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***Title:***

**ASSESSMENT OF BONE AGE AMONG SUDANESE  
CHILDREN AND YOUNG ADULTS**

*A thesis submitted in fulfillment for the requirement of the MSc degree in Human  
Anatomy*

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## الآية

### VERSE

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَلَقَدْ خَلَقْنَا الْإِنْسَانَ مِنْ

سُلَالَةٍ مِّن طِينٍ ﴿١٣﴾ ثُمَّ جَعَلْنَاهُ نُطْفَةً فِي قَرَارٍ مَّكِينٍ ﴿١٣﴾

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الْمُضْغَةَ عِظْمًا فَكَسَوْنَا الْعِظْمَ لَحْمًا ثُمَّ أَنْشَأْنَاهُ خَلْقًا

ءَاخِرَ فَتَبَارَكَ اللَّهُ أَحْسَنُ الْخَالِقِينَ ﴿١٤﴾

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***DECLARATION OF AUTHORSHIP***

I hereby declared that this thesis had been generated by me with the assistant of the supervisor, and it was the result of my own interpretations and investigations.

When I had consulted and quoted from the published work of others, this was always clearly cited and attributed.

It had neither been submitted nor accepted for any other degree in this university or any other academic institution.

The data collection, analysis and interpretation were the sole work of the author, except where acknowledged.

The writing of this thesis is the sole work of the author.

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## ***DEDICATION***

*To Allah the almighty, this work is dedicated to my parents, Belgees and Mohammed, who they are always, stand behind my success. My wife thanks for sharing this life. To Mariam my soul this work is for your beautiful attendance.*

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## LIST OF ABBREVIATIONS

BAA	Bone age assessment
BA	Bone age
SA	Skeletal age
CA	Chronological age
PHC	Primary health care
G&P	Greulich and Pyle
TW	Tanner Whitehouse
TW1	Tanner Whitehouse1
TW2	Tanner Whitehouse2
TW3	Tanner Whitehouse3
ROI	Regions of interest
GP	Greulich-Pyle
SPR	Society of pediatric radiology
KS	Korean standard of bone age chart
MRI	Magnetic Resonance Imaging
SBA	Shorthand bone age assessment method
DXA	Dual energy X-ray absorptiometry
IOPA	Intraoral periapical radiograph
ER	Eklöf and Ringertz
PA	Posterior-anterior
SPSS	Statistical Package for Social Sciences

## ABSTRACT

Bone age assessment is the procedure performed in pediatric outpatients by radiologist to evaluate child's bones. The aim of this study was to investigate whether the Greulich–Pyle (GP) method is adequate for Sudanese children and young adults. A group of 76 individuals (35 girls and 41 boys) aged (3-10) months old were studied. Bone age (BA) from plain radiographs of the left hands and wrists were estimated in reference to GP standard atlas. The total mean difference between CA and SA in males was  $20.9 \pm 45.0$  months, i.e., skeletal age was less when compared to chronological age by 20.9 months in males, and the total mean difference between CA and SA in females was  $14.1 \pm 27.2$  month, i.e., skeletal age was less when compared to chronological age by 14.1 months in females. The results of this study suggested that the mean differences between BA and CA are low to be of great practical significance. This concluded that Greulich-Pyle method was not applicable in Sudanese children and young adults. Therefore it is recommended that in future research the samples should be collected from different areas of the Sudan to cover different races, tribes and areas. This will enable to draw an atlas for Sudanese children and young adults bone growth development.

**Keywords:** Greulich–Pyle (GP) method, bone age, chronological age, skeletal age, Sudanese children.

## ملخص الدراسة

الهدف من هذه الدراسة هو التحقق مما إذا كانت طريقة غريوليتش- بايل كافية للتطبيق علي الأطفال والشباب البالغين السودانيين. تمت دراسة مجموعة من ٧٦ فردا (٣٥ فتاة و ٤١ ذكر) بين عمر ٣ الي ٢٤٠ شهرا . وقد تم تقدير عمر العظام من التصوير الاشعاعي بالاشعة السينية من اليد اليسرى والمعصم من قبل معايير غريوليتش- بايل . كان معدل الفرق الكلي بين متوسط العمر الزمني ومتوسط عمر العظام في الذكور  $20,9 \pm 45,0$  شهرا ، أي ان متوسط عمر العظام مقارنة بالعمر الزمني يكون بنسبة ٢٠,٩ شهر في الذكور، ومعدل هذا الفرق كبير (P = القيمة = ٠,٠٠٥). كما ان متوسط الفرق الكلي بين العمر الزمني وعمر العظام في الإناث كان  $14,1 \pm 27,2$  شهرا ، أي المتوسط عمر العظام مقارنة مع العمر الزمني يكون بنسبة ١٤,١ شهر في الإناث، ومعدل هذا الفرق كبير ايضا. وتشير نتائج هذه الدراسة إلى أن متوسط الفروق بين العمر الزمني وعمر العظام كبير جدا ويعتبر فرق معنوي وأن معدل الأعمار في قاموس غريوليتش- بايل لا يمكن استخدامه بين الأطفال والشباب السودانيين.



# *Chapter One*

*Introduction*

*Rationale*

*Objectives*

# CHAPTER ONE

## Introduction

### 1.1 Background

Bone age is the degree of maturation of a child's bones. As a person grows from fetal life through childhood, puberty, and finishes growth as a young adult, the bones of the skeleton change in size and shape. These changes can be seen by x-ray. Estimation of bone age usually is performed in the radiological departments based on the skeletal indicators of bone development. Bone age is assessed and compared with the chronological age. Inconsistency between these two values can highlight abnormal bone growth. In primary health care (PHC) birth records, monitoring the mental and physical child growth and treatment follow-up are a serious problem in the Sudan. Therefore bone age estimation participates strongly in solving these problems. Bone age is a crucial factor of identification which many social events may rely on, such as recruitment in a job, retirement, joining the army, and legal- criminal incidents. Absent birth data is a big problem in Africa. In South Asia, 65% of all births are not registered by the age of 5 years. The need for accurate estimation of age arises in conditions which necessitate proper accuracy as immigration in lawsuits and in competitive sports. In these cases, bone age is used to provide the closest estimate of chronological age.

## **1.2 Rationale**

For decades, the determination of bone maturity has relied on a visual evaluation of skeletal development, recently bone age evaluate by using Greulich-Pyle skeletal age atlas was derived from white children of upper social economies level during the 1930s. To our knowledge, the Greulich and Pyle standard have not been reassessed for both black and white children, one of the purposes of this study to reassess that applicability of these standards to today's children. Genetical and nutritional factors can play important rule in bone maturation and growth by considering these serious points bone age assessment among Sudanese using Greulich and Pyle atlas must be reassessed.

Boundary of the hand bones in hand x-ray images can easily to extracted, ossification centers of the hand bones are proceed in close time (started prenatally and mostly completed by age of 20th years old) and the risks of radiation received per each hand x-ray is comparable to natural background radiation for just 3 hours, all these explanations are reasons for this study.

## **1.3 Objectives:**

### **1.3.1 General objectives**

1. To determine bone age based on appearance ossification center in the hand from normal children in the age group of 0-20 years.
2. To compare the differences in bone age between Sudanese citizens and other races.
3. Assessment of bone development on the social events such as beginning a job, marriage, retirement and joining the army.

### **1.3.2 Specific objectives**

1. To assess applicability of Greulich-Pyle standard among Sudanese children and young adults.
2. To evaluate whether the estimated skeletal age correlates with the chronological age.
3. To compare between the skeletal age of males and females.
4. To compare between the results with that of Greulich –Pyle standards and likewise with other surveys performed in Sudan.

# *Chapter Two*

## *Literature Review*

# CHAPTER TWO

## Literature Review

### 2.1 Definition of bone:

Bone is a special form of connective tissue and consists of cells, fibers, and extracellular matrix. Because of mineral deposition in the matrix, bones become calcified. The process of Bone formation called ossification. Bone development begins in the embryo by two distinct processes: endochondral ossification and intramembranous ossification(Allen, 2008).

### 2.2 Anatomy of the hand bones

The skeleton of the hand is subdivided into three segments: the carpus or wrist bones; the metacarpus or bones of the palm and the phalanges or bones of the digits. The carpal bones, eight in number, are arranged in two rows. Those of the proximal row, from the lateral radius to the medial ulna are named as the scaphoid (navicular), lunate, triangular (triquetral), and pisiform. Those of the distal row are named as trapezium (greater multangular), trapezoid (lesser multangular), capitate, and hamate in the same order. Each of the carpal bones is ossified from a single center, Ossification proceeds in the following manner: capitate and hamate, during the first year, the former preceding the latter, the triquetral during the third year, in the lunate and trapezium during the fifth year, the former preceding the latter, navicular during the sixth year, the trapezoid during the eighth year and about the twelfth year is the pisiform (Gray, 2012).

The skeleton of the hand is made up of three zones of bone; carpus (eight bones), metacarpals (five bones), and phalanges (three for each of the medial four fingers and two for the thumb).

### **2.2.1 Carpus:**

Carpal bones are short bones type, they arranged in two rows. In the proximal row Medio laterally are; pisiform, triquetral, lunate and scaphoid. The distal row includes; hamate, capitate, trapezoid and trapezium (Sinnatamby, 2011).

### **2.2.2 Metacarpals:**

Which are long bones arranged from lateral to medial as there; 1st, 2nd, 3rd, 4th and 5th for the thumb, index, middle, ring and little respectively?

### **2.2.3 Phalanges:**

They are long bone (because they have two ends connected by the middle shaft) they are 14 in number three for each of the medial four fingers and two phalanges for the thumb. All carpal, metacarpal, phalanges of the hand with ulna and radius develop by the endochondral ossification (Agur and Dalley, 2017).

## **2.3 Bone development:**

The degree of skeletal maturity depends on growth of the underlying ossification centers and deposition of minerals (mainly calcium) in bone.

Skeletal age is an indicator of the skeletal and biological maturity of an individual. This is different from chronological age, which is calculated using the date of birth of an individual (Manzoor Mughal et al., 2014b).

In the majority of healthy children, there is an established sequence of ossification for the carpal, metacarpal, phalangeal bones and distal ends of ulna and radius.

Calcification commences with the 8th or 9th weeks of intrauterine life, the 13th week of fetal period marks the appearance of most primary centers in the long bone in the region of the diaphysis. At the birth, all diaphysis are entirely ossified (from primary centers) while epiphysis is still cartilaginous.

Carpal bones of the hand ossify entirely from a single primary center which appears in the body of the bone. The metacarpal bone and phalanges ossify from two centers of ossification (primary and secondary centers); the secondary center appears in the cartilage of the long bone extremity. The Diaphysis ossified from the primary center and that of the epiphysis is ossified from the secondary center. Ossification of secondary center continues to replace all cartilages with bone except in the epiphyseal plate (located between epiphysis and diaphysis) which remains cartilage until the development of bone is completed.

### **2.3.1 Endochondral ossification:**

It occurs during the sixth week of intrauterine life. In this type of ossification, the model hyaline cartilage enlarges and begins to calcify. During calcification the flow of blood vessels and gases decreases leaving cavities in the cartilage and the fragmented calcified matrix serves as a structural framework of bony material. Ossification center formed by the union of mesenchymal connective tissue, osteoblasts and blood vessels in the developing bone (Allen, 2008). The carpal bones are each ossified from a single center, the metacarpal bones are each ossified from two centers: one for the body and one of the distal extremity of each of the second, third, fourth, and fifth bones; one for the body and one for the base of the first metacarpal bone. The phalanges are each ossified from two centers: one for the body, and one for the proximal extremity. Ossification begins in the body, about the



eighth week of fetal life. Ossification of the proximal extremity commences in the bones of the first row between the third and fourth years, and a year later in those of the second and third rows. The two centers become united in each row between the eighteenth and twentieth years(Gray, 2012).

## **2.4 Bone age assessment:**

Bone age is often requested by pediatricians and endocrinologists for comparison with the chronological age for diagnosing diseases which result in tall or short stature in children. Serial measurements are also used to assess the effectiveness of treatments for these diseases. Formulae have also been designed for computing the final adult height of children with bone age values in normal healthy children. Calculation of bone age is also employed for estimation of chronological age in conditions, where accurate birth records are not available.

### **2.4.1 Hand-wrist X-ray:**

An X-ray image of the left hand-wrist is commonly used for bone age assessment for several reasons(2000):

1. Hand-wrist are can easily extracted from the other parts of the body, and exposure to harmful radiation of the rest of the adjacent area can be minimized;
2. This hand- wrist area of includes a lot of ossification centers that appear or change morphologically or even fuse in the established model;
3. The epiphysis of the distal radius is the last area to fuse, and occurs relatively late in adulthood.

#### **2.4.2 Clinical importance of bone age assessment:**

Bone age assessment (BAA) is a common radiological examination used in pediatrics to determine any discrepancy between a child's skeletal age (the developmental age of their bones) and their chronological age in years, taken from birth date (Gertych et al., 2007).

#### **2.5 Method of bone age assessment:**

For many years, various studies have been conducted to determine methods to identify the age of living persons. Nowadays, the most commonly used method for the identification of age is bone age assessment. Several methods have been forwarded for the evaluation of bone age assessment with the advent of digital imaging.

The classical method of skeletal bone age assessment (BAA) utilizes the recognition of changes in the radiographic appearance of the maturity indicators in a hand-wrist radiograph by comparison with a reference data set which consists of a series of radiographs grouped according to sex and age. The most commonly used reference atlas is the atlas published by Greulich and Pyle (G&P). The atlas was derived from the population of the middle socioeconomic class of Caucasian children from Midwest and USA from 1931-1942. The atlas remains unchanged from its initial publication and is commonly used in clinical practice to assess the bone age of children of Caucasian, African American, Hispanic, Asian, and other descents. The examination is subjective because the radiologist analyses each individual bone of the hand and wrist, determines the overall bone age, and finally fits the amalgamated results into the closest match to the reference radiographs in the atlas (Gertych et al., 2007).

### **2.5.1 Greulich and Pyle's Radiographic Atlas of Skeletal Development of the Hand and Wrist (G&P):**

Contains left-hand radiographs selected as sex-specific developmental standards at different ages. G&P also contains data tables of sex-specific mean skeletal ages and standard deviations at various chronological ages, from which calculations can be made to determine whether a child's skeletal maturity is normal or not(Bunch et al., 2017).

### **2.5.2 Tanner Whitehouse TW2 methods:**

The Tanner &Whitehouse (TW) method, in contrast, is not based on the age; it is rather based on the level of maturity for 20 selected regions of interest (ROI) in specific bones of the wrist and hand in each age population. The development level of each ROI is categorized into specific stages labeled as (A, B, C, D. . . I), the numerical score is given to each stage of development for each bone individually. By summing up all these scores from the ROIs, a total maturity score is calculated. This score is correlated with the bone age separately for males and females. TW method is comparatively more complex and requires more time; however, it is more accurate and reproducible when compared to GP method(Manzoor Mughal et al., 2014b).

### **2.5.3 Computer Assisted Techniques for Bone Age Assessment Determinations:**

Computer-assisted bone age estimation systems are generally based on imaging techniques that evaluate the degree of ossification in the carpal bones and the epiphyses of the phalanges. The different stages of computer-assisted assessments contain obtaining hand and wrist radiographies(Aydoğdu and Başçiftçi, 2014).

## **2.6 Factors affecting age assessment:**

Bone development occur during the time and in different age groups of children in various stages of growth, This is why it is difficult to find any relationship between the chronological age and biological growth (Somkantha et al., 2011).

## **2.7 Radiation hazard:**

The hand radiographs are quite safe to obtain as the effective dose of radiation received during each exposure is between 0.0001-0.1 mSV. This dose is less than 20 minutes of natural background radiation or the amount of radiation received by an individual on 2 minutes transatlantic flight (Manzoor Mughal et al., 2014b).

## **2.8 Bone age groups:**

To aid skeletal age assessment, skeletal development subdivided into six categories depend on skeletal indicators which are the appearance of ossification centers for each of the carpus, metacarpals, phalanges and distal ends of radius and ulna as follow:

### **2.8.1 Infancy**

*(Females: Birth to 10 months of age and Males: Birth to 14 months of age)*

Ossification of carpus, metacarpals, distal ends of both radius and ulna and epiphysis of all phalanges are lacking during this stage of development, the only useful observable indicators during this stage is appearance of ossification centers of capitate and hamate (former proceeds first) which starts to be visible during the third month, 10 months of age for girls and about 1 year and 3 months of age for boys the ossification center of distal radial epiphysis is very clear to estimate



**Figure [2.1] : (Gilsanz and Ratib, 2012).**

*During Infancy, bone age is primarily based on the presence or absence of ossification of the capitate, the hamate and the distal epiphysis of the radius. The capitate usually appears slightly earlier than the hamate, and has a larger ossification center and rounder shape. The distal radial epiphysis appears later.*

### **2.8.2 Toddlers:**

*(Females: 10 months to 2 years of age and Males: 14 months to 3 years of age);*

The ossification centers for the epiphyses of phalanges and metacarpals become distinguishable during this stage, usually in the middle finger proceeds earlier than the fifth finger. Skeletal age determination during this period depends on the ossification centers of epiphysis which are identified as follow;

- ✚ Proximal phalanges.
- ✚ Metacarpals.
- ✚ Middle phalanges.
- ✚ Distal phalanges.

This regulation of ossification shows two exceptions:

- The appearance of the ossification center of the distal phalanx of the thumb which is recognizable at 1 year and 3 months in males, and 1 year and six months in females.
- Late appearance of the ossification center of the middle phalanx of the fifth finger, which is the last phalangeal epiphysis developed. Lunate and trapezoid can be recognized during this stage.



**Figure [ 2.2]: (Gilsanz and Ratib, 2012)**

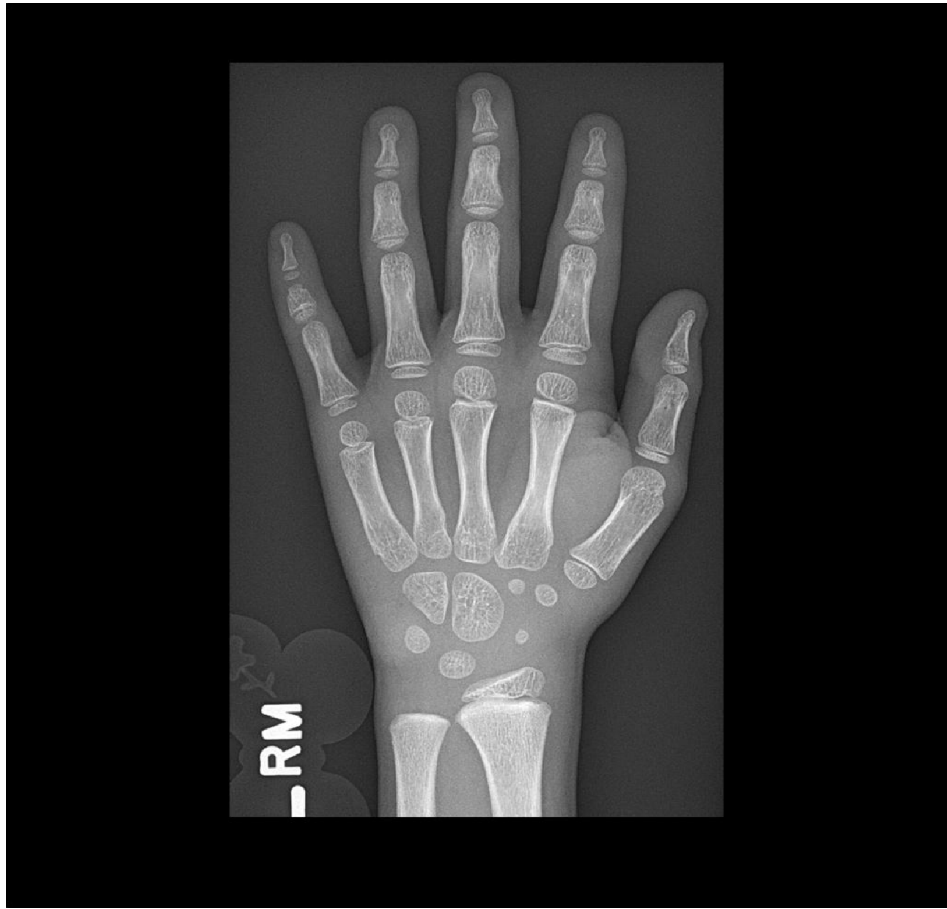
*Estimation of bone age is subject to recognizable ossification centers of metacarpal bone and phalanges.*

### **2.8.3 Pre-puberty:**

*(Females: 2 years to 7 years of age and Males: 3 years to 9 years of age);*

Assessments of bone age indicators in pre-pubertal stage depends on the epiphyseal size of the phalanges as they related to the adjacent metaphysis and the appearance of the lunate ossification center. Here ossification centers for the epiphyses increase in width as in the metaphysis. This stage of maturation is characterized by recognizable ossifications centers of the distal epiphysis of ulna and all the carpal bone except that of the pisiform which is normally the last one.





**Figure [2.3] : (Gilsanz and Ratib, 2012).**

*Assessment of bone age is characterized by appearance of trapezium and other carpal bone (except pisiform) and at the age of 5.5 years distal epiphysis of ulna is distinguishable*



**Figure [2.4] : (Gilsanz and Ratib, 2012).**  
*Epiphysis of distal and middle phalanges grows faster and embraces the metaphysis before the stage of tinny horn.*

#### **2.8.4 Early and mid-puberty:**

*(Females: 7 years to 13 years of age and Males: 9 years to 14 years of age);*

Assessments of skeletal maturity in early and mid-puberty are also based on the size of the epiphyses in the distal phalanges (first) and the middle phalanges (second). The epiphyses at this stage continue to grow and their widths become greater than the metaphysis. Thereafter, the epiphyses of distal and middle phalanges continue to grow and start to overlap the metaphysis like cap and looks like tiny horns on both sides of the shaft.

### **2.8.5 Late puberty:**

*(Females: 13 years to 15 years of age and Males: 14 years to 16 years of age);*

Assessments of Bone age at this time are mainly based on the degree of epiphyseal fusion (with the metaphysis) of the distal phalanges. Fusion of the epiphyses to the metaphysis in the long bones of the hand tends to take place in an orderly characteristic pattern as follows:

1. Fusion of the distal phalanges.
2. Fusion of the metacarpals.
3. Fusion of the proximal phalanges.
4. Fusion of the middle phalanges.



**Figure [ 2.5.1] (Gilsanz and Ratib, 2012).**

*Assessments of bone age in late stages of puberty and sexual maturity are based on the degree of epiphyseal fusion of the distal phalanges (first) and on the degree of fusion of the middle phalanges (second)*



**Figure [ 2.5.2] (Gilsanz and Ratib, 2012)**

*Assessments of bone age in late stages of puberty and sexual maturity are based on the degree of epiphyseal fusion of the distal phalanges (first) and on the degree of fusion of the middle phalanges (second)*



**Figure [2.6]: (Gilsanz and Ratib, 2012).**

### **2.8.6 Post-puberty:**

*(Females: 15 years to 17 years of age and Males: 17 years to 19 years of age)*

Degree of epiphyseal fusion of the ulna and radius is the only landmark of this stage of skeletal maturity; phalanges, metacarpals and carpal bone get their final adult shape.

## **2.9 Sequences of ossification:**

According to Greulich-Pyle atlas of skeletal maturity ossification centers of carpal bones takes place in the following manner;

### **2.9.1 In male:**

- ✚ Capitate and hamate before the 8th month (former proceeds first).
- ✚ By the 16th month distal radial epiphysis is start to ossify.
- ✚ Triquetrum at the age of 20th month.
- ✚ Lunate at the 3rd years.
- ✚ Trapezium and distal epiphysis of ulna at 4.5 years.
- ✚ Trapezoid one year after trapezium.
- ✚ Scaphoid when the male reach the age of 6th years.
- ✚ Sesamoid of adductor pollicis of the thumb appear at the 14th year.

### **2.9.2 In female;**

- Capitate and hamate prior the 8th month (former proceeds first).
- By the 10th month distal epiphysis of radius is appearing.
- Triquetrum at the age of 20th month.
- Lunate at the 24th month.
- Trapezium and trapezoid together at the 3.5th of development.
- By the 4th year the scaphoid is proceeds to ossification.
- 6th year characterized by appearance of distal epiphysis of ulna.
- Sesamoid of adductor pollicis of the thumb appear at the 11th year.



**Note:**

- ❖ Pisiform cannot be standard for skeletal maturity because it comes under cover of triquetrum and difficult to evaluate.
- ❖ Ossification centers of carpal bone look earlier in female.

**2.10 Recent studies:**

Several studies are done all over the world for bone age assessment because of the importance of these procedures and wide application. These studies include;

- ✚ Society of pediatric radiology (SPR) aims to conclude which of the bone age assessment methods which are used by the pediatric radiologist and their confidence in these methods. Society for Pediatric radiology invited 937 members for an online survey to evaluate three groups of bone age (Infants (<1-year-old), 1- to 3-year-olds and 3- to 18-year-old). Those were asked to use their confidence method to determine the skeletal age of the above-mentioned age groups. Of these 937 SPR members only, 441 are reports (47%). For infants group, 70% of these answered using Greulich-Pyle. For age group (1-3 years) 86% used Greulich and Pyle. For 3- to 18-year-old age group 97% used Greulich and Pyle (Breen et al., 2016).
- ✚ Departments of Radiology and Pediatrics at Dankook University Hospital, Cheonan in Korea. Left hand-wrist radiographs of 212 pre-pubertal healthy Korean children aged 7 to 12 years were obtained for the evaluation of the traumatic injury in the emergency department. The intention of this study was to compare the reliability of the Greulich-Pyle (GP) method, Tanner-Whitehouse 3 (TW3) method and Korean standard bone age chart (KS) in the evaluation of bone age of pre-pubertal healthy Korean children. They conclude that The KS (Korean standard bone age chart), GP, and TW3 methods showed good reliability

in the calculation of the bone age of pre-pubertal healthy Korean teenagers without significant difference between them(Kim et al., 2015).

- ✚ Plain radiographs of left hands and wrists data collected from the Khartoum Teaching Hospital, Gafar Ibn-Auf Pediatrics Hospital, UmDurman Teaching Hospital, Abo-Sed Teaching Hospital, Khartoum North Teaching Hospital, Alsheik Hospital and Ibrahim Malek Teaching Hospital from Sudanese children. The study was conducted on aged 0-2 years in female and 0-3 years in males using the digital atlas of skeletal maturity which is established by Greulich-Pyle standard. This study concludes that the digital atlas of skeletal maturity is applicable for Sudanese infancy and toddlers(H. Karrar Alsharif et al., 2014).
- ✚ Two hundred and twenty children (139 males, 81 females) between ages of 56 and 113 months (4.5 to 9.5 years) randomly selected from 4 primary schools of Shireen Jinnah & Clifton, Karachi. (Manzoor Mughal, A.Hassan, and N.Ahmed) Aim to evaluate the degree of applicability of skeletal age calculated by Greulich & Pyle Atlas in the estimation of chronological age for therapeutic and medico-legal purposes. They found that the Greulich & Pyle Atlas misjudges the chronological age by 6.65 +/- 13.47 months in females and 15.78 +/- 12.83 months in males (p-values < 0.001). They therefor think Greulich-Pyle standard can be used in cases related just to therapeutic cases (Manzoor Mughal et al., 2014a).
- ✚ Others conclude that MRI images and their three-dimensional segmentation demonstrate the hand-wrist bone features very clearly. Scoring of this skeletal feature, according to the Tanner-Whitehouse Japan system the results are a strongly positive correlation with chronological age. And their results demonstrate the validity and reliability of skeletal age assessment using MRI(Terada et al., 2013).

- ✚ Benton Heyworth; shorthand bone age assessment method (SBA) offers a simple, efficient, and accurate and alternative to current bone age assessment methods. (SBA) offers a method which is derived from a Greulich-Pyle method. 260 left-hand radiographs (140 male and 160 female) previously assigned for skeletal aging ranging from 12.5 to 16 years in males and 10 to 16 years in females by musculoskeletal radiologists using the Greulich and Pyle radiographs were assessed by three attending pediatric orthopedic surgeons and an orthopedic surgery resident. The shorthand method utilizes a single, univariable criterion for each age, rather than a multivariable subjective comparison to a radiographic atlas of Greulich-Pyle. The upshot of the study concludes that the SBA method readings demonstrated substantial agreement with readings by the Greulich and Pyle atlas in a simple way(Heyworth et al., 2013).
- ✚ Heppe, D. H., Taal, H. R., Ernst, G. D. And other use dual-energy X-ray absorptiometry (DXA) as a method to assess bone age in children and compare their results with the Greulich-Pyle method. Participants were selected from the outpatient clinic of the Department of Pediatric Endocrinology of the Erasmus Medical Center, Sophia Children's Hospital, and Rotterdam, Netherlands. Paired dual-energy X-ray absorptiometry (DXA) scans and X-rays of the left hand were performed in 95 children who attended the pediatric endocrinology outpatient clinic of University Hospital Rotterdam, Netherlands. The outcome of comparing bone age assessments by DXA scan with those performed by X-ray using Greulich-Pyle atlas show the difference between bone age assessed and therefore conclude that (DXA) method give similar results and can be used to calculate skeletal age in a pediatric hospital-based population(Heppe et al., 2012).

- ✚ Cantekin, K., Celikoglu, M., Miloglu, O., Dane, A., and Erdem, A. examined whether the Greulich-Pyle (GP) method was applicable for Turkish children. From a total of 767 individuals (425 girls and 342 male children) age group between 7 and 17 years, plain radiographs of left hands and wrists by GP standards were estimated. The total mean differences between (BA) and chronological age (CA) for girls and boys were found to be 0.20 and -0.13 years, respectively, and there were significant differences between BA and CA in age groups 7-, 8-, 10-, 11-, 12-, 13-, 15-, and 16-year-olds for girls and 7-, 10-, and 12-year-olds for boy(Cantekin et al., 2012).
- ✚ To validate Greulich-Pyle atlas among Pakistani children, hand, wrist radiographs collected from 889 individuals of age group 0-216 months after exclusion of metabolic, nutritional and growth disorder. The 889 radiographs are reviewed by radiologists whom they blinded from chronological age. This paper results in a variation of 13 months between chronological and skeletal age calculated by radiologists by using the Greulich-Pyle atlas. The study concludes that Greulich-Pyle atlas (GP) is not applicable for Pakistani children's(Zafar et al., 2010).
- ✚ Bala, M., Pathak, A. And Jain, R. L. (2010) looking for an Assessment of skeletal age used MP3 and hand-wrist radiographs and its correlation with dental and chronological ages of children. 160 North-Indian healthy children (80 male and 80 female) in the age group 8-14 years was studied. A radiograph for a middle phalanx of the third finger of the right hand and intraoral periapical X-ray for the right permanent maxillary canine were done. Skeletal age assessed from MP3 according to Greulich and Pyle standards shows high correlation in all the age groups for both sexes while the dental age assessed from IOPA radiographs based on Nolla's calcification stages showed high correlation with dental age in 12-14 years age group. The result of this

study discussed that Chronological age showed inconsistent correlation with dental and skeletal ages(Bala et al., 2010).

- ✚ Hsieh, C. W. And other presenters developed a computerized skeletal age calculation system which is based on the analysis of geometric features of carpal bones. Bone age categorized into 4 groups, linear, nearest neighbor, back-propagation neural network, and racial group. These four features groups were extracted by computerized shape and area description. The hand X-ray radiographs of 465 boys and 444 girls served as their database, statistical analysis represented similar results of that of Greulich and Pyle atlas. This study also shows the ossification sequence of trapezium and trapezoid bones between Taiwanese and the Atlas of the GP method is quite different(Hsieh et al., 2007).
- ✚ Haiter-Neto F, Kurita LM, Menezes AV, and Casanova MS aim to evaluate and compare Greulich-Pyle (GP), Tanner-Whitehouse (TW3), and Eklöf and Ringertz (ER) methods of bone age estimation. 360 left-hand radiographs are collected from Brazilian children (180 boys and 180 girls) the age ranging 7-15 years. The analysis of this data showing the age calculated by Greulich-Pyle and Tanner-Whitehouse (TW3) methods are close to the chronological age, but that method of Eklöf and Ringertz (ER) seems to have the great variation with the chronological age(Haiter-Neto et al., 2006).
- ✚ Mentzel HJ, Vogt S, Vilser C, Schwartz T, Eulenstein M, Böttcher J, Tsoref L, Kauf E, and Kaiser WA. Used a different procedures the new sonographically method based on the Greulich-Pyle method to evaluate skeletal age,by consecutive 160 left-hand X-ray data collected (77 male and 83 female), at the same date and situation. Ultrasound examination was performed using the bone age system Sunlight Medical Ltd., Israel. Which evaluates the relationship between the velocity of the wave (speed of sound) passing through the distal

radial and ulnar epiphyses and growth, using gender- and ethnicity-based algorithms.). Three professional investigators (blinded to the chronological age) were invited to explore the X-ray and examine the skeletal age by using Greulich and Pyle Atlas (G and P). Results of the investigators and that of the Bone age system were performed using SPSS. Of 160 patients 152 performed successfully. The correlation between investigators using (GP) method was between 0.977 and 0.980, and the correlation between investigators and the Bone age system was between 0.902 and 0.920. The assumption of this study is there are Bone age device demonstrates the ability to produce a sufficient measure of bone age using an ultrasound (Mentzel et al., 2005).

✚ Yasemin Bilgili, MD, Selda Hizel, MD, Simay Altan Kara, MD, Cihat Sanli, MD, Haydar Hüseyin Erdal, MD, and Deniz Altinok, MD conduct a study at the American Institute of Ultrasound in Medicine study, which aimed to create ultrasonography version of Greulich-Pyle method for skeletal age estimation of children at a range of age 0-6years. Left hand-wrist radiographs and ultrasonographic images of ninety-seven child were processed for this study, both techniques of measurements applied and statistically compared based on Greulich-Pyle method. This study finds out 71.1% of males had the same age in both methods, and in 84.4% of patients, the difference was less than 6 months. In 65.5% of female patients, both methods revealed the same age, and in 88.5% of them, the difference was less than 6 months. This study concludes that the ultrasonographic version of (GP) can be applied without radiation hazard(Bilgili et al., 2003).

✚ On 2015 , the Journal of Pharmacy and Bioallied Sciences published study tested on Andhra children living in India by a total of 660 children (330 boys & 330 girls) age group between 9-20 years randomly selected from department of oral medicine in GITAM dental college, Andhra Pradesh. The Hand-wrist

radiographs assessed by Greulich and Pyle atlas for determination of skeletal age, this study results in underestimated SA ( $0.23 \pm 1.53$ ) years for boys and overestimated SA by ( $0.02 \pm 2$ ) for girls. This study concludes that G-P standards are reliable for bone age assessment among South Indian Andhra children of age 9-20 years (Gopalakrishnan, 2015).

# Chapter Three

## *Materials and Methods*



# CHAPTER THREE

## Material & Methods

### 3.1 Study design:

Comparative study, by conventional plain radiographs of the hands and wrists were obtained from people that fit the study criteria, and then we use indicators of skeletal maturity in children and adolescents. The purpose of this section is to describe which bones in the hand and wrist are the most suitable indicators of skeletal maturity during the different phases of child development. In the majority of healthy children, there are organized sequence of ossification for the carpal, metacarpal, phalangeal bones and distal epiphysis of radius and ulna. Overall, the first ossification center to appear in hand and wrist radiograph is the capitate, and the last is, most often, the sesamoid of the adductor pollicis of the thumb. The first epiphyseal center to appear is that of the distal radius, followed by those of the proximal phalanges, the metacarpals, the middle phalanges, the distal phalanges, and, finally, the ulna. There are, however, two main exceptions to this sequence: the epiphysis of the distal phalanx of the thumb commonly appears at the same time as the epiphyses of the metacarpals, and the epiphysis of the middle phalanx of the fifth finger is frequently the last to ossify. Since the predictive value of the ossification centers differs and changes during growth, the reviewer should primarily focus on the centers that best characterize skeletal development for the subject's chronological age.

### 3.2 Study area:

Data was collected from various hospitals in Khartoum province i.e. the data was gathered by random ways, the hospitals Included GafarIbn-

Auf Children's Hospital, Royal Care International Hospital and Military Hospital Helipad.

### **3.3 Study period:**

Two years from November 2015 to November 2017.

### **3.4 Study population:**

Images were obtained from children attend the emergency department or orthopedic outpatient department because of suspected trauma. The study group consisted of (76) children (41 male, 35 female).

### **3.5 Sample size:**

A total of 76 Sudanese children (41 male and 35 female) were collected randomly.

### **3.6 Criteria of sample selection:**

1. All the samples had documentary evidence of birth.
2. Chronological age of samples ranged from 3 months to age of 20 years.
3. They should be free from any physical disability involving hand-rest region, nutritional and endocrinal disorders at the time of radiography.

### **3.7 Study tool and technique:**

Data tables were formed in order to collect information from the Plain radiographs of the hands and wrists, hand X-rays were taken by using an X-ray generator machine which is a device used to generate X-rays. These devices are commonly used by radiographers to acquire an X-ray image from the object's inside (as in medicine or non-destructive testing) but they are also used in sterilization or fluorescence.

### **Steps of doing x-ray:**

A hand X-ray is a black and white image that shows the inner structures of hand, such as bones and soft tissues. This diagnostic tool can help for locate and understand injuries or degenerative diseases that affect investigated hand. Also hand X-rays used to monitor the growth of bone.

X-rays are taken using radiation. A technician in the radiology department at a hospital or another medical facility usually performs X-rays.

A standard posterior-anterior (PA) view Plain radiographs of the hand and wrist achieved great advancement for skeletal age assessment

### **Preparing for a hand X-Ray:**

Hand X-rays don't require special preparation. Remove wearing rings, bracelets, or a watch. This will make it easier for the technician to manipulate hand into the right position for your X-rays. It will also allow radiologist to read the X-rays without mistaking of bone fractures or deformity.

Technician must know if the sample is pregnant. There's a slight risk that radiation exposure could damage the fetus. As a precaution, women and children are usually draped with an apron lined with lead to protect their reproductive organs and developing fetuses.

### **Hand X-ray procedure:**

Patient was requested to place his/her hand on an examination table. Stay as still as possible while the X-rays are being taken. The X-ray technician may move patient's hand into different positions to take different images.

The X-rays themselves aren't painful. However, X-rays are used to diagnose conditions such as bone fractures, tumors, and arthritis. In some cases, these conditions can create pain during the X-ray procedure.

### **3.8 Statistical analysis:**

Statistical analysis performed by using programs (SPSS) statistical package for social Sciences, The chronological age and skeletal age were compared using the paired Student's t-test, unpaired Student's-test and Pearson correlation coefficient and Excel, after improving the images' resolution by Using paint and Microsoft office picture manager programs.

### **3.9 Difficulties:**

The study carried out randomly among children's in various geographical locations in the Sudan. The study will be conducted by conventional X-Ray was taken from subjects aged 3 months to 20 years of both sexes; images be made mostly from the emergency orthopedic pediatric outpatient departments.

It had been noticed that the filing and preservation of the data is poor and lacks documentation. Therefore in future studies it must be made sure that the data are properly preserved and documented.

# *Chapter Four*

## *Results*

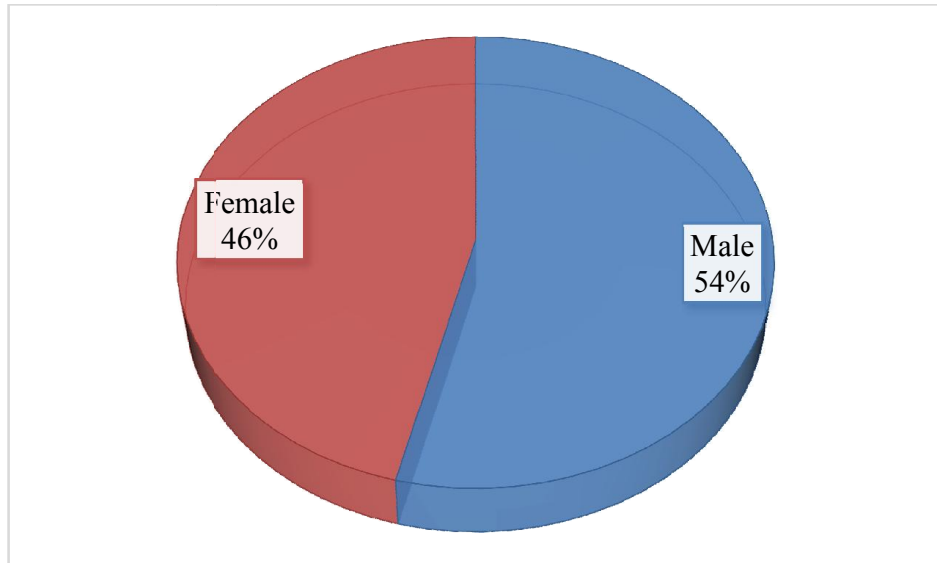
## CHAPTER FOUR

### Results:

The study comprised a total of seventy six person, 41 males and 35 females in the age group of 3-240 months. Skeletal age estimation was done using Greulich-Pyle method .The following are the results obtained:

**Table (4.1): Distribution of sample study according to gender**

<b>Gender</b>	<b>Frequency</b>	<b>Percent</b>
<b>Male</b>	41	53.9 %
<b>Female</b>	35	46.1%
<b>Total</b>	76	100.0%



**Figure [4.1]: Distribution of sample study according to gender**

**Table (4.2): Correlation between chronological age, skeletal age**

<b>Pearson's correlation</b>		<b>Skeletal Age In Months</b>	<b>Inference</b>
<b>Chronological Age in Months</b>	<b>Correlation Coefficient</b>	0.849	Very highly significant
	<b>P-value</b>	0.000	

Pearson's correlation coefficients were used to measure the association between the chronological age and skeletal age. Chronological age was found to be strongly positively correlated to skeletal age and found to be statistically significant (P-value < 0.01), and correlation coefficient of 0.849. Table (2).



**Table (4.3): Mean chronological age and skeletal age**

	Mean $\pm$ SD	Mean Difference	P-value	95% Confidence Interval of the Difference		Inference
				Lower	Upper	
<b>Chronological Age in Months</b>	109.5 $\pm$ 71.2	17.8	0.000	9.1	26.4	Very highly significant
<b>Skeletal Age In Months</b>	91.8 $\pm$ 64.2					

Paired Student's t-test was used to measure the difference between mean of chronological age and skeletal age, the mean chronological ages and skeletal age of samples were determined as 109.5  $\pm$  71.2 month and 91.8  $\pm$  64.2 month, respectively.

The mean difference between chronological age and skeletal age were 17.8 month, i.e., skeletal age was lower compared to chronological age by 17.8 month, and this difference is very highly significant (P-value < 0.01), we 95% confident this difference lies between (9.1, 26.4) month. Table (3)

**Table (4.4): Mean chronological age and skeletal age of males and females**

<b>Sex</b>		<b>Mean ± Std.D</b>
<b>Chronological Age in Months</b>	<b>Male</b>	116.4 ± 75.9
	<b>Female</b>	101.4±65.4
<b>Skeletal Age In Months</b>	<b>Male</b>	95.5±68.3
	<b>Female</b>	87.3±59.7

The mean chronological ages of male and female samples were determined as  $116.4 \pm 75.9$  month and  $101.4 \pm 65.4$  month, respectively, and the mean skeletal ages of male and female samples were determined as  $95.5 \pm 68.3$  month and  $87.3 \pm 59.7$  month, respectively.

**Table (4.5): Comparison of chronological age and skeletal age in gender**

	Mean Difference	P-value	95% Confidence Interval of the Difference		Inference
			Lower	Upper	
<b>Chronological Age in Months</b>	15.1	0.361	-17.6	47.8	Not significant
<b>Skeletal Age In Months</b>	8.2	0.581	-21.3	37.8	Not significant

By comparing chronological age, and skeletal age, the following was observed:

The mean difference in chronological age between males and females were 15.1 month, i.e., females was reduced compared to males by 15.1 month, and this difference is not significant (P-value = 0.361). Table (5).

The mean difference in skeletal age between males and females were 8.2 month, i.e., females was reduced compared to males by 8.2 month, and this difference is not significant (P-value = 0.581). Table (5).

**Table (4.6): Difference mean between mean chronological age and skeletal age of males and females**

Sex		Chronological Age in Months&Skeletal Age In Months	P-value
Male	Mean ± SD	20.9 ± 45.0	0.005
Female	Mean ± SD	14.1 ± 27.2	0.004

The mean difference in chronological age between and skeletal age in males were  $20.9 \pm 45.0$  month, i.e., skeletal age was reduced compared to chronological age by 20.9 month in males, and this difference is significant (P-value = 0.005).Table (6).

The mean difference in chronological age between and skeletal age in females were  $14.1 \pm 27.2$  month, i.e., skeletal age was reduced compared to chronological age by 14.1 month in females, and this difference is significant (P-value = 0.004).Table (6).

# *Chapter Five*

*Discussion*

*Conclusion*

*Recommendations*

## CHAPTER FIVE

### 5.1 Discussion

Bone age assessment is important to evaluate whether the growth of Sudanese children and young adult are normal or not according to international data. This procedure is used widely in pediatric endocrinology and forensic medicine departments. The most common method used in bone age estimation is Greulich-Pyle atlas of bone age estimation. The atlas is made of standard PA left hand and wrist radiographs of individuals at different stages of skeletal maturation. This study was carried out randomly among children and young adults in various geographical locations in the Sudan .Moreover the dates of births are poorly documented in Sudan, especially in rural areas. However, assessment of BA is very important in identifying criminal and legal responsibility and for social events. Therefore, this study investigated the reliability of the GP method for Sudanese children and youth. In a previous study in Sudan,(H. Karrar Alsharif et al., 2014),which investigated the reliability of the GP atlas method in infants and toddlers and reported that the mean BA was less by 2 to 4 months in comparison to Caucasians. It also reported that the sex differences did not exist. Those results did not match with current study results. This might be due to poor sample size in that study. In this study the total mean difference between CA and SA in males were  $20.9 \pm 45.0$  month,

i.e., skeletal age was less when compared to chronological age by 20.9 month in males, and this difference is significant (P-value = 0.005), and the total mean difference between CA and SA in females were  $14.1 \pm 27.2$  month, i.e., skeletal age was less when compared to chronological age by 14.1 month in females, and this difference is significant (P-value = 0.004).

## **5.2 Conclusion**

The results of this study concluded that the (GP method) standard established by Greulich-Pyle was not applicable in Sudanese children and young adults. The differences of bone age growth in Sudanese was significantly less in comparison to Caucasians, This might be due to genetical, racial, socioeconomical reasons and the difference in diet and atmosphere between the two locations.



### **5.3 Recommendations**

From this study, it was recommend that:

1. In the future research the samples should be collected from different areas of the Sudan to cover different races, tribes and areas. This will enable to draw an atlas for Sudanese children and young adults bone growth development.
2. Further researches which explain the causes of the differences between the Sudanese and Caucasians children.
3. Establishment of Sudanese standard of bone age computer software assistant sequences of hand bone development (including distal radius & ulna) in Sudanese.
4. Further studies to evaluate constitutional delay among Sudanese children and young adults
5. Documentation of X-ray data to facilitate such researches.

# *Chapter Six*

*References*

## CHAPTER SIX

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