بسم الله الرحمن الرحيم

Sudan University of Science and Technology

College of Graduate Studies

Assessment of Gestational Age in Second and Third Trimester by Occipto-frontal Diameter using Ultrasound

تقييم عمر الجنين بالقطر القحفي الامامي في المرحلتين الثانية والثالثة بإستخدام الموجات فوق الصوتية

A thesis Submitted for Partial of the Requirement of M.Sc. Degree in Medical Diagnostic Ultrasound

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2016

الآيـة

بسم الله الرحمن الرحيم

قال تعالى :

﴿ اللَّهُ لَا إِلَهَ إِلَّا هُوَ الْحَيُّ الْقَيُّومُ لَا تَأْخُذُهُ سِنَةٌ وَلَا نَوْمٌ لَهُ مَا فِي السَّمَاوَاتِ وَمَا فِي الْأَرْضِ مَنْ ذَا الَّذِي يَشْفَعُ عِنْدَهُ إِلَّا بِإِذْنِهِ يَعْلَمُ مَا بَيْنَ أَيْدِيهِمْ وَمَا خَلْفَهُمْ وَلَا يُحِيطُونَ بِشَيْءٍ مِنْ عِلْمِهِ إِلَّا بِمَا شَاءَ وَسِعَ كُرْسِيُّهُ السَّمَاوَاتِ وَالْأَرْضَ وَلَا يَئُودُهُ حِفْظُهُمَا وَهُوَ الْعَلِيُّ الْعَظِيمُ ﴾

سورة البقرة الاية (**255**)

Dedication

To:

- **My Unreadable Mother**
- **My wisdom father**
- **My decently &patience husband**
- **My lovely son**
- **My Colleagues**
- **My all staff particularly Dr. Mohammed Elfadil.**

Acknowledgment

Firstly I would like to thank Allah for the great help in preparing this research. Special thanks to Dr. Mohammed Elfadil for his great cooperation, guidance, encouragement and patience during all the stages of this research, from whom I understand that the life without knowledge mean nothing.

I generally indebted to thank my family for their helpful, special thank extended to my awesome husband who always supporting me to achieve this degree, Also I would like to appreciate the helpful of my friends Mazahir, and the staff of Elsouady hospital & Zahra, Manar Abass staff of Turkish hospital.

I never forget I am very so fortunate to have unique person in my educational life like Dr. Ahmed Abdelrahim who always supportive, encouragement and great help to keep me going.

Finally, I am so proud of *Dr. Mohammed Mohamed Omer*, and Dr. Alsafi Ahmed because I was one student of them really I didn't know how to appreciate them for their efforts and good advices.

Dalia S. Serey

ABSTRACT

The objective of this study was to estimate the gestational age using the occipitofrontal diameter in the second and third trimester using the known last minstrel period as a reference in estimating the accurate GA.

The study was conducted at Alsouady hospital / Turkish teaching hospital on October 2016-December, 2016 by using ultrasound machine with convex transducer with variable frequencies ranging from (3-4 MHz).electronic caliper system set at a velocity of 1540m/s.

This is a descriptive and analytical study of a cross sectional type with prospective data collection. The data of this study were collected from 50 uncomplicated pregnant women between 14 and 40 weeks of gestation who presented for routine ultrasound. Only singleton pregnancies were included. Pregnant women with concomitant disease possibly affecting fetal growth (e.g. diabetes mellitus, asthma, hypertension, renal disease, thyroid disease) were not included as were those with complications of pregnancy.

The results of this study showed that the mean value of the OFD was 81.1±24.6 mm which is the long axis of the head diameter versus the shorter diameter (BPD) was 63.7±20.2 mm with cephalic index (CI) of 0.81±0.1, the average GA using FOD was 26.5±7.3 weeks versus 26.5±7.7 weeks using LMP. There is no

significant difference between the LMP calculation of GA and GA estimated using OFD. The result also showed that GA increases by 0.3 weeks/mm of OFD. In conclusion OFD can be used to estimate the GA with an accuracy > 92% in i.e. the OFD can explain more than 92% of the changes occur in the GA.

Finally, the study showed the OFD can be used safely to predict the GA, but consideration of cephalic index is important to avoid over or under estimation of GA. The OFD mainly had exponential relationship with the GA rather than the linear trend although both trend gives insignificant difference from the LMP-GA.

المستخلص

الهدف من هذه الدراسة تقييم عمر الجنين عن طريق قطر الراس الطولي باستخدام الموجات الفوق صوتية في الطور الثاني و الثالث للحصول علي نتيجه دقيقه لعمر الجنين قمنا بتسجيل موعد اخر دوره شهريه.

تم إجراء هذه الداسه في كل من المستشفي السعودي و المستشفي التركي التلعيمي في الفتره من نوفمبر 2016 الي يناير 2017 باستخدام جهاز موجات صوتيه ذات مسبار محدب بتردد متغيره تترواح ما بين (3_4) ، ونظام مؤشر الكتروني مدرج مضبوط علي سرعة 1540م/ث.

هذه دراسه وصفيه من نوع المقطعي مع جمع البيانات المحتمله، بيانات هذه الدراسه جمعت من 50 امرأة حامل في الفتره من الأسبوع الرابع عشر و حتي الأربعون .اثناء المتابعة الروتينيه تضمنت الدراسه كل الحوامل ذوي الحالات المستقره لايعانوا من اي امراض عرضيه مثل (السكري ، ضغط ، ازمه ، امراض كلي، او غده درقيه).

نتائج هذه الدراسة توضح ان متوسط قطر الرأس الرئيس يسوي 81.1±24.6 وقطر الرأس الثاني يساوي 63.7±20.2 و النسبة بينهم تساوي 0.81±0.1 . متوسط تقدير عمر الجنين بأستخدام قطر الرأس الرئيس يساوي 26.5±7.5 و بأستخدام حساب اخر دورة شهرية كان يساوي 26.5±7.7 مما يدل علي عدم وجود فرق معنوي بين الاثنين. اثبتت هذه الدراسة ان عمر الجنين يزيد بمقدار 0.3 اسبوع لكل مليمتر زيادة في قطر الرأس الرئيس.

ايضا قطر الرأس الرئيس يمكن استخدامه لتقدير عمر الجنين بدقة اكثر من 92% مما يعني ان طول قطر الرأس الرئيس يفسر التغيرات في عمر الجنين بنسبة 92%.

اخيرا اثبت الدراسه ان مقياس الراس الطولي يمكن ان يستخدم كمؤشر امن لي تقييم عمر الجنين ، لكن يعتبر المؤشر الراسي ذات اهميه لي تجنب الذياده او النقصان في تقييم عمر الجنين.

قطر الراس الطولي ذو علاقه اسيه مع عمر الجنين اكثر من علاقه الاتجاه الخطي بالرغم من ان كل من الاتجاهين يعطي اختلافا ملحوظ من عمر الجنين بمعياد اخر دروه شهريه.

List of Content:

List of Figures

List of Tables

Chapter one

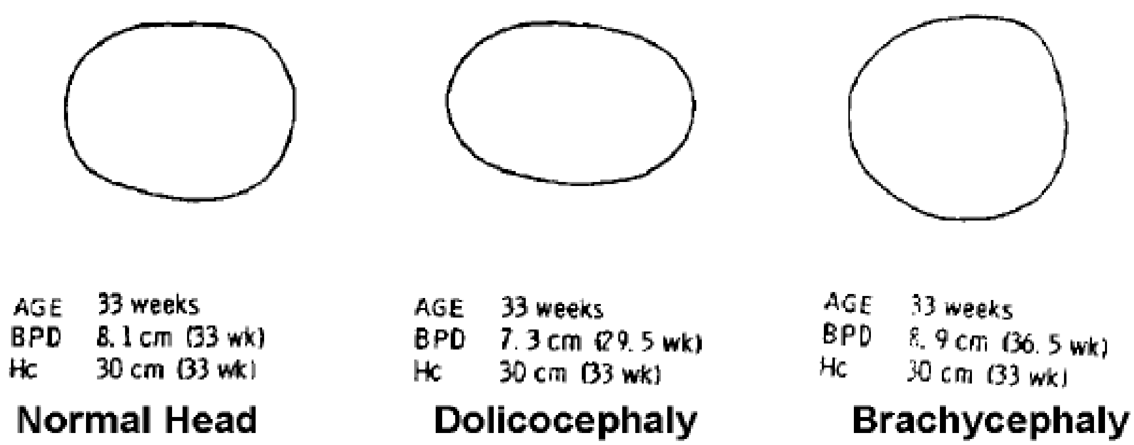
Introduction

CHAPTER (ONE)

INTRODUCTION

1.1. Introduction

The occipitofrontal diameter (OFD) may be used as an alternative measurement if the Biparietal Diameter (BPD) is unsatisfactory because of low fetal head position. Several data for OFD measurements against gestational age have been published. The main use of the OFD is to determine head circumference from the ellipse formula when there is no tracing calipers and determination of the cephalic index (CI). Synonyms for occipitofrontal include frontooccipital and anteroposterior (Buscicchio1 et al. 2008 and Mador et al 2010 and 2012).



What is the significance of an abnormal Cephalic Index? A CI which falls below 0.70 or 70 indicates a fetal head with an abnormally narrow BPD relative to the OFD and is associated with *dolicocephaly*, which defines a head shape with a narrow BPD in proportion to the occipitofrontal diameter (the head is oblong or sausage-shaped. With dolicocephaly, the BPD underestimates gestational age. The most common cause of dolicocephaly is oligohydramnios. Other causes include multiple pregnancy (twins, triplets, etc...), breech position, and primigravida. A CI value which falls above 0.86 or 86 indicates a fetal head which is rounder than normal and is known as *brachycephaly* (a CI of 86 indicates the BPD is 88% the OFD value; if the CI was 1 or 100%, the BPD and OFD would be equal). With *brachycephaly*, the BPD overestimates gestational age. Brachycephaly is much less common than dolicocephaly. It is reported to be most commonly associated with multiple pregnancies. Another less common cause of brachycephaly is trisomy, most often trisomy 21 (Al-Hilli 2009, Lubuskya et al. 2007, Shan and Madheswaran 2009).

1.2 The problem of the study

The estimation of the Gestational Age (GA) and hence the Expected Delivery Date (EDD) is one of the routine tasks that carried out by the sonologist for pregnant women using some parameter like the Biparietal Diameter (BPD) and Femoral Length (FL) of the fetus. Where the BPD might potentially include some errors in case of head anomalies like dolicocephaly which affect the GA estimation. In the same essence estimation of GA using head circumference (HC) does not affected by these discrepancy; this means Occipitofrontal Diameter (OFD) play a major role in this rectification since both measurements (BPD and OFD) play a role in head circumference calculation even with the contribution of the affected BPD. Therefore estimation of the GA using OFD in a quadratic equation for Sudanese in the second and third trimester might give a better estimation with minimum error relative to other methods. (Kazan & Levine 2007).

1.3 Objectives

1.3.1 General objective

To evaluate the robustness of the OFD in estimation of the GA and hence EDD for Sudanese in order to overcome the limitation that might be associated BPD measure in certain circumstances. By other words we can say the main objective to assess the gestational age in Second and Third trimester using Occipitofrontal diameter.

1.3.2 Specific objectives

- To measure the Occipitofrontal, Biparietal diameter and head circumference.
- To estimate the GA and EDD using OFD, BPD and HC by quadratic equations.
- To find the significant differences and correlation of theses estimations with last menstrual period (LMP) calculations.

- To find the accuracy and sensitivity of the estimation results.
- To find the effect of GA (using LMP), BPD/OFD ratio, maternal age and parity on the accuracy of the results

1.4 Significant of the study

This study will highlight the application of OFD diameter as one of the crucial factor in GA estimation for Sudanese, and hence it will provide a Sudanese index the can be incorporated in an indigenous equation, which will fit their ethnic diversity.

1.5 Overview of the study

This study will falls into five chapters, with chapter one is an introduction which include background about concerning the ultrasound and it is application in obstetric evaluation as well as the problem of the study, objectives and significance of the study. While chapter two which include literature review, it will present the previous study that carried out by the scholar in the field of this study. In the same essence chapter two will present the material used to collect the data and the technique followed to accrue the collected data. Chapter four include data presentation that illustrated in tables and figures. Finally chapter five will include discussion of the illustrated results, conclusion of the study and recommendation.

Chapter Two

Literature review

Chapter (Two)
Literature review

2.1 Background

2.1.1 Fetal head Shapes

The shape and echogenicity of the fetal skull or calvarium may be abnormal and provide clues for the diagnosis of central nervous system and skeletal anomalies, and syndromes. The normal skull produces a high amplitude echo which is very echogenic compared to the brain. Diminished echogenicity of the fetal skull is most commonly seen with osteogenesisimperfecta and hypophosphatasia respectively (Nahum 2000).

Abnormal skull mineralization should be suspected if the falxcerebri appears to be as or more echogenic than the skull. Poor or absent calvarial ossification is also associated with “superb” imaging of brain anatomy due to lower sound attenuation and fewer bone-related artifacts which normally hamper good visualization of the brain nearest the transducer. The sonographer should be alerted to a mineralization abnormality if the brain is seen with unusual clarity. Other findings associated with poor mineralization of the skull include increased compressibility of the fetal head and increased acoustic transmission. Normal skull sutures can be seen as short breaks in the skull echo. The coronal suture is routinely seen in the BPD image between the temporal and frontal bones. The general shape of the normal fetal head in the axial plane in the 2nd/3rd trimester should appear smooth and oval (BPD/HC image). In the 1st trimester (10-14 weeks LMP), the head appears more spherical than oval since brain development and growth has not yet influenced the shape of the head. Abnormalities in the shape of the fetal head are associated with different conditions and can be very helpful in searching for anomalies, including syndromes. The following list describes the most common abnormalities in fetal head shape described in the sonographic literature (Rumack 2011, Danhnert 200 and Patterson 1985).

Dolicocephaly- describes a fetal head with a relatively narrow biparietal diameter (BPD) and a long occipitofrontal diameter (OFD). Most commonly associated with oligohydramnios.

Brachycephaly - describes a fetal head which is rounder than usual. Most commonly seen with multiple pregnancy (due to intrauterine crowding), and can be a late feature associated with trisomy 21 (Down’s syndrome).

Lemon Sign - describes a fetal head with bilateral denting of the frontal bones. Most commonly associated with spina bifida.

Cloverleaf-shaped Skull - describes a trilobed appearance of the head that is believed to occur as a result of premature closure of the coronal, lambdoidal, and squamosal sutures. It is most commonly associated with than atophoric dysplasia and homozygous achondroplasia, both lethal skeletal limb reduction syndromes.

Strawberry-Shaped Skull **-** describes a fetal head with a normal BPD and a narrow frontal diameter. Similar to the lemon sign except that there is no obvious concavity to the frontal bones. Most commonly associated with trisomy 18.

Spalding's sign - describes a flattened and misshapen fetal head with overlapping of cranial bones. Associated with fetal demise (Figure 2-1and 2-2)

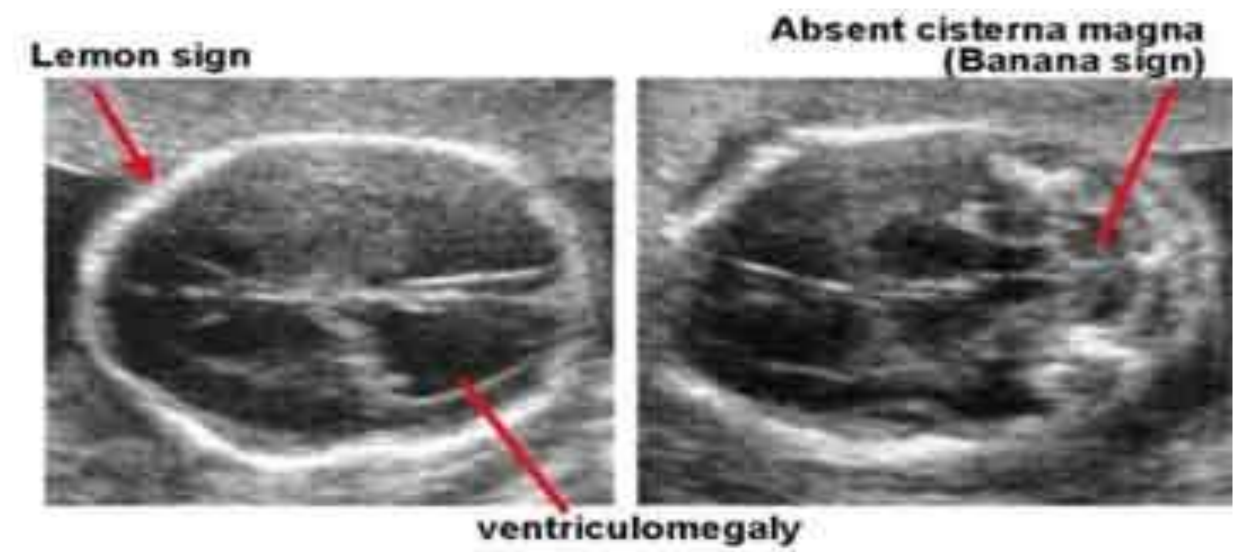


Figure 2-1 Strawberry-Shaped Skull

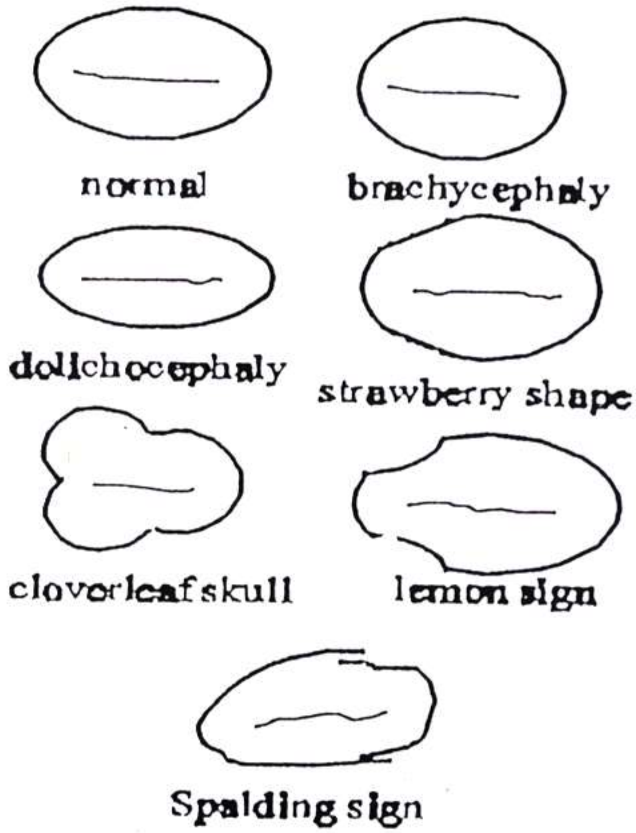


Figure 2-2 Different fetal skull shape

2.1.2 Fetal Scalp

The fetal scalp is normally very thin and barely noticed (scalp thickness is normally <3 mm). In the late third trimester, fetal hair may be seen as short, stringy echoes arising from the scalp. Scalp edema is a manifestation of fetal hydrops and is seen as scalp thickening (scalp thickness more than 3mm) (Chudleigh 2004).

2.1.3 Anomalies of the Fetal Head

Neural Tube Defects:

The embryonic brain and spinal cord develop from the neural tube. Anomalous development of the neural tube results in neural tube defects (NTD's) of varying degrees and significance. NTD's may be either open or closed. An open defect indicates the neural tissue (brain or spinal cord) is not covered by the normal integuments or covering tissue layers such as skin and subcutaneous fat. Cranial NTD's include anencephaly, anencephalocele, and cranial meningocele. Spinal NTD's include spina bifida, spinal meningocele, and meningomyelocele. Open NTD's are usually associated with elevated maternal serum and amniotic fluid alpha-fetoprotein concentrations. NTD's are among the most common of all congenital anomalies. The incidence of NTD's varies significantly with geography and has been estimated to be as high as 16 per 10,000 births(Kazan 2007 and Rumack 2011).

Anencephaly:

Anencephaly is defined as absence of the cranial vault and higher brain (cerebrum). Absence of the cranial vault with a variable amount of disorganized brain tissue is defined as acrania. With advancing gestational age, acrania is associated with progressive degeneration of the fetal brain such that acrania progresses to anencephaly, namely the acrania-anencephaly sequence. Although anencephaly technically means absence of the brain, functioning neural tissue (brain stem and portions of the midbrain) is usually present and the majority of fetuses grows and is born alive. Anencephaly is the most common anomaly of the neural tube and results from failure of the neural tube to completely close at its cephalic end. Closure of the neural tube occurs between the second and third weeks of embryonic development thus the renatal diagnosis of anencephaly can be made in the first trimester with good equipment and technique. The highest risk factor is a history of previous anencephalic fetus with the recurrence rate estimated to be about 4% and rising to 10% after two successive affected fetuses (Figure 2-3).

Figure 2-3 Acrania, anencephalocele

Although the cranium is absent with anencephaly and acrania, the base of the skull and orbits are normally present. About one-half or 50% of affected fetuses also have rachischisis (extensive spina bifida) (this finding does not alter the prognosis or management). After 20 to 24 weeks of gestation, polyhydramnios is associated with about one-half of cases (probably due to a decreased ability of affected fetuses to swallow amniotic fluid). The ultrasound diagnosis of acrania and anencephaly can be made reliably by 14 weeks gestation with standard TAS technique, and as early as 10 weeks gestation with EVS providing a specific search is made for the sonographic features for this condition. Acrania is characterized on ultrasound by absence of the normal cranial vault with disorganized (dysmorphic) brain tissue above the orbits which is usually best demonstrated in a coronal view of the fetal head. An interesting and highly specific appearance of acrania at the end of the first trimester is the "Mickey Mouse" sign representing a coronal view of the dysmorphic fetal brain and face. Another characteristic feature of acrania or anencephaly is bulging eyes (exophthalmos). This sonographic feature has been dubbed the "frog face" or "eyeglass" sign. Failure to identify normal cranial morphology and brain tissue above the orbits is the most reliable sonographic feature of anencephaly. The CRL measurement in anencephalic fetuses may be normal or small-for-dates depending on the status of e cerebral brain tissue. In one group of anencephalic fetuses the mean fetal CRL was significantly reduced but it was below the 5th percentile of the normal range in only one-quarter of the cases. A frequent, indirect sign of acrania-anencephaly sequence is echogenic amniotic fluid in the first trimester. Amniotic fluid at this stage of pregnancy is normally clear or echo free at normal gain settings. Eight of nine cases in the series by Calcfic had some degree of amniotic fluid echogenicity. It is hypothesized the amniotic fluid echoes are the result of exfoliating fetal neural debris from the exposed and mechanically traumatized fetal brain and associated bleeding (proven in some cases by aspiration of neural cells and red blood cells by amniocentesis). Variability in the degree of echogenicity of the amniotic fluid is related to gestational age at diagnosis or a more rapid turnover of the amniotic fluid. Sonographers should be heightened of the possibility of acrania anencephaly sequence if the amniotic fluid appears echogenic in relation to the fluid in the chorionic cavity especially in view of increased use of first-trimester nuchal translucency screening(Kazan 2007 and Rumack 2011).

Cephalocele:

Cephalocele is a developmental defect in the cranium (skull) resulting in an extracranial mass consisting of variable elements. If the cephalocele contains only protruding meninges and CSF, it is called a cranial meningocele; if the cephalocele also contains brain tissue, it is called an encephalocele or meningoen cephalocele. Most cephaloceles are covered by normal scalp tissues and do not cause maternal alpha-fetoprotein concentrations to be abnormally elevated. Cephaloceles are the least common form of open NTD's. Most cephaloceles are midline (symmetric), with the majority occurring in the occipital region (~3/4 or 75% of cases). These lesions may be isolated or featured with other anomalies in syndromes, most notably amniotic band syndrome (ABS), limb-body-wall complex (LBWC), and Meckel- Gruber syndrome. Cephaloceles associated with ABS and LBWC are typically multiple and in an asymmetric or lateral location such as the parietal or temporal region of the head. Sonographically, a cephalocele appears as an extracranial mass of variable dimension and sonographic appearance (cystic, complex, or solid mass) associated with a definitive skull defect. Identification of a skull defect is the predominant distinguishing feature between cephalocele and other cranial masses such as cystic hygroma, teratoma, and other lesions. Other sonographic findings may include the "lemon sign" of the frontal bones in the BPD image and ventriculomegaly (obstructive hydrocephalus) (Kazan 2007 and Rumack 2011).

2.1.4 Choroids Plexus Cysts (CPC):

CPCs arise from neuroepithelial folds in the choroid plexus, with the atrial region of the lateral ventricle being the most common site. CPCs are typically unilateral, spherical, anechoic, and relatively small (range 1 to 20 mm, with most cysts being less than 5 mm). CPCs are infrequently multiple, bilateral, or odd-shaped Most CPCs are seen between the 18th and 24th weeks of gestation, with the majority regressing and disappear spontaneously. The majority of CPCs are isolated findings in otherwise normal fetuses however they may be associated with other structural anomalies and aneuploidy. The most common chromosome abnormality associated with CPCs is trisomy 18. There does not appear to be any statistical differences between the association of isolated fetal choroid plexus cysts and the sex of the fetus). The clinical management of isolated CPCs in low-risk women remains somewhat Controversial. Some investigators have dismissed the isolated CPCs as a normal variant that usually resolves by the 3rd trimester whereas others have quoted a significantly increased risk of aneuploidy for all cysts even if isolated or transient. The sonographic detection of CPCs depends on the size of the cyst, gestational age, and background heterogeneity of the CP, transducer and equipment resolution capabilities. As shown by Turner et al, the background echo texture of CP is more heterogeneous in younger fetuses and small anechoic areas are normal features of developing CP). Consequently, these small anechoic areas in the CP may be falsely mistaken for small CPCs. Based on their interesting experiment with embedded prototype cysts of different sizes at different gestational ages, Turner advocates “that cysts must be at least 2.5 mm in the screening period of 13 to 21 weeks’ gestation to be reproducibly and accurately detected and at least 2 mm from 22 to 38 weeks’ gestation. It is important to recognize that there is a lower limit of size below which the diagnosis of a CP cyst should not be made, and the possibility of a false diagnosis due to the background heterogeneity is great. We think that, hence tenets should guide the development of diagnostic criteria, help standardize the literature, and, it hoped, reduce the number of false-positive diagnoses and unwarranted amniocenteses, which generate needless anxiety in prospective parents (Kazan 2007 and Rumack 2011).

Cerebral Ventriculomegaly and Hydrocephalus:

Cerebral ventriculomegaly refers to dilatation of the cerebral ventricles without defining the cause. The fetal head may be normal, enlarged, or even small-for-gestational age depending on the underlying cause and the time of the diagnosis during the pregnancy. Fetal head size is therefore not crucial for the diagnosis of cerebral ventriculomegaly. Hydrocephalus (hydrocephaly) is ventriculomegaly most commonly associated with increased intracranial pressure and is usually due to a lesion causing obstruction of the CSF pathway. Fetal hydrocephalus is characterized in the third trimester by macrocephaly and brain atrophy. The most common causes of fetal ventriculomegaly include Arnold-Chiari malformation, open neural tube defects, congenital aqueductal stenosis, and Dandy- Walker malformation. The prognosis depends on the severity, underlying cause, and the association with other anomalies. In the majority of cases ventriculomegaly is bilateral and symmetric. Asymmetric bilateral and/or unilateral ventriculomegaly are very uncommon. As an isolated finding, fetuses with unilateral cerebral ventriculomegaly generally have a good developmental outcome. Fetuses with unilateral ventriculomegaly have a better prognosis than those with bilateral ventriculomegaly suggesting that both ventricles should be evaluated in every fetus. The underlying cause of fetal ventriculomegaly determines the components of the ventricular system that enlarge. For example, with Arnold-Chiari malformation, the 4th, 3rd, and both lateral ventricles are dilated, and with aquaductal stenosis, the 3rd ventricle and both lateral ventricles are dilated whereas the 4th ventricle is normal is normal since the obstruction is proximal.

Anatomic appearance and several measurements have been described to assess ventricular size including the transverse atrial diameter, combined anterior horn diameter, and the lateral ventricle-to-hemisphere ratio. The atrial measurement is currently the best indicator of ventriculomegaly and will be the only measurement technique considered here (Kazan 2007 and Rumack 2011).

2-4 Previous study:

Biparietal diameter (BPD) is a cross-sectional view of the fetal head at the level of thethalami; ideal angle of insonation is 90◦ to the midline echoes; - symmetrical appearance of both hemispheres; continuous midline echo (falxcerebri) broken in middle by the cavumseptipellucidi and thalamus; no cerebellum visualized. *Caliper placement.* Both calipers should be placed according to a specific methodology, because more than one technique has been described (e.g. outer edge to inner edge or 'leading edge' technique vs. outer edge to outeredge), at the widest part of the skull, using an angle that is perpendicular to the midline falx. The same technique as that used to establish the reference chart should be used. The cephalic index is a ratio of the maximum head width to its maximum length and this value can be used to characterize fetal head shape. Abnormal head shape (e.g. brachycephaly and dolichocephaly) can be associated with syndromes. This finding can also lead to inaccurate estimates of fetal age when the BPD is used; in these cases, HC measurements are more reliable (Bhargava, 2010).

Head circumference (HC) described for the BPD, ensuring that the circumference placement markers correspond to the technique described on the reference chart. *Caliper placement.* If the ultrasound equipment has ellipse measurement capacity, then the HC can be measured directly by placing the ellipse around the outside of the skull bone echoes. Alternatively, the HC can be calculated from the BPD and occipitofrontal diameter (OFD) as follows: the BPD is measured using a leading edge technique as described in the previous section whereas the OFD is obtained by placing the calipers in the middle of the bone echo at both the frontal and occipital skull bones. HC is then calculated using the equation: $HC = 1.62 \times (BPD + OFD)$, (Salomon et al 2010).

An accurate assessment of gestational age is fundamental in managing both low and high risk pregnancies. In particular, uncertain gestational age has been associated with adverse pregnancy outcomes including low birth weight, spontaneous preterm delivery and perinatal mortality, independent of maternal characteristics. Making appropriate management decisions and delivering optimal obstetric care necessitates accurate appraisal of gestational age. For example, proper diagnosis and management of preterm labor and post-term pregnancy requires an accurate estimation of fetal age. Many pregnancies considered to be preterm or post term are wrongly classified. Unnecessary testing such as fetal monitoring and unwarranted interventions including induction for supposed post term pregnancies may lead to an increased risk of maternal and neonatal morbidity. In addition, pregnancies erroneously thought to be preterm may be subject to avoidable and expensive hospitalization stays as well as excessive and potentially dangerous medication use including to colitis therapy. In one study by Kramer et al that assessed over 11,000 pregnant women who underwent early ultrasound, one-fourth of all infants who would be classified as premature and one-eighth of all infants who would be classified as post term by menstrual history alone would be misdiagnosed. Accurate pregnancy dating may also assist obstetricians in appropriately counseling women who are at imminent risk of a preterm delivery about likely neonatal outcomes. Precise knowledge of gestational age is also essential in the evaluation of fetal growth and the detection of intrauterine growth restriction. During the third trimester, fundal height assessment may be helpful in determining appropriate fetal growth by comparing the measurement to a known gestational age. In addition, dating a pregnancy is imperative for scheduling invasive diagnostic tests such as chorionic villus sampling or amniocentesis, as appropriate timing can influence the safety of the procedure. Certainty of gestational age is also important in the interpretation of biochemical serum screening test results and may help avoid undue parental anxiety from miscalculations and superfluous invasive procedures, which may increase the risk of pregnancy loss. Assessment of gestational age is also crucial for counseling patients regarding the option of pregnancy termination (Hall 1985).

Traditionally, the first day of the last menstrual period (LMP) has been used as reference point, with a predicted delivery date 280 days later. The estimated date of confinement (EDC) can also be calculated by Nagele's rule by subtracting three months and adding seven days to the first day of the last normal menstrual period. However, there are inherent problems in assessing gestational age using the menstrual cycle. One obstacle in using the LMP is the varying length of the follicular phase and the fact that many women do not have regular menstrual cycles. Walker et al evaluated 75 ovulatory cycles using luteinizing hormone levels as a biochemical marker and found that ovulation occurred within a wide range of 8–31 days after the LMP. Similarly, Chia all collected over 30,000 recorded menstrual cycles from 2316 women and found that only 77% of women have average cycle lengths between 25 and 31 days. Another barrier in using a menstrual history is that many women do not routinely document or remember their LMP. Campbell et al demonstrated that of more than 4000 pregnant women, 45% were not certain about their LMP as a result of poor recall, irregular cycles, bleeding in early pregnancy or oral contraceptive use within two months of conception Campbell et al. 1985).

Other methods used to assess gestational age have included uterine size assessment, time at quickening and fundal height measurements. However, these clinical methods are often suboptimal. Robinson noted that uterine size determination by bimanual examination produced incorrect assessments by more than two weeks in over 30% of patients. Similarly, fundal height estimation does not provide a reliable guide to predicting gestational age. Beazley et al found up to eight weeks variation in gestational age for any particular fundal height measurement during the second and third trimesters. Quickening, or initial perception of fetal movement can vary greatly among women. While these modalities may be useful adjuncts, they are unreliable as the sole tool for the precise dating of a pregnancy (Salomon et al 2010).

In recent years, ultrasound assessment of gestational age has become an integral part of obstetric practice. Correspondingly, prediction of gestational age is a central element of obstetric ultrasonography. Fetal biometry has been used to predict gestational age since the time of A-mode ultrasound. Currently, the sonographic estimation is derived from calculations based on fetal measurements and serves as an indirect indicator of gestational age. Over the past three decades, numerous equations regarding the relationship between fetal biometric parameters and gestational age have been described and have proven early antenatal ultrasound to be an objective and accurate means of establishing gestational age (Kalish et al 202 and Kurtz et al 1996).

Although routine ultrasonography at 18–20 weeks gestation is controversial, it is practiced by many obstetricians in the United States. In addition to screening for fetal anomalies, sonographic gestational age assessment may be of clinical value in that it has been shown to decrease the incidence of post term as well as preterm diagnoses and thus the administration of tocolytics. In addition, uncertain gestational age has been associated with higher perinatal mortality rates and an increase of low birth weight and spontaneous preterm delivery (Ewigman 1993).

While ultrasound has proven to be useful in the assessment of gestational age in the first and second trimesters, accuracy in the third trimester is not as reliable. Biologic variation can be a major factor that affects accuracy in gestational age prediction, and this variability greatly increases with advancing pregnancy. Doubilet and Benson evaluated late third trimester ultrasound examinations of women who had also received a first trimester exam and found the disparity in gestational age assessments to be three weeks or greater. Thus, third trimester sonographic estimates of gestational age should be used with caution, if at all.

Recent advances in ultrasound image quality and the wide availability of accurate biometric formulas have greatly improved physicians' ability to calculate gestational age. However, properly dating a pregnancy sonographically still depends on adherence to good ultrasound technique. Obtaining a clear and precise image of each bio-metric indicator is essential. Errors in estimation may arise from technical difficulties including obtaining the proper axis for measurement, movement of the mother or fetus, machine sensitivity settings or caliper placement. If a certain biometric indicator is not well visualized or is difficult to measure, it is better to use an alternative indicator rather than include a suboptimal measurement. In addition, it is helpful to obtain several measurements of each indicator and use an average to ensure a more precise calculation of fetal age (Filly and Hadlock 2000).

Buscicchioet al. (2008) analyzed fetal biometric measurements to compare fetal biometric measurements with standard growth charts for ultrasound parameters existing from the last 30 years. Their study included 1000 pregnant women with uncomplicated singleton pregnancy between $14^{th}$and 41weeks of gestation. All recruited pregnant women enrolled had an abdominal ultrasonography for fetal biometry. For each measurement, regression models were fitted to estimate the mean and SD. The results were compared with existing references from the last 30 years using Student's distribution. *Results:* One thousand normal fetuses from pregnant women, between 22th and 23th weeks, between 32th and 33th weeks and at 38th week, were thoroughly measured. There were significant differences from the comparison with their data for each gestational age: femur length and homer length, abdominal circumference, head circumference and occipito-frontal diameter were longer than all parameters of existing references from the last 30 years. Their study concluded that; fetus is grown up across the years. It is necessary to modify the standard growth charts for ultrasound parameters existing from the last 30 years with actually fetal biometric measurements. It is helpful for a correct clinical approach and for an appropriate management mother-fetus.

Madoret al. (2010) evaluated fetal Gestational age dependent biometric parameter because there is limited data on fetal cranial dimensions of Nigerian population. This is important because the study of normal and abnormal growth of children has become an increasingly important part of the practice and research in all fields related to child health; more so that prenatal and postnatal growth is one continuous process. Their study is a cross-sectional study conducted on 13,740 Nigerian fetuses ranging from 12 weeks to 42weeks at the Centre for Reproductive Health Research Jos; bi parietal and occipitofrontal diameters were measured using ultrasound machine in order to calculate fetal cephalic index. The values were statistically analyzed after deriving the relevant indices. Their results using regression equation as calculated between gestational age and cephalic index of fetuses of Nigerian women. This equation $y = 1.3x + 59.88$; showed a linear relationship which was stronger from 12 to 16 weeks of gestation. Above 16 weeks gestation, the relationship was found to be quite weak. Coefficient of correlation is $R^2 = 0.9844$ ($p < 0.0001$). In conclusion: The fetal skulls were found to be mesocephalic in the early weeks and brachycephalic at term.

Chapter three 3
Methodology

Chapter three

Methodology

Material and methods

3-1 Material:

3-1-1 Patient:

A fifty pregnant women were referred to the ultrasound department for check up to assess the gestational age at Turkish teaching hospital, and Elsoudy hospital.

3-1-2 Equipment:

In this study, the data was collected using Philips SDR 1000 Real time ultrasound machine equipped with 3.5 MHz transducer and an electronic caliper system set at a velocity of 1540m/via trans-abdominal scan.

Figure(3-1) Ultrasound machine

3-2 Method of study:

Each patient scanned twice in an international scanning guidelines, first by the researcher and then by a qualified sinologist to confirm the findings and diagnosis.

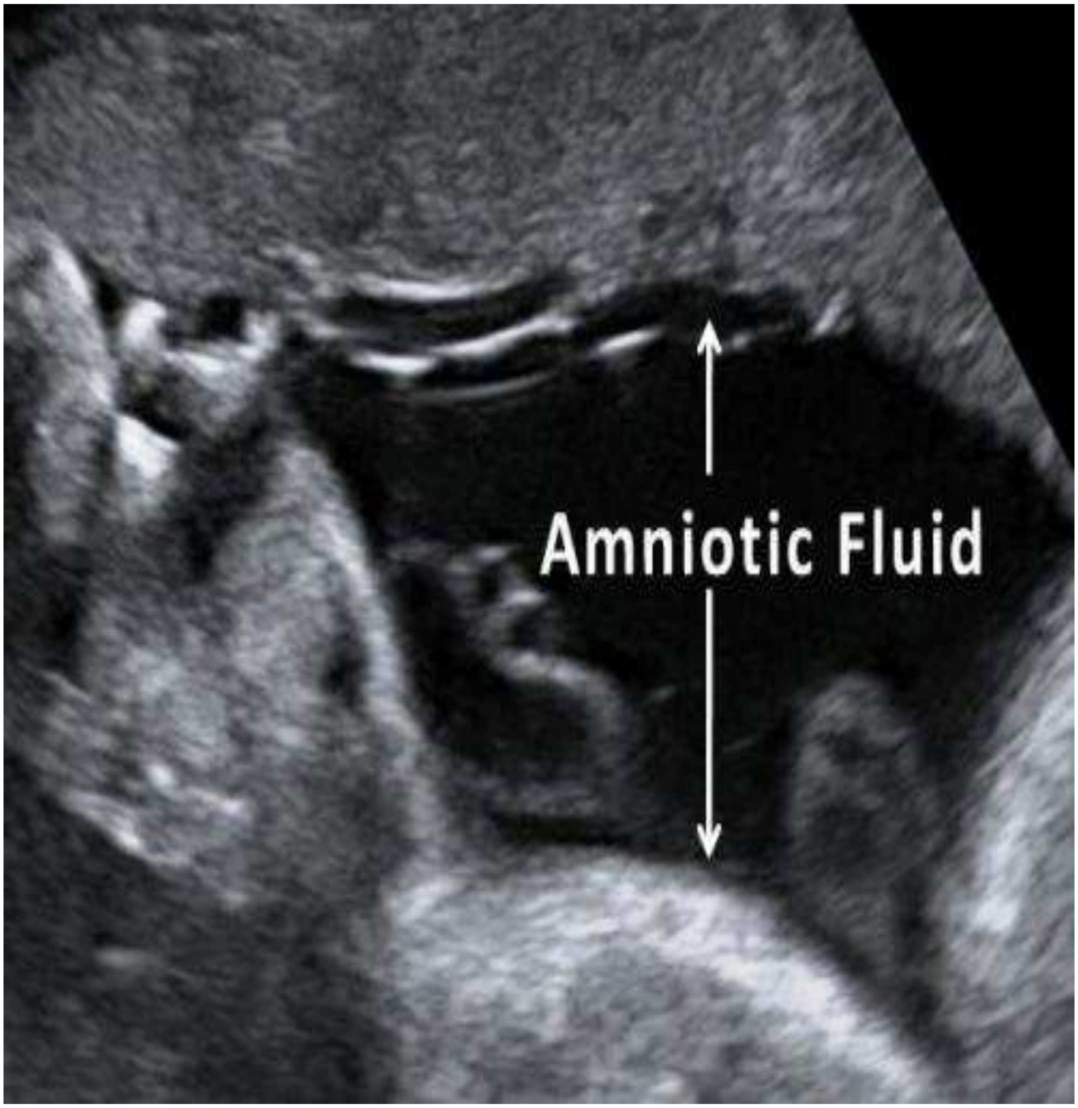


Figure (3-2) Ultrasound technique of Amniotic fluid index

Shows the convex transducer in longitudinal axis and patient supine to measure the amniotic fluid index. (Henry 2012).

3-2-1 Design of the study

This is a descriptive study of a cross sectional type with prospective data collection

3.2.2 Method of data collection (technique)

Every fetus will be measured and included only once so that a pure cross-sectional set of data was constructed. For each patient the gestational age was recorded, as were last menstrual period, maternal age and parity. Maternal age was calculated in completed years at the moment of the ultrasound. Fetal biparietal diameter measurements were made in an axial plane at the level where the continuous midline echo is broken by the cavum septum pellucidum in the anterior third and that includes the thalamus. This transverse section should demonstrate an oval symmetrical shape. BPD is measured at the level of Thalamai and Cavum Septic Pellucidi. The Cerebellar hemispheres should not be visible in this scanning plane. The measurement is to be taken from the outer edge of the proximal skull to the inner edge; then other measurement were taken from outer to outer to obtain HC. The occipitofrontal diameter (OFD) was measured in the same plane between the leading edge of the frontal bone and the outer border of the occiput. The cephalic index was calculated as the ratio of the same two diameters (BPD/OFD × 100). The head circumference will be calculated using the following equation: HC = 3.14 (BPD + OFD)/2

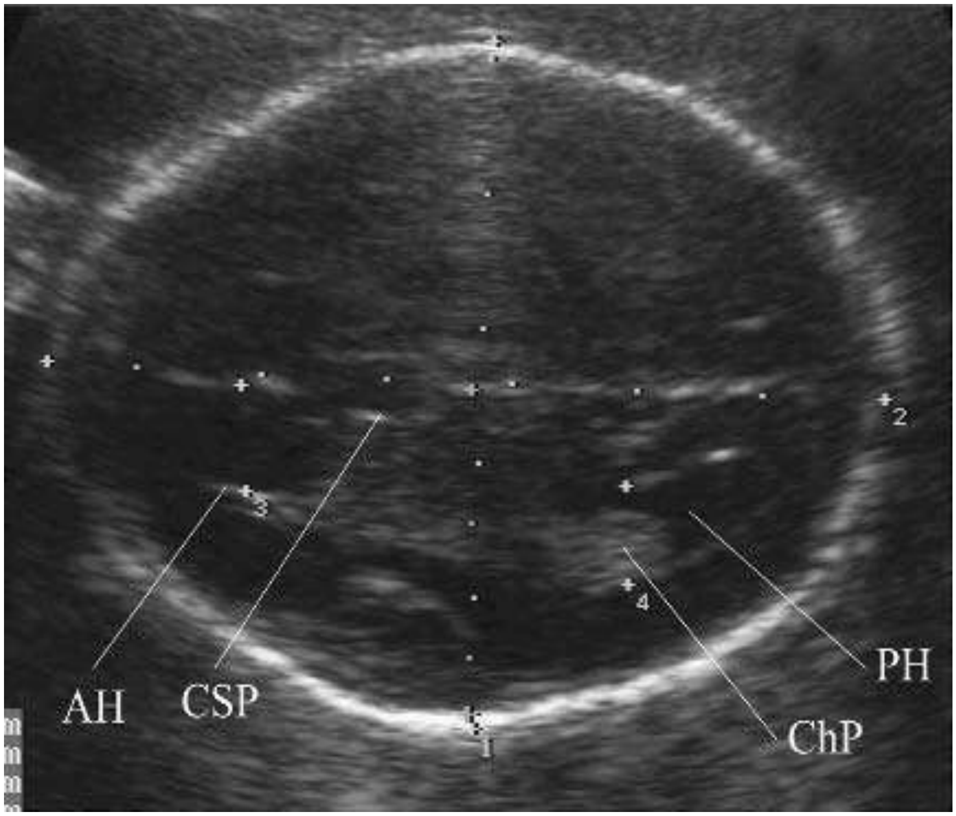


Figure (3-3) is a Transverse section of the fetal head demonstrating the landmarks required to measure the BPD using the thalami view. CP, cerebral peduncles; CSP, cavum septum pellucidum; TH, thalami.

3.2.3 Sample size and type

The data will be collected from 50 pregnant women in the second or third trimester visited the ultrasound department fetal assessment. The sample will be chosen conveniently.

3.2.4 Variables of the study

The data will be collected using the following variables: maternal age, parity, LMP, BPD diameter (inner to outer), Occipitofrontal diameter, GA (using LMP, and BPD), HC, BPD and OFD ratio,

3.2.5 Method of data analysis

The data will be analyzed by Microsoft Excel and SPSS version 21 under windows; where the frequency distribution of the included variables will be obtain as well as the estimation of the GA using OFD through a linear regression model and quadratic one will carried using the LMP calculation as a reference. A significant difference between the estimated GA using OFD, BPD and HC will be made; also the effect of maternal age, parity and BPD/OFD ration will be investigated. Accuracy and sensitivity of the estimated GA using OFD will be calculated.

3.2.6 Ethical approval

The researcher will grant an ethical approval from the hospital and the ultrasound department as well as written consent from the patient. The collected data will be used for scientific research only and the ID of the patient or their personality will not be disclosed under any circumstances.

Chapter four
Results

Chapter four

Results

The results of this study presented in tables and figures. The tables show the paired samples statics the mean and slandered deviation. Also the other table showed Paired Samples Correlations projected the relationship between the Gestational age using LMP and the fetal head parameters.

Table 4.1: Paired Samples Statistics:

		Mean	Std. Deviation
Pair 1	GA_LMP	29.9288	6.92259
	GA_BPD	29.9690	6.97746
Pair 2	GA_LMP	29.9288	6.92259
	GA_OFD	29.9892	6.97240
Pair 3	GA_LMP	29.9288	6.92259
	GA_FL	29.9268	6.96150
Pair 4	GA_LMP	29.9288	6.92259
	GA_HC	30.06392	6.943664

Table 4.2: Paired Samples Correlations:

		Correlation	Sig.
Pair 1	GA_LMP & GA_BPD	.996	.000
Pair 2	GA_LMP & GA_OFD	.992	.000
Pair 3	GA_LMP & GA_FL	.997	.000
Pair 4	GA_LMP & GA_HC	.997	.000

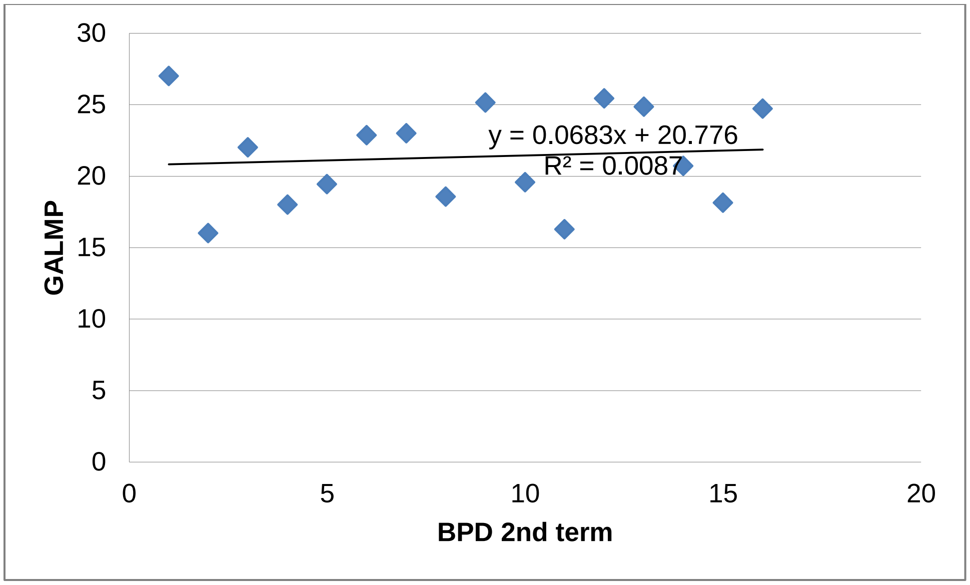


Figure 4- 1 Scatter plot of BPD versus GA from LMP with a trend line depicted a direct linear association in **2nd term.**

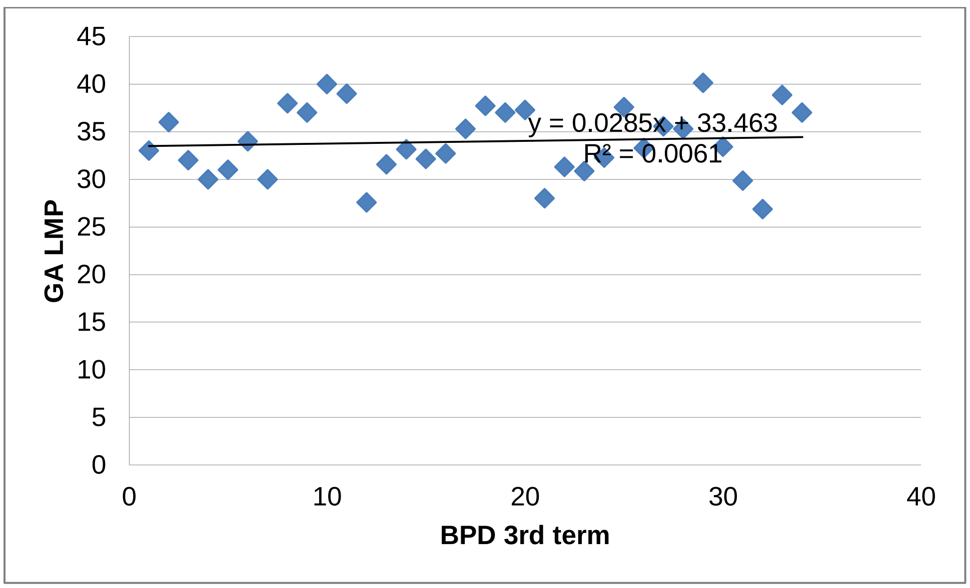


Figure 4- 2 Scatter plot of BPD versus GA from LMP with a trend line depicted a direct linear association in 3rd term.

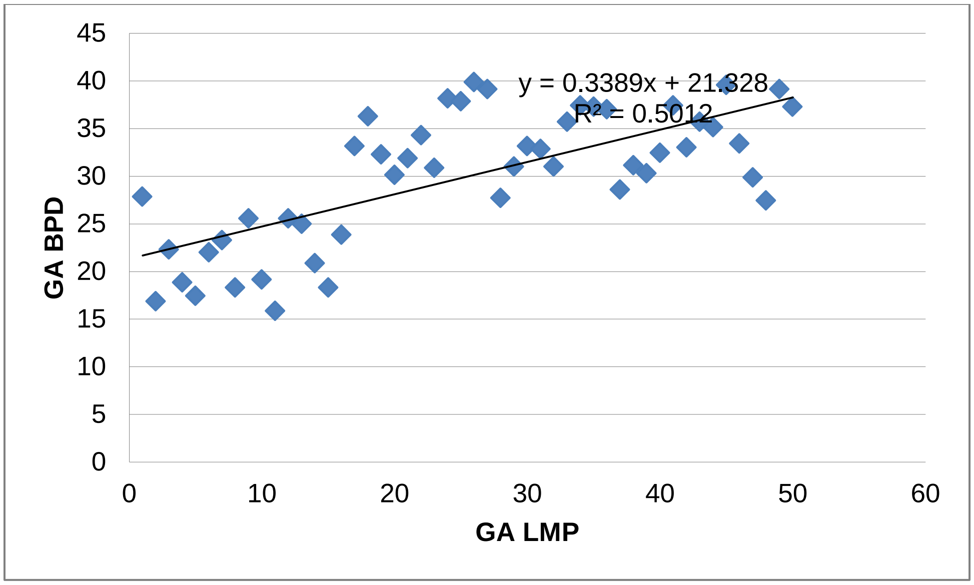


Figure 4-3 Scatter plot of BPD versus from LMP with a trend line depicted a direct linear association.

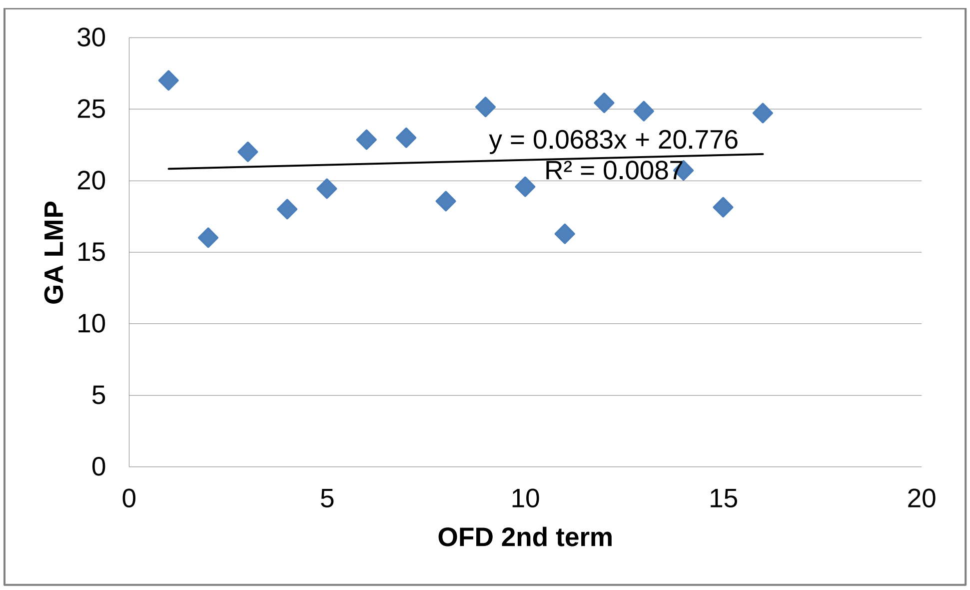


Figure 4-4 Scatter plot of BPD versus OFD with a trend line depicted an exponential association in **2nd term.**

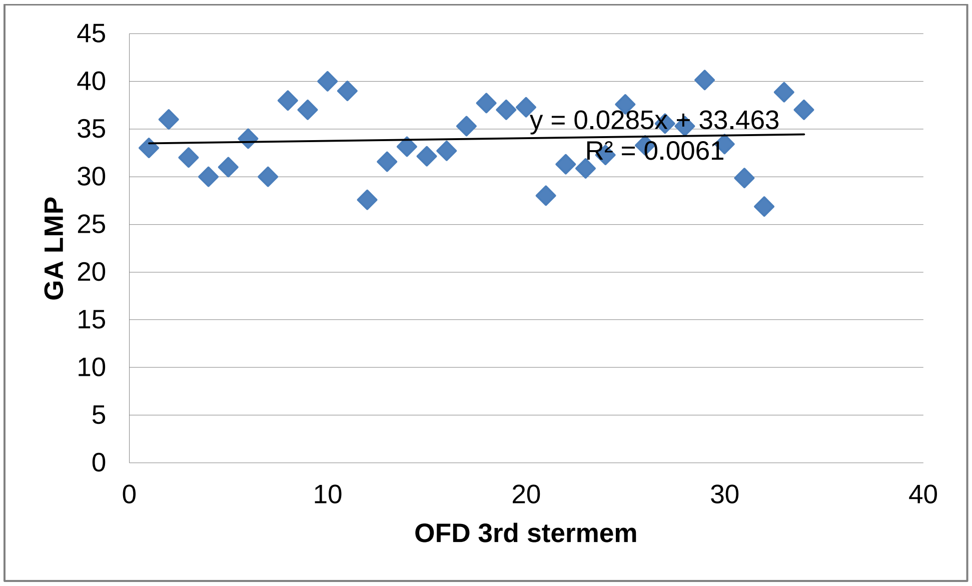


Figure 4-5 Scatter plot of BPD versus OFD with a trend line depicted an exponential association in third term.

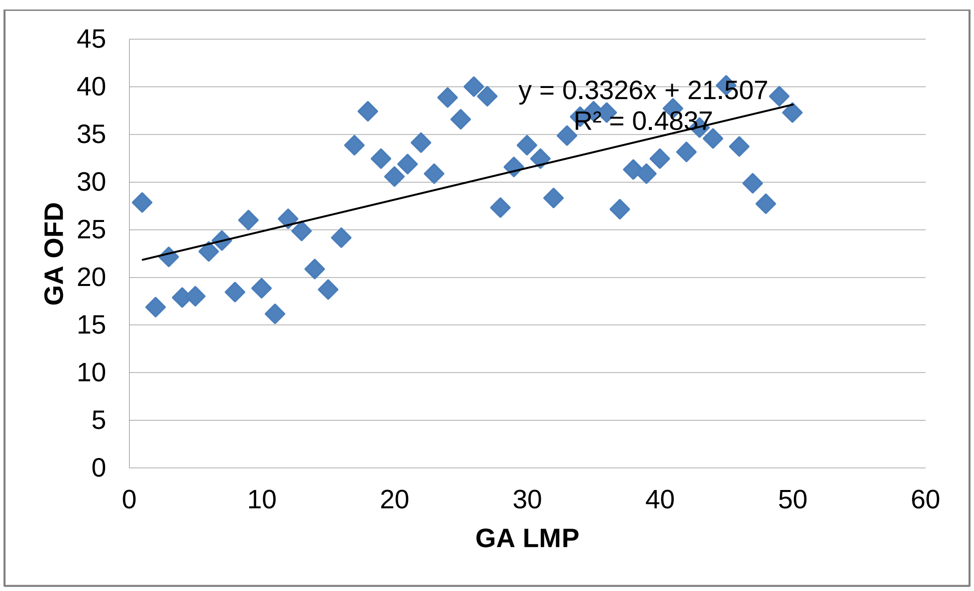


Figure 4-6 Scatter plot of BPD versus OFD with a trend line depicted an exponential association

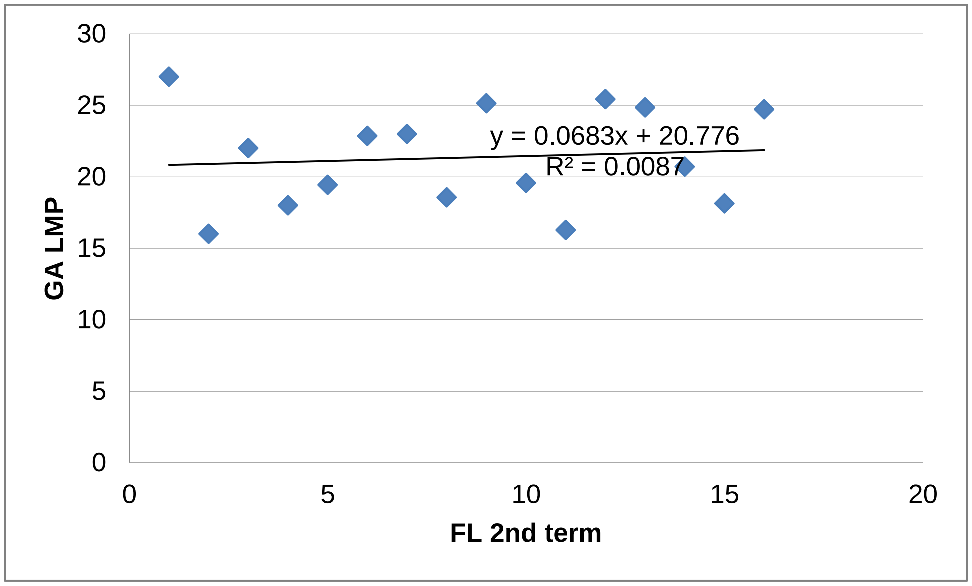


Figure 4-7 Scatter plot of femur length versus GA from LMP with a trend line depicted a direct linear association in 2nd term.

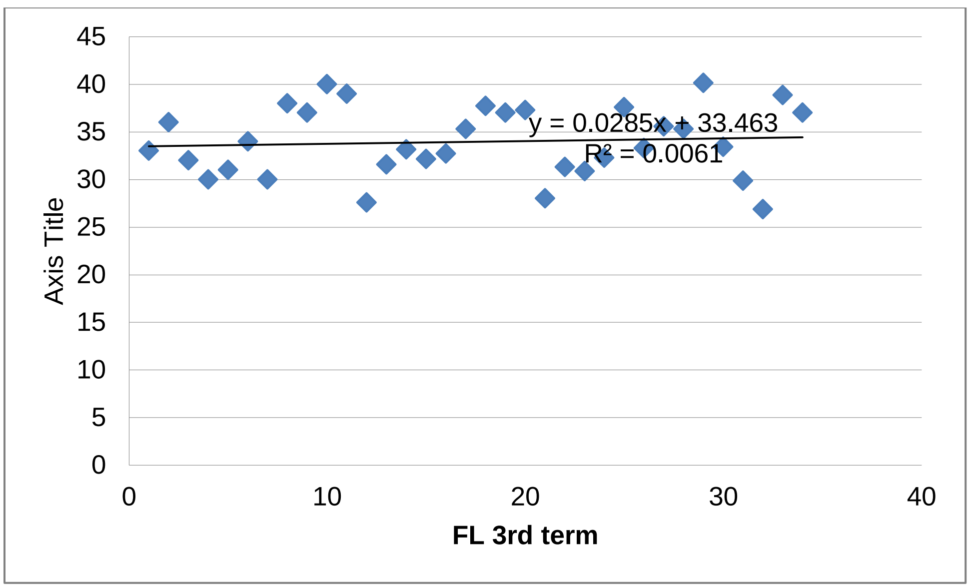


Figure 4-8 Scatter plot of femur length versus GA from LMP with a trend line depicted a direct linear association in third term.

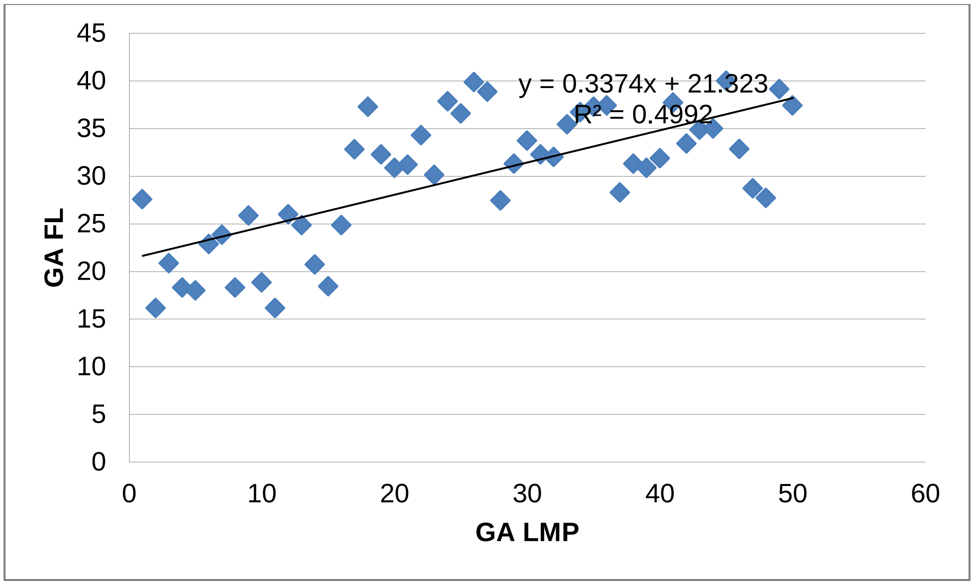


Figure 4-9 Scatter plot of femur length versus GA from LMP with a trend line depicted a direct linear association in third term.

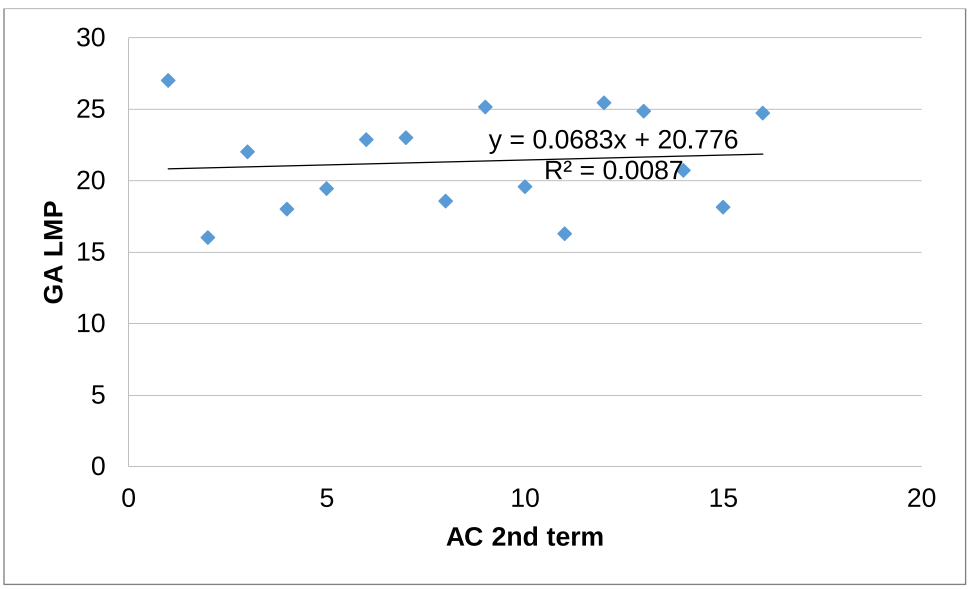


Figure 4-10 Scatter plot of abdominal circumference versus GA from LMP with a trend line depicted a direct linear association in 2nd term.

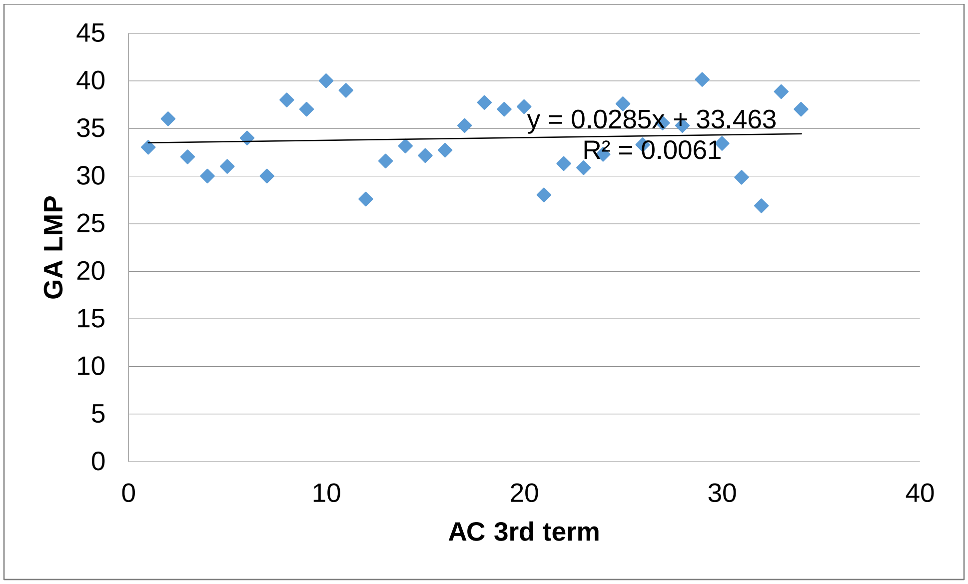


Figure 4-11 Scatter plot of abdominal circumference versus GA from LMP with a trend line depicted a direct linear association in third term.

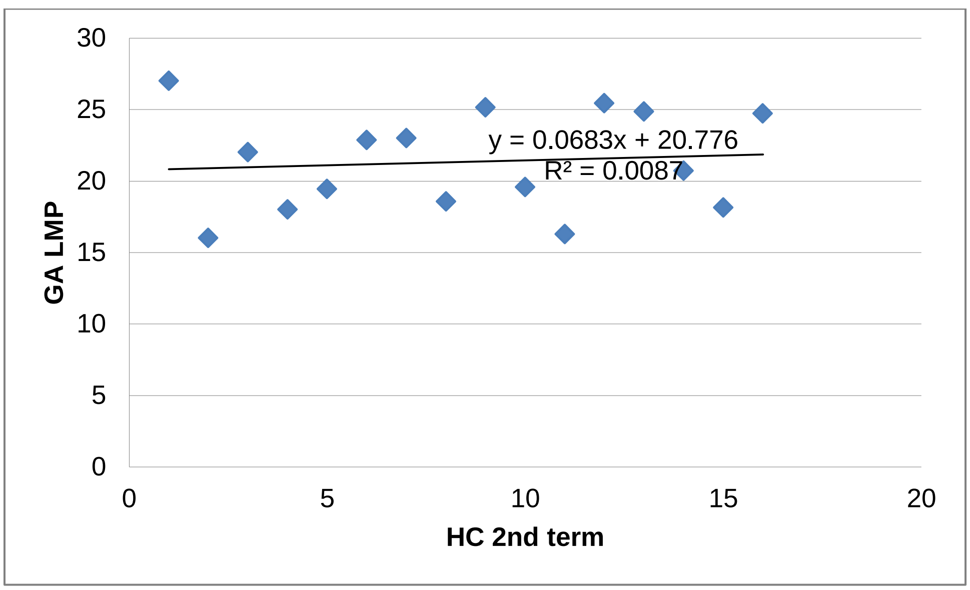


Figure 4-12 Scatter plot of head circumference versus GA from LMP with a trend line depicted a direct linear association in 2nd term.

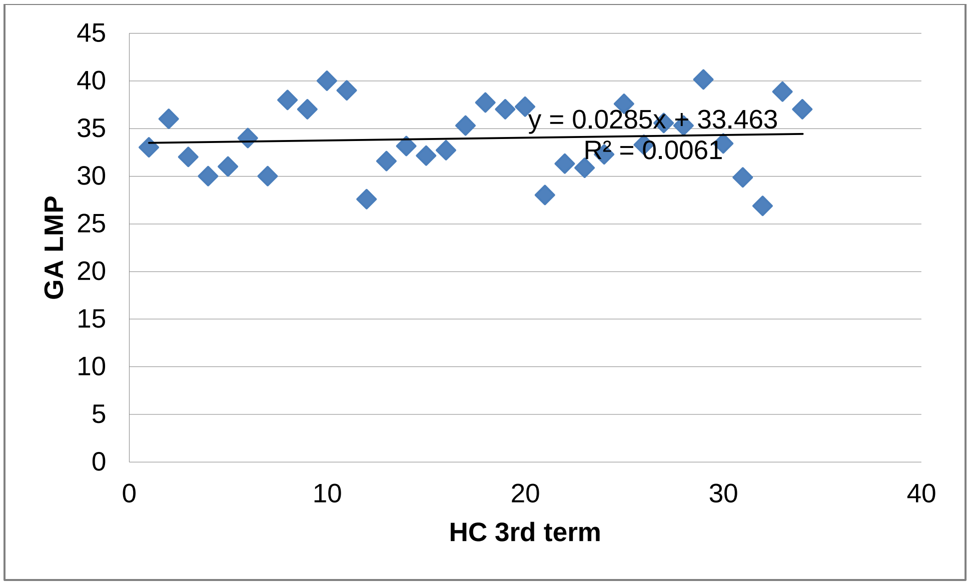


Figure 4-13 Scatter plot of head circumference versus GA from LMP with a trend line depicted a direct linear association in third term.

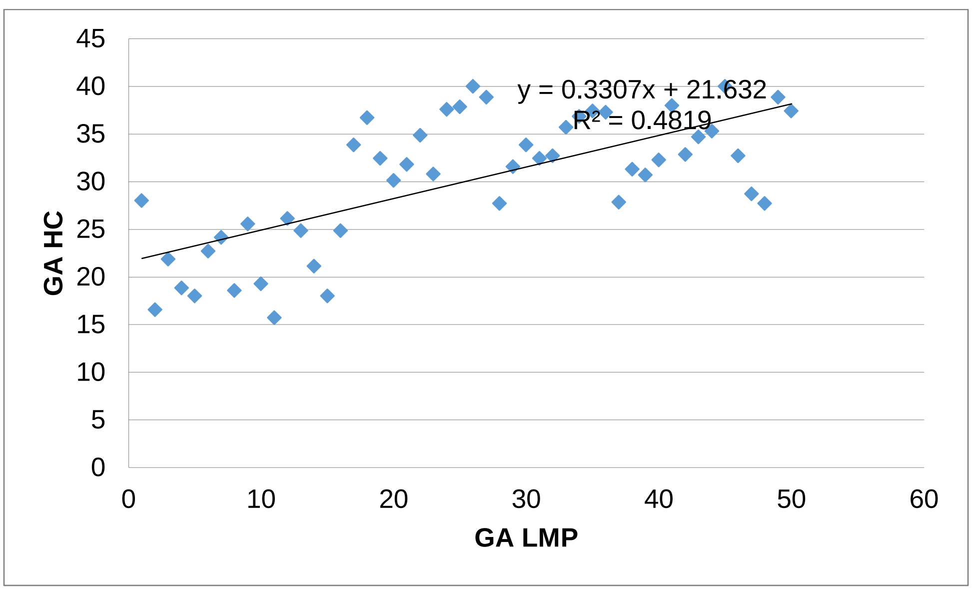


Figure 4-14 Scatter plot of head circumference versus GA from LMP with a trend line depicted a direct linear association in $3r^{d}$ term.

Table 4-3 a paired t-test result between the GA calculated using LMP and GA estimated using OFD, BPD and HC

Significance test		t	Sig. (2tailed)
Pair 1	GA_LMP GA_BPD	.484	.631
Pair 2	GA_LMP GA_OFD	.500	.619
Pair 3	GA_LMP GA_FL	.026	.979
Pair 4	GA_LMP GA_HC	1.675	.100

Chapter five

***Discussion**

***Conclusion**

***Recommendations**

Chapter Five
(Discussion, conclusion and recommendation)

The main objective of this study was to estimate the gestational age using the occipitofrontal diameter in the second and third trimester using the known last minstrel period as a reference in estimating the accurate GA.

5-1 Discussion:

The results of this study showed a significant correlation between the BPD and OFD where 97.4% of the OFD variation can be explained successfully by using the BPD, therefore the OFD increases by 1.24 mm for every 1 mm of the BPD (Figure 4-3). In the same essence there is a significant correlation between the GA using LMP (26.5±7.7 weeks) and the OFD, in which the OFD can explain 92% of the changes in GA perfectly, where the GA increases by 0.3 weeks/mm of OFD starting at 2.3 weeks with an average estimation equal to 26.5±7.3 weeks (Figure 4-6). But when exponential relationship was assumed the predicting power increases to 93% of the GA (Figure 4 &5).

The BPD as well showed as expected strong and significant correlation with the LMP-GA, hence the BPD can explain 96% of the changes in GA perfectly where the GA increases by 0.99 week/mm of BPD (Figure 4-12) with an average estimated GA of 26.7±7.6 weeks. Similarly HC had a significant correlation with GA and it can explain 92% of the changes in GA. The GA increases by 0.105 week/mm of HC (Figure 4-7) with an average estimated GA of 26.4±7.4 weeks.

As it can be seen clearly the estimation of gestational age using OFD, BPD and HC alone gives results in average almost similar with minimal variation in respect to standard deviation. This difference was inconclusive using paired *t*-test between the estimated GA using the measured parameters and the GA using LMP at $p = 0.05$ which means the OFD can be used safely to estimate the GA specially in cases where the BPD can't be accessed easily as well as a comparative measure when the short axis showed abnormal dimension.

5-2 Conclusion:

This study was generally is an attempt to estimate the gestational age using front occipital diameter as a predictor variable and compare the result to last menstrual period gestational age calculation as well as BPD and HC.

The data in this prospective, cross-sectional study were collected from 50 pregnant women in the second and third trimester, visited Alsouady and Turkish hospital in the period from October 2016 to December 2016 using trans-abdominal scan through 3.5 MHz transducer.

The results of this study showed that OFD can be used in linear equation and exponential one to estimate the gestational age with a predicting power of 93% as follows: $GA = (0.2958\times OFD) + 2.3$ or $GA = 9.6774e^{0.0118\times OFD}$, similarly for BPD and HC can be used to estimate the GA as follows: $GA = (0.9915 \times BPD) + 0.03$ and $GA = (0.1046 \times HC) + 2.05$. The results also emphasizes that the estimated GA were not significantly different from the LMP-GA at $p = 0.05$ using *t*-test.

In conclusion OFD can be used safely to predict the GA, but consideration of cephalic index is important to avoid over or under estimation of GA. The OFD mainly had exponential relationship with the GA rather than the linear trend although both trend gives insignificant difference from the LMP-GA.

5-3 Recommendations:

- Further study can be done to relate head measurements OFD, BPD and HC to abdominal circumference and femur length to find fetal growth index.
- Also further study can be done to find the accuracy of the head measurements together and separate in the second trimester then third trimester to compare the accuracy in each trimester.
- Cephalic index must be evaluated first before using head measurement for GA estimation.
- OFD and HC should be done as a routine in Sudan to estimate GA because Sudanese have different ethnic groups, which it has impact on the skull diameter specially the BPD.
- OFD should be programmed in all ultrasound machines to have a good benchmark for comparison.

Further study could be done to authenticate the reliability of OFD in cephalic and breach pregnancy.

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Appendices

Appendix (A)

Term of preg.	*BPD*	*OFD*	*FL*	*HC*	*AC*	*GA_LMP*	*GA_BPD*	*GA_OFD*	*GA_FL*	*GA_HC*
2	7.14	9.4	5.16	25.81	23.58	27	27.86	27.86	27.57	28
2	3.32	5.86	2.24	13.25	14.02	16	16.86	16.86	16.14	16.57
2	5.48	5.98	4.23	17.92	16.34	22	22.29	22.14	20.86	21.86
2	3.63	3.99	2.14	11.95	10.25	18	18.86	17.86	18.29	18.86
2	4.04	5.14	2.65	14.43	14.93	19.43	17.43	18	18	18
2	5.48	6.65	2.88	17.92	15.22	22.86	22	22.71	22.86	22.71
2	7.74	8.5	2.5	25.92	23.95	23	23.29	23.86	23.86	24.14
2	3.63	3.93	1.99	11.95	9.25	18.57	18.29	18.43	18.29	18.57
2	7.88	10.3	4.23	31.55	28.82	25.14	25.57	26	25.86	25.57
2	5.88	7	3.58	19	17.25	19.57	19.14	18.86	18.86	19.29
2	4.79	6.22	2.46	19.86	17.52	16.29	15.86	16.14	16.14	15.71
2	6.55	8.22	3.15	20.81	19.98	25.43	25.57	26.14	26	26.14
2	6.89	7.03	2.84	21.22	17.95	24.86	25	24.86	24.86	24.86
2	9.44	11.49	4.07	26.08	23.44	20.71	20.86	20.86	20.71	21.14
2	7.54	8.94	2.68	29.84	26.86	18.14	18.29	18.71	18.43	18
2	6.83	9.14	3.47	24.84	21.84	24.71	23.86	24.14	24.86	24.866
3	8.44	10.79	6.39	30.42	28.42	33	33.14	33.86	32.81	33.86
3	9.06	11.43	7.3	32.4	33.96	36	36.29	37.43	37.29	36.71
3	8.17	10.39	6.32	24.38	27.91	32	32.29	32.43	32.29	32.43
3	7.59	9.29	5.32	26.34	25.19	30	30.14	30.57	30.86	30.14

3	7.62	10.1	5.86	28.46	26.04	31	31.86	31.86	31.19	31.81
3	9.46	11.04	6.29	32.15	33.69	34	34.29	34.14	34.29	34.86
3	8.6	10.26	5.44	26.22	25.18	30	30.86	30.86	30.14	30.81
3	9.58	10.56	6	28.53	27	38	38.14	38.86	37.86	37.57
3	9.1	10.62	5.88	26.02	26.81	37	37.86	36.57	36.57	37.86
3	9.71	10.59	6.22	30.04	28.37	40	39.86	40	39.86	40
3	9.12	10.44	5.98	29.22	27.16	39	39.12	39	38.86	38.86
3	7.1	8.92	5.12	25.53	24.8	27.57	27.71	27.29	27.43	27.71
3	8	10.15	6.02	28.71	28.1	31.57	31	31.57	31.29	31.57
3	8.44	10.79	6.42	30.42	28.42	33.14	33.14	33.86	33.71	33.86
3	8.19	10.39	6.23	29.39	27.94	32.14	32.86	32.43	32.29	32.43
3	8.1	10.62	6.16	29.55	28.88	32.71	31	28.3	32	32.71
3	8.6	11.52	6.88	26.22	24.09	35.29	35.71	34.86	35.43	35.71
3	9.14	10.42	4.25	31.77	29.52	37.71	37.43	36.86	36.71	36.86
3	10.4	11.54	5.39	32.49	29.33	37	37.29	37.43	37.29	37.43
3	9.1	10.62	4.23	26.02	23.05	37.29	37	37.29	37.43	37.29
3	6.9	8.85	3.24	24.85	22.09	28	28.57	27.14	28.29	27.86
3	7.82	9.22	3.66	27.73	25.29	31.29	31.14	31.29	31.29	31.29
3	7.67	9.42	2.78	27.51	25.2	30.86	30.29	30.86	30.86	30.71
3	8.71	9.58	3.22	30.22	28.28	32.29	32.43	32.43	31.86	32.29
3	7.85	9.55	4.22	32.08	29.89	37.57	37.43	37.71	37.71	38
3	9.28	11.25	5.18	36.01	34.24	33.29	33	33.14	33.43	32.86

3	9.12	11.25	4.48	26.01	23.26	35.57	35.71	35.71	34.86	34.71
3	9.19	10.08	3.55	30.84	27.94	35.29	35.14	34.57	35	35.29
3	10.22	12.39	5.28	34.05	31.88	40.14	39.57	40.14	40	40
3	8.54	10.53	3.85	36.24	32.29	33.43	33.43	33.71	32.86	32.71
3	8.99	11.65	3.95	34.85	31.89	29.86	29.86	29.86	28.71	28.71
3	6.84	8.74	2.99	29.71	27.09	26.86	27.43	27.71	27.71	27.71
3	9.84	11.98	6.27	36.42	33.84	38.86	39.14	39	39.14	38.86
3	8.73	10.25	4.75	32.43	29.64	37	37.29	37.29	37.43	37.43

Appendix (B)
Ultrasound Images

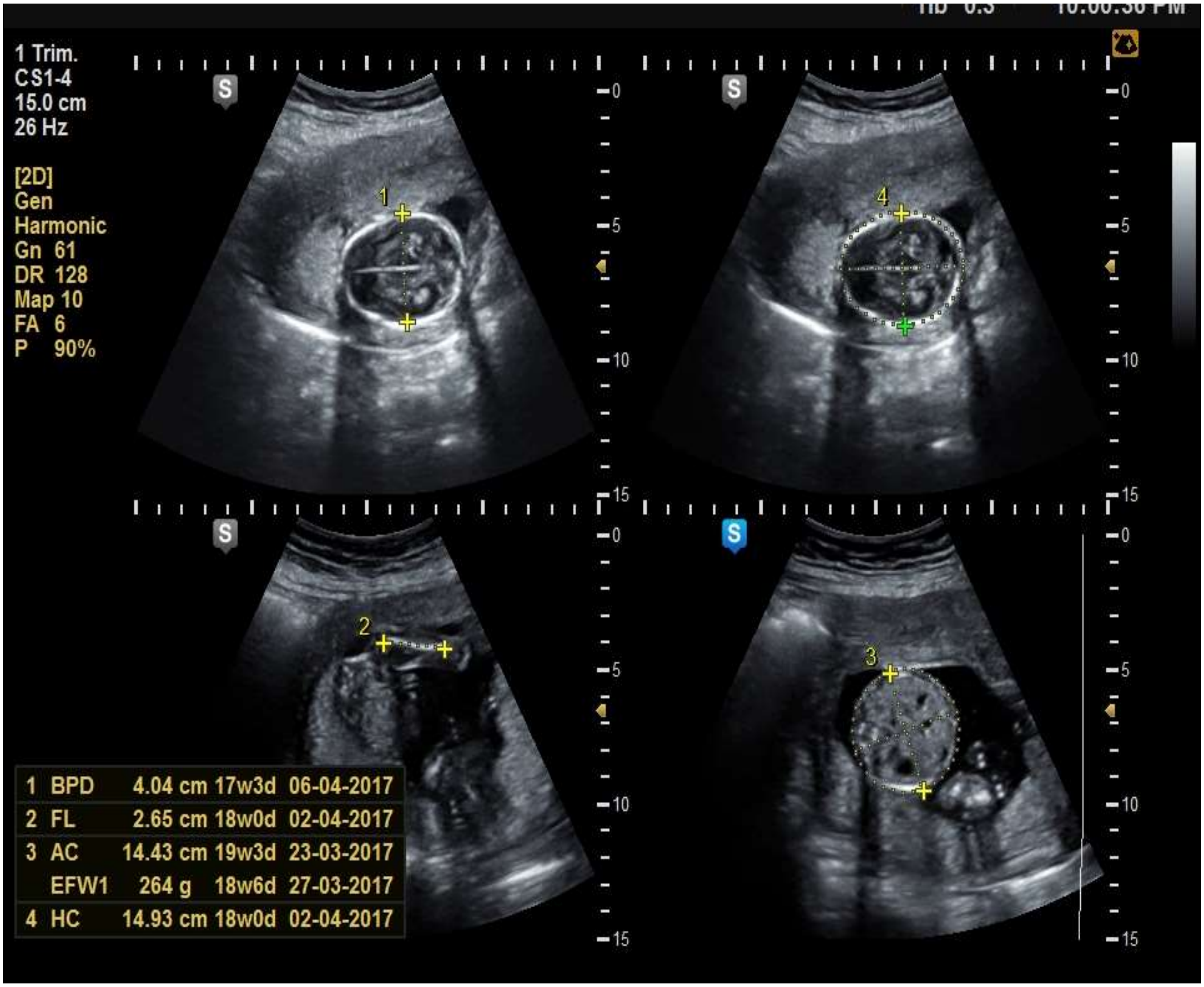
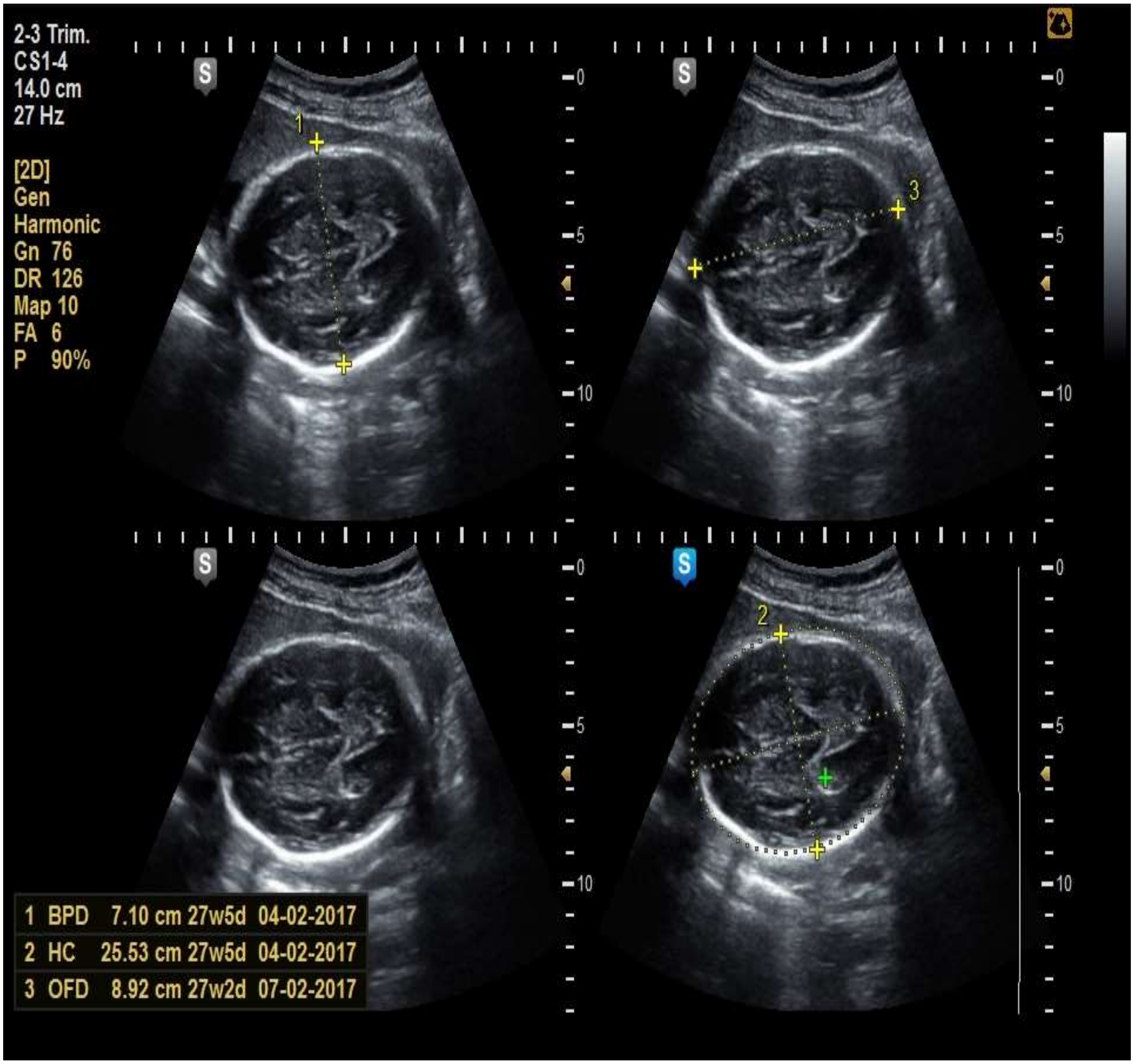


Figure B-1: Fetal head& femur length ultrasound images.
Has **18** Weeks gestational age



B- Figure 2: Fetal head ultrasound images.
With **27** Weeks + **5** days gestational age.

Figure B-3: Fetal head& femur length ultrasound images.
The fetal has **27** Weeks + **6** days GA.

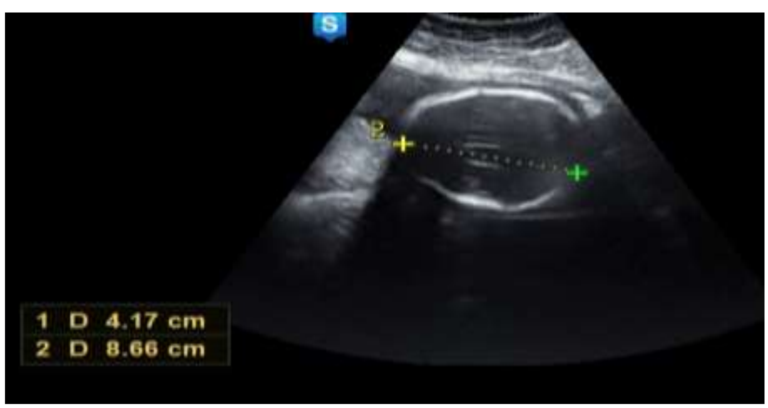


Figure B-4: Fetal head ultrasound image.

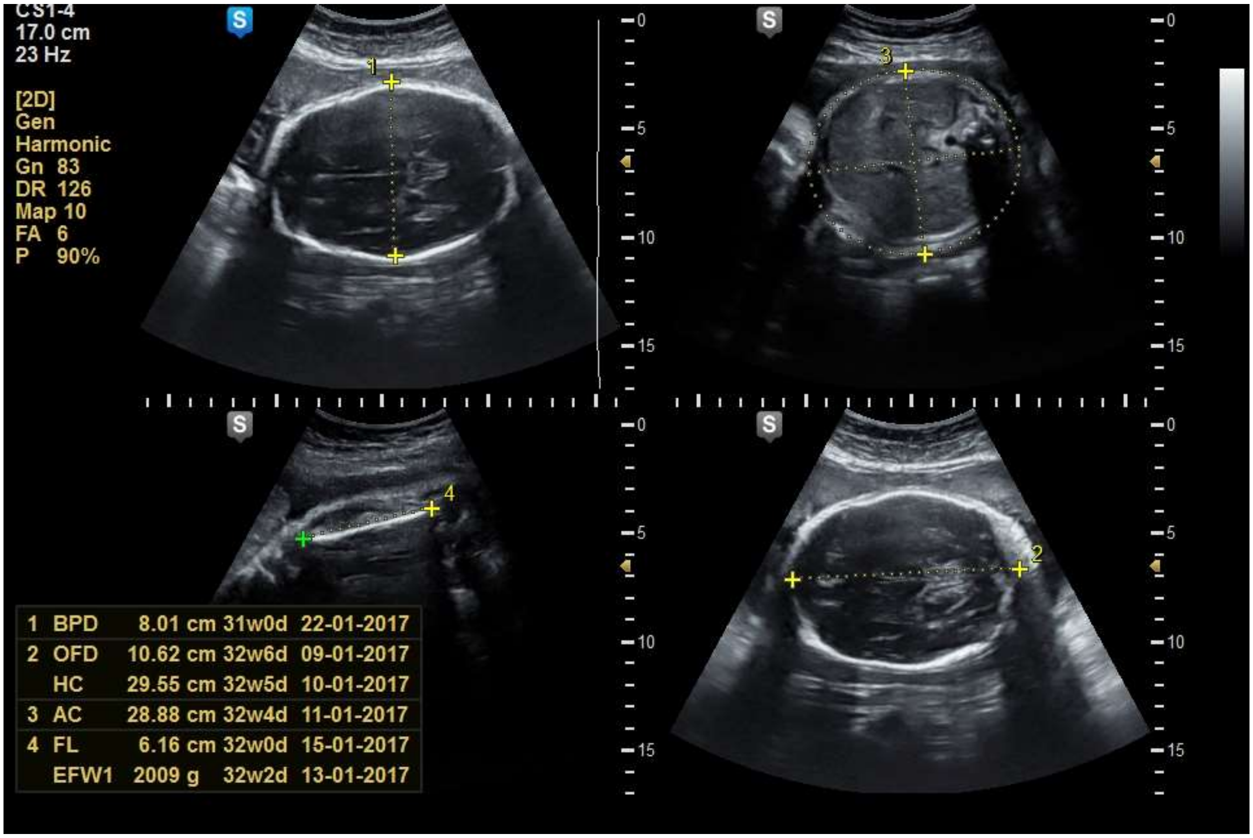


Figure B-5: Fetal head& femur length ultrasound images.
The gestational age is **32** weeks + **4** days.

Figure B-6: Fetal head ultrasound image.

Figure B-7: Fetal head& femur length ultrasound images.
The fetal had **30** weeks + **2** days.

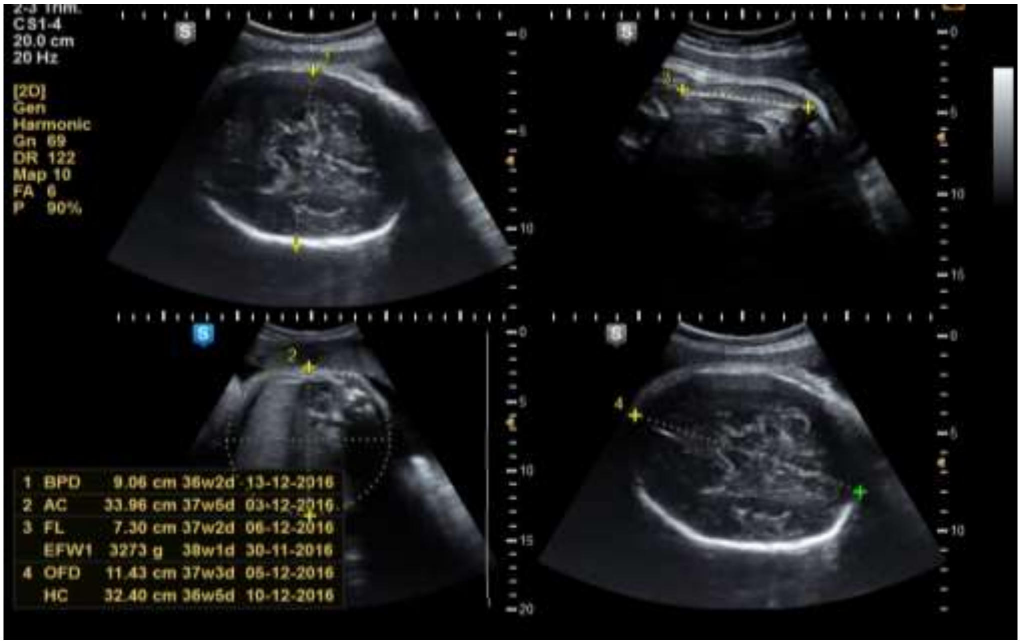


Figure B-8: Fetal head& femur length ultrasound images.
GA is **37** weeks + **3** days.

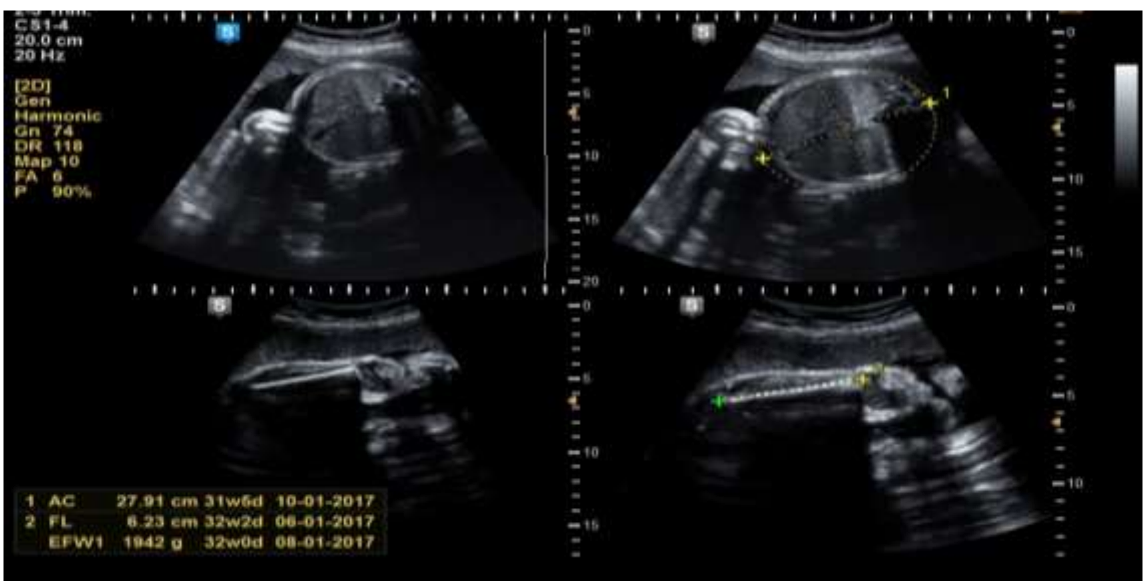


Figure B-9: Fetal head& femur length ultrasound images.
GA is **32** weeks

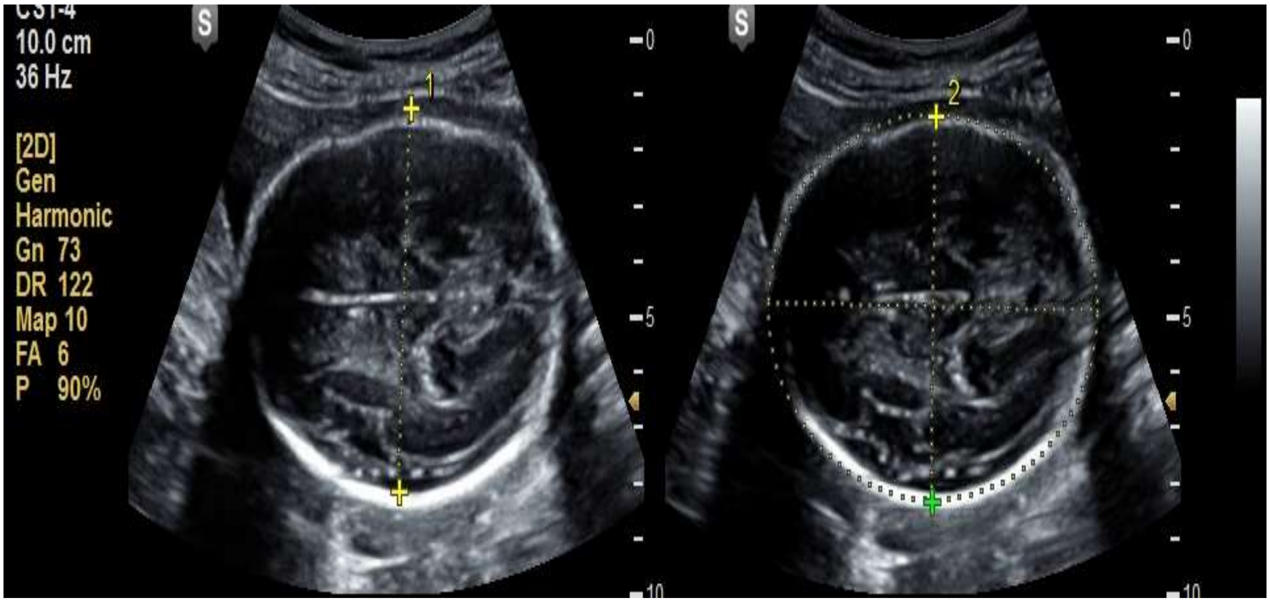


Figure B-10: Fetal head ultrasound images has GA **37** weeks.

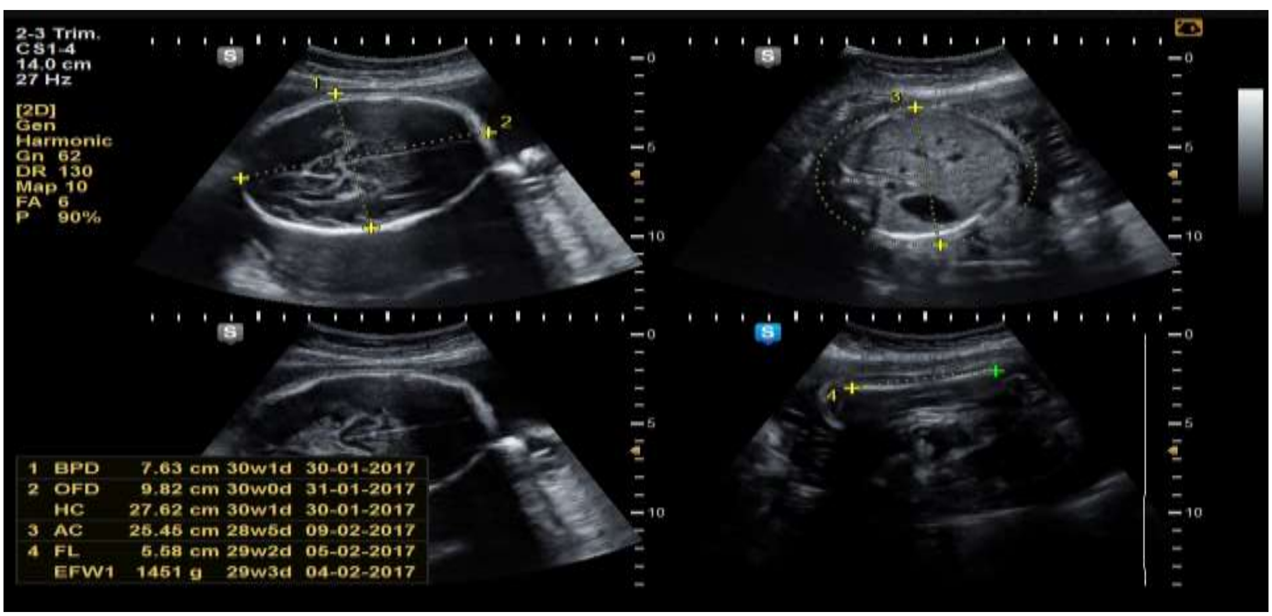


Figure B-11: Fetal head& femur length ultrasound images.
Gestational age is **30** weeks

o

Figure B-12: Fetal head ultrasound image

Figure B-13: Fetal head ultrasound image

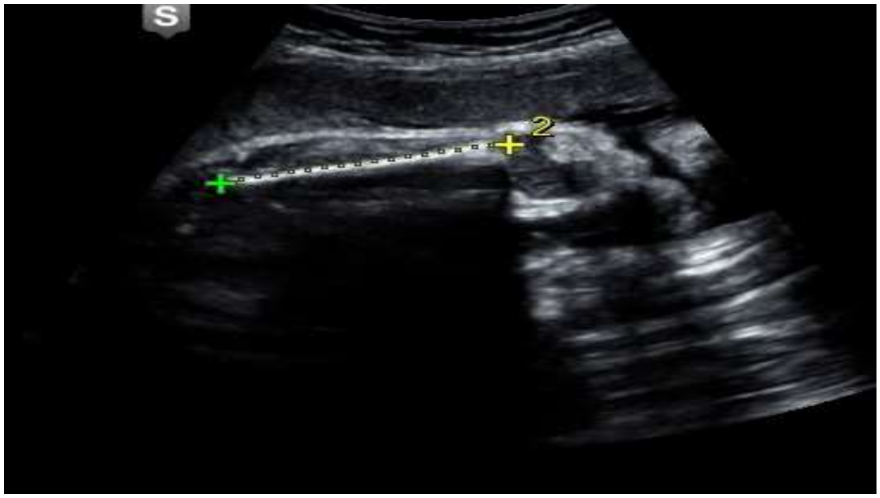


Figure B-14 : Femur length ultrasound image.

Figure B-15: Fetal head ultrasound image

LMP		GA(LMP)		EDD(LMP)		Gravida	Para
Composite GA	Average	GA(AUA)	30w4d	EDD(AUA)	03-06-2017	Aborta	Ectopic

EFW1	HADLOCK2	BPD,AC,FL	1611 g	(3lb 9oz)	30w2d	WILLIAMS

Fetal Biometry

	Label	Value	GA		m1	m2	m3	Method	Av.US
BPD	ASUM	7.88 cm	30w5d	±2w1d	7.88			Avg	☑
FL	HADLOCK	5.68 cm	29w6d	±2w1d	5.68			Avg	☑
AC	ASUM	26.58 cm	30w3d	±2w3d	26.58			Avg	☑
OFD	ASUM	10.04 cm	30w6d	±2w0d	10.04			Last	☑
HC	HADLOCK	28.35 cm	31w1d	±3w0d					☑

Fetal HR

Label	Value	m1	m2	m3	Method
Fetal HR	132 bpm	132			Last

2D Calculations

CI	HADLOCK	78.4 %	(70.0 %~86.0 %)	FL/AC	HADLOCK	21.4 %	(20.0 %~24.0 %)
FL/BPD	HOHLER	72.1 %	(71.0 %~87.0 %)	FL/HC	HADLOCK	20.0 %	(~)

Sample of Fetal Biometry Report Page

تم بحمد الله