Sudan University of Science and Technology

Collage of Graduate Studies

Estimation of Gestational Age using Humeral Length in Ultrasonography

تقدير عمر الجنين بطول عظم العضد باستخدام التصوير بالموجات فوق الصوتية

Thesis Submitted for Partial Fulfillment for the Requirements of M.sc Degree in Medical Diagnostic Ultrasound

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2019

الآيـة

قال الله تعالى :

﴿ثُمَّ خَلَقْنَا النُّطْفَةَ عَلَقَةً فَخَلَقْنَا الْعَلَقَةَ مُضْغَةً فَخَلَقْنَا الْمُضْغَةَ عِظَامًا فَكَسَوْنَا الْعِظَامَ لَحْمًا ثُمَّ أَنشَأْنَاهُ خَلْقًا آخَرَ ۚ فَتَبَارَكَ اللَّهُ أَحْسَنُ الْخَالِقِينَ﴾

صدق الله العظيم

سورة المؤمنون الآية (14)

Dedication

Many thanks to my greatest parents for their helps and support in my scientific career and to my mother, brother and sister.

Acknowledgement

My gratefulness to my supervisor Dr. Bakier Abdelwahab for his great effort in the advising and correcting me during this research.

Special acknowledgement to the ultrasound department of Omdurman Maternity hospital and Altohami medical Center for giving me a chance to collect the research data.

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Abbreviations	Meaning
AC	Abdominal circumference
ADD	Actual date of delivery
BPD	Biparietal diameter
CRL	Crown rump length
EDD	Expected date of delivery
FL	Femur length
GA	Gestational age
HC	Had circumference
HL	Humeral length
IUGR	Intrauterine growth retardation
IVF	In vitro fertilization
LFD	Large for date
LMP	Last menstrual period
SD	Standard deviation
SFD	Small for date
MHz	Mega hertz
U.S	Ultrasound

Abstract

This is a descriptive, cross sectional study was carried out on ultrasound department in the Omdurman maternity hospital, the main problem for this research is an accurate measurement of gestational age in third trimester , the study aim to assess the reliability of humeral length and the femur length in predicating gestational age and prediction of menstrual age. 50 healthy pregnant women were enrolled in the study; their age ranged 18-35 year is a safe period for the pregnancy, delivery and have less chance of congenital anomalies. Ultrasound devices with option of measuring humeral length were used.

The result revealed that there was no significant difference between gestational age obtained with femur length and that obtained with humeral length. Furthermore, a significant correlation was noticed between gestational age and HL, this correlation also seen between FL and gestational age.

The ultrasound plays a great role to assess fetal bone biometrics as it is sensitive and accurate. The study concluded that both femoral and humeral length s were similar and reliable to estimate the gestational age.

The study recommended that the humeral length must be used as routine measurement in calculation the gestational age in the third trimester .

ملخص الدراسة

هذه دراسة وصفية مقطعية ، تم عملها في قسم الموجات الصوتية بمستشفى أم درمان لأمراض النساء والتوليد ومركز التهامي الطبي (المهندسين) هدف هذه الدراسة دقة قياس عمر الجنين باستخدام طول عظم العضد مقارنةبعمر الجنين باستخدام طول عظم الفخذ وعمر الجنين بزمن الدورة الشهرية ، المواصفات التي تم عليها تحديد النساء الحوامل لتشملهم الدراسة ، هي أن يكون عمر المرأة ما بين 18 – 35 سنة وهو العمر المناسب للحمل السليم ، والولادة الآمنة ، واقل احتمالية للإصابات بالتشوهات الخلقية للجنين ، الصفة الثانية هي ان تكون السيدة الحامل معافاة لا تشكو من أي امراض وان يكون الجنين واحد داخل الرحم وسليم ليس لديه تشوهات خلقية ، الصفة الثالثة هي أن تكون السيدة في الشهر الرابع حتى التاسع ، تم إستخدام اجهزة موجات فوق صوتية بها خاصية تحديد عمر الجنين باستخدام طول عظم العضد بالجنين ، عينة البحث هي خمسين سيدة حامل حضرت الى قسم الموجات الصوتية بمركز التهامي الطبي المهندسين ومستشفى الولادة أم درمان ثم تم تحليل البيانات بواسطة برنامج التحليل الاحصائي ، نتيجة البحث هي انه لم يوجد فرق بين عمر الجنين المأخوذ بواسطة طول عظم العضد وطول عظم الفخذ.

Chapter One
Introduction

1-1 Introduction:

Obstetric ultrasound introduced since 1950, obstetric ultrasound has evolved into a major specialty of sonography. Ultrasound is safe non ionizing easy operative relatively inexpensive techniques painless procedure that offers invaluable information to the obstetrician, The use of ultrasound in pregnancy greatly increase in the last 10 years at present 40 to 60 percent of pregnancy are evaluated by ultrasound. Current technology offers complete assessment of the fetus with high resolution images sophisticated measurements and computations, and the ability to analyzed fetal hemodynamic (Donofrio, et. al., 2014).

In the past gestational age was established by a combination of the historical information and the physical examination. Reliance was placed on the menstrual history and the maternal sensation of fetal movement ("quickening"). Other factors include assessment of uterine size by bimanual examination in the first trimester, initial detection of fetal heart tones by Doppler (10–12 weeks) or auscultation (19–21 weeks), and uterine fundal height measurement. However, both the history and the findings on physical examination are fraught with error, even in the best of circumstances, It has been estimated that 20% to 40% of women cannot relate the LMP with certainty.6,7 Some of the reasons for this uncertainty include oligomenorrhea, metrorrhagia, bleeding in the first trimester of pregnancy, pregnancy following use of oral contraceptives or intrauterine devices, and becoming pregnant in the postpartum period. Hertz and co- workers9 reported that menstrual history was considered reliable in only 18% of women. In another report, even among women with known LMP, neonatal age assessment differed markedly from that assigned by certain menstrual dates in

15%.8 Physical examination also tends to be inaccurate, especially with advancing gestational age.10 Bimanual examination in the first trimester may be accurate within ±2 weeks; however, fundal height measurement, which is more commonly used to assess gestational age, is only accurate within ±4 to 6 weeks.

Clearly, the inaccuracies of history and physical examination may limit their usefulness in assessment of gestational age. Methods that assess the time of ovulation or conception can accurately establish gestational age.

Timed ovulation, either by basal body temperature recording or semi quantitative assessment of luteinizing hormone surge, predicts gestational age within ±4 to 6 days. Ovulation induction with agents such as clomiphene citrate and Personal, also accurately predicts gestational age. In vitro fertilization, with known date of conception, is likely the most accurate means of predicting gestational age (±1 day). However, in most pregnancies, the date of ovulation or conception cannot be as accurately predicted as outlined above and gestational age must be established by other methods.

a real time scanner using endovaginally in first 5 weeks of gestation or transabdominally is used. Normal pregnancy 40 weeks divided to first trimester 13weeks diagnosed by yolk sac gestational sac and crown rump length at least 7weeks or 10mm should be determine the gestational age which is an accurate indicator of fetal age fetal cardiac activity start 6weeks vaginally 7weeks transabdominally, after 13weeks CRL un reliable because of spine affect flexibility so biparietal dimeter is accurate up to 24weeks, second trimester 14weeks to 27weeks the standard level of measuring biparietal diameter (BPD), is include cavil septum pellucidum and thalami head circumference is the same level but is accurate till delivery associated with abdominal circumference (AC) which is detected by junction of the umbilical vein and portal sinus AC may allow detection of growth retardation and macrosomia when compared with BPD. After

24weeks estimation of fetal age is accurate by fetal limb femur length (FL), humeral length (HL), tibia, and ulna length, the estimation of fetal age at the second trimester is more accurate it is prediction approximatly7 Days before 20weeks and 10 days after 20 weeks and 21 Days in 3rd trimester femur length is very useful biometric parameters in the second and third trimester of pregnancy it grows linear throughout an is best measured after 14weeks of gestation (Mukherjee, 2014).

The FL measured at the long axis of femoral shaft when the ultrasound beam is perpendicular to the shaft these parameters are help full in the estimation of fetal age in patients whose fundal height on abdominal examination does not corresponding to the last menstrual period (LMP).The fetal humeral length is not widely used as biometric parameters for determination the gestational age also it easy to be imaged with ultrasound and measured (Donofrio, et. al., 2014).

The study aim to clarify the role of humeral length in determining gestational age with comparison with FL and HL may be useful when BPD unreliable or abnormal to be used in BPD: FL ratio, and BPD: HL ratio as categorical variable in Down syndrome or as comparison with HC and AC in Achondroplasia. A few studies were done in Sudan concerning the estimation of GA using fetal humeral length HL.

This research is conducted to introduce a new way in measuring the gestational age in the third trimester using the humors length, by the proving the accuracy by comparing the obtained gestational age by that which obtained from the femur length. The benefit of this option is its use at when the fetal position is unreliable for easiest way to measure the femur length so instead we use the length of humerus.

1-2: Problem of the study:

The main problems deliver from an inaccurate measurement of biparietal diameter after 24 weeks and femur length (FL) due to combination of fetal movement and delay use of freeze button, as well as an abnormal fetal presentation can affect measuring the gestational age by using the .

1-3: Objectives:

1-3-1 General objective:

To estimate of gestational age using humeral length in ultrasonography

1-3-2 Specific objective:

- To estimate the accurate measurement in the third trimester using humeral length and femoral length.
- To assess gestational age correlated to HL and FL.

Chapter Two
Literature Reviews

2-1: Anatomy:

2-1-1: anatomy of Humerus:

The humerus articulates with the scapula at the shoulder joint and with the radius and ulna at the elbow joint. The upper end of the humerus has a head, which forms about one third of a sphere and articulates with the glenoid cavity of the scapula. Immediately below the head is the anatomic neck. Below the neck are the greater and lesser tuberosities, separated from each other by the bicipital groove. Where the upper end of the humerus joins the shaft is a narrow surgical neck. About halfway down the lateral aspect of the shaft is a roughened elevation called the deltoid tuberosity. Behind and below the tuberosity is a spiral groove, which accommodates the radial nerve .The lower end of the humerus possesses the medial and lateral epicondyles for the attachment of muscles and ligaments, the rounded capitulum for articulation with the head of the radius, and the pulley-shaped trochlea for articulation with the trochlear notch of the ulna. Above the capitulum is the radial fossa, which receives the head of the radius when the elbow is flexed. Above the trochlea anteriorly is the coronoid fossa, which during the same movement receives the coronoid process of the ulna. Above the trochlea posteriorly is the olecranon fossa, which receives the olecranon process of the ulna when the elbow joint is extended (Kijowski, et. al., 2004).

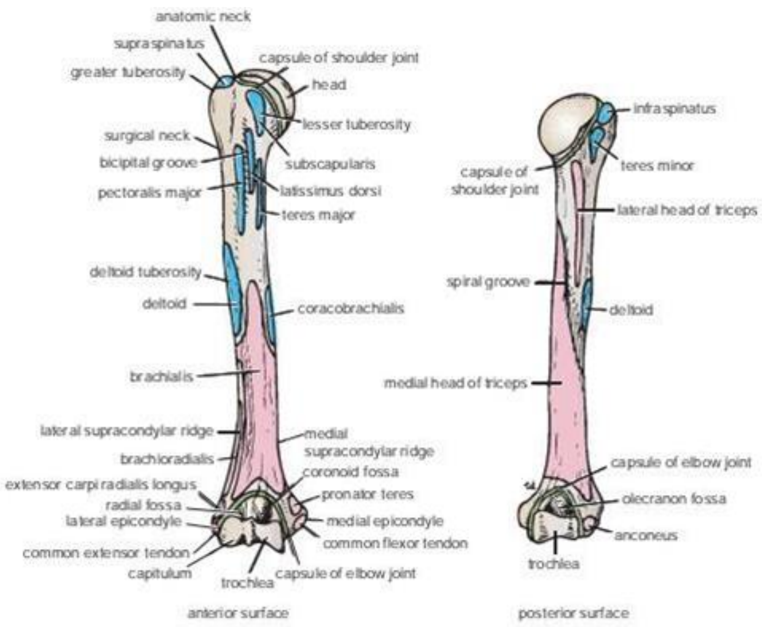

Figure (2. 1) Show the anatomy of humerus, with presentation of muscle attachment and insertion (Kijowski, et. al., 2004).

2-1-2: Anatomy of the Femur:

The femur articulates above with the acetabulum to form the hip joint and below with the tibia and the patella to form the knee joint. The upper end of the femur has a head, a neck, and greater and lesser trochanters. The head forms about two thirds of a sphere and articulates with the acetabulum of the hip bone to form the hip joint. In the center of the head is a small depression, called the fovea capitis, for the attachment of the ligament of the head. Part of the blood supply to the head of the femur from the obturator artery is conveyed along this ligament and enters the bone at the fovea. The neck, which connects the head to the shaft, passes downward, backward, and laterally and makes an angle of about 125° (slightly less in the female) with the long axis of the shaft. The size of this angle can be altered by disease. The greater and lesser trochanters are large eminences situated at the junction of the neck and the shaft. Connecting the two trochanters are the inter trochanteric line anteriorly, where the iliofemoral ligament is attached, and a prominent intertrochanteric crest posteriorly, on which is the quadrate tubercle .The shaft of the femur is smooth and rounded on its anterior surface but posteriorly has a ridge, the linea aspera, to which are attached muscles and intramuscular septa. The margins of the linea aspera diverge above and below. The medial margin continues below as the medial supracondylar ridge to the adductor tubercle on the medial condyle. The lateral margin becomes continuous below with the lateral supracondylar ridge. On the posterior surface of the shaft below the greater trochanter is the gluteal tuberosity for the attachment of the gluteus maximus muscle. The shaft becomes broader toward its distal end and forms a flat, triangular area on its posterior surface called the popliteal surface. The lower end of the femur has lateral and medial condyles, separated posteriorly by the intercondylar notch. The anterior surfaces of the condyles are joined by an articular surface for the patella. The two condyles take part in the formation of the knee joint. Above the condyles are the medial and lateral epicondyles. The adductor tubercle is continuous with the medial epicondyle (Kijowski, et. al., 2004).

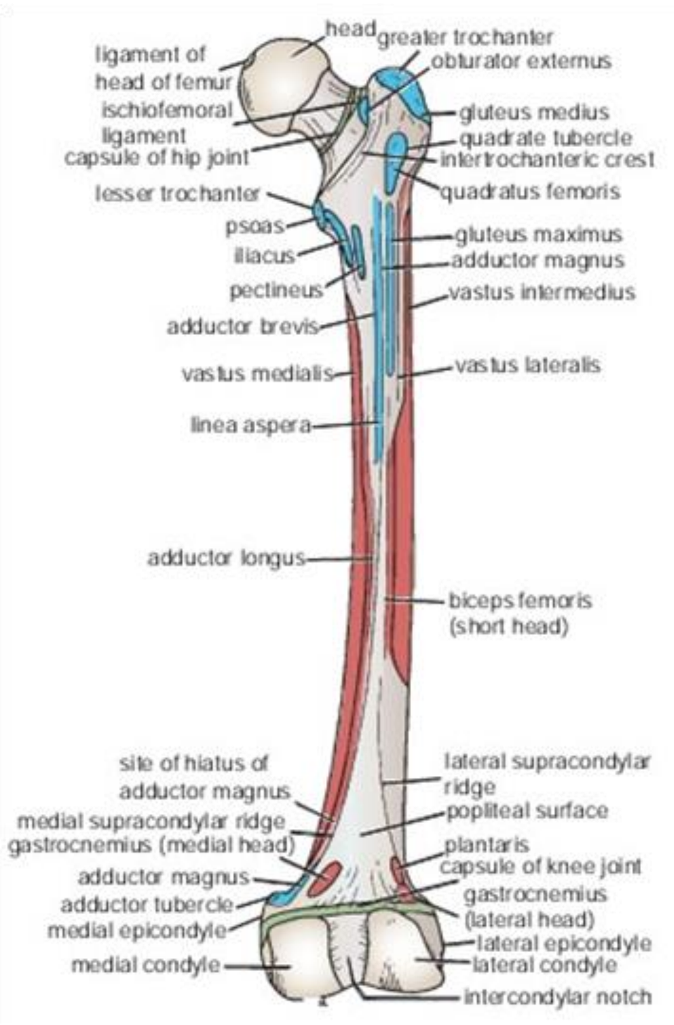

Figure (2. 2) Show the anatomy of femur, with presentation of muscle attachment and insertion (Kijowski, et. al., 2004).

2-2 Emberology:

2-2-1 limb growth and development:

The limbs, including the shoulder and pelvic girdles, comprise the appendicular skeleton. At the end of the fourth week of development, limb buds become visible as outpocketings from the ventrolateral body wall. The fore-limb appears first followed by the hind limb 1 to 2 days later. Initially, the limb buds consist of a mesenchymal core derived from the parietal (somatic) layer of lateral plate mesoderm that will form the bones and connective tissues of the limb, covered by a layer of cuboidal ectoderm. Ectoderm at the distal border of the limb thickens and forms the apical ectodermal ridge (AER). This ridge exerts an inductive influence on adjacent mesenchyme, causing it to remain as a population of undifferentiated, rapidly proliferating cells, and the progress zone. As the limb grows, cells farther from the influence of the AER begin to differentiate into cartilage and muscle. In this manner, development of the limb proceeds proximodistally.

By the sixth week of development, the first hyaline cartilage models, foreshadowing the bones of the extremities, are formed by these chondrocytes. Joints are formed in the cartilaginous condensations when chondrogenesis is arrested, and a joint interzone is induced. Cells in this region increase in number and density, and then a joint cavity is formed by cell death. Surrounding cells differentiate into a joint capsule. Factors regulating the positioning of joints are not clear, but the secreted molecule WNT14 appears to be the inductive signal. Ossification of the bones of the extremities, endochondral ossification, begins by the end of the embryonic period. Primary ossification centers are present in all long bones of the limbs by the 12th week of development. From the primary center in the shaft or diaphysis of the bone, endochondral ossification gradually progresses toward the ends of the cartilaginous model. At birth, the diaphysis of the bone is usually completely ossified, but the two ends, the epiphyses, are still cartilaginous. Shortly thereafter, however, ossification centers arise in the epiphyses. Temporarily, a cartilage plate remains between the diaphyseal and epiphyseal ossification centers. This plate, the epiphyseal plate, plays an important role in growth in the length of the bones. Endochondral ossification proceeds on both sides of the plate. When the bone has acquired its full length, the epiphyseal plates disappear, and the epiphyses unite with the shaft of the bone. In long bones, an epiphyseal plate is found on each extremity; in smaller bones, such as the phalanges, it is found only at one extremity; and in irregular bones, such as the vertebrae, one or more primary centers of ossification and usually several secondary centers are present. Synovial joints between bones begin to form at the same time that mesenchymal condensations initiate the process of forming cartilage.Thus, in the region between two chondrifying bone primordia, called the interzone (for example between the tibia and femur at the knee joint), the condensed mesenchyme differentiates into dense fibrous tissue. This fibrous tissue then forms articular cartilage, covering the ends of the two adjacent bones; the synovial membranes; and the menisci and ligaments within the joint capsule (e.g., the anterior and posterior cruciate ligaments in the knee). The joint capsule itself is derived from mesenchyme cells surrounding the interzone region. Fibrous joints (e.g., the sutures in the skull) also form from interzone regions, but in this case the interzone remains as a dense fibrous structure (Mohammed, A., 2019).

2-3: Congenital anomalies of the fetal bones:

Congenital bone disorders are a heterogeneous group of disorders primarily affecting the growth and development of the musculoskeletal system. There are three major categories. The skeletal dysplasias are developmental disorders of chondro-osseous tissue caused by single gene disorders with prenatal and postnatal manifestations. thedysostoses are single-gene disorders resulting in mal formations of individual bones caused by transient abnormalities of signaling factors. Disruptions are morphologic defects of an organ or larger region resulting from extrinsic breakdown or interference with an originally normal developmental process.The prevalence of skeletal dysplasias, also called osteochondro-dysplasias, diagnosed prenatally or during the neonatal period, excluding limb amputations, is 2.4 to 4.5 per 10,000 births.

Nonetheless, the majority of lethal skeletal dysplasias, including thanatophoric dysplasia, a chondrogenesis, and osteogenesis imperfect (OI), type II, can be diagnosed solely on the basis of prenatal ultrasound. Lethal skeletal dysplasias were identified correctly by prenatal ultrasound; however, only 13 of 27 (48%) received an accurate specific antenatal diagnosis (Wyatt-Ashmead, J., 2014).

2-3-1 lethal skeletal dysplasia:

The lethal skeletal dysplasias are characterized by severe micromelia and small thoracic circumference with pulmonary hypoplasia.The most important determinant of lethality is the presence and degree of pulmonary hypoplasia. The three most common lethal skeletal dysplasias are thanatophoric dysplasia; achondrogenesis, and osteogenesisimperfecta type II, overall accounting for 40% to 60% of all lethal skeletal dysplasias (Wyatt-Ashmead, J., 2014).

2-3-1-1Thanatophoric Dysplasia:

Thanatophoric dysplasia is the most common lethal skeletal dysplasia, with a prevalence of 0.24 to 0.69 per10,000 births. The key features are severe micro melia with rhizo melic predominance and macrocrania (disproportionately large head) in association with decreased thoracic circumference but a normal trunk length. Mineralization is normal, with no fractures present. Typically, the extremities are so foreshortened that they protrude at right angles to the body. The skin folds are thickened and redundant secondary to a relatively greater rate of growth of the skin and subcutaneous layers than the bones. Clinical presentation is usually caused by large-for-date measurements secondary to poly hydramnios (Wyatt-Ashmead, J., 2014).

2-3-1-2: Thanatophoric dysplasia:

Thanatophoric dysplasia has many phenotypic similarities to homozygous achondroplasia. Both conditions may appear identical from ultrasound and radiographic perspectives. They can be distinguished by the positive family history, in which both parents are affected with the heterozygous form of achondroplasia (Wyatt-Ashmead, J., 2014).

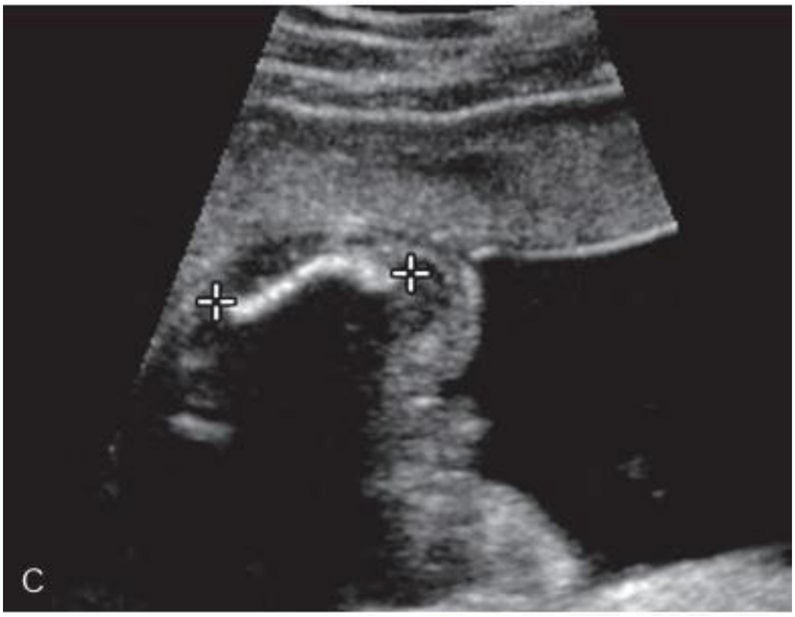

Figure (2. 3) Thanatophoric dysplasia at 22 weeks, curved femur (Wyatt-Ashmead, J., 2014).

2-3-1-3 Platyspondyly:

Platyspondyly, or flattened vertebral bodies, is one of the most characteristic features on AP radiographs of a thanatophoric dwarf. There is a U or H configuration of the vertebral bodies and a relatively increased height of the disc spaces. Platyspondyly appears on ultrasound as a wafer-thin vertebral body with a relatively larger, hypo echoic disc space on either side of the vertebral body (Wyatt-Ashmead, J., 2014).

2-3-1-4: Achondrogenesis:

Achondrogenesis is the second most common lethal skeletal dysplasia, with a prevalence of 0.09 to 0.23 per10,000 births. It is a phenotypically and genetically diverse group of chondrodysplasias characterized by severe micromelia, macrocranium, decreased thoracic circumference and trunk length, and decreased mineralization (Wyatt-Ashmead, J., 2014).

2-3-1-5 Osteogenesis Imperfecta (OI):

Osteogenesis imperfecta is a clinically and genetically heterogeneous group of collagen disorders characterized by brittle bones resulting in fractures. The incidence is1: 60,000 births. Until recently there were four types of OI, all with an autosomal dominant mode of inheritance and associated with mutations in the COL1A1 orCOL1A2 genes. In the past several years a few more conditions that can be categorized phenotypically into one of the four categories, but of a different etiologies and some with autosomal recessive modes of inheritance, have been detected (Wyatt-Ashmead, J., 2014).

2-3-1-6 Hypophosphatasia:

Hypophosphatasia congenita, the lethal neonatal form of hypophosphatasia, is an autosomal recessive skeletal dysplasia caused by a deficiency of tissue-nonspecific alkaline phosphatase. Frequency of hypo phosphatasiacongenita is approximately 1 in 100,000 births. The key features are severe micromelia, decreased thoracic circumference with normal trunk length, and decreased mineralization with occasional fractures. Cranial vault size remains normal. The demineralized long bones may be bowed with occasional angulations caused by fractures. The bones appear thin and delicate and may appear entirely absent (Wyatt-Ashmead, J., 2014).

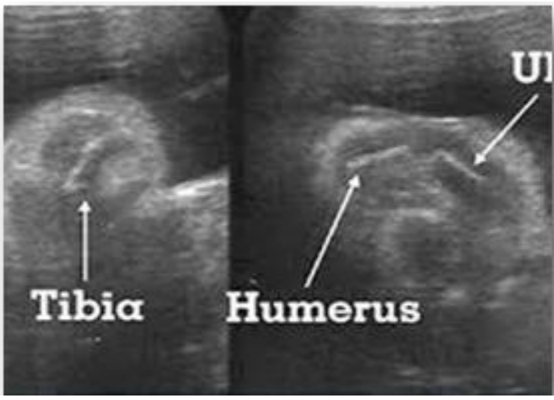

Figure (2. 4) Hypophophatasia at 20 weeks

2-3-1-7 Campomelic Dysplasia:

Campomelic dysplasia, or bent-limb dysplasia, is a rare autosomal-dominant condition that usually results from a new dominant mutation in the SOX9 gene (sex-determining protein homeobox 9 mapped to 17q24.3). The incidence is 0.5 to 1.0 per 100,000 births. Most cases are lethal because of respiratory insufficiency from laryngotracheomalacia in combination with a mildly narrowed thorax.The characteristic skeletal features of campomelicdys-plasia are a short and ventrally bowed tibia and femur, a hypoplastic or absent fibula, talipesequinovarus (club-foot), and hypoplastic scapulae (Wyatt-Ashmead, J., 2014).

Figure (2. 5) Bowing of femur at 30 weeks (Wyatt-Ashmead, J., 2014).

2-3-1-8: Short-Rib Polydactyly Syndromes:

Short-rib polydactylydysplasias are a heterogeneousgroup of rare and lethal skeletal dysplasias with an autosomal recessive mode of inheritance. All forms are characterized by severe micromelia and decreased thoracic circumference. The cranial vault measurements and bone mineralization are normal. Polydactyl, cardiac, and genitourinary abnormalities are found in most cases (Wyatt-Ashmead, J., 2014).

Figure (2. 6) polydactyl syndrome**.** http://www.google com

2-3-1-9: Fibrochondrogenesis:

Fibrochondrogenesisis a rare, lethal, autosomal recessive rhizomelicchondrodysplasia. The typical features include narrow chest (short ribs with cupping), short long bones with irregular metaphyses with peripheral spurs, and extra-articular calcifications giving the appearance of stippling, platyspondyly with decreased ossification (particularly cervical vertebrae), and vertebral midline clefts. Other features include flat facies and cleft palate (Wyatt-Ashmead, J., 2014).

2-3-2 Nonlethal skeletal dysplasia:

2-3-2-1 Heterozygous Achondroplasia:

Heterozygous achondroplasia is the most common nonlethal skeletal dysplasia. About 80% of cases are the result of a spontaneous dominant mutation associated with advanced paternal age, and the remainder is inherited from parental heterozygous achondroplasia. The incidence is approximately 1 in 26,000 births. Previously considered a diagnosis of the third trimester, recent studies have shown that a second trimester diagnosis is possible (Wyatt-Ashmead, J., 2014).

2-3-2-2 Diastrophic Dysplasia:

Diastrophic dysplasia is an autosomal recessive disorder with variable expression and a predominantly rhizomelicform of micromelia. The term diastrophic implies "twisted,'' which reflects the multiple postural deformities, dislocations, joint contractures, and kyphoscoliosis present. The most characteristic feature is the “hitch-hiker thumb’’ caused by a lateral positioning of the thumb in association with a hypoplastic first metacarpal (Wyatt-Ashmead, J., 2014).

2-3-2-3 Asphyxiating Thoracic Dysplasia:

Asphyxiating Thoracic Dysplasia, or Jeune syndrome, is an autosomal recessive disorder with variable expressivity. The incidence is 1 in 70,000 to 130,000 births. The perinatal mortality is high as a result of pulmonary hypo-plasia. Those who survive may develop renal and hepatic fibrosis. The key features are a mild to moderate form of micromelia (60%) with rhizomelic predominance, a long narrow thorax with short horizontal ribs, inverted “handlebar” appearance of the clavicles, renal dysplasia and cysts, and postaxial polydactyly in 14% (Wyatt-Ashmead, J., 2014).

2-3-2-4 Ellis–van Creveld Syndrome:

Ellis–van Creveld syndrome, or chondroectodermal dysplasia, is an autosomal recessive disorder with an incidence of 1 per 150,000 births. The condition has a high prevalence among inbred populations, such as the Amish and the Arabs of the Gaza strip.It is generally a nonlethal disorder, but death can result from pulmonary hypoplasia. Key features include mild to moderate form of micromelia with a mesomelic predominance, short horizontal ribs, postaxial or ulnar polydactyly that is almost 100% in the hands and 25% in the feet,and CHD (50%), most often atrial septal defect (Wyatt-Ashmead, J., 2014).

2-3-2-5 ChondrodysplasiaPunctata:

Chondrodysplasiapunctata, or stippled epiphyses, is a heterogeneous group of disorders with many small calcifications (ossification centers) in the cartilage, in the ends of bones, and around the spine. Known associated conditions include single -gene disorders such as rhizomelic chondrodysplasiapunctata, ConradiHünermann syndrome, and Zellweger syndrome (cerebrohepatorenal syndrome); chromosomal abnormalities such as trisomy 21 and 18; maternal autoimmune diseases; and teratogen exposure (e.g., warfarin, alcohol) (Wyatt-Ashmead, J., 2014).

2-3-2-6 Dyssegmental Dysplasia:

Dyssegmental dysplasia is a rare autosomal recessive skeletal dysplasia characterized by gross vertebral disorganization. The findings typically include micromelia, short narrow thorax, joint rigidity, anisospondyly (gross irregularity of the size and shape of the vertebral bodies) which may include malsegmentation, clefting or "over-size" bodies, kyphoscoliosis, and multiple ossification centers (Wyatt-Ashmead, J., 2014).

2-3-2-7 Osteogenesis Imperfecta (OI) Types I, III, IV-Nonlethal Types:

2-3-2-7-1Osteogenesis imperfecta type I:

Is a mild, "tarda'' variant inherited in an autosomal dominant manner as a result of mutation in the COL1A1 (on chromosome 17) or COL1A2 (on chromosome 7) and possibly in other collagen genes. OI type I is a generalized connective tissue disorder characterized by bone fragility and blue sclerae. The bones are of normal length, and only 5% present at birth with fractures. Most fractures occur from child-hood to puberty. There is progressive hearing loss in approximately 50% of type I cases (Wyatt-Ashmead, J., 2014).

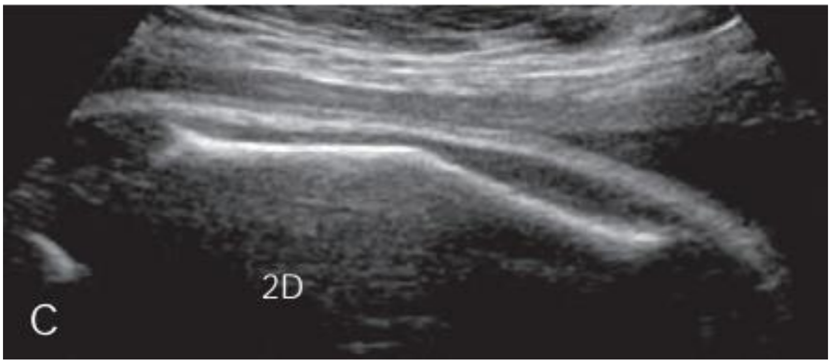

Figure (2. 7) Type I. Nonlethal variant of OI with a mildly angulated femur of normal length. (Wyatt-Ashmead, J., 2014).

2-3-2-7-2 Osteogenesis imperfecta Type III:

Has a heterogeneous mode of inheritance. This is a nonlethal, progressively deforming variety of OI that often spares the humeri, vertebrae, and pelvis. Rib involvement is variable. The blue sclerae will normalize, and there is no associated hearing impairment (Wyatt-Ashmead, J., 2014).

2-3-2-7-2 Osteogenesis imperfecta Type IV:

Is an autosomal dominant form of OI. It is the mildest form, involving isolated fractures. The sclera is blue at birth but normalize over time. There is no associated hearing impairment (Wyatt-Ashmead, J., 2014).

2-3-2-7-3Down syndrome:

Down syndrome (DS or DNS, known as Down's syndrome in the UK), also known as trisomy 21, is a genetic disorder caused by the presence of all, or part of a third copy of chromosome 21. It is typically associated with physical growth delays, characteristic facial features, and mild to moderate intellectual disability. The average IQ of a young adult with Down syndrome is 50, equivalent to the mental age of an 8- or 9-year-old child, but this can vary widely.

2-4 Physiology:

2-4-1 Deposition and Absorption of Bone-Remodeling of Bone:

Deposition of Bone by the Osteoblasts. Bone is continually being deposited by osteoblasts, and it is continually being absorbed where osteoclasts are active. Osteoblasts are found on the outer surfaces of the bones and in the bone cavities. A small amount of osteoblastic activity occurs continually in all living bones (on about 4 per cent of all surfaces at any given time in an adult), so that at least some new bone is being formed constantly (Rodan, G.A., 2003).

2-4-2 Absorption of Bone-Function of the Osteoclasts:

Bone is also being continually absorbed in the presence of osteoclasts, which are large phagocytic, multinucleated cells (as many as 50 nuclei), derivatives of monocytes ormonocyte-like cells formed in the bone marrow. The osteoclasts are normally active on less than 1 per cent of the bone surfaces of an adult. Later in the chapter we see that PTH controls the bone absorptive activity of osteoclasts. Histologically, bone absorption occurs immediately adjacent to the osteoclasts. The mechanism of this absorption is believed to be the following: The osteoclasts send out villus like projections toward the bone, forming a so called ruffled border adjacent to the bone.The villi secrete two types of substances: (1) proteolytic enzymes, released from the lysosomes of the osteoclasts, and (2) several acids, including citric acid and lactic acid, released from the mitochondria and secretory vesicles.The enzymes digest or dissolve the organic matrix of the bone, and the acids cause solution of the bone salts. The osteoclastic cells also imbibe by phagocytosis minute particles of bone matrix and crystals, eventually also dissoluting these and releasing the products into the blood (Rodan, G.A., 2003).

2-4-3 Bone deposition and absorption are normally in equilibrium:

Normally, except in growing bones, the rates of bone deposition and absorption are equal to each other, so that the total mass of bone remains constant. Osteo-clasts usually exist in small but concentrated masses, and once a mass of osteoclasts begins to develop, it usually eats away at the bone for about 3 weeks, creating a tunnel that ranges in diameter from 0.2 to 1 millimeter and is several millimeters long. At the end of this time, the osteoclasts disappear and the tunnel is invaded by osteoblasts instead; then new bone begins to develop. Bone deposition then continues for several months, the new bone being laid down in successive layers of con-centric circles (lamellae) on the inner surfaces of the cavity until the tunnel is filled.

Deposition of new bone ceases when the bone begins to encroach on the blood vessels supplying the area. The canal through which these vessels run, called the Haversiancanal, is all that remains of the original cavity. Each new area of bone deposited in this way is called an osteon (Rodan, G.A., 2003).

2-5 Routine Parameter Scanning:

After ascertaining the fetal head position, serial scans were made in a plane transverse to the fetal head. The BPD was measured in a scan that shows the widest diameter at the level of midline echo complex; two lateral ventricle, thalami, and cavum septum pellucidum . The three measurements were made using freeze frames with electronic calipers. The reference point for BPD is the measurement from the inner margin of distal skull interface to the outer margin of proximal skull interface . The fetal spine was traced from the skull downward till a large anechoic area (fetal bladder) identified anterior to the sacral spine. The transducer was then placed at right angle to mid of heart and bladder to get to the level of AC which was completely circular and included the liver ,horizontal portion of portal sinus, as well as the stomach bubble and the fetal spine. The AC was measured with maximum diameter using outer to outer technique (Patre, V., et. al., 2015).

For measuring the FL, the transducer was placed at right angles to the fetal spine and passed down the fetus maintaining this angle to the caudal end. Since the distal femur is usually flexed, the transducer was rotated from this position through 30-45 degrees toward the abdomen until the full length of the femur was visualized. An attempt was made to define both ends of the calcified portion of the femur which was measured when the maximum length was obtained (Patre, V., et. al., 2015).

The HC measurements were taken after obtaining a horizontal section of the fetal head which included both the BPD (corona plane) and the occipitofrontal diameter (sagittal plane, the measurements were taken when the head appeared as an ovoid and echoes from the third ventricle were detected in the midline. After noting BPD, HC, AC, HL, and FL, the complete information was recorded, and then each parameter was compared with its respective standard chart. The graph was plotted between GA and individual and the accuracy of each parameter evaluated and compared amongst each other (Patre, V., et. al., 2015).

2-5-1 Femur length (FL):

It is a standard practice to assess femur length (FL) as part of the evaluation of fetal size and morphology. Although measurement of all the long bones is not required in a routine obstetric ultrasound, an overall evaluation of the fetal skeleton should be performed to ensure the presence and bilateral symmetry of the tubular bones. The longest femur measurement, excluding both proximal and distal epiphyses, is usually chosen. The inclusion of the distal femur point, or the specular reflection of the lateral aspect of the distal femoral epiphysis cartilage, is the most common reason for overestimating FL. An oblique FL measurement will result in under measurement. The lateral border of the femur in the near field of the transducer appears straight, whereas the medial border of the femur in the far field has a curved appearance (Wyatt-Ashmead, J., 2014).

2.6. Previous studies:

Gameraddin et.al, in 2015 studied The Role of Fetal Humeral Length in Determination of Gestational Age Compared with Femoral Length Using Ultrasonography.

Assessment of fetal gestational age with ultrasound provides high accuracy and reliability, as ultrasound is safe, easy operating and cheap imaging modality.

Objectives: to estimate the GA with HL and FL, to establish the role of HL which could be applied to determine the fetal GA, to compare between FL and HL?

Methods: there were 113 normal pregnancies (singleton) had been selected for the study during the second and third trimesters. They were scanned with ultrasound using 3.5MHz probe applying the obstetrics protocol to measure the fetal bony biometrics. The length of femoral diaphysis was measured from upper end to lower end excluding epiphysis. The humeral length was measured from upper to lower end of diaphysis. The fetal humerus was identified by the region of the chest in which the pumping heart is a gross marker. The fetal femur is visualized at the region of fetal pelvis when the fetal urinary bladder is clear, then the probe is swept at various degrees and motions.

Results: Statistical tests such as correlation and T-test had been used between humeral length and fetal length to analyze and get the correlation coefficients and significant values. There was a strong positive correlation between gestational age (last menstrual period) and humeral length (r=0.80).

Also strong correlation exists between gestational age and femoral length(r=0.89). There was no significant difference between humeral length and femoral length (p-value=0.630).

Conclusion: The estimation of gestational age with fetal humeral length and femoral length still remain the most common measurements to assess the fetal growth. The fetal humeral length is an accurate biometry as well as femoral length. Evaluation of gestational age with humeral length and femoral length joined together is more accurate than using femoral length alone (Gameraddin et.al, 2015).

Patre, et.al in 2015 studied Ultrasonographic Evaluation of Fetal Humerus Length for Assessment of Gestational Age and Its Comparison with Other Conventional Parameters.

Introduction: Ultrasonography is proved to be an ideal imaging method, as it is safe for the mother and fetus. It being a painless, non-invasive, non-ionizing, and relatively inexpensive technique used to evaluate fetal growth parameter many times during pregnancy.

Purpose: To estimate the gestational age (GA) with humerus length (HL) and establish the accuracy of it as a reliable indicator for prediction of GA in comparison with other routine parameters.

Materials and Methods: Prospective study was performed on 100 normal singleton pregnancies at second and third trimesters. The study was conducted on a gray scale real-time ultrasound scanner using linear and sector transducers to measure the fetal biometrics. After visualizing the heart, the transducer is moved to image the scapular spine located on the dorsal surface to the head of the humerus. A straight measurement was made from the one end of the diaphysis to the other.

Results: Biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) were compared with standard charts and scatter graphs were plotted. Coefficient of correlation were calculated which were 0.9620, 0.8632, 0.8208, 0.9853 for BPD, HC, AC, and FL, respectively, proving them reliable indicators except for AC. HL measured in the present study was compared with standard nomogram. A statistically significant curvilinear correlation was found between the HL and

GA indicating it to be a reliable indicator of GA. Significant coefficient of correlation (0.9704) was observed between HL and GA indicating it to be a reliable parameter.

Conclusion: The HL was most accurate parameter next to FL in assessing GA.The study also indicates that combination of BPD, HC, AC, FL, HL is more accurate in predicting GA than any single parameter, particularly in the third trimester of pregnancy. HL would contribute to maximum accuracy next to FL amongst all the parameters (Patre, et. al., 2015).

Nagesh, et al, 2016 studied Ultrasonographic Estimation of Foetal Gestational Age by Humerus Length and Its Comparison with Femur Length.Aims and Objectives: To estimate foetal gestational age by measuring humerus length on ultrasonography in second and third trimesters of normal pregnancies. To compare it with conventional parameter femur length for verification of its accuracy and usefulness in foetalbiometry. *Material and Methods:* this prospective cross-sectional study includes 100 healthy women with uncomplicated singleton gestations in the period of 14 to 40 weeks. The average gestational age of the foetus was calculated by using routine biometric parameters. The foetal femur length and humerus length were measured and are compared with standard tables. The gestational age was correlated with femur and humerus lengths. The humerus length was compared with femur length.

*Results:*Data obtained from 100 normal singleton gestations pertaining to gestational age, femur length and humerus length were statistically analysedand compared. Correlation coefficients and p-values were calculated. The association of GA with FL and HL showed positive correlation and are significant. [Gestational age and femur length: r-0.995, p<0.001**, Gestational age and humerus length: r-0.993, p<0.001**, Femur length and Humerus length: r-0.998, p<0.001**] Scatter graphs for GA and

FL, GA and HL, FL and HL also shown good correlation between the variables.

Conclusions: Humerus length is a good parameter for estimation of foetal gestational age. Compared with femur length, humerus length is similar and reliable in estimation of foetal gestational age and there is no much difference between the two parameters (Nagesh, et. al., 2016).

Chapter Three
Material and Method

3.1 Materials:

3.1.1 Subject:

A comparative observational study to estimate the GA by HL and FL in the third trimester with B-mode gray scale ultrasonography. It has been carried out in ultrasound department of Omdurman maternity hospital.50 pregnant female aged between 18-35 year in the third trimester presented to the ultrasound department of Omdurman maternity hospital with previous normal ultrasound finding, or with current normal ultrasound finding, are included in the research sample. Pregnant women with previous abnormal ultrasound finding (fetal growth retardation, small gestational age, large gestational age, bleeding and women with age out of the range of 18-35 year old were excluded.

3.1.2Machine used

The study was performed on gray scale real time scanner Shimadzu - 355SDU and Shimadzu - Aspire with a 3.5 MHz linear and 5.3MHz sector transducers. These devices have a facility to estimate the gestational age by measuring humeral length.

3.2 Method:

3.2.1 Technique used:

By convex probe 3.5 MHz the fetus examined in the following sequences, firstly the patient lie supine with exposed abdomen, then the probe is applied to the center of the abdomen vertically, to determine the fetal lie, and presentation, then the FL is measured and its gestional age is calculated, and HL and its estimated gestional age is obtained.

After visualizing the heart, the transducer is moved to image the scapular spine which is dorsal to the humerus head. The full length of the humerus was then obtained in a plane as close as possible to right angles of the ultrasound beam. A straight measurement was made from the center of one end of the diaphysis to the other, disregarding any curvature.

All the patients were examined in supine position using 3.5 MHz convex transducer. Fetal head was identified to determine presentation of the fetus and then heart was located to confirm viability. A general survey of the fetus was done to rule out any anomalies. Liquor quantity was assessed. Placental location and maturity was noted. The measurement of femur and humerus were done as follows: To locate fetal femur, the transducer was moved transversely across the abdomen till iliac bones and bladder were seen. Then, turning the probe sagittaly, the long femur bone was identified manipulating the probe depending upon the position of thigh. Both the calcified ends of the femur were defined in long axis. Ultrasound cursers were placed at both ends of the diaphysis and the length was measured in mms

To locate humerus bone, the transducer was slided upwards transversely towards thorax of the fetus to locate beating heart of the fetus. Then, with a probe rotation of 90 degrees, probe was moved side wards to identify scapula and then the adjoining long bone, the humerus, with probe movements depending upon the position of fetal arm. The ends of the diaphysis of humerus in long axis were imaged. By placing the ultrasound cursers on both ends of the diaphysis, the length was measured in mms.

It is measured in a plane such that the bone was as close as possible to a right angle to the ultrasound beam. Care was taken to ensure that the full length of the bone was visualised and the view was not obscured by shadowing from adjacent bony parts. The foetal gestational age was calculated by using BPD, HC, AC and FL measurements in weeks. Femur length measurements were compared with standard nomogram by Hadlock et al. The humerus length measurements were compared with standard nomogram by Jeanty et al to obtain gestational age

3.2.2 Data collection:

The collected data include the age of pregnant women, gestational age using LMP, gestational age using FL, gestational age using HL, average gestational age from the previous estimated gestational ages, femur length and Humeral length in millimeter.

32.3 Data analysis:

The data is analyzed by using Statistical Package for the Social Sciences (SPSS). Descriptive statistic, Paired samples t-test and Pearson correlation test were used.

Chapter Four

Data analysis and result

4.1 Result

Fifty pregnant women came for the routine ultrasound examination, in the ultrasound department of Omdurman maternity hospital were selected to be the sample of the research, then the gestational age using the femur length and the humeral length is obtained.

Table (4. 1) Comparison between the femoral length and the humeral length in association with age of pregnant women.

	N	Minimum	Maximum	Mean	Std. Deviation
Age	50	18	35	27.04	5.014
FL /mm	50	53	78	67.60	6.462
HL /mm	50	46	68	59.66	5.363

Table (4. 2) Present the correlation of the gestational age with femoral length and humeral length.

Paired Samples Statistics

			Std. Deviation	Std. Error Mean
Pair 1 GA/ LMP GA / FL	35.22	50	3.228	.457
Pair 2 GA/ LMP	34.74	50	3.056	.432
GA / HL	35.22	50	3.228	.457
	34.58	50	3.071	.434

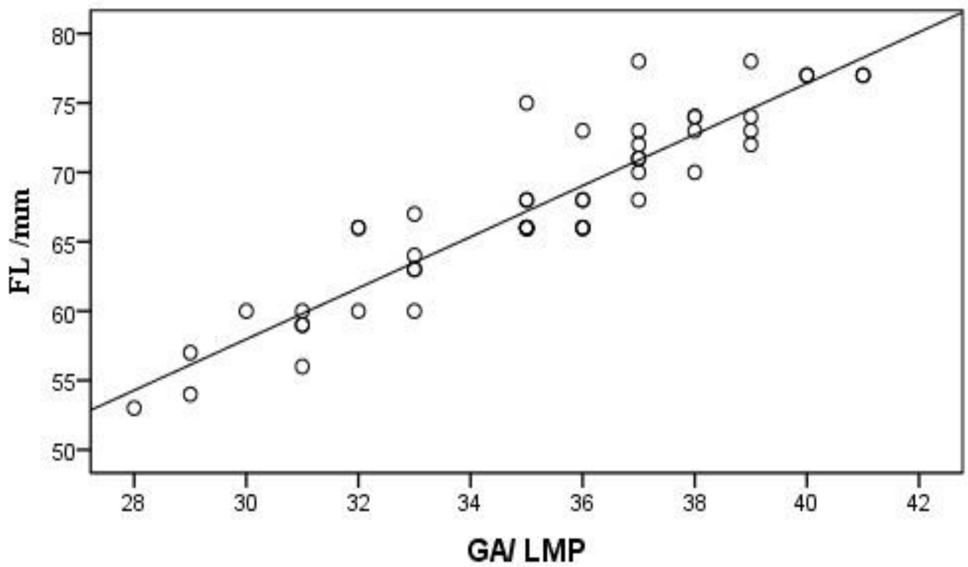

Figure (4. 1) Scatter plot shows the predication system to estimate the gestational age in weeks by using the femur length in mm.

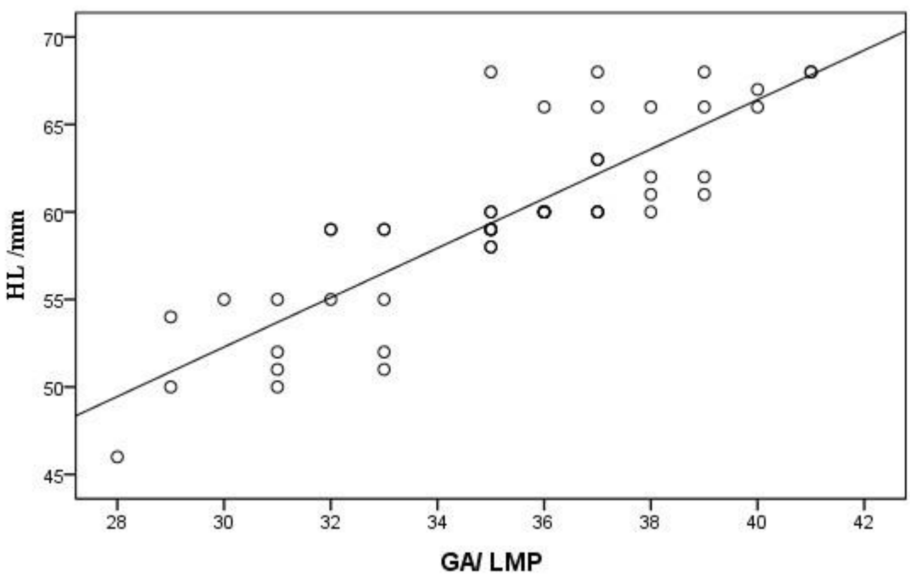

Figure (4. 2) Scatter plot shows the predication system to estimate the gestational age in weeks using the humeral length in mm.

Table 4-3. Show the mean and the stander deviation of gestational age measured using the FL and the HL.

Paired Samples Statistics

	Mean	N	Std. Deviation	Std. Error Mean
Pair 1 GA / FL	34.74	50	3.056	.432
GA / HL	34.58	50	3.071	.434

Table 4-4. Show the correlation between the gestational age using the LMP versus FL, LMP versus HL, and FL versus HL.

Correlations

		GA/ LMP	GA / FL	GA / HL
GA/	Pearson Correlation	1	.941**	.905**
	Sig. (2-tailed)		.000	.000
	N	50	50	50
GA / FL	Pearson Correlation	.941**	1	.962**
	Sig. (2-tailed)	.000		.000
	N	bs350	50	50
GA / HL	Pearson Correlation	.905**	.962**	1
	Sig. (2-tailed)	.000	.000	
	N	50	50	50

**. Correlation is significant at the 0.01 level (2-tailed).

Chapter Five

Discussion, Conclusion and Recommendations

5.1 Discussion

Fifty pregnant women came for the routine ultrasound examination, in the ultrasound department of Omdurman maternity hospital.

FL is used as standard method to estimate gestational age to be compared with the other gestational age that obtained with HL and the LMP.

The study revealed that the mean gestational age measured using the HL is 34.58 which is less than week difference from the gestational age calculated from the FL , so this clarify that there is no significant difference between the both measured gestational age in the third trimester by using the FL and HL.The result is similar to previous study (Moawia et.al, 2015). However, A study conducted by Rosati et al., (2002) revealed that the differences in accuracy in predicting bone length using formulae derived from data acquired during early pregnancy can be related to the fact that systematic variations in the measurement of FL and HL occur particularly during the first trimester of pregnancy, a period in which the upper and lower bones are quite difficult to measure accurately (Rosati et al, 2002). In this study, the humeral length and femur length were measured to confirm the role of fetal humeral length as biometric parameter which could be used to determine the gestational age.

Use of the multiple parameters method of assessing gestational age is valid when the gestational age estimates of the various ultrasound parameters are similar. If the gestational age estimates of one or several parameters is greater than 2 weeks different than the estimates of the other parameters, either the abnormal ultrasound parameters should be excluded or a different method should be used to estimate gestational age. When the various ultrasound parameters predict different gestational ages the fetus should be further evaluated to explain these differences. In this study a significant correlation was noticed between gestational age and HL, this correlation also seen between FL and gestational age. Thus HL can be added to the formulae that used in the estimation of gestational age. In the pregnancy with unknown menstrual dates or a discrepancy between menstrual dates and mean gestational age predicted by multiple parameters of more than 3 weeks, fetal age should be estimated by the multiple parameters method. However, the potential error of this method in the third trimester of pregnancy may not be acceptable.

In conclusion, assessment of gestational age is fundamental to obstetric care and should be a carefully thought. Furthermore, HL could be used in estimation of gestational age.

5.2 Conclusion:

From this result we can conclude that the humeral length measurement in the third trimester is accurate in calculation of the gestational age in the single fetus with no fetal anomalies, of the healthy pregnant women with normal uncomplicated pregnancy.

The gestational age calculated using the humeral length is another standard parameter used in the third trimester to precise measurement of the gestational age.

There is no significant difference between the gestational age calculated using the femur length, last menstrual period, and the humeral length.

5.3 Recommendations:

1. From the above result we can see that in this research the gestational age that calculated by the measuring the humeral length is another accurate measurement for the fetal age in the third trimester and should be used as standard measure when the femur length is difficult to be obtain.
2. The humeral length must be used as routine measurement in calculation the gestational age in the third trimester, to confirm the accuracy of the femur length measurement, and the precise of the last menstrual period in the calculation of the third trimester gestational age.
3. The expected date of the delivery (EDD) should never be reported, unless is confirmed by using the EDD that obtained from measuring the HL.
4. Machine to use HL to be used as routine ultrasound .
5. High quality.

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Data collection sheet

NO	Maternal age	LMP	G	P	BPD(mm)	FL(mm)	HL(mm)	Gestational age(wk)