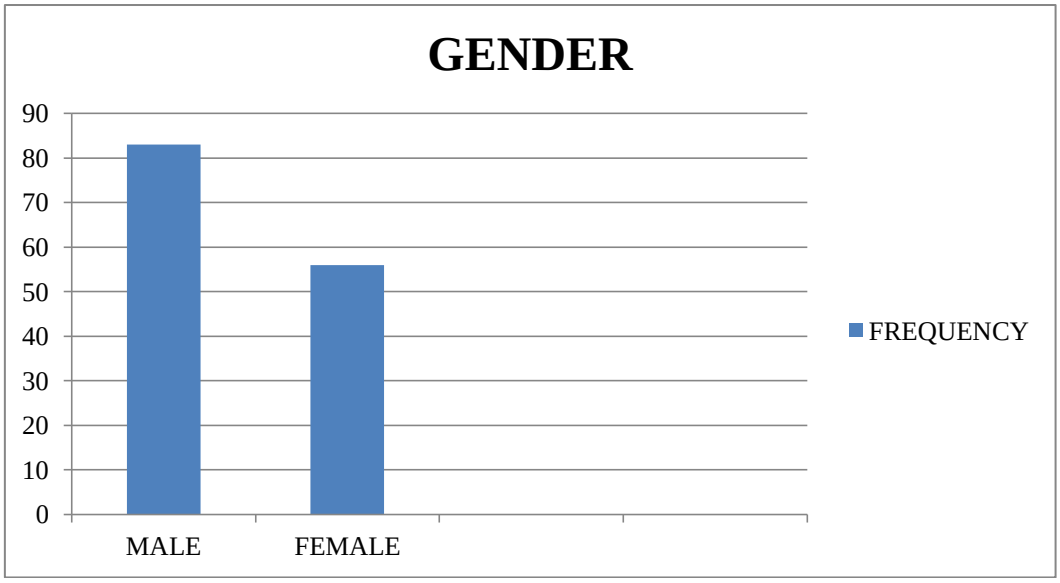

Figure 6: Gender of the study participants

4.4 Estimated age using the GP method

The mean GP age was 8.69 years with a Standard deviation of 5.491.

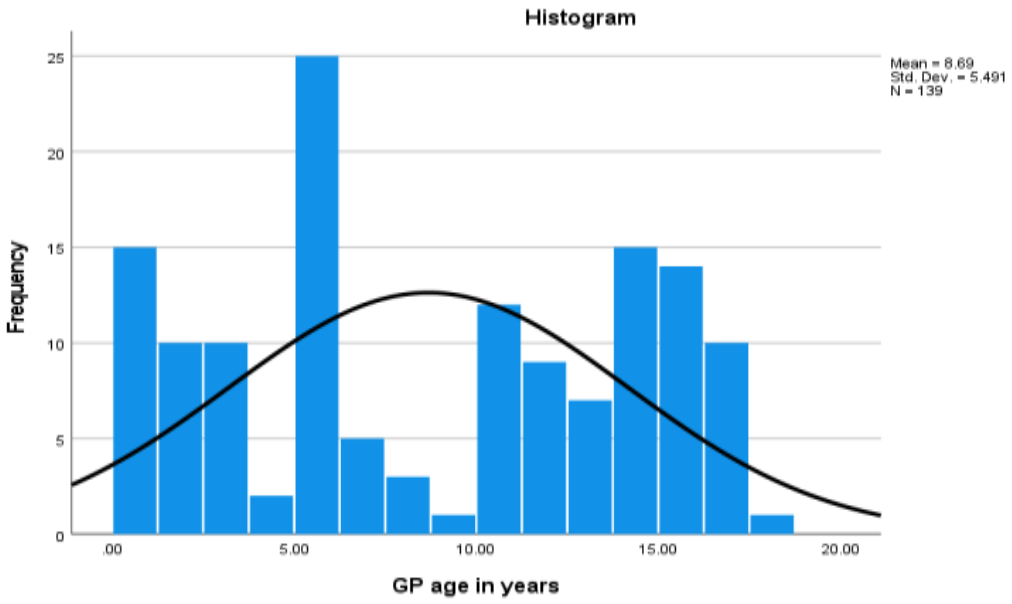

Figure 7: Histogram showing the mean GP age in years

4.5 Comparison of chronological age versus GP age in males.

There was a statistically significant difference between chronological age and GP age among the male participants. Chronological age was 0.150 years higher than the GP age (t_{82} =2.433, P value=0.017). GP underestimates CA in 58% and overestimates CA in 31% of the male participants.

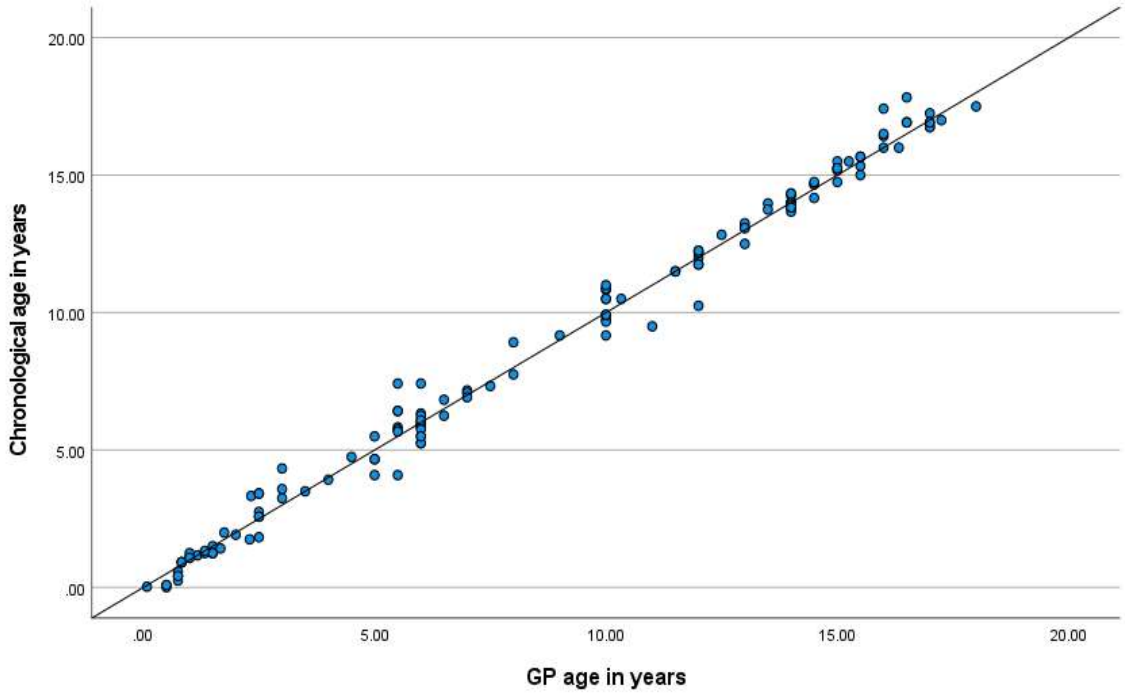

Figure 8: Scatter plot of chronological age against GP age in males

Table 1: Gender and GP age estimation

Interpretation	Gender		p-value
	Male (n=83)	Female (n=56)	
GP underestimate CA	48(58%)	21(37%)	0.004[f]
GP overestimate CA	26(31%)	33(59%)	
GP correct estimate CA	9(11%)	2(4%)	

[f] Fishers Exact Test

4.6 Comparison of chronological age versus GP age in females.

There was no statistically significant difference between the chronological age and GP age among the female participants ((t_{55}=-1.427, P value=0.159). GP underestimates CA in 37% and overestimates CA in 59% of the female participants.

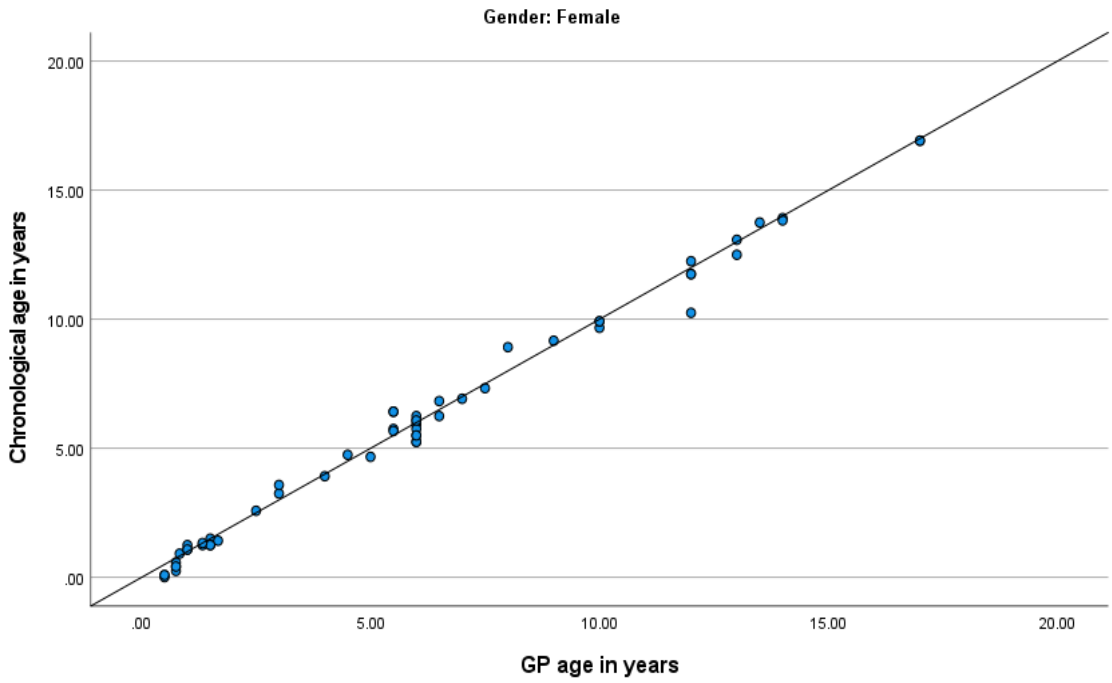

Figure 9: Scatter plot of chronological age against GP age in females

4.7 Reliability of Greulich and Pyle method of age determination

There was no statistically significant differences between chronological age and GP age in years (t_{138} =1.286, P value=0.201). On average, chronological age was 0.057 years higher than GP age (95% CI -0.031, 0.145).

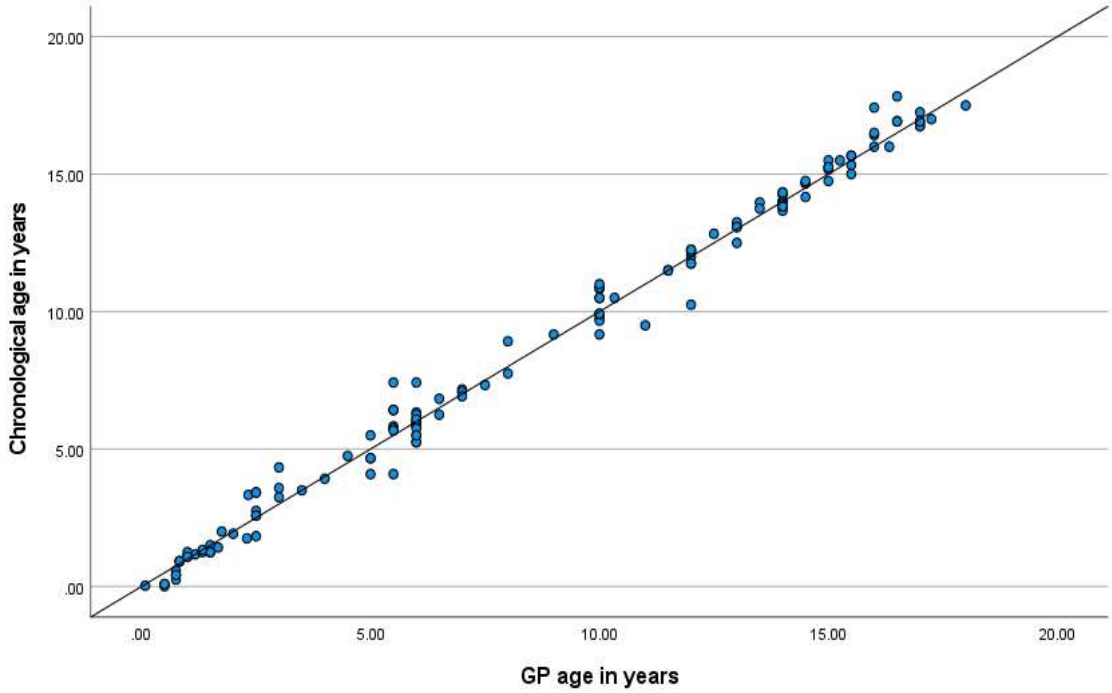

Figure 10: Scatter plot of chronological age against GP age

No proportion bias was noted when a linear regression was done with the coefficient being close to zero (0.009) and the p value was not significant (P value=0.272).

Table 2: Linear regression

		Unstandardized Coefficients		Standardized Coefficients		
		B	Std. Error	Beta	t	Sig.
1	(Constant)	-.021	.083		-.248	.804
	mean	.009	.008	.094	1.104	.272

a. Dependent Variable: difference

When a Bland Altman plot was plotted, near perfect agreements between the chronological age and GP age was demonstrated. 95% of the data points lie within ±1.96 SD of the mean difference which was the limits of agreement (red and blue line.

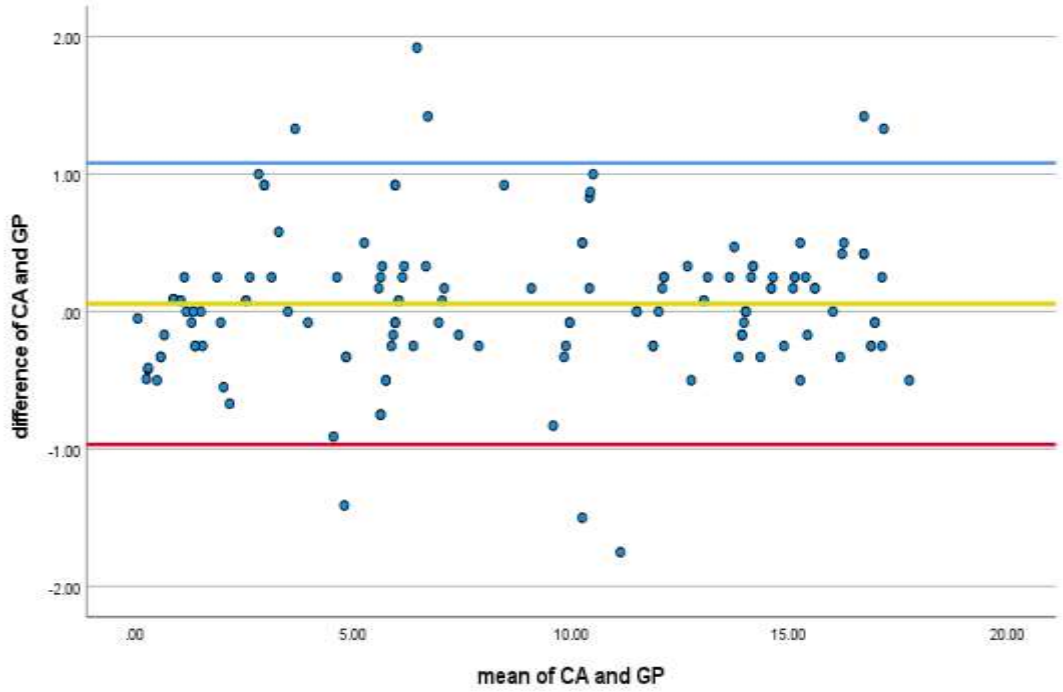

Figure 11: Bland-Altman plot

Paired Mean differences between Chronological age and GP age in months

Table 3: Paired mean difference between CA and GP age

Subject	Paired Mean difference	Standard deviation	95% CI	t	df	P value
All	.684	6.268	-.368,1.735	1.286	138	.201
Men	1.801	.741	.328, 3.275	2.433	82	.017
Female	-.973	.682	-2.340, .394	-1.427	55	.159

Table 4: Paired sample T-test

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Chronological age in years - GP age in years	.05698	.52233	.04430	-.03062	.14458	1.286	138	.201
Pair 2	Chronological age in months - GP age in months	.68374	6.26799	.53164	-.36748	1.73496	1.286	138	.201

SAMPLE IMAGES

Image 1: Left wrist radiograph of a female patient who presented with left wrist pain after a fall on an outstretched hand. Age by GP method was determined to be 6.5 years. Chronological age was 6.83 years. Linear transverse fracture of the distal radius and buckling of the distal ulna cortex noted.

Image 2: Left wrist radiograph of a female patient who presented with left wrist pain. Age by GP method was determined to be 13 years. Chronological age was 13.08 years. The wrist radiograph was normal.

Image 3: Left wrist radiograph of a male patient who presented with history of fall on an outstretched arm. Age by GP method was determined to be 13.5 years. Chronological age was 13.97 years. Linear fracture at the ulna styloid demonstrated.

Image 4: Left wrist radiograph of a male patient who presented with wrist swelling after trauma. Age by GP method was determined to be 5 years. Chronological age was 4.67 years. Mild buckling at the distal radius cortex demonstrated.

Image 5: Left wrist radiograph of a female patient who presented with suspected fracture of the distal radius. Age by GP method was determined to be 5.5 years. Chronological age was 5.75 years. Normal left wrist radiograph.

Image 6: Left wrist radiograph of a male patient who presented with wrist swelling. Age by GP method was determined to be 2.5 years. Chronological age was 3.42 years. Normal left wrist radiograph.

Image 7: Left wrist radiograph of a male patient who presented with suspected fracture after trauma. Age by GP method was determined to be 14 years. Chronological age was 14.33 years. Transverse mildly displaced fracture of the distal radius demonstrated.

Image 8: Left wrist radiograph of a male patient who presented with wrist swelling after trauma. Age by GP method was determined to be 10.33 years. Chronological age was 10.5 years. Transverse non-displaced fracture of the distal radius demonstrated.

Image 9: Left wrist radiograph of a female patient who presented with wrist pain after trauma. Age by GP method was determined to be 6.5 years. Chronological age was 6.25 years. Normal left wrist radiograph.

CHAPTER FIVE: DISCUSSION

5.1 Demographics

Majority of the study participants in this study were male – 59.7% (n=83). The male to female ratio was 1.4:1. Similar findings were obtained in a study by Tsehay et al in Debre Hospital, Ethiopia on Assessment of Reliability of Greulich and Pyle (GP) Method for Determination of Age of Children where the male to female ratio was 1.5:1(Tsehay et al., 2017b). Alcina et al, in a study at the university hospital of the University of Barcelona, Spain found comparable results where 590(51.3%) of the study participants were male and 560 (48.3%) were female. In this study by Alcina et al, the male to female ratio was 1.1:1(Alcina et al., 2018). These findings were further supported by Manzoor et al in a study at the Ziauddin hospital in Karachi, Pakistan where 139 (63.2%) of the 220 study participants were male(Manzoor Mughal et al., 2014c). The reason for the male dominance in this study is unclear. However, we postulate that this is because males have a higher bone density hence their bones are more likely to fracture when a similar force is applied, as compared to females. Schneider et al, in a study in Austria showed that the higher the bone density, the higher the chance of sustaining fractures from trivial force. Majority of our study participants (n=75, 54%) presented with suspected fractures.

5.3 Comparing chronological age and age by GP method in males

The mean difference between the GP age and the chronological age was 0.15 years. This was statistically significant with a p value of 0.015.

This compares well with findings by various authors. Van Rijn et al, in a study in Netherlands titled ‘Is the Greulich and Pyle atlas still valid for Dutch Caucasian

children today?' found a mean difference of 0.27 years which was statistically significant, with a p value of <0.001(van Rijn et al., 2001).

Our findings also compare well with those of Gungor et al, in their study on the reliability of the Greulich and Pyle atlas when applied to a Southern Turkish population, they found a mean difference ranging between 0.07 to 1.11 years, which was statistically significant with a p value of <0.001(Gungor et al., 2015).

Our findings however differ from those of Paxton et al in Australia. In their study on the reliability of the Greulich and Pyle method in bone age determination among Australian children, they found a mean difference between GP age and CA to be 0.125 with a p value of>0.05(Paxton et al., 2013). This can be attributed to the difference between the population studied by Paxton and our study population. Paxton's study participants were Caucasians, same race as the reference population.

When grouped in one year intervals, GP method under-estimated chronological age in 58% (n=48) among the male participants. The mean under-estimation was 0.4 years, with a minimum of 0.08 years and a maximum of 2.3 years. This compares well with findings of various researchers from different countries. Tsehay et al, in a study in a study on the Assessment of Reliability of Greulich and Pyle (GP) Method for Determination of Age of Children at Debre Markos Referral Hospital, East Gojjam Zone in Ethiopia, found under-estimation in 18 % of the male study participants. The mean under-estimation in this study was 0.7 years(Tsehay et al., 2017b).

These findings however differ from those by Paxton in Australia. In his study on the reliability of the Greulich–Pyle method in bone age determination among Australian children, he found a mean difference of 0.125 years(Paxton et al., 2013).

The greatest under-estimation was in the age between 2-3 years with a mean of 0.7 years. Tsehay et al found the greatest under-estimation of 3 years to be in the age group of 22 years. This can be explained by the fact that in this study, the study participants' ages ranged between 10-22 years.

The least under-estimation was in the ages between 13-14 years by a mean of 0.08 years. Tsehay et al found the least under-estimation to be in the study participants in the age category of 17 years.

GP method over-estimated the chronological age in 31% (n=26). This contradicts to findings by Tsehay et al who had 9.23% of the study participants whose chronological age was over-estimated by GP method.

The mean over-estimation was 0.4 years with a minimum of 3 weeks and a maximum over-estimation by 1.5 years. The greatest over-estimation was in the ages between 7-9 years by a mean of 0.8 years. The least over-estimation was in the ages between 1-2 years by a mean of 0.3 years. Tsehay et al found the greatest over-estimation to be in the age group of 15 years and the least over-estimation to be in the age group of 14 years. Zabet et al, in a study titled 'Can the Greulich and Pyle method be used on French contemporary individuals?' done at the Radiology department of the University Hospital of Tours in France found a mean over-estimation by 0.2 years among the male participants(Zabet et al., 2014). Patil et al, in a study on the applicability of the Greulich and Pyle skeletal age standards to Indian children found an over-estimation of 0.01- 2.1 years among the male participants(Patil et al., 2012).

GP method correctly estimated age in only 11% (n=9) of the male study participants. The 9 participants were distributed across all age groups. In the study by Tsehay et al,

GP did not correctly estimate the chronological age in any of the age groups. His study participants however had a range of 10-22 years.

5.3 Comparing chronological age and age by GP method for females

The mean difference between the GP age and the CA was 0.08 years. This was not statistically significant with a p value of 0.159.

This compares well with findings by various authors. Hackman et al, in a study in Scotland on the reliability of the Greulich and Pyle atlas when applied to a modern scottish population, they found a mean difference of 0.1 years which was not statistically significant with a p value of 0.7(Hackman & Black, 2013).

Findings also agree with those of Zabet et al. In their study titled, 'Can the Greulich and Pyle method be used on French contemporary individuals?', they found a mean difference of 0.53 years which was not statistically significant with a p value of >0.05(Zabet et al., 2014).

Our findings however differ from those of Patil et al. In their study in India on the applicability of Greulich and Pyle skeletal age standards to Indian children, they found a mean difference of 0.33 years which was statistically significant with a p value of <0.05(Patil et al., 2012). This could be attributed to differences in diet and genetic make-up, which have been shown to affect the rate of growth and bone maturation.

GP method under-estimated chronological age in 37% (n=21) among the female participants. This compares well to several studies by various authors. In a study in 2017 on the Assessment of Reliability of Greulich and Pyle (GP) Method for Determination of Age of Children at Debre Markos Referral Hospital, East Gojjam

Zone in Ethiopia, Tsehay et al found under-estimation of chronological age by the GP method in 13.7 % of the female study participants.

The mean under-estimation was 0.3years, with a minimum of 0.08 years and a maximum of 1.75 years. Tsehay et al found a mean under-estimation of 0.98 years.

The greatest under-estimation was in the age between 8-9 years with a mean under-estimation of 0.92 years. The least under-estimation was in the age group of 13 years, by a mean of 0.02 years.

It over-estimated the chronological age in 59% (n=33). The findings contradict to findings by Tsehay et al, who found GP to have over-estimated the chronological age in 2.3% of the female study participants. The mean over-estimation was 0.33 years with a minimum of 0.08 years and a maximum over-estimation by 1.75 years. The greatest over-estimation was in the ages between 10-11 years by a mean of 1.75 years. The least over-estimation was in the ages between 4-5 years by a mean of 0.04 years. Zabet et al, in France, in a study titled 'Can the Greulich and Pyle method be used on French contemporary individuals?' found a mean over-estimation by 0.54 years among the female participants(Zabet et al., 2014).Patil et al in India, in a study on the applicability of the Greulich and Pyle skeletal age standards to Indian children found an over-estimation of chronological age by GP method by 0.82 years in females(Patil et al., 2012).

These differences can be attributed to the difference in genetic make-up, differences in geographical location and diet between the study populations and our study population. These factors have been shown to affect the rate of bone maturation hence differences in the estimated bone ages.

GP method correctly estimated age in 4% (n=2) of the female study participants. This compares well with a study by Tsehay et al, where GP method correctly estimated the chronological age in 6.9% of the study participants.

5.5 Reliability of Greulich and Pyle method of age determination

The overall absolute mean difference between chronological age and GP age was 0.057 years which was statistically significant with a p value of0.201. This compares well with studies from various researchers. Van Rijn et al, in their study titled 'Is the Greulich and Pyle atlas still valid for Dutch Caucasian children today?' found an absolute mean difference of 0.14 years, which was not significant with a p value 0.14(van Rijn et al., 2001).

In a study in 2017 at Debre Markos Referral Hospital, East Gojjam Zone, Ethiopia on the Assessment of Reliability of Greulich and Pyle (GP) Method for Determination of Age of Children, Tsehay et al found a mean difference of 8.7 months for males and 11.8 months for females. Sumit T. Patil in 2012, in a study on the Applicability of Greulich and Pyle skeletal age standards to Indian children in Government Medical College, GMC Nagpur, Nagpur, Maharashtra, India found a mean difference of 8.4 months in males and 4 months in females. In 2002 in a study at the Queen Elizabeth Central Hospital in Malawi on the Delay in skeletal maturity in Malawian children, C.P. Lewis found the mean age difference to be 20.7months for males and 18.9 months for females. SC Braude et al in a study in South Africa on the Accuracy of bone assessments for verifying age in adolescents-application in sport in 2007 found the mean difference to be 6.8 months for males and 12 months for females.

Our findings are further supported by those of Manzoor et al. In their study in 2014 on the applicability of the Greulich& Pyle Atlas for bone age assessment in primary

school-going children of Karachi, Pakistan, he found a mean difference between age as determined by the GP method and chronological age of 6.7 months in males and 15.8 months among the female participants.

Our findings however differ from those of Gungor et al. In their study on the reliability of the Greulich and Pyle atlas when applied to a Southern Turkish population, they found a mean difference of 0.81 which was statistically significant with a p value of <0.05. The reason for this difference is not clear. However, we postulate that this could be due to difference in methodology between this study and the study by Gungor et al. Gungor only studied children between the ages of 10-18 years(Gungor et al., 2015)

The findings in this study also vary from those by Paxton in Australia. In a study on the reliability of the Greulich–Pyle method in bone age determination among Australian children in 2012, he found the mean difference to be 1.5 months for males. The mean difference among the female participants was also not statistically significant. This could be explained by the geographical setting and the ethnicity from where the study population was drawn from. Paxton did his study in North Queensland, Australia where majority of the children studied were Caucasians. The population which was studied to come up with the GP standards of age estimation was normal white children in the United States.

Our findings also differ from that of Hackman and Black. In a study on the reliability of the Greulich and Pyle atlas when applied to a modern Scottish population in 2012, they found a mean difference between bone age as determined by GP method and chronological age to be-1.6 in males and -1.9 in females. The negative values in this study indicate that GP method under-estimated the age in both

the male and the female cohorts. In this study however, analysis was made by subtracting the GP age from the chronological age. In our study, analysis was made by subtracting the chronological age from the GP age.

In our study, GP seems to be a fair estimate of chronological age for children between 12to 16 years. The accuracy of GP method did not improve or worsen by age.

Our findings differ from those of Paxton in 2012. In his study in Australia, he found that GP over-estimated chronological age in children up-to the age of 8.3 years, above which GP generally under-estimated chronological age. The reason for this is not clear. However, we postulate this could be due to the fact that Paxton did his study in a predominantly Caucasian population.

Our findings also differ from those of Ozge et al. In their study in 2015 on the reliability of the Greulich and Pyle atlas when applied to a Southern Turkish population, they found that GP over-estimated chronological age in males in the age cohorts between 10-15 years. GP was a fair estimate of chronological age between 15-18 years.GP under-estimated the chronological age in all the age groups in females (10-18 years). This could be explained by the fact that Ozge et al studied children of ages between 10-18 years.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1Conclusions

1. The mean difference between the GP age and chronological age among males is statistically significant.
2. There is no statistically significant difference between the mean GP age and CA among females
3. GP method of age determination among children in MTRH is reliable

6.2 Recommendations

1. GP chart should be interpreted with caution especially in males when high accuracy is required.

2. Further studies should be done and a customized bone age chart developed for the local population.

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APPENDICES

APPENDIX I: CONSENT FORM

English Version

Investigator: My name is Dr. Kanyotu Reuben Njoroge. I am a qualified doctor, registered with the Kenya Medical Practitioners and Dentists Board. I am currently pursuing a Master degree in Radiology and Imaging at Moi University. I would like to recruit your child into my research which is to study the reliability of Greulich and Pyle method in age determination among children at Moi Teaching and Referral Hospital.

Purpose: This study will seek to determine the association between age determined by GP method and chronological age at MTRH.

Procedure: Children scheduled to undergo wrist and hand x-ray will be identified at the radiology department, MTRH and recruited into the study after written informed consent is sought from the parents and/or guardians. Data on demographic characteristics will be obtained. Wrist and hand x-rays will then be reviewed and age determined. The patients' birth certificate or notification will then be reviewed and date of birth recorded. Chronological age will be calculated. Clinical, radiologic and demographic findings will be collected on data collection forms. Data collecting material will be kept in a locked cabinet during the study period.

Benefits: There will be no direct benefits of participating in this study. Study subjects will be accorded same quality of management as non-study subjects.

Risks: There are no anticipated risks to the participants attributable to this study.

Confidentiality: All information obtained in this study will be treated with utmost confidentiality and shall not be divulged to any unauthorized person.

Rights to Refuse: Participation in this study is voluntary; there is freedom to refuse to take part or withdraw at any time. This study has been approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital.

Sign or make a mark if you agree to take part in the study.

Parent/Guardian: ……Investigator: …….. Date: ……

Kiswahili version

Mpelelezi: Jina langu ni Daktari Kanyotu Reuben Njoroge.Mimi nidaktarialiyehitimu nakusajiliwa na bodi ya Kenyaya Madaktari naMadaktari wa meno.Kwa sasanatafutashahada ya uzamili katikaRadiologyna ImagingkatikaChuo Kikuu cha Moi. Ningependakusajili mtoto wakokatikautafiti wanguambao ni wa kujifunza uwiano wa uchunguzi wa umri kutumia njia iliyopendekezwa na Greulich na Pyle na umri kamili wa mtoto kutoka tarehe aliyozaliwa miongoni mwa watoto wanaofanyiwa x-ray ya mkono katika hospitali ya mafundisho na rufaa ya Moi.

Kusudi: Utafiti huu utachunguza uwiano kati ya umri utakaobainishwa kutumia njia iliyopendekezwa na Greulich na Pyle na umri kamili wa mtoto kutoka tarehe aliyozaliwa.

Utaratibu: Watoto waliokusudiwa kufanyiwa xray ya mkono watasajiliwa katika utafiti huu ikiwa wazazi na/au walezi wao watakubali baada ya kuelezwa juu ya utafiti. Umri wa watoto utatabiliwa kutoka kwa xray ya mkono kutukia njia iliyopendekezwa na Greulich na Pyle. Umri kamili wa mtoto utahesabiwa kutoka kwa tarehe iliyo kwenye stakabadhi za kusajili watoto wanapozaliwa na kurekodiwa. Data zitakusanywa kwenye fomu za ukusanyaji data. Hifadhi zitakazo tumika katika ukusanyaji wa data zitawekwa katika kabati iliyofungwa na mpelelezi mkuu katika kipindi cha utafiti.

Faida: Hakutakuwa na faida ya moja kwa moja ya kushiriki katika utafiti huu. Wanaofanyiwa utafiti watakuwa na haki nakupewa matibabu sawa na wale ambao hawatahusishwa na utafiti huu.

Hatari: Hakuna hatari inayotarajiwa kwa washiriki kutokana na utafiti huu. **Usiri:** Habari zote zitakazopatikana katika utafiti huu zitawekwa kwa usiri mkubwa na wala hazitatolewa kwa mtu yeyote asiyehusika na utafiti.

Haki ya kukataa: Kushiriki katika utafiti huu ni kwa hiari yako; kuna uhuru wa kukataa kusajiliwa au kutoka kwenye utafiti wakati wowote. Utafiti huu umepitishwa na Utafiti wa Taasisi na Kamati ya Maadili (IREC) ya Chuo Kikuu cha kufundishia Moi na Hospitali ya Rufaa.

Tia sahihi au kufanya alama kama unakubali kushiriki katika utafiti

Mgonjwa: ..... Mpelelezi: .....

Tarehe: .....

APPENDIX II: ASSENT FORM
English version

Information

This informed assent form is for children above 7 years of age who are scheduled to undergo wrist and hand x-ray

What is medical research?

Medical research is a process which involves a doctor or any other researcher collecting information to learn more about disease or illness. This helps doctors in understanding more about illnesses and coming up with new and better ways of managing illnesses.

What is this study about?

This study research is on children who have been scheduled to undergo wrist x-rays. The wrist is part of the body which connects the hand to the forearm. X-rays are used by doctors to see whether there is any injury or abnormality to the bone or other internal tissues of the body. In this study, bone age will be determined using one of the methods of age determination, that is Greulich and Pyle method and then compared to the chronological age, calculated from the birth date to decide whether the G.P method of age determination is reliable. This will be of help to children who will need age determination in future.

Who is doing this research?

My name is Dr Kanyotu Reuben Njoroge. I am a qualified medical doctor. I am currently studying for my Masters degree in Radiology & Imaging at Moi University.

What will happen to me in this study?

I will request you to be part of this study. If you agree to participate, your x-rays will be reviewed, and age determination done using GP method. You will then be

requested to provide your birth certificate and the chronological age calculated from the date of birth indicated in the birth certificate.

There are no risks or benefits of participating in this study and you will be accorded the same quality of medical care as the children who will participate in the study. You can choose to participate or not to participate in this study. I have explained to your parent(s)/ guardian(s) and they know that I am seeking for your permission to be part of the study. In case you refuse to be part of the study, you will not be forced by anybody, including your parent(s) or guardian(s)

In case you have any question, feel free to ask and I will be happy to answer.

Certificate of assent

Do you understand this research and are willing to participate?

Yes..... No.....

Has the researcher answered allyour questions?

Yes..... No.....

Do you understand that you can pull out of the study at any time?

Yes..... No.....

I agree to take part in the study.

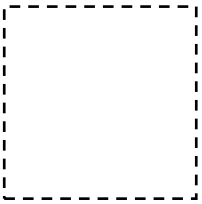
OR

i do not wish to take part in the study and I have not signed the assent below

.....

Only if child assents

Name of the child.....

Child's thumb print 

Date .....

Kiswahili version

Fomu hii ya idhini ni ya watoto walio na umri wa miaka saba na wamepangiwa kufanyiwa x-ray ya mkono.

Utafiti wa matibabu ni nini?

Utafiti wa matibabu ni njia inayotumiwa na madaktari na wachunguzi wengine kupata ujuzi mpya kuhusu magonjwa na matatizo mengine yanayoadhiri watu.

Utafiti huu unahusu nini?

Utafiti huu unahusisha watoto waliopangiwa kufanyiwa x-ray ya mkono. X-rays hutumiwa na madaktari kuona mifupa ili kujua kama imevunjika ama kuna shida nyingine yeyote ndani ya mwili. Katika utafiti huu, umri utatabiliwa kwa kuchunguza x-ray ya mkono na kutumia njia iliyopendekezwa na Greulich na Pyle. Umri huu utalinganishwa na umri utakaohesabiwa kutoka kwa tarehe ya kuzaliwa iliyonakiliwa kwenye cheti cha kuzaliwa ili kujua kama njia iliyopendekezwa na Greulich na Pyle ni bora kutabili umri.

Nani anafanya utafiti huu?

Jina langu ni Dkt. Kanyotu Reuben Njoroge.Mimi nidaktarialiyehitimu nakusajiliwa na bodi ya Kenyaya Madaktari naMadaktari wa meno.Kwa sasanatafutashahada ya uzamili katikaRadiologyna ImagingkatikaChuo Kikuu cha Moi.

Nini kitakachofanyika kwangu katika utafiti huu?

Nitakualika kushiriki katika utafiti huu. Iwapo utakubali, picha yako ya x-ray ya mkono itakaguliwa na umri kuhesabiwa kutumia njia iliyopendekezwa na Greulich na Pyle.Umri kamili wa mtoto utahesabiwa kutoka kwa tarehe iliyo kwenye stakabadhi za kusajili watoto wanapozaliwa na kurekodiwa.

Hakuna hatari au faida za kushiriki kwenye utafiti huu. Utapewa huduma sawa za matibabu na watoto wengine watakaoshiriki kwenye utafiti huu. Uko na uhuru wa

kuchagua kama ungependa kushiriki kwenye utafiti huu. Nimezungumza na mzazi na/au mlezi wako na anajua ya kwamba tunaomba ruhusa yako ya kushiriki kwenye utafiti huu. Ikiwa utakataa kushiriki, huwezi kulazimishwa hata na mzazi au mlezi wako kushiriki.

Ikiwa uko na swali lolote, jisikie huru kuuliza nami nitafurahi kujibu.

Hati ya kukubali

Je, unaelewa utafiti huu na uko tayari kushiriki?

Ndio..... La.....

Je, mtafiti alijibu maswali yako yote?

Ndio..... La.....

Je, unaelewa kwamba unaweza kujiondoa kwenye utafiti huu wakati wowote?

Ndio..... La.....

Nakubali kushiriki kwenye utafiti huu

AU

Sitaki kushiriki kwenye utafiti huu na sijapeana idhini hii.....

Ikiwa tu mtoto ataidhinisha:

Jina la mtoto.....

Alama ya kidole cha gumba cha mtoto

Tarehe .....

APPENDIX III: DATA COLLECTION FORM

1. All sections to be filled appropriately.
2. Writings should be and legible.
3. Bone age determined using the GP method to be filled in by the principal investigator. Chronological age to be filled by the assistant once the patient's age is confirmed from the birth certificate/notification

SOCIO-DEMOGRAPHICS

Date: ……..

Gender…….

County of residence**.....**

Serial Number…….

Contact……

INDICATIONS FOR THE HAND/WRIST X-RAYS

Pain ☐ ☐

Suspected fracture ☐ ☐

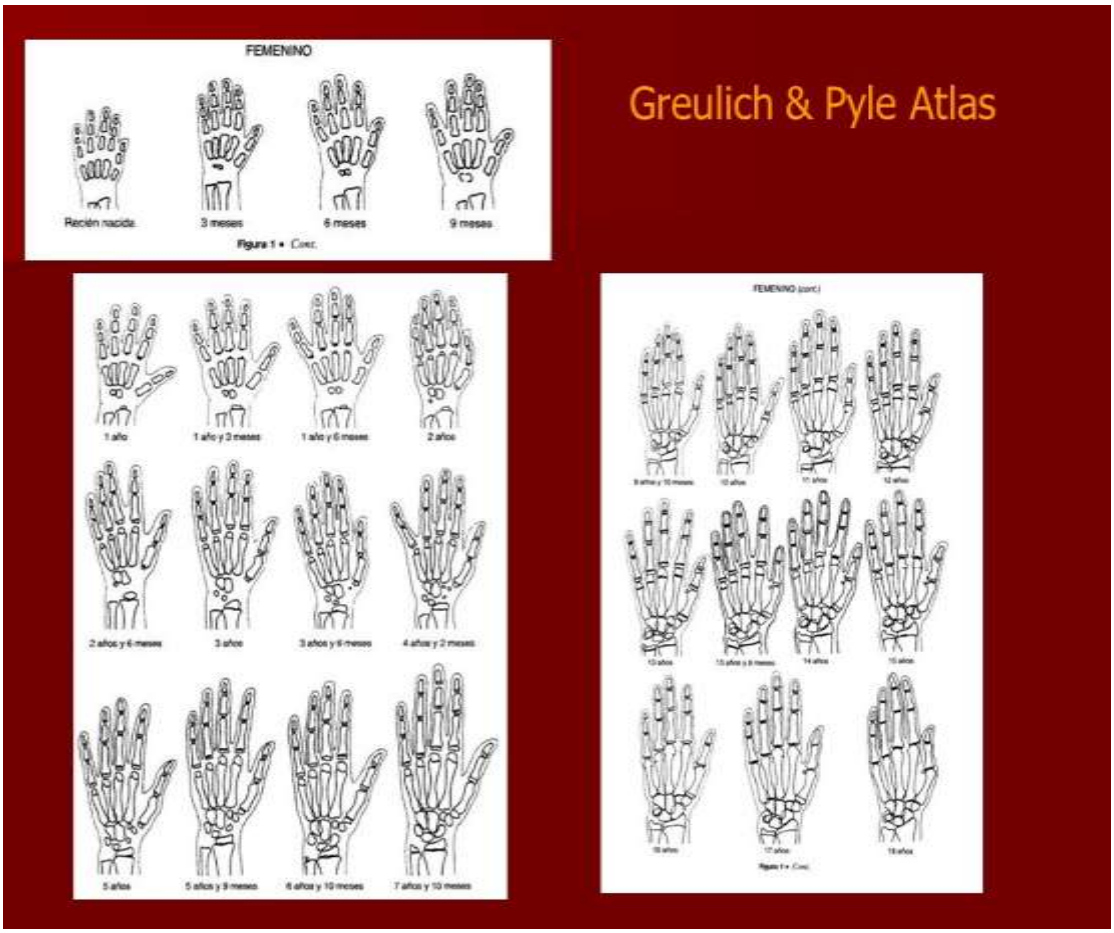
FINDINGS ON WRIST AND HAND X-RAY

Estimated age using GP method in years and months: ……

CHRONOLOGICAL AGE IN YEARS AND MONTHS

Age: ……..

APPENDIX IV: GREULICH AND PYLE CHART



APPENDIX V:IREC APPROVAL

MU/MTRH-INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471/2/3

MOI UNIVERSITY
COLLEGE OF HEALTH SCIENCES
P.O. BOX 4606
ELDORET

Reference: IREC/2018/326
Approval Number: 0003296

3rd April, 2019

Dr. Kanyotu Reuben Njoroge,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
03 APR 2019
APPROVED
P. O. Box 4606-30100 ELDORET

Dear Dr. Njoroge,

RE: FORMAL APPROVAL

The MU/MTRH- Institutional Research and Ethics Committee has reviewed your research proposal titled: -

"Reliability of Greulich-Pyle Method of Age Determination among Children Undergoing Wrist X-Rays at Moi Teaching and Referral Hospital".

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 3296*** on 3rd April, 2019. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; hence will expire on 2nd March, 2020. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date. You will be required to submit progress report(s) on application for continuation, at the end of the study and any other times as may be recommended by the Committee.

Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. You will also be required to seek further clearance from any other regulatory body/authority that may be appropriate and applicable to the conduct of this study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc	CEO	-	MTRH	Dean	-	SOP	Dean	-	SOM
	Principal	-	CHS	Dean	-	SON	Dean	-	SOD

APPENDIX VI: HOSPITAL APPROVAL (MTRH)

An ISO 9001:2015 Certified Hospital

MOI TEACHING AND REFERRAL HOSPITAL

Telephone :(+254)053-2033471/2/3/4
Mobile: 722-201277/0722-209795/0734-600461/0734-683361
Fax: 053-2061749
Email: ceo@mtrh.go.ke/directorsofficemtrh@gmail.com

Nandi Road
P.O. Box 3 – 30100
ELDORET, KENYA

Ref: ELD/MTRH/R&P/10/2/V.2/2010

8th April, 2019

Dr. Kanyotu Reuben Njoroge,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Reliability of Greulich-Pyle Method of Age Determination among Children Undergoing Wrist X-Rays at Moi Teaching and Referral Hospital".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR. WILSON K. ARUASA, *MBS*
CHIEF EXECUTIVE OFFICER
MOI TEACHING AND REFERRAL HOSPITAL

cc - Senior Director, (CS)
- Director of Nursing Services (DNS)
- HOD, HRISM