

# **GROWTH PROFILE OF FETUS IN OUR POPULATION**



## **PhD Thesis**

Submitted by  
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Submitted to the Dhaka University as partial fulfillment of the  
requirements for the degree of Doctor of Philosophy.

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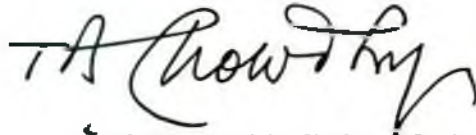
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## SUPERVISORS' CERTIFICATE

The work of this Thesis was done under our supervision, as partial fulfillment of the requirements for the degree of Doctor of Philosophy (PhD), of Dhaka University by Dr. Sabrina Quddus. The whole Thesis is her own work and it is up to our expectations.



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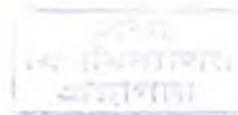
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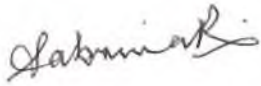
my teachers and patients who enriched me with knowledge and wisdom.

and

my husband Dr. Harun ar Rashid and children Shahrin and Amer Rashid.

## DECLARATION OF THE STUDENT

I do hereby declare that, the work described in this thesis titled 'Growth Profile of Fetus in our population', is completely unaided unless otherwise acknowledged. The whole thesis is based upon my own work and was done under the supervision of my guides. No part of this work has been previously submitted elsewhere for any other degree.



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## TABLE OF CONTENTS

<b>General Section:</b>		
Title page	...	Pg. i
Supervisors' certificate	...	ii
Declaration	...	iii
Dedication	...	iv
Acknowledgements	...	v
Table of Contents	...	vi-vii
List of Tables	...	viii
List of Graphs	...	ix
Abbreviations	...	x
<b>Technical Section:</b>		
<b>1. INTRODUCTION</b>	...	1-4
1.1: Statement of the problem	...	1
1.2: Purpose of the study	...	2
1.3: Assumption	...	4
1.4: Hypothesis	...	4
<b>2. AIMS AND OBJECTIVES</b>	...	5-7
2.1: General Objective	...	5
2.2: Specific Objective	...	5
<b>3. REVIEW OF LITERATURE</b>	...	8-37
3.1: Introduction	...	8
3.2: Gestational age assessment	...	11
3.3: Biparietal diameter	...	13
3.4: Head circumference	...	14
3.5: Femur length	...	15
3.6: Abdominal circumference	...	17
3.7: Estimated fetal weight	...	20
3.8: Ratios determined	...	22
3.9: Fetal growth	...	25
3.9a: Growth restricted fetus	...	28
3.9b: Growth accelerated fetus	...	32
3.10: Variability	...	34

3.11: Accuracy	...	...	34
3.12: Amniotic fluid evaluation	...	...	35
3.13: Body mass index	...	...	36
3.14: Safety of ultrasonography	...	...	37
3.15: Sample size in a study	...	...	37
<b>4. SUBJECTS AND METHODS</b>	...	...	<b>38-51</b>
4.1: Place & duration	...	...	38
4.2: Study design	...	...	38
4.3: Sample size and sampling technique	...	...	39
4.4: Sample selection	...	...	40
4.5: Ethical consideration.	...	...	42
4.6: Social class	...	...	42
4.7: Methodology	...	...	42-44
4.8: Out-come variables	...	...	44
4.8: Dependent variables:	...	...	45-48
4.8a: Biparietal diameter	...	...	45
4.8b: Head circumference	...	...	46
4.8c: Femur length	...	...	46
4.8d: Abdominal circumference	...	...	47
4.8e: Estimated fetal weight	...	...	48
4.8f: Ratios determined	...	...	48
4.8g: Estimated fetal weight accuracy	...	...	48
4.9: Procedure of data collection	...	...	49
4.10: Procedure of data analysis	...	...	50-51
<b>5. OBSERVATIONS AND RESULTS</b>	...	...	<b>52-96</b>
<b>6. DISCUSSION</b>	...	...	<b>97-121</b>
6.1 Discussion	...	...	97
6.2 Limitations	...	...	121
<b>7. SUMMARY AND CONCLUSION</b>	...	...	<b>122-123</b>
7.1 Summary	...	...	122
7.2 Conclusion	...	...	122
7.3 Recommendations	...	...	123
<b>8. REFERENCES</b>	...	...	<b>124-141</b>
<b>APPENDICES</b>	...	...	<b>xi-xx</b>
Questionnaire, consent form	...	...	xi-xiii
Obstetrics report sheet/CRF	...	...	xiv
Plates of U/S images	...	...	xv- xvi
Definitions, Stats, Formulae	...	...	xvii -xx



## LIST OF TABLES

Table I:	Summary of fetal BPD measurements	...	...	Pg.56
Table II:	Fitted centiles of fetal BPD	...	...	57
Table III:	Summary of fetal HC measurements	...	...	60
Table IV:	Fitted centiles of fetal HC	...	...	61
Table V:	Summary of fetal FL measurements	...	...	64
Table VI:	Fitted centiles of fetal FL	...	...	65
Table VII:	Summary of fetal AC measurements	...	...	68
Table VIII:	Fitted centiles of fetal AC	...	...	69
Table IX:	Summary of EFW	...	...	72
Table X:	Fitted centiles of EFW	...	...	73
Table XI:	Summary of FL/AC Ratio	...	...	76
Table XII:	Fitted centiles of FL/AC Ratio	...	...	77
Table XIII:	Summary of HC/AC Ratio	...	...	80
Table XIV:	Fitted centiles of HC/AC Ratio	...	...	81
Table XV:	Summary of FL/BPD Ratio	...	...	84
Table XVI:	Fitted centiles of FL/BPD Ratio	...	...	85
Table XVII:	Summary of BPD/AC Ratio	...	...	88
Table XVIII:	Fitted centiles of BPD/AC Ratio	...	...	89
Table XIX:	Summary of FL/HC Ratio	...	...	92
Table XX:	Fitted centiles of FL/HC Ratio	...	...	93
Tables XXI:	Accuracy of EFW	...	...	96
Table XXII:	Descriptive Statistics	...	...	96

## LIST OF GRAPHS

Graph 1	: Parity of patients	...	...	Pg.54
Graph 2	: Sample size	...	...	54
Graph 3	: Raw data of BPD with fitted centiles	...	...	58
Graph 4	: Standard deviation score of BPD	...	...	58
Graph 5	: Raw data of HC with fitted centiles	...	...	62
Graph 6	: Standard deviation score of HC	...	...	62
Graph 7	: Raw data of FL with fitted centiles	...	...	66
Graph 8	: Standard deviation score of FL	...	...	66
Graph 9	: Raw data of AC with fitted centiles	...	...	70
Graph 10	: Standard deviation score of AC	...	...	70
Graph 11	: Raw data of EFW with fitted centiles	...	...	74
Graph 12	: Standard deviation score of EFW	...	...	74
Graph 13	: FL/AC Ratio graph (fitted centiles)	...	...	78
Graph 14	: FL/AC Ratio graph (SD score)	...	...	78
Graph 15	: HC/AC Ratio graph (fitted centiles)	...	...	82
Graph 16	: HC/AC Ratio graph (SD score)	...	...	82
Graph 17	: FL/BPD Ratio graph (fitted centiles)	...	...	86
Graph 18	: FL/BPD Ratio graph (SD score)	...	...	86
Graph 19	: BPD/AC Ratio graph (fitted centiles)	...	...	90
Graph 20	: BPD/AC Ratio graph (SD score)	...	...	90
Graph 21	: FL/HC Ratio graph (fitted centiles)	...	...	94
Graph 22	: FL/HC Ratio graph (SD score)	...	...	94
Graph 23	: EFW accuracy graph	...	...	96

## **ABBREVIATIONS**

AC- Abdominal circumference  
AFI- Amniotic fluid index  
AIUM- American institute of ultrasound in medicine  
BCPS- Bangladesh College of Physicians and Surgeons  
BIRDEM- Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders.  
BMI- Body mass index  
BPD- Biparietal diameter  
BSMMU- Bangabandhu Sheikh Mujib Medical University  
CI- Confidence interval  
CRL- Crown rump length  
DC- Differential count of WBC  
EFW- Estimated fetal weight  
ESR- Erythrocytes sedimentation rate  
FL- Femur length  
GA- Gestational age  
Hb- Hemoglobin  
HC- Head circumference  
HCG- Human chorionic gonadotrophin  
ICDDRDB- International center for Diarrhoeal Disease Research, Bangladesh.  
IUGR- Intrauterine growth restriction  
LBW- Low birth weight  
LGA- Large for gestational age  
LMP - Last menstrual period  
MA- Menstrual age  
R/E- Routine examination  
S/D ratio- systolic/diastolic ratio  
SD- Standard deviation  
SGA- Small for gestational age  
TC- Total count of WBC  
USG/ US- Ultrasonography/ Ultrasound  
VDRL- Venereal disease research laboratory test  
WBC- White Blood corpuscles  
WHO- World Health Organization

## ABSTRACT

Ultrasonography has opened new vistas for medical science. It offers a far better way of studying human development than we have ever had before. Crucial decisions can be made on the basis of fetal biometric measurements. The biometric measurements that are used as references should be population based. If tables and charts that are used for fetal biometry are derived from a different population, then they may mislead the obstetricians. A fetus may be genetically small for date but will appear to be growth restricted if a table derived from another race is used, or it may appear to be macrosomic in the same way. Many studies in Bangladesh showed that the western tables that are used here are not appropriate for Bengalis and often give wrong information especially in the third trimester which can lead to wrong decisions by the obstetricians. Population specific nomograms should therefore be used. So we need to prepare Bangladeshi standards. To this end this study was designed.

### SUBJECTS AND METHODS

This study was conducted in Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), on consecutive healthy gravid patients, who had met the criteria. The subjects were Bangladeshi Bengalis, belonging predominantly to the middle class. A 3.5 MHz curvilinear transducer was used. Standard methods and techniques were used for the ultrasonographic measurements of the parameters. Fetal weights were estimated from head circumference, femur length and abdominal circumference by using the model generated by Hadlock and colleagues in 1985. Accuracy of estimated fetal weight was also determined.

The five basic parameters of the fetuses, biparietal diameter (BPD), head circumference (HC), femur length (FL), abdominal circumference (AC) and estimated fetal weight (EFW) and their ratios were studied.

## RESULTS

A total of 1223 healthy, gravid subjects were included, from 13 to 40 weeks gestational age. Size charts were prepared of the four main measurements of the fetus. Growth profile of estimated fetal weight was also produced. Tables of observed values of the parameters were prepared as a function of gestational age and then tables of estimated values were produced after fitting models to the data. These tables provided the distribution of patients in each week, mean, 2 standard deviations, and 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles. Graphs of scatter diagrams with percentile curves superimposed on them and graphs showing goodness of fit of models and expected 2 standard deviations were prepared. Similarly tables of observed values and estimated values of the ratios FL/AC, HC/AC, FL/BPD, BPD/AC, FL/HC, were also prepared. Graphs of percentile curves superimposed on scatter charts and graphs of goodness of fit of ratios were also produced. Lastly two tables and a graph to show accuracy of estimated fetal weight were constructed, based on the birth weights of seventy three infants.

## CONCLUSION

The aims and objectives of the study were all met. Tables and graphs as mentioned above were prepared. These nomograms of fetal growth profile were produced for the first time in Bangladesh with fitted models. Fetal growth can now be followed more reliably by using Bangladeshi standards. Growth restriction, growth acceleration and fetal skeletal anomalies can now be detected earlier and accurately to impart treatment timely to get the best possible results.

These nomograms are unique for Bangladeshi population because of their different stature and characteristic socio- economic condition. These can be used as standards for Bangladesh, till more such studies are conducted on a broad based population. Computer software can also be produced to install these tables and graphs in the ultrasound machines so that growth assessment of a fetus can be made based on a Bangladeshi study. The fetus can thus be taken care of in the best possible way so that a healthy, normal infant is born. This can ensure to a great extent a healthy, well grown adult. As studies have now shown that a growth restricted fetus can have long term problems with health, intellect and physical growth.

# CHAPTER 1

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## *INTRODUCTION*

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1.1: STATEMENT OF THE PROBLEM	...	...	1
1.2: PURPOSE OF THE STUDY	...	...	2
1.3: ASSUMPTION	...	...	4
1.4: HYPOTHESIS	...	...	4

---

## INTRODUCTION

The growth and development of fetus is one of the most important issues to the obstetrician caring for the well being of the fetus and the mother. That is because a normally growing fetus with its size within the normal limits means fewer complications during its prenatal and postnatal stages. It also means fewer complications in its infant and childhood stages. Not only that, it also means a healthy, intelligent and well grown adult.

### 1.1: STATEMENT OF THE PROBLEM

Any kind of abnormality in fetal growth whether growth restriction or growth acceleration is worrisome because it is associated with risk of prenatal and postnatal morbidity and mortality. Prenatal diagnosis of these conditions is therefore very important to the physician concerned because it can help him/her decide not only the time but also the mode of delivery. This in turn reduces the risk.

The problem that the doctors face in Bangladesh is that, all the growth charts of fetal parameters that are used here to follow fetal growth have been generated by studies on western population. But their stature is different from Bengalis and so these charts are not appropriate for this population. Therefore charts prepared on Bangladeshi population are needed, in order to guide the obstetricians for better management of pregnancy.

Bangladesh is a developing country, maternal and infant mortality rates here are one of the highest in the world. To improve this gloomy situation maternal antenatal care is mandatory. Here ultrasound can play a vital role, by helping the obstetrician in assessing the growth of the fetus accurately.

The use of ultrasound evaluation in obstetrics provides the potential for improvement in antenatal care by allowing recognition of abnormalities of dates and size in utero. Early

ultrasound examination before 20 menstrual weeks provides very accurate characterization of the menstrual age of the fetus (2 standard deviations =  $\pm 1$  week). More recently ultrasound evaluation has been applied to fetal size in utero so that fetuses that are small for gestational age or large for gestational age can be recognized and managed appropriately. It is a well known fact that across different communities and races, the measurements and therefore the growth profile vary. For this reason, population standards have been developed (Hadlock, 1994). The identification of intrauterine growth restriction is one of the key issues in antenatal care. Growth restriction is associated with adverse perinatal outcome and neonatal and long-term problems (Gardosi et al, 1998). A small-for-gestational age baby may be small because of constitutional variation or because of pathological causes associated with reduced intrauterine growth (De Jong et al, 1999).

As nutritional status of the majority of Bangladeshi population is below optimum, there is greater risk for the fetus to be growth restricted or small for date. But if the calibration is done by western tables more fetuses will appear to be small than the actual number leading to confusion in diagnosis and management of such cases.

A fetus born at the 5th percentile for weight that has reached its genetic potential may be small in relation to the reference population but it is not actually growth retarded (Hadlock, 1994). This is the problem that the obstetricians and sonologists of Bangladesh face when using the tables based on Caucasian population.

The assessment of the growth of fetus reliably has long been a challenge to all who care for pregnant women. Clinical parameters have some value, but they lack the necessary consistency to provide for optimal perinatal care. With recent advances in diagnostic imaging, fetal growth can now be assessed with high accuracy. But population based charts are needed for that.

## **1.2: PURPOSE OF THE STUDY**

The purpose of this study is to prepare fetal growth charts and tables or fetal growth profiles of Bangladeshi population for accurate assessment of fetal size and growth in Bangladesh. This will be done based on the fetal biometry of the five main parameters, biparietal diameter (BPD), head circumference (HC), femur length (FL), abdominal circumference (AC) and



estimated fetal weight (EFW), by ultrasonography. Nomograms of fetal ratios will also be generated. Accuracy of fetal weight estimation by ultrasonography will also be determined to show the reliability of ultrasonographic measurements.

If gestational age and fetal development are to be estimated, measurements must be obtained and then compared with local standard values. One should make sure to use tables that are appropriate for one's patients and not derived from some quite different population (Palmer, 1995). Normative values must be evaluated to determine which are most appropriate for the population being studied. If appropriate standards cannot be found, then they must be developed (Deter et al, 1983). In one study here, it was found that if the western charts prepared on Caucasian population are followed, the abdominal circumference measurements even in normal Bangladeshi fetuses lagged much behind (by 2 or more weeks) after 33 weeks gestational age and would therefore indicate a false low growth rate (Quddus, 2000). There was a discrepancy of 12 to 26 mm between head circumference at term in different western studies and a study on Bangladeshi population (Quddus, 2006). Clinically significant difference in predicting gestational age by biparietal diameter appeared from 32 weeks onwards, by 2 to 3 weeks (Quddus, 2007). Therefore different studies conducted here recommended that studies done on Bangladeshi population should be used for reference in this country (Quddus, 2007, 2006, 2005, 2004, 2002, 2000, 1999; Quddus and Khatun, 2001; Moslem et al. 1996; Bala, 1991).

The sonographic growth profile used for identification of growth retarded fetuses is equally useful in recognition of growth accelerated fetuses (Hadlock et al, 1984). Therefore sonographic estimates of fetal weight also help in detection of macrosomia and population specific fetal weight charts help in its early and accurate detection in pregnancy for early management.

On following fetal growth profile using charts and graphs derived from studies on Bangladeshi population, when any disturbance is detected in fetal growth, it will be more accurate. Treatment can be then given to improve its birth weight and also to determine the appropriate time and route of delivery– normal or caesarian, so that the baby can be taken care of in the best possible way, to give it a chance to a healthy normal life. So that it does not become a liability on its family, society and the country. As it is now clear that decreased weight is associated with increased mortality and morbidity (Paul et al, 1979; Warsof, 1977).

This indicates that any persistent growth abnormality is significant and should be treated vigorously. Early detection allows early treatment and thus minimizes damage to fetus (Deter et al, 1983).

By using the nomograms and growth profile charts based on Bangladeshi population, doctors can find out the growth percentile of the fetus more accurately and timely for proper management of the fetus.

### **1.3: ASSUMPTION**

The growth charts that are used in Bangladesh are all of foreign origin. As the reference group of population is different not only in size and stature but also in socio-economic condition, so will be their fetal biometry and growth charts. Therefore the references may not be appropriate for Bangladeshi population.

The population specific nomograms generated in this study will improve the antenatal care of Bangladeshi fetuses by the obstetricians, who have to rely heavily on ultrasound determination of fetal size and weight in many cases.

### **1.4: HYPOTHESIS**

There is a good co-relation between gestational age and fetal biometric parameters. For this reason these variables are used to determine fetal size and growth in relation to fetal age. Fetal size and growth is less in Bangladeshis compared to the Caucasians whose tables are used here. Therefore by measurement of the five basic parameters, biparietal diameter, head circumference, femur length, abdominal circumference and estimated fetal weight normative charts and graphs need to be prepared as population specific standards. This will go a long way for accurate determination of fetal size and growth in Bangladeshi population for their best possible management and optimum pregnancy outcome.

## CHAPTER 2

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### *AIMS AND OBJECTIVES*

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2.1: GENERAL OBJECTIVE	...	...	5
2.2: SPECIFIC OBJECTIVE	...	...	5

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## **AIMS AND OBJECTIVES**

Growth charts and tables that are used in our country on our patients were generated by studies on western populations. Since we belong to a different race and our size and stature is different from theirs, so our foetal growth profile is likely to be. Therefore the present study was conducted on our population with the following aims and objectives.

### **2.1: GENERAL OBJECTIVE**

The objective of this study was to establish reference growth charts and tables of our own population by ultrasonography, as standards, to follow the growth of Bangladeshi fetuses and also to detect the type of fetal growth abnormalities as well as fetal skeletal anomalies.

### **2.2: SPECIFIC OBJECTIVE**

- a. To construct fetal growth profile charts and tables of estimated fetal weights (EFW), from 13 to 40 weeks gestational age.
- b. To produce nomograms and growth charts of fetal biparietal diameter (BPD), head circumference (HC), femur length (FL) and abdominal circumference (AC) measurements
- c. To prepare normative charts and tables of FL/AC, HC/AC, FL/BPD, BPD/AC and FL/HC ratios.
- d. To determine accuracy of fetal weight estimation by ultrasonography by correlating it with birth weight.

Many studies were conducted on our population and it was found that the western nomograms were not appropriate for our population and gave inaccurate assessment of fetal growth especially in the third trimester (Quddus, 2006, 1999; Quddus and Khatun, 2001; Moslem et al, 1996; Bala, 1991).

There is considerable increase in perinatal morbidity and mortality for pre-term or post-term fetuses and for fetuses born too small or too large for menstrual age (Battaglia and Lubchenco, 1967). In a developing country like ours, maternal malnutrition and consequent low birth weight of the neonate is quite common. In many such cases a timely and early delivery becomes mandatory. A discrepancy of two weeks can be critical for the survival of an infant who has to be delivered early because of some antenatal complication (Palmer, 1995).

In developed countries they have fetal growth profiles of their own population which is mainly Caucasian. Since we belong to a different race our genetic growth potential is different from theirs, also our nutritional and socioeconomic status is lower than theirs, so our fetal growth profile may also be different. Therefore their profile is not applicable here.

It has become obvious that different populations show considerable variations in their birth weight characteristics. The Aberdeen birth-weight data, when applied to the Glasgow population for example, suggest that substantially more babies are small-for-dates than if local, Glasgow derived figures are used (Forbes and Smalls, 1983). Another study found that it is almost invalid to use the standard estimated fetal weight (EFW) growth curves when plotting the fetal growth of a constitutionally small ethnic group, as Asians. A fetus could be labeled as small for gestational age whereas its size might be totally appropriate for its heritage (Rosenberg and Chervenak, 1995).

Such a study on our population is therefore long over due, to help the obstetricians provide proper management timely to improve the growth rate and therefore the birth weight of the fetuses, which is imperative for their well being.

It is the duty of the sonologists to help the clinician determine which fetuses are small because of intrauterine growth restriction, so that appropriate management may optimize fetal outcome (Hadlock, 1994). For this, evaluation of growth profile would be required if intrauterine growth restriction in all its forms were to be detected (Deter et al, 1982). Small for dates or small for gestational age are babies with birth weights under the 10<sup>th</sup> percentile

for the gestational age at which they are delivered. Ideally, the chart used to decide that they are small should be derived from the population being studied.

The problems of low birth weight and intrauterine growth restriction are more acute in a developing country like Bangladesh than in the developed ones. So a study of this kind will be helpful for the future generation's health and well being.

More fetuses will appear to be growth restricted than the actual number, if Bangladeshi standard measurements are not used here. Because Bengali fetuses could be smaller from western ones due to other factors like racial, maternal nutrition, parity and child bearing age.

The ultimate objective was, to detect fetal growth abnormalities as well as fetal skeletal anomalies, by using population specific standards. These nomograms and growth profile charts would be useful to both the obstetricians and sonologists who would be able to predict more accurately the growth and the weight of the fetuses. Therefore the management and treatment of both the growth restricted and growth accelerated fetuses and their follow-up will become more accurate and reliable.

## CHAPTER 3

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### *REVIEW OF LITERATURE*

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3.1: INTRODUCTION	...	...	8
3.2: GESTATIONAL AGE ASSESSMENT	...	...	11
3.3: BIPARIETAL DIAMETER	...	...	13
3.4: HEAD CIRCUMFERENCE	...	...	14
3.5: FEMUR LENGTH	...	...	15
3.6: ABDOMINAL CIRCUMFERENCE	...	...	17
3.7: ESTIMATED FETAL WEIGHT	...	...	20
3.8: RATIOS DETERMINED	...	...	22
3.9: FETAL GROWTH	...	...	25
3.9a:GROWTH RESTRICTED FETUS	...	...	28
3.9b:GROWTH ACCELARATED FETUS	...	...	32
3.10: VARIABILITY	...	...	34
3.11: ACCURACY	...	...	34
3.12: AMNIOTIC FLUID EVALUATION	...	...	35
3.13: BODY MASS INDEX	...	...	36
3.14: SAFETY OF USG	...	...	37
3.15: SAMPLE SIZE IN A STUDY	...	...	37

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## **REVIEW OF LITERATURE**

### **3.1: INTRODUCTION & HISTORICAL BACKGROUND**

The introduction of sonography to obstetrics by Ian Donald and colleagues in 1958 is now regarded as one of the major milestones of modern medicine. For the first time it became possible to obtain information about the fetus and its environment directly with a noninvasive diagnostic procedure considered safe even when used repeatedly (Johnson, 1998). The 1980s was an amazing decade for fetal sonography. During that decade, real time sonography became the standard modality, color Doppler was introduced, and intracavitary transducers became available for general clinical practice. These new tools, in those 10 years, have given more information about the development of human fetus than had been available during the rest of human history (DuBose, 1996).

Accurate ascertainment of fetal size and growth in both normal and abnormal pregnant women is of prime clinical importance. As the effects of maternal disease on fetal development and the penalties of prematurity become more clearly understood, precise measurement of fetal size in relation to maturity will assume increasing importance. Ultrasonographic cephalometry has shown a high degree of accuracy in forecasting fetal maturity and weight (Hellman et al, 1967). For this reason nowadays assessment of fetal growth by ultrasonography in relation to menstrual age is an indispensable part of maternal antenatal care.

If gestational age and fetal development are to be estimated, measurements must be obtained and then compared with local standard values (Palmer, 1995). Fetal growth problems are a serious cause of perinatal mortality and morbidity in current obstetric practice, the understanding of the biology of intra-uterine growth remains incomplete. There are both growth promoting and restraining factors, most of which are under some form of genetic



control. This is complicated by extrinsic factors which may include maternal nutrition, infection and habits such as smoking and alcohol abuse (Whittle 2001).

A major aim of antenatal care is to detect the fetus whose growth deviates from a normal pattern. This is very important to the obstetrician because of the complications as follows:

Fetuses that have excessive growth rates cause difficulties with delivery. The head of a large baby may not be able to pass through its mother's pelvis (cephalopelvic disproportion) or if the head is delivered the shoulders may get stuck (shoulder dystocia). Disproportion causes long painful labors that commonly end in caesarian section. The fetus may suffer from lack of oxygen (fetal distress) or may be subject to a difficult instrumental delivery with associated birth trauma. Shoulder dystocia may result in the baby dying during delivery or being delivered with paralysis of the nerves to its face and arms. Breech presentation in large fetuses may mean that the baby is delivered as far as its head, then gets stuck resulting in severe birth asphyxia and trauma or death (Patricia and Pearce, 1992).

A study reported that perinatal death rate was nearly eight times higher than that in their total study population when the weight was between the 10<sup>th</sup> and 3<sup>rd</sup> percentiles and nearly 20 times higher when the weight fell below the 3<sup>rd</sup> percentile (Scott and Usher, 1966). The most common definition of intrauterine growth restriction (IUGR) is that a fetus is growth restricted if its weight is below the 10<sup>th</sup> percentile for gestational age (Reed and Droegmueller, 1983; Doubilet and Benson, 1990). The current WHO criteria for low birth weight is a weight less than 2,500g (5 lb, 8 oz) or below the 10<sup>th</sup> percentile for gestational age. Fetal growth and birth weight are subject to a variety of influences, which include physiological and pathological factors. Physiological variables, such as maternal stature and parity affect birth weight and fetal growth. Smallness defined by individually adjusted, customized centiles has been found to reflect pathological pregnancy outcomes better than an unadjusted, population-specific standard (De Jong et al, 1998).

The complications associated with IUGR are well known. Among the aids used in the antenatal monitoring of potentially growth retarded fetuses, the diagnostic ultrasound has been shown to be of value in making a positive diagnosis. A number of authors have described their results, either by serial ultrasonic measurements of fetal biparietal diameter (BPD) to detect abnormal growth patterns or by a single measurement, to estimate weight and

to screen for IUGR. The incidence of IUGR in the total obstetric population is approximately 5% (Wittmann et al, 1979).

The earliest and the most basic method for studying fetal growth was by constructing a table or graph from the measurements of a group of normal fetuses. These graphs and tables show how rapidly a parameter changes with time, and the data in the graphs are known as growth curves. Basically, three tools are available for estimating the size of a fetus from sonographic measurements: the table, the graph, and the regression formula, with the additional tool of ratio to compare the relative size of one parameter with that of another.

A woman's reported last normal menstrual period (LMP) is used to estimate gestational age. LMP is used only for the date reported by a woman as the first day of her last menstrual period. Other means, such as sonographic fetal measurements, beta-hCG levels, multiple fetal parameter average age, GIFT (gamete-intrafallopian transfer) dates, and others, are also used to determine gestational age. Optimal menstrual histories are present when the patient has a certain last normal period (preferably recorded on a calendar), regular menses, no exposure to oral contraceptives, and no unusual bleeding.

Sonographic studies designed to evaluate fetal growth rely on cross-sectional evaluation of a large number of patients with known dates of the beginning of the last normal menstrual period and no compounding variables in the menstrual history to question its validity. Rosavik and Fishburne (1989) demonstrated that such populations are equivalent to populations with known conception dates for studies of this type. Most studies also eliminate multiple gestation and those with a history that might adversely affect fetal growth. In a properly designed cross-sectional analysis of any fetal biometric parameter, measurements are made in a large number of fetuses evenly distributed over the entire range of menstrual ages, with each fetus being measured only once in gestation; the later point is important in avoiding bias in variability estimates. The data is then analyzed using regression analysis.

Estimation of the fetal weight, on its own and in relation to gestational age, can influence obstetric management decisions concerning the timing and route of delivery. Early delivery may benefit a fetus that is small for dates (SFD). Such a fetus may be inadequately supplied by its placenta with oxygen and nutrients and may therefore do better in the care of a neonatologist than in utero. When the fetus is large, cesarean section may be preferred route of delivery, particularly in pregnancies complicated by maternal diabetes. In view of these

considerations, fetal measurements should be a component of every obstetric sonogram (AIUM, 2003). The rate of increase in the size of a fetus is a reliable indicator of its state of health. A diabetic woman's fetus may gain weight too fast and have difficulty in delivery; hydrops fetalis and other problems are also possible. In twin gestations, one or both twins may increase in size too slowly and require close monitoring to determine the optimum time and method of delivery (DuBose, 1996).

The use of multiple measurements is important when one considers several points. It is not uncommon for normal fetuses to have measurements that are above or below the expected mean value at a given age and these differences are not always in the same direction. And the process of plane selection of the fetal head, abdomen, and femur allows a detailed look at important anatomic structures and, therefore, facilitates detection of abnormalities in those areas (Filly and Hadlock, 2000). The relative differences in the distributions are greater for body parameters than for cranial parameters; both increase with time. The distributions for the cranial parameters are approximately 3 to 5% of the age, whereas the body parameter residuals are approximately 7% to 10% of the age. The body parameters thus are approximately twice as variable as those of the head (DuBose, 1996).

It has become apparent that different populations show variations in their birth weights. Apart from defining a normal population, important factors that influence birth weight include birth order, parental height (particularly the mother's), and ethnic group. Studies in Singapore, allow the comparison of three different ethnic groups living under similar circumstances, show clear differences in birth weight distribution. Social and economic status remains an important influence on perinatal outcome, and fetal growth in particular; the reasons for this may be partly nutritional or related to habits such as smoking. The effect of diet is difficult to assess, but the starvation of women during the Dutch famine and the siege of Leningrad during the Second World War caused a significant increase in the number of SFD babies (Whittle, 2001).

### **3.2: GESTATIONAL AGE ASSESSMENT**

The true measure of age is the number of days since conception, termed conceptual age. Historically, pregnancies were dated by the number of days since the first day of the last

menstrual period (LMP), termed menstrual age. The term most often used to date pregnancies is gestational age (GA). In 28-day cycles, gestational age and menstrual age are equal (Benson and Doubilet, 2005). To assess fetal growth gestational age assessment in the 1<sup>st</sup> trimester or before 20 weeks (w) gestation is very important. This can be done accurately by ultrasonography (USG). Sonographic estimates of age before 20w gestation are highly reliable for pregnancy dating. It represents the most accurate scientific information establishing the menstrual age (Filly and Hadlock, 2000). It can be estimated as follows:

1. By detection of a gestational sac at 3 to 5 week of gestation. Gestational sac diameter yields an accuracy of only  $\pm 2$  to 3 week in 90% of cases (Hohler, 1984).
2. The crown rump length (CRL) is the most accurate sonographic technique for establishing gestational age up to the 11<sup>th</sup> week. The accuracy is  $\pm 5$  days with a 95% confidence interval (CI) (Sabbagha et al, 1982).
3. In the second trimester BPD is most widely accepted for estimating gestational age. Between 17 and 26 week gestational age the predictive value is  $\pm 11$  days (95% CI) (Sabbagha et al, 1982).

In cases of IUGR caused by asphyxia or reduced utero-placental blood flow, centralization of fetal circulation occurs, thus preserving blood flow to the brain at the expense of the trunk (Campbell, 1976). Therefore BPD is affected less than abdominal circumference (AC) and can be used for gestational age determination. A single BPD measurement was more predictive of estimation of confinement than an optimal menstrual history (Campbell et al, 1977). That is why dating by Ultrasonography (USG) is now widely and readily accepted by obstetricians.

A study found that in Bangladeshi population the gestational age by LMP and Ultrasound (by using western tables) correlates very well up to 18w. From 19-36w, gestational age by BPD and femur length (FL) are similar though a week smaller than the LMP age. But after 36w FL age is closer to the menstrual age than the BPD age is. So after 36w, if we use the western charts FL age should rather be preferred as it is closer to the LMP age (Quddus, 1999). By composite gestational age estimated by ultrasonography using BPD, FL and AC, 83% were closer to LMP age. Composite gestational age was more reliable than that of individual parameter like BPD (37.53%), FL (74.92%) and AC (54.3%) (Biswas et al, 2006).

Fig.1 shows a full term human fetus.



Figure showing a full-term human fetus in uterus, placenta, amnion, chorion, umbilical chord, cervix, vagina (Williams, ed., 1995).

Fig. No: 1

### 3.3: BIPARIETAL DIAMETER

The biparietal diameter (BPD) of the head is one of the first fetal sonographic measurements. It is also one of the easiest and most accurate, if the head is normally shaped. The BPD is not a very reliable predictor of IUGR for many reasons. The first is the 'head sparing' theory. This is associated with asymmetric IUGR. Fetal blood is shunted away from other vital organs to nourish the fetal brain, giving the fetus an appropriate BPD ( $\pm 1$  standard deviation) (SD) for the gestational age. The second problem is the alteration in the fetal head shape secondary to oligohydramnios, often associated with IUGR. Dolichocephaly can lead to underestimation of fetal weight, and brachycephaly can lead to over estimation of fetal weight. Head circumference (HC) measurement is a more consistent parameter, but a

combination of all growth parameters should be used (BPD, HC, AC, and FL) when diagnosing a fetal growth discrepancy (Rosenberg and Chervenak, 1995). Thirdly although an easy measurement to make, the BPD becomes increasingly inaccurate in the later weeks of pregnancy, just when the assessment of growth may be most important. Finally the spread of normal BPD size becomes very wide after 32w, again reducing the value of the method as means of identifying a small fetus (Whittle, 2001).

It was noted that by employing serial cephalometry and separating fetuses into three percentile growth patterns, it becomes possible to predict fetal age from sonar BPD with greater precision. Also it is suggestive that a fall from the BPD growth pattern is more likely to lead to small neonates, some of whom maybe frankly, growth retarded. This study also shows that 95% of fetuses whose sonar BPD readings consistently fall above the 75<sup>th</sup> percentile, have a birth weight in excess of 3000g - with two thirds of these fetuses weighing over the 50<sup>th</sup> birth weight percentile (Sabbagha et al, 1976).

In certain circumstances (e.g., ruptured membranes, breech presentations, and multiple gestations) shape changes in the fetal head may lead to errors. The two most frequently noted alterations in head shape are dolichocephaly and brachycephaly. Cephalic index is used to assess the head shape. The range of normal is 75% to 85%. >85% suggests brachycephaly and <75% suggests dolichocephaly (Jeanty and Romero, 1984).

A comparison of studies showed that BPD varies with race. In various Bangladeshi (Quddus, 2005; Moslem et al, 1996; Bala, 1991) and western studies the difference was of 2-5mm at term (Hadlock et al, 1982; Shepard and Filly, 1982).

Maternal exposure to tobacco smoke in early pregnancy, as measured by serum cotinine concentration at 20-24w of gestation, adversely affects fetal BPD. Preventive measures need to be undertaken to encourage pregnant women to stop smoking and avoid passive exposure to tobacco smoke from the very beginning of pregnancy (Hanke et al, 2004).

### **3.4: HEAD CIRCUMFERENCE**

Although reproducibility of head circumference (HC) is not as precise as that of biparietal cephalometry, the advantages of using the circumference measurement outweighs this small loss of precision (Campbell and Thomas, 1977). Prenatal compression of the fetal skull is

common. It occurs more often in fetal malpresentation, such as breech, or in conditions of intrauterine crowding, such as multiple pregnancies. The fetal skull can also be compressed in vertex presentations without any obvious reason or as a result of an associated uterine abnormality (Hohler, 1984). HC is less affected than BPD by head compression. Because the BPD can be misleading in cases with head shape changes (Hadlock et al, 1981) the HC is the measurement of choice for evaluation of head growth in utero (Hadlock et al, 1982).

A number of groups have produced charts of HC against gestational age: the two most often used are very similar (Hadlock et al, 1982; Deter et al, 1982). Both show that changes in HC, like BPD, tend to tail off towards term, but the SD are much smaller, so the likelihood of identifying the IUGR may be higher. In addition HC is much less dependent on head shape. However, all head measurements become harder to perform in late pregnancy, and the brain-sparing effect in growth restriction affects both HC and BPD (Whittle, 2001).

Head circumference varies with race, at term there was a discrepancy of 12-26mm, between the western (Hadlock et al, 1982; Deter, 1982) and Bangladeshi studies (Quddus, 2006). Head circumference also varies with sex. Statistically significant but low levels of HC sexual dimorphism are present in early life. On average males have HC about 2% larger than females of comparable femur/body length (Joffe et al, 2005).

A highly significant association between small HC and maternal smoking was found. More alarming was that given a certain level of IUGR, infants of smoking mothers were at an increased risk of small HC compared to infants of non-smoking mothers. Maternal smoking during pregnancy affects brain development negatively (Kallen, 2000).

Birth weight, birth length, and HC were significantly greater among infants born to women who used no drugs, compared with women with any cocaine, opiate, alcohol, tobacco, or marijuana use during pregnancy. Tobacco affects birth weight (deficit of 232g), length (deficit of 0.8cm) and HC (deficit of 0.7cm), whereas cocaine affects birth weight (deficit of 250g) and head size (deficit of 0.98cm) (Shankaran et al, 2004).

### **3.5: FEMUR LENGTH**

The use of real-time ultrasound has become universal. It allows fast reliable determination of gestational age as well as fetal size and growth assessment. Because of its size, visibility, and

ease of measurement, the femur is generally preferred over the other long bones. It usually lies 30 to 70 degrees to the long axis of the body. Like other parameters its variability increases as the pregnancy advances.

Femur length (FL) helps in the assessment of fetal growth by giving an accurate gestational age. The 95% confidence limits for this from 12 to 23w gestation would appear to be even more accurate than predictions made from the measurements of the BPD (O'Brien et al, 1981). Fetal long bones have the disadvantage of a larger variation than the cranial parameters. The FL and humeral length are particularly reliable because they are easy to locate. It can also be used to detect developmental anomalies, though some anomalies of the extremities do not manifest until the 25<sup>th</sup> week (DuBose, 1996).

In any routine obstetric evaluation, the FL is usually the only long bone measured, but if there is a 2w or longer difference between FL and all the other biometric parameters, all fetal long bones should be measured and a targeted examination of the fetal anatomy should be performed. An association was found between shortened femur and humerus lengths and trisomy 21 (Benacerraf et al, 1991). Dwarfism and constitutional hereditary growth factors are also a possibility (Rosenberg and Chervenak, 1995). FL shortening in the second trimester appears to be a useful screening parameter for fetal Down's syndrome in a Thai population (Tannirandorn et al, 2001). Using institution-specific FL was more efficient in screening for Down's syndrome than published expected FL (Borgida et al, 2003).

The use of FL in the estimation of fetal growth is limited, although it has been combined with other measurements to estimate fetal size (Whittle, 2001). Transvaginal FL measurement is easy to perform between 10 and 16w of gestation. The high degree of intra- and inter-observer repeatability indicates it to be a reproducible method (Rosati et al, 2004).

The diagnosis of small for gestational age (SGA) fetuses, based on ultrasound AC measurement of <10 centile, was made 9w (range 5-14) after the finding of a short FL. Half of these cases also developed pre-eclampsia (Todros et al, 2004). In pregnant adolescents with age of  $15.9 \pm 1.1$ y, fetal femur length was significantly lower with consumption of <2 servings of dairy products/day as it may negatively affect fetal bone development by limiting the amount of calcium provided to the fetus (Chang et al, 2003).

Less-than-expected FL was noted among the fetuses of Asian mothers, and greater than expected FL were noted among the fetuses of black mothers, compared with femurs of



fetuses of white mothers. The implications for the use of fetal FL as a component of the genetic sonogram in patients of various races require further study (Shipp et al, 2001). At 40w the mean fetal FL in Bangladesh is 73mm whereas it is 77mm in caucasian population (Hadlock et al, 1984). The mean is 4mm smaller here, at term (Quddus and Begum, 2004).

Bone length may also be compared with gestational age or BPD. A femoral or humeral measurement can be considered normal if it falls within 2SD of the mean. It is proportional to the BPD if that measurement falls within 2SD of the mean BPD. A FL is short if it is >2SD below the mean. A skeletal dysplasia is likely only if the FL is 5mm smaller than 2SD below the mean (Palmer, 1995). Smoking was associated with a reduction in fetal FL ( $p=0.005$ ) and AC as well as birth weight, length and HC but not skin fold thickness, suggesting smoking results in a reduction in organ size and function (Pringle et al, 2005).

### **3.6: ABDOMINAL CIRCUMFERENCE**

Abdominal circumference (AC) is useful as a parameter to assess fetal size. It is not very predictive of gestational age. It is probably the single most valuable biometric parameter used in assessing fetal growth. 4 of 4 macrosomic fetuses were predicted when a change in AC was greater than or equal to 1.2cm a week between the 32<sup>nd</sup> and 39<sup>th</sup> weeks of pregnancy (<4000g). 17 out of 21 (81%) of the fetuses with birth weights between 4000g and 4499g, and 5 out of 6 (83%) whose weight exceeded 4500g. When the abdominal growth was less than 1.2cm/w (between 32 and 39w), normal fetal growth was correctly identified in 89.1% of cases (Landon et al, 1989). An abdominal circumference less than 5<sup>th</sup> percentile is abnormal and suggests IUGR (Palmer, 1995).

In 1975, Campbell and Wilken first described the use of the fetal AC in predicting fetal weight. The AC is very useful in monitoring normal fetal growth and detecting fetal growth disturbances, such as IUGR and macrosomia, also isoimmunization. The AC may change shape with fetal breathing activity, transducer compression, intrauterine crowding as in multiple pregnancies or oligohydramnios or secondary to fetal position, as in breech presentation. When discrepancies do occur in AC measurements, multiple measurements should be taken and averaged to ensure accuracy (Rosenberg and Chervenak, 1995).

Abdominal circumference is useful for assessing proportionality and relative size. Fat fetuses have large AC, and thin fetuses have smaller AC. It is a factor in most regression formulas for estimating fetal weight. Many disease factors can affect the abdominal circumference and liver size (Williamson and Williamson, 1992).

The AC is undoubtedly the best index with which to assess both fetal size and growth because the measurement is taken at the level of the fetal liver, which constitutes about 4% of the total fetal weight and which steadily increases in size with gestational age. Tabular data for normal values of fetal growth and gestational age suggest a fairly linear growth throughout, in contrast to head measurements, although the SD widens towards term. In contrast to the brain, liver growth seems very sensitive to reduction in the supply of nutrients and so provides a potentially useful marker of intrauterine starvation. Thus an asymmetrical pattern of growth restriction develops because of continuing head growth with little or no increase in abdominal girth, leading to a high HC/AC ratio. This is more often observed when IUGR has a vascular or uteroplacental basis (Whittle, 2001).

By using umbilical vein as a reference point the reproducibility of AC measurement is improved; the mean SD of three independent fetal AC measurements is 2.95mm (Campbell, 1976) which represents an acceptable 2% error. In addition, sections at the level of the umbilical vein and fetal liver would seem to be particularly appropriate in studies on the SFD fetuses (Campbell and Thomas, 1977).

Of the four basic ultrasound measurements, AC has the largest variability (Hill, et al, 1992). This is partly attributed to the fact that AC is more acutely affected by growth disturbances than the other basic parameters. Of the four recommended measurements, AC is the most difficult to obtain. Depletion of hepatic glycogen and subcutaneous fat stores in IUGR fetuses lead to an early decrease in fetal AC, making this parameter an early and sensitive predictor of asymmetrical IUGR (Campbell and Thomas, 1977; Hadlock et al, 1983).

In IUGR the fetal liver is one of the most severely affected body organs, which alters the fetal AC (Crane and Kopta, 1979). The fetal AC is the most sensitive measurement for predicting IUGR, which is associated with increased risk of intrapartum fetal distress. A single measure of the fetal AC made within one week prior to delivery is superior to an assessment of growth rate of fetal AC in the third trimester in discriminating patients who require cesarean section for fetal distress (Williams and Nwebube, 2001).

The simplest way to screen for SGA with ultrasound is by measurement of the fetal AC at 32-36w gestation. This will detect approximately 85% of SGA fetuses. Any fetus with an AC of less than 25cm at 32w, 29cm at 34w or 30.5cm at 36w should have the HC measured and HC: AC ratio calculated. The fetus should then be measured serially (Patricia and Pearce, 1992). In fetal growth restriction, reduction is more pronounced for hepatic volume than for head or upper AC; hepatic volume is a better discriminator than HC (Boito et al, 2002).

Intrapartum ultrasonographic evaluation of AC for suspected macrosomic babies in early labor is an easy, practical method that should be adopted in decision making (Al-Inany et al, 2001). In a study to determine if AC can identify macrosomia ( $\geq 4000\text{g}$ ) at or beyond 37w, it was found that AC is slightly useful in detecting macrosomia among term parturients. AC  $\geq 350\text{mm}$  can identify macrosomic fetuses (Henrichs et al, 2003).

The technique of measurement is important in the assessment of abdominal circumference size (Tamura et al, 1986). The measurements obtained by direct measurement around the circumference were consistently (by about 3.5%) greater than those obtained by derivation from measurement of the abdominal diameters (Chitty et al, 1994). Negative prediction of large birth weight is more accurate than positive prediction. At 3<sup>rd</sup> trimester sonography with maternal diabetes, the AC percentile is potentially useful and should be routinely reported (Holcomb et al, 2000). Fetal hyperinsulinism is a strong predictor for excessive growth and fetopathy in pregnancies complicated by diabetes. AC  $\geq 75^{\text{th}}$  percentile determined by a third trimester ultrasound examination may discriminate between pregnancies at low versus high risk of amniotic fluid (AF) insulin  $\geq 16$  microU/ml. This AF insulin concentration is associated with considerable neonatal and long term morbidity (Schaefer-Graf et al, 2003).

Abdominal circumference ratio was a good predictor of twin birth weight discordance at any gestational age. An AC ratio cutoff of 0.93 yielded a sensitivity and specificity of 61% and 84%, respectively (Klam et al, 2005). Transverse cerebellar diameter/AC (TCD/AC) ratio remained constant in second half of pregnancy. Correlation coefficient was found to be statistically significant,  $r = 0.98$ ,  $p < 0.0001$ . Cases with IUGR can be diagnosed if local nomograms can be prepared for different ethnic groups (Malik et al, 2006).

A number of other fetal structures can be imaged and measured for fetal size and age estimation, like occipito-frontal diameter, lateral cerebral ventricles, TCD, intra-orbital diameter, extra-orbital diameter, inter-orbital and binocular distance, cranial volume, coronal

HC, 3D BPD correction, spine, mandibular length, liver, kidney length and diameter, renal pelvic diameter, humerus, radius, ulna, finger, tibia, fibula, foot, metacarpal length, thigh circumference, clavicle length, fetal nasal bone, and soft tissues at various places on the fetus. The cerebellum does not seem to be affected by IUGR (Whittle, 2001). Fetal nasal bone length (NBL) and BPD are linearly related in the second trimester. Fetal NBL in the Korean population is shorter than Caucasian and African- Americans (Shin et al, 2006).

### **3.7: ESTIMATED FETAL WEIGHT**

Disturbances of fetal growth- intrauterine growth restriction (IUGR) and macrosomia- are associated with increased risk of perinatal morbidity and mortality. Prenatal diagnosis of these conditions can aid in decision making concerning the timing and route of delivery, thereby reducing perinatal risk (Doubilet et al, 2000).

Fetal weight has been the primary parameter used in identifying infants with IUGR (Deter et al, 1982; Bard, 1970) and it is well known that the outcome of the pregnancy is related to the weight of the fetus (Paul et al, 1979). For these reasons estimating fetal weight from parameters determined by ultrasound has been the objective of a great many investigations (Deter et al, 1981).

It has become obvious that different populations show considerable variations in their birth weight characteristics. The Aberdeen birth-weight data, when applied to the Glasgow population, suggest that substantially more babies are SFD than if local, Glasgow derived figures are used (Forbes and Smalls, 1983). Similarly Bangladeshi population studies found EFW at term to be, 0.2 to 0.8 kg less than western studies (Quddus, 2002; Quddus and Khatun, 2001; Miah, et al, 1998). Both parents' races are important determinants of birth weight and fetal growth among twin pregnancies, with greater maternal influence than paternal influence (Tan et al, 2004).

The most reliable EFW formulas incorporate all fetal parameters, such as HC, AC and FL. This is important because an over all reduction in the size and mass of these parameters gives a below- normal EFW. An abnormally low weight of the fetus is usually observed after the AC and head: body ratio have become abnormal (Palmer, 1995).

The estimation of fetal weight involves errors of up to 160g/kg of fetal weight. Formulae that involve the measurement of two fetal parameters are about 5% more accurate than those which involve only one parameter, whilst the addition of a third parameter improves the estimation by about a further 1% (Patricia and Pearce, 1992). Overall, accuracy of fetal weight prediction improves with increasing number of body parts up to three. No further improvement is achieved by adding a fourth or fifth body part to the formula. Predicted weight will fall within 15% to 18% of the actual weight in 95% of cases, when measurements of fetal head, abdomen and femur are used (Benson and Doubilet, 2005). For these reasons the 3 parameters HC, AC and FL were used to estimate fetal weight in this study.

Prior to the availability of ultrasound, manual examination of the maternal abdomen was the only approach that could be used to estimate fetal size. Physical examination provides only a rough approximation of fetal weight because the palpated dimensions of the uterus are affected by several factors other than fetal size. These are amniotic fluid volume, placental bulk, presence of fibroids and maternal obesity (Benson & Doubilet, 1998).

Sonographic measurements of fetal body parts provide a direct way of assessing fetal size. Numerous formulas have been published for estimating fetal weight from one or more of the following fetal body measurements:

Head (BPD or HC), Abdomen (abdominal diameters or AC), and Femur (FL) (Campbell and Wilkin 1975; Warsof, 1977; Shepard et al, 1982).

AC may be among the most sensitive indicators of impending IUGR (Deter et al, 1983). A substantial literature indicates that measurement of AC with BPD provides the best estimates of fetal weight (Deter et al, 1981). The most widely used formulae were generated by Shepard, et al using the BPD and AC plus those of Hadlock, et al using the FL and AC (Warsof et al, 1977). More recently the later have revised their formula and introduced their formula of using BPD, AC and FL (Hadlock et al, 1985). Shepard et al's, prediction has an accuracy of  $\pm 20\%$  (Shepard et al, 1982). The formula does not take into consideration HC and FL, which contribute to fetal mass. It also ignores that BPD can be altered because of normal variations in head shape. These variations can occur in association with oligohydramnios, which may be found with IUGR (Rosenberg and Chervenak, 1995). Hadlock et al use three basic measurements: HC, AC and FL (Hadlock et al, 1985). The use

of HC instead of BPD has improved the predictive value to  $\pm 15\%$ . That is why this formula was used in this study to estimate fetal weight.

Other measurements use such as, thigh circumference (Vintzileo et al, 1987), and formulas for three-dimensional (3-D) sonography (Lee et al, 2001), and 3-D magnetic resonance imaging (MRI) have also been published (Uotila et al, 2000).

A weight between 10<sup>th</sup> and 90<sup>th</sup> percentiles is generally considered to be appropriate for gestational age. When it falls outside this range, the diagnosis of small or large-for-gestational age fetus is suggested. Median fetal weight/week increases progressively until 36w of gestation, reaching a maximum rate of 220g/w (Brenner et al, 1976). After 36w, the rate of weight gain steadily decreases in the normal fetus (Benson and Doubilet, 2005).

The sonographic growth profile used for identification of growth retarded fetuses is equally useful in the recognition of the growth accelerated fetus (Hadlock et al, 1984). Sonographic estimates of fetal weight would appear to be a natural tool for the detection of macrosomia and the development of an in-utero fetal weight curve should allow diagnosis early in pregnancy (Hadlock, 1994). Brenner et al (1976) and Hadlock et al (1985) have prepared prenatal fetal weight charts of Caucasian population. A derivative semi-quantitative approach can also be used. IUGR can be diagnosed with confidence when the EFW is <6<sup>th</sup> centile for gestational age and can be excluded when the EFW is >20<sup>th</sup> centile. When the EFW is between 6<sup>th</sup> and 20<sup>th</sup> centiles, the fetus is likely to be IUGR if there is oligohydramnios or maternal hypertension and is likely to be normal if amniotic fluid is normal to elevated and the mother is normotensive (Benson et al, 1990).

Fetal growth is assessed by serial sonograms, tracking estimated fetal weight and weight percentile. Fetal weight gain significantly below the norm of 100 to 200g/w in the third trimester or a falling weight percentile is worrisome (Hadlock et al, 1991).

### **3.8: RATIOS DETERMINED**

To assess fetal size, ratio is a common tool. It is used to compare relative size of one parameter with another. The generally accepted wisdom is that ratios are the best method for evaluating the proportions of a fetus. Ratios, also called an index, have no unit because they cancel out algebraically. Percentages are ratios multiplied by 100, expressing the numerator

as a percentage of the denominator. Ratios are sensitive to changes in the relative size of the two parameters. However, because the various parameters of the fetal body usually grow at different rates, a table or graph must be used to determine if any particular ratio is appropriate at a particular time in the pregnancy (Sokal and Rohlf, 1981). When a particular ratio is abnormal, the numerator or the denominator is abnormal. If a ratio is large for the fetal age, then it must be determined if the numerator is too large, or denominator is too small, or if both are only moderately large and small, respectively. If the ratio is too small, the conditions are reversed. It is also possible that both numerator and denominator may be abnormal in the same direction, both too large or both too small, resulting in a normal ratio.

### 3.8a: FEMUR LENGTH/ ABDOMINAL CIRCUMFERENCE

The femoral ratios are the most constant after 20w gestational age (DuBose, 1996). If AC is to be used in age estimate, one must examine the relationship between FL and AC (FL/AC). If this ratio is low, one should avoid using AC because of possible macrosomia; and if it is high one should avoid using AC because of possible IUGR (Hadlock et al, 1983). This is a time-independent proportionality index. It was able to predict only 63% macrosomic fetuses (Hadlock et al, 1985), which shows that this ratio has a limited clinical application.

An elevated FL/AC ratio has a low positive predictive value; the likelihood of IUGR is no more than 20% when this criteria is positive (Doubilet et al, 2000).

### 3.8b: HEAD CIRCUMFERENCE/ ABDOMINAL CIRCUMFERENCE

The head: body ratio is calculated by dividing the HC by the AC (HC/AC). Malformations may change the size of the head or abdomen. With normal anatomy, the head: body ratio can be considered normal if it lies between 5<sup>th</sup> and 95<sup>th</sup> centiles for the gestational age. The ratio determines whether the growth retardation is symmetrical or asymmetrical. If the fetus is small and the ratio is normal, the fetus is symmetrically growth retarded. If the AC or weight is low and the ratio is elevated (>95<sup>th</sup> percentile), there is asymmetrical growth retardation. Asymmetrical IUGR is easier to diagnose than symmetrical IUGR (Palmer, 1995).

The ratio that is most often used in fetal USG is the Campbell and Thomas' (1977) HC/AC ratio to detect IUGR in cases of uteroplacental insufficiency. For each gestational age the ratio is assigned with SD. In an appropriate-for-gestational-age pregnancy the ratio decreases as the gestation increases. In IUGR, with the loss of subcutaneous tissue and fat, the ratio increases. The HC/AC ratio is at least 2SD above the mean in approximately 70% of fetuses

affected with asymmetric IUGR. The HC/AC ratio is not very useful in predicting symmetric IUGR, as the fetal head and abdomen are equally small (Rosenberg and Chervenak, 1995). Crane and Kopta (1979) also found HC/AC ratio to be highly predictive of IUGR.

Discordant twins with HC/AC asymmetry have an increased risk of morbidity. In the absence of asymmetry, outcomes are comparable among discordant and concordant twins (Dashe, et al, 2000). At each visit the AC and HC should be measured, the HC/AC ratio calculated, and all three should be plotted on charts. In this fashion deviations from expected growth patterns can be recognized (Patricia and Pearce, 1992). This ratio works very well for the assessment of relative fetal size as fat fetuses have fat abdomens. The skull is normal in most cases and the HC includes only the skull, not the scalp, which may be affected by fat (DuBose, 1996).

Fetal HC measurement was used when determining the ratio between head and body because the BPD is only a single dimension of the head and is frequently not truly representative of the total fetal head and brain size. HC measurement is more representative of brain size and this is supported by our finding that normal weight dolichocephalic fetuses have HC measurements within normal range (Campbell and Thomas, 1977).

The best criterion for IUGR is the HC/AC ratio, with a positive predictive value of 62%, but IUGR cannot be diagnosed with confidence because 38% of fetuses will not be growth restricted (Benson and Doubilet, 2005). The measurement of both HC and AC allow the independent assessment of head and abdominal growth which differs under circumstances of vascular or placental failure as head growth is maintained for some time while abdominal growth slows or even ceases. Causing the HC/AC ratio to rise making it possible to identify the truly growth restricted fetus from a single study (Whittle, 2001). Normally the ratio falls with increasing gestational age and is equal to one at 36w (Patricia and Pearce, 1992).

### 3.8c: FEMUR LENGTH/ BIPARIETAL DIAMETER

These are most useful to evaluate the normalcy of the long bones. Fetal head shape should be normal. Short stature increases a woman's risk of having an abnormal FL: BPD ratio (FL/BPD) at later gestational ages. This finding indicates that risk assessment of fetal Down's syndrome for such patients might be inaccurate (Pierce et al, 2001).

### 3.8d: BIPARIETAL DIAMETER/ ABDOMINAL CIRCUMFERENCE

A number of sonographic parameters besides EFW have also been proposed to predict large for gestational age (LGA) and macrosomia: measurements of a number of fetal parts, like



fetal abdomen and head, also ratios of body parts, such as the FL/AC and BPD/AC. The positive predictive value of most of these parameters for diagnosis of LGA in diabetic and nondiabetic mothers have proven to be only moderately high. In general, the positive predictive values are considerably higher in diabetic mothers compared with nondiabetic mothers (Doubilet et al, 2000). As there is more asymmetry in fetuses of diabetic mothers.

### 3.8e: FEMUR LENGTH/ HEAD CIRCUMFERENCE

This ratio should be more useful to evaluate the normalcy of long bones as it is independent of head shape. BPD can vary due to brachycephaly and dolicocephaly. Therefore FL/BPD may not be so reliable in such cases to assess normalcy of long bones. FL/HC is more reliable.

## 3.9: FETAL GROWTH

One of the earliest investigations into the clinical importance of IUGR occurred more than three decades ago when Lubchenco first plotted neonatal birth weights against gestational age at delivery. Their analysis revealed increased perinatal morbidity and mortality in infants with birth weights  $\leq 10^{\text{th}}$  percentile for gestational age (Lubchenco et al, 1963). Abnormally small fetuses have a relatively poor prognosis because some of the causes of subnormal size, such as inadequate supply of oxygen and nutrients through the placenta, chromosomal anomalies, and infections, adversely affect fetal outcome (Reed and Droegmueller, 1983). Obstetric diagnosis of IUGR, based on US and menstrual age and subsequent birth weight, correlated better with adverse outcome and with premature delivery. Antenatal diagnosis of IUGR may be more accurate than one that was based on neonatal assessment of gestational age and birth weight (Lackman et al, 2001). Adverse outcome was seen only when the antenatal diagnosis of IUGR was actually associated with a confirmed neonatal diagnosis of SGA. Poor intrauterine growth up to 32w was associated with increased mortality and with serious morbidities often associated with adverse long term problems (Thomas et al, 2004). A complete evaluation of fetal growth will require measurement of BPD, HC, AC and FL. Comparison of fetal size and gestational age can provide a valuable indicator of IUGR. During the first routine scan US age is defined based on CRL, head measurement and FL. Using the BPD alone, about 60% of growth-retarded fetuses will be detected. Using the AC as well as other measurements, the sensitivity increases to 70-80%. Tables used to estimate gestational age, fetal weight or development must be appropriate for the social group of the

patient (Palmer, 1995). Fetal growth is a dynamic process, therefore serial US measurements are required to measure a growth rate (Whittle, 2001).

When several examinations have been performed, fetal growth can be depicted graphically by means of a trend plot, or growth curve. One form of growth curve plots the EFW versus gestational age, with the curve of the fetus superimposed on lines depicting 10<sup>th</sup>, 50<sup>th</sup> and 90<sup>th</sup> centiles. An alternative mode of display plots the EFW centile versus gestational age. In this, the graph for a normally growing fetus will be a horizontal line (Benson and Doubilet, 2005). Fetal growth restriction is one of the most challenging obstetric problems. Due to confusing terminology, there is lack of uniform diagnostic criteria. At present most authors do not distinguish between the terms 'small for gestational age' (SGA) and 'intrauterine growth restriction' (IUGR). These two clinical entities are not the same. The term 'SGA' should be used for an infant who has failed to achieve a weight threshold (10<sup>th</sup> centile). Conversely an IUGR infant has, by definition not reached his/her genetic growth potential due to an insult in utero. It implies a pathological process. Clinicians tend to manage both conditions in the same way by delivering affected cases, often by elective caesarean section and often prematurely. This strategy represents an over treatment (Bamberg and Kalache, 2004).

The rate of growth of fetus and its birth weight is genetically determined but is modified by environmental factors. The closest associations with birth weight are maternal weight at the start of the pregnancy and mother's own birth weight. Most fetus show a decline in growth after 38w. The 'fall off' in growth is related to the overall weight of the 'litter' and the decline is demonstrated once litter weight achieves 3.2kg. Thus it occurs at 38w in singleton, 30w in twins, 27w in triplets and 26w in quadruplets (Patricia and Pearce, 1992).

Low birth weight includes two pathological conditions and one normal condition. The normal condition refers to the healthy but constitutionally small baby. The pathologic conditions include preterm delivered and IUGR. According to the definition of IUGR as a birth weight <10<sup>th</sup> centile, the incidence of IUGR should be 10%. One third have true IUGR, and the remaining two thirds are constitutionally small. Some authors apply the term "small for gestational age" to the later group of infants (Vandenbosche and Kirchner, 1998).

Fetal growth is the end product of a variety of genetic, maternal, fetal and placental factors. Maternal size is a dominant determinant of fetal weight. Specific nutrients and their availability modify genetically determined metabolic and transfer systems. Hormones and

growth factors of maternal, fetal, and placental origin regulate nutrient transfer and fetal organ development. Fetal development is determined by dynamic interactions between all of these factors (Sacks, 2004). Primary placental insufficiency is a diagnosis of exclusion, by ruling out the other causes. It is the most common cause of IUGR (Doubilet et al, 2000).

Fetal growth restriction remains an important problem and it seems likely that about 25% of babies who weigh less than 2.5kg at birth and who contribute to the perinatal mortality are in fact growth restricted. In addition babies who survive and who are severely growth restricted are over-represented among children who develop long term handicap (Whittle, 2001). The fetus is uniquely vulnerable, as it must rely for its nutritional support on the vascular supply to the uterus and on the function of the placenta (Clapp et al, 1980). Placenta may modulate fetal growth, not only by changes in nutrient supply but also through the secretion of growth-controlling substances (Hay, 1989).

In order to assess fetal growth the age of the fetus must be accurately established before 24 week gestation. Any fetal organ or part of the fetal body that can be measured serially can have its growth rate studied but in normal fetuses we are only interested in growth rates of the head and abdomen (Patricia and Pearce, 1992).

Numerous growth curves are available, the one chosen must be appropriate for the population. Symmetric IUGR cannot be diagnosed in a single examination. The interval growth can be plotted on a graph to show growth sequence. Ethnicity, previous obstetric history, paternal size, fetal gender, and the results of tests of fetal well-being must be considered before IUGR is diagnosed rather than a healthy SGA. A study with US confirmed dates showed that in addition to gestation and gender, maternal weight at first visit, height, ethnic group, and parity were significant determinants of birth weight. Correction factors were entered into a computer program to adjust the normal birth weight percentile limits. With adjusted centiles they found that 28% babies that conventionally fit the criteria for SGA and 22% of those who were LGA were in fact within normal limits. Conversely, 24% and 26% identified as small or large, respectively, with adjusted centiles were missed by conventional unadjusted centile assessment (Gardosi et al, 1992).

Growth analysis requires two or more studies. IUGR tends to be progressive, and if the AC is approaching -2SD in the second trimester, then that AC age may be below -2SD near term. This is not a hard and fast rule because other processes may affect the AC by causing liver

enlargement (DuBose, 1996). Fetal size assessment is a complex issue. Fetal growth analysis requires an early dating sonogram followed by a second for growth evaluation. When any abnormality is suspected, Doppler, close observation (biophysical profile), and follow-up studies to monitor growth are advised (DuBose, 1996). Sonography is useful for diagnosing IUGR and evaluating and monitoring the fetus after IUGR has been diagnosed (Doubilet et al, 2000). The Doppler finding with the greatest impact on pregnancy management is absent or reversed end-diastolic flow in the umbilical artery (Fouron et al, 1993).

Lower maternal weight at the first antenatal visit was associated with a significantly smaller placental volume at 17 and 20w gestation ( $p < 0.002$  and  $< 0.0001$ ). Maternal weight gain was directly related to fetal anthropometry (AC, HC, FL and BPD) (Thame et al, 2004).

Intrauterine growth restriction is described as a decreased rate of fetal growth. IUGR complicates 3% to 7% of all pregnancies (Hadlock et al, 1984). It is often difficult to differentiate the fetus that is constitutionally small from one that is growth restricted. IUGR babies are at a greater risk of antepartum death, perinatal asphyxia, neonatal morbidity, and later developmental problems. Mortality is increased 6 to 10 fold. Before abnormal growth can be diagnosed it is necessary to accurately determine the gestational age. In the prenatal period an accurate LMP or a first trimester US can be used. If the first trimester US was not performed, then in the 2<sup>nd</sup> or 3<sup>rd</sup> trimester the standard BPD, HC, AC and FL should be used in conjunction with other tests of fetal well being (e.g. Biophysical profile and fetal Doppler velocimetry). An early diagnosis of IUGR and close fetal monitoring is of significant help in managing IUGR (Rosenberg and Chervenak, 1995).

### 3.9a: GROWTH RESTRICTED OR SMALL FOR DATE FETUS (SFD)

Babies are small because they are born too soon (preterm) or too light in weight (SFD) or both. Many of the problems of these conditions overlap. In general SFD infants can be divided into two groups: symmetrical and asymmetrical. The differentiation between these two is important because they have different causes and different prognosis, and require different management.

An antenatal diagnosis of IUGR in general correlates well with the same adverse outcomes that neonatal diagnosis of SGA or a standard definition of birth weight less than the 10<sup>th</sup> percentile for gestational age. Thus, obstetricians can more safely make their decisions on the basis of information presented in this and other similar studies using neonatal definitions of

IUGR/SGA. Similarly this information is vital to the neonatologists. It can also improve clinical counseling and decision making in these critical situations (Garite et al, 2004).

Gestational age at onset of growth restriction is more important than the cause in producing a symmetric versus an asymmetric fetus. Neonatal morbidity and mortality rates were higher in symmetric IUGR (Lin et al, 1998). The overall prevalence of IUGR must be 10%, because it includes all fetuses whose weight falls <10<sup>th</sup> centile. But it is not uniform. In healthy and well nourished population, IUGR occurs in 3-5% of patients. In women of hypertension or previous IUGR fetus, the prevalence rises to 25% or higher (Simon et al, 1990).

Accurate antenatal diagnosis offers the best opportunity to reduce the complications associated with IUGR. IUGR fetuses have a four to eight fold increased risk of perinatal mortality (Seeds, 1984). Doppler USG and biophysical profile stratify IUGR fetuses into risk categories, but their results do not show a consistent relationship with each other. Further research is warranted to investigate how they are best combined (Baschat et al, 2006).

#### I. SYMMETRICAL SMALL FOR GESTATIONAL AGE (SGA)

Symmetrical growth restriction or low profile fetuses are perfect miniatures, in that they are correctly proportioned but are small. In most cases they represent the lower end of the normal range, i.e. they are genetically determined to be small and are not abnormal. However, some will be small because of chromosomal, infective or environmental factors that exert an influence early in pregnancy and therefore become apparent early. Growth is <5<sup>th</sup> centile both for HC and AC, so the HC/AC ratio remains within the normal range. Symmetric SGA or growth retardation is characterized by a fetus that is small in all physical parameters (e.g. BPD, HC, AC and FL) this is usually the result of a severe insult in the first trimester (Sabbagha, 1984). In many cases the specific cause of IUGR cannot be determined. Regardless of the etiology they have a poor prognosis. Their mortality is four to eight times that of non-IUGR fetuses (Lockwood and Weiner, 1986). Majority of these will be normal but it is very important that the abnormal babies be detected as soon as possible. Potential problems associated with symmetrical SGA are: reduced intellect and learning ability, short stature, and increased incidence of death in the first year (Patricia and Pearce, 1992).

#### II. ASYMMETRICAL SMALL FOR GESTATIONAL AGE (SGA)

This is the more common variety and occurs in most cases of primary or secondary placental insufficiency. In asymmetrical growth retardation—late growth deceleration, the fetal insults

occur later in gestation (after the 32<sup>nd</sup> week) when fat accumulation should be the greatest. The AC will be significantly lower than normal and the head: body ratio will also be abnormal. Such growth retardation results from placental insufficiency in mothers with pre-eclampsia, edema, proteinuria and hypertension. The prognosis for the fetus is improved by adequate maternal treatment (Palmer, 1995).

It should be noted that IUGR fetuses have been born to mothers who have no high risk factors, so all pregnancies undergoing US examinations should be evaluated for IUGR. Asymmetric IUGR is characterized by an appropriate BPD and HC with a disproportionately small AC. This reinforces the 'brain sparing effect'. The BPD and HC may be slightly smaller, but this usually does not happen until the late 3<sup>rd</sup> trimester (Rosenberg and Chervenak, 1995). This form of IUGR usually begins in late 2<sup>nd</sup> or early 3<sup>rd</sup> trimester.

These infants are long and thin. They have a head size appropriate for gestational age but have wasted bodies, as though they have been starved. The placenta supplies the fetus with nourishment and oxygen, and removes wastes. When the placenta begins to fail, its ability to supply nourishment declines before its ability to supply oxygen. Detecting failure in growth is an early warning that the oxygen supply to the fetus will decline in the near future.

Fetuses that have little or no glycogen stores are those that are preterm or are asymmetrically small. In the case of preterm infants, labor occurs before the fetus has completed its stores of glycogen. In asymmetrically small infants the fetus has used its stores of glycogen to allow its brain to grow. If delivered before they become short of oxygen then they exhibit 'catch up' growth and are as well grown and intellectually able as appropriately grown babies.

Initially growth of HC continues, reflected in a rise in HC:AC ratio. Eventually the HC stops growing. Growth of AC slows 2-3w before that of the HC, and eventually stops. As timely delivery will prevent perinatal death and handicap, careful monitoring is necessary. Potential problems associated with asymmetrical SGA are: one half of infants suffer serious short or long term morbidity, still birth, antenatal and perinatal asphyxia, leading to cerebral palsy and/or major mental handicap, hypoglycemia, hypothermia, hypocalcaemia, polycythemia, premature delivery, meconium aspiration pneumonia (Patricia and Pearce, 1992).

Long term morbidity in the IUGR babies include statistically significant excess of learning and psychomotor problems (Fitzhardinge et al, 1978). More recently it has been found that there is an apparent increase in the risk of developing hypertension and diabetes in later life

(Barker, 1992). Therefore the identification of the SFD fetuses has an important impact on perinatal mortality and morbidity in current obstetric practice.

Ideally, all pregnant women should have fetal growth monitored by measurements of HC and AC every 4 weeks, or more frequently if growth deviates from expected lines. This is obviously not feasible for all women. Therefore serial measurements can be done in women at 'high risk' of having small or large fetus. They are:

1. Maternal weight less than 10<sup>th</sup> centile for height (or under 45 kg as a rough guide).
2. Previous infant was SGA or poor maternal weight gain.
3. Maternal vascular disease- essential hypertension, pregnancy-induced hypertension, diabetes mellitus, collagen disorders.
4. Maternal cardiac disease that is severe enough to cause polycythaemia.
5. Heavy smokers, alcoholics and drug addicts.
6. Women with sickle cell disease.
7. Women with recurrent antepartum hemorrhage or uterine anomaly.
8. Women with raised maternal serum alpha feto-protein (MSAFP) but a structurally normal fetus (Patricia and Pearce, 1992) and fetal factors are:

1. Chromosomal disorders, especially trisomies 13 and 18.
2. Infections- viral like rubella, cytomegalovirus etc.
3. Non-chromosomal syndromes.
4. Multiple pregnancy.
5. Birth order.

Severe damage results in spontaneous abortion, but occasionally the pregnancy survives to term, when the disturbance may manifest itself as growth restriction (Whittle, 2001).

Intrauterine growth restriction is also associated with poor postnatal growth. The majority of children with IUGR demonstrate catch-up growth in the first 2 years of life. Those who don't, have a high risk of long-term growth problems. There is evidence of impaired growth hormone activity in IUGR who have persistent poor growth in the postnatal period (Yanney and Marlow, 2004). The importance of establishing the diagnosis in this group is underlined by the fact that when perinatal loss occurs it is much more likely to result in a still birth rather than a neonatal death (Whitfield, 1986).

Compared with the other options, biophysical profile was the best strategy to guide physicians on the timing of the delivery of the IUGR fetus (Odibo et al, 2004). Doppler US has shown that in fetuses with asymmetric IUGR, vascular resistance increases in the aorta and umbilical artery and decreases in fetal middle-cerebral artery. Increased vascular resistance is reflected by an increased Systolic/Diastolic (S/D) ratio or pulsatility index. A ratio of >3.0 in the umbilical artery after 30w is abnormal (Schulman et al, 1984). In the umbilical circulation, elevated resistance causing absent or reversed end-diastolic flow velocity waveforms are associated with high rates of morbidity and mortality (Rochelson et al, 1987).

The SGA fetus with an increased umbilical artery S/D ratio is at much higher risk for poor perinatal outcome than a small fetus with a normal ratio (Trudinger et al, 1985). Doppler can play useful role in determining the prognosis of fetus with IUGR. 'Reversed diastolic flow' in the umbilical artery carries a grave prognosis, and 'absent diastolic flow' or an 'elevated S/D ratio' is associated with poor prognosis, including increased likelihood of fetal distress in labor, admission to the intensive care unit, and perinatal mortality (Reuwer et al, 1987).

Intrauterine growth restriction can be diagnosed most accurately by using a combination of three parameters: EFW centile, amniotic fluid volume, and maternal blood pressure (Doubilet et al, 2000), using the definition of hypertension during pregnancy as a diastolic pressure of at least 90mm Hg or a systolic pressure of at least 140mm Hg or a rise in the former of at least 15mm Hg or in the later of at least 30mm Hg (Roberts, 1994). US features to be followed also include biophysical profile score and umbilical artery Doppler. A worsening trend in one or more of these features should prompt consideration of early delivery (Benson and Doubilet, 2005).

In general, Doppler criteria are not as good as non-Doppler Sonographic criteria for IUGR (Benson and Doubilet, 1998). IUGR fetuses have increased risk of perinatal mortality, of those who survive 50% have significant short or long- term morbidity (Doubilet et al, 2000).

### **3.9b: GROWTH ACCELERATED FETUS OR MACROSOMIA**

Sonographic estimation of fetal weight to determine macrosomia is of value. Large for gestational age (LGA) is another term applied to a large fetus or neonate. LGA is most often defined as a weight above the 90<sup>th</sup> percentile for gestational age (Doubilet et al, 2000).



Currently available formulas to estimate fetal weight assume a uniform density of tissue (Bernstein and Catalano, 1992). Because fat tissue is less dense than lean body mass, it can be hypothesized that US estimation of fetal weight particularly in diabetic mothers is the consequence of an elevated proportion of body fat. Weight estimation has positive predictive values of up to 51% for LGA and 67% for macrosomia (Benson and Doubilet, 2005).

10% of all infants have birth weights  $>90^{\text{th}}$  centile for GA and are considered LGA infants. 8% to 10% have birth weights  $>4000\text{g}$ , and are classified as macrosomic. Accurate Sonographic prediction of macrosomia is invaluable to the obstetrician in managing and delivering the fetus. Macrosomia was 1.2 to 2 times more frequent than the normal in women who are multiparous,  $\geq 35$  years, have a pre-pregnancy weight  $>70\text{kg}$ , have a post date pregnancy, or have a history of LGA fetus (Boyd et al, 1983).

Macrosomia is also a common result of poorly controlled maternal diabetes mellitus. The frequency of macrosomia in the offspring of mothers with diabetes ranges from 25% to 45% (Landon et al, 1989) versus 8% to 10% among nondiabetic mothers (Mintz and Landon, 1988). Macrosomic infants of insulin-dependent diabetic mothers are usually heavy and show a characteristic organomegaly. In addition to adipose tissue, the liver, heart and adrenals are increased in size (Morris, 1984). There is increased fat and muscle mass, leading to increase in size of fetal abdomen and shoulders. As a result they are at a greater risk for complications during labor than is a fetus of similar weight of a non-diabetic mother (Gross et al, 1987).

Not all infants of diabetic mothers are overgrown; those with severe vascular disease may have IUGR. Fetal abdominal fat layer of  $\geq 5\text{mm}$  was the most useful predictor of macrosomia at term. An AC  $\geq 90^{\text{th}}$  percentile, however, had a better sensitivity. The usefulness of routine fetal abdominal fat layer measurement in the early third trimester in the management of diabetic pregnancies is worthy of further evaluation (Bethune and Bell, 2003).

The macrosomic fetus has an increased incidence of morbidity and mortality as a result of head and shoulder injuries and cord compression. Shoulder dystocia, clavicular fracture, facial and brachial plexus palsy, meconium aspiration, perinatal asphyxia, neonatal hypoglycemia, and other metabolic complications are significantly increased in macrosomic pregnancies (Golditch and Kirkman, 1978). The incidence of macrosomia increased from 1.7% at 36w to 21% at 42w (Boyd et al, 1983). Women with US diagnosis of a LGA fetus more frequently received epidural anesthesia and had more cesarean deliveries (Levine et al,

1992). Fetuses of insulin-dependent and gestational diabetic mothers are exposed to high levels of glucose throughout pregnancy and so produce excess insulin. This leads to overgrowth of fetal trunk and abdominal organs, while the head and brain grow at a normal rate. US measurements of fetuses of diabetic mothers demonstrate accelerated growth of the fetal thorax and abdomen beginning between 28 and 32w gestation. LGA occurs in 25-42% and macrosomia in 10-50% of infants of diabetic mothers (Landon et al, 1989). If vaginal delivery is contraindicated for the macrosomic fetuses of diabetic mothers, the EFW should be taken into account when selecting the route of delivery (Benson and Doubilet, 2005).

Large fetuses especially those weighing >4000g, are at increased risk for perinatal complications. These are greatest for large fetuses of diabetic mothers, and most occur as a result of attempted vaginal delivery. Antenatal US diagnosis of large fetus can prompt cesarean section, preventing these complications. The most accurate US approach to diagnosis of macrosomia is via EFW. An EFW >4000g should prompt cesarean delivery, especially if the mother is diabetic (Doubilet et al, 2000). When the EFW is >90<sup>th</sup> centile, LGA can be diagnosed with greater confidence in the presence of polyhydramnios.

A large AC ( $\geq 90^{\text{th}}$  centile) or a fetus with accelerated growth should suggest the possibility of maternal diabetes mellitus. More so if there is associated polyhydramnios (amniotic column of >8cm) and a large (>4cm thick) placenta. Excessive growth, especially if accompanied by polyhydramnios, suggests poor control of maternal diabetes.

### **3.10: VARIABILITY**

The variability of fetal parameters increases as pregnancy advances. The increase in variability is undoubtedly for the most part due to actual differences in fetal size, because it has been demonstrated consistently in populations with optimal menstrual histories, with known dates of conception, and in whom age was established early in pregnancy by use of CRL measurement. The reason for variability of fetal biometry is the genetic variation in actual fetal size as pregnancy advances and, to a lesser extent, the measurement errors associated with their use (Filly and Hadlock, 2000).

### **3.11: ACCURACY**

The accuracy of weight prediction formula is determined by assessing how well the formula works in a group of fetuses scanned close to delivery. An important measure of a formula's

performance is its 95% confidence interval (CI). If the 95% CI is  $\pm 18\%$ , then the EFW will fall within 18% of the actual weight in 95% of cases, and the error will be greater than 18% in only 5% of cases. The accuracy of weight prediction formulas improves as the number of measured body parts increases up to three, achieving greatest accuracy when measurements of the head, abdomen and femur are used. There is no apparent improvement by adding the thigh circumference as a 4<sup>th</sup> measurement, nor is there proven benefit from using 3D USG or MRI. Even when based on measurements of the head, abdomen and femur, sonographic weight prediction has a rather wide 95% CI of at least  $\pm 15\%$ . Based on the AC and either the head or femur, the range is at least  $\pm 16\%$  to  $\pm 18\%$  (Benson and Doubilet, 2005).

The accuracy of Sonographic measurements has been questioned, as a consequence of large interobserver variations (Sarmandal et al, 1989). One point however is that the AC measurement has the greatest interobserver and intraobserver variability of all measurements reported in the literature (Hadlock, 1994) and it is an important part of all the EFW formulas. Accuracy appears to be less in fetuses that weigh less than 1000 grams than in larger fetuses (Townsend et al, 1988). Weight prediction is less accurate in diabetic than in non-diabetic mothers. In diabetics, with measurements of head, abdomen and femur, 95% CI is of  $\pm 24\%$ , whereas it is  $\pm 15\%$  in the general population (Hadlock et al, 1985).

In a study calculated weights from a 90-sec single-shot fast spin-echo sequence MR acquisition with 8-mm-thick slices in the axial plane at term were better than USG estimates by Hadlock's formula (Hassibi et al, 2004). Breech babies weighing  $>4\text{kg}$  at birth have 3-6 times the perinatal mortality rate of breech babies weighing 2.5-4kg; hence the need for an accurate fetal weight estimate in late pregnancy, especially in patients with breech presentations (Patricia and Pearce, 1992).

A study conducted here demonstrated that reliable estimates of fetal weight can be made by USG, to help the Obstetricians in the proper management of a case. The mean percentage error in EFW with BPD/AC formula was found to be  $-2.5\%$  (Quddus and Khatun, 2001).

### **3.12: AMNIOTIC FLUID EVALUATION**

The association between IUGR and decreased amniotic fluid (oligohydrannios) is well recognized. Oligohydrannios has also been associated with fetal renal anomalies, rupture of intrauterine membranes, and the postdate pregnancy. Amniotic fluid index (AFI) is used to

evaluate and quantify amniotic fluid volume (AFV) during the course of a pregnancy. Normal value of the sum of four quadrants or AFI, is 8 to 22cm, decreased is less than 5cm, increased is greater than 22cm (Phelan et al, 1987). The “eyeball technique” is also quite acceptable. It is a subjective survey to evaluate the overall amount of AFV and is probably the most commonly used method. Halpern has defined oligohydramnios as occurring when the largest vertical pocket is <3cm, whereas Manning reported <1cm to be true oligohydramnios (Halpern et al, 1985; Manning et al, 1981). In the presence of oligohydramnios, care should be taken when evaluating the fetal growth parameters, since they can be compressed. This may alter the EFW.

Amniotic fluid volume should provide direct evidence of pathological growth restriction, as the production of amniotic fluid is reduced in the presence of either vascular or placental deficiency. Most studies suggest that pregnancy outcome is impaired when the AFV is reduced, and the perinatal mortality rises sharply (Whittle, 2001). There is a relationship between fetal size and AFV. In particular, the prevalence of polyhydramnios is higher in pregnancies of nondiabetic mothers with LGA fetus than with a non LGA fetus and the prevalence of oligohydramnios is lower (Benson et al, 1991).

A study found that there was no significant relationship between the AFI and EFW ( $r = 0.08$ ;  $p = .10$ ) over all. In pregnancies with female fetuses, the AFI was positively associated with EFW centile before 38w, at 38w or later. A positive relationship between the AFI and EFW centile in pregnancies with male fetuses was noted only at 38w or later (Perni et al, 2004).

In Bangladesh, at 16w gestational age the mean (2SD) AFI was found to be 11.1cm ( $\pm 4$ cm) and at 40w it was 11.7cm ( $\pm 8$ cm), maximum AFI was 18cm ( $\pm 7$ cm) at 23w gestational age (Quddus and Rashid, 2005). Normal AFI in Bangladesh was found to correlate well with the AFI found on the Caucasian population. Only the maximum AFI was 18.1cm in this study whereas it was 14.7cm in their study, at 24w of gestation (Quddus, 2006).

### **3.13: BODY MASS INDEX (BMI)**

In Tech. Rep. Series No. 724 (FAO/ WHO/ UNU- 1985 Energy and Protein requirement), it has been mentioned that the desired body mass index (BMI) for Male and Female should be 20.1-25 and 18.7- 23.8 respectively. BMI below these levels has been considered as suffering from chronic energy deficiency and BMI  $\geq 28.6$  in female and  $\geq 30$  in male as obese.

When dealing with developing countries, it is suggested that the lower limit of “normality” for individuals of 20 is too high and a limit of 18.5 has therefore been proposed on the basis of the usual distribution of adult weights (WHO, 2003). Relative to women with a normal pre-pregnancy BMI, underweight women (BMI <18.5) were more likely to have a growth restricted fetus (Doherty et al, 2006).

### **3.14: SAFETY OF ULTRASONOGRAPHY**

Although ultrasound can produce permanent damage to tissue directly at high energies and reversible damage at somewhat lower energies, the danger is obviated in the use of diagnostic ultrasound by the use of pulsed sound at energy levels several hundred times lower than those necessary to produce minimal temperature rise in tissue (Hellman et al, 1967). Sunden has carried out a series of careful experiments on pregnant and non-pregnant rats. With the intensities employed in ultrasound machines he could neither damage maternal tissue, nor provoke abortion or damage to the newborn rat (Sunden, 1964). Food and drug administration guidelines (USA) state that the spatial peak-temporal average intensity (SPTA, a unit used to measure ultrasound intensity) has to be less than 94 mW/cm<sup>2</sup> in situ. Most commercial equipments use variable acoustic outputs between 1 and 46 mW/cm<sup>2</sup>.

### **3.15: SAMPLE SIZE IN A STUDY**

Technically, the sample size should be large enough to provide a confidence interval (CI) of desired width (95 out of 100%). It is called 95% CI. If the sample size covers 95% CI, the sample is said to be precise and representative. Thus precision depends on the size of a sample. When the sample size is 30 or more, their mean value will be closer to each other and also will be adjacent to the population mean and covers 95% CI. Therefore to get precise sample size, the number of subjects should not be less than 30. Any information obtained on 30 subjects, could be considered as the representative sample. However, greater is the sample size, more is the precision of the study and desired information representing the population can be obtained. But then, in general it is much better to increase the accuracy of data collection than to increase sample size after a certain point. The main objective of sampling is to get maximum information about the population with minimum effort and with minimum resource (Chowdhury, 2002).

## CHAPTER 4

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### *SUBJECTS AND METHODS*

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4.1: PLACE & DURATION	...	...	38
4.2: STUDY DESIGN	...	...	38
4.3: SAMPLE SIZE & SAMPLING TECHNIQUE	...	...	39
4.4: SAMPLE SELECTION	...	...	40
4.5: ETHICAL CONSIDERATION	...	...	42
4.6: SOCIAL CLASS	...	...	42
4.7: METHODOLOGY	...	...	42-44
4.8: OUT-COME VARIABLES	...	...	44
4.8: DEPENDENT VARIABLES:	...	...	45-48
4.8a: BIPARIETAL DIAMETER	...	...	45
4.8b: HEAD CIRCUMFERENCE	...	...	46
4.8c: FEMUR LENGTH	...	...	46
4.8d: ABDOMINAL CIRCUMFERENCE	...	...	47
4.8e: ESTIMATED FETAL WEIGHT	...	...	48
4.8f: RATIOS DETERMINED	...	...	48
4.8g: ESTIM. FETAL WEIGHT ACCURACY	...	...	48
4.9: PROCEDURE OF DATA COLLECTION	...	...	49
4.10: PROCEDURE OF DATA ANALYSIS	...	...	50-51

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## **SUBJECTS AND METHODS**

### **SUBJECTS**

#### **4.1: PLACE AND DURATION**

This research work was carried out in the Radiology & Imaging department in collaboration with the department of Obstetrics and Gynecology of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), located in the capital city of Dhaka, in Bangladesh.

The study was conducted over a period, starting from December 2004 to November 2007.

#### **4.2: STUDY DESIGN**

This was a prospective, cross sectional study, of consecutively scanned healthy, gravid women. Therefore each patient was included once only in the study. As it is recommended that cross sectional data should be used to develop reference centiles for fetal size (Altman and Chitty, 1994).

The calculation of reference centiles was based on single observations as that was the usual clinical practice. The study population was homogenous.

To determine the accuracy of estimated fetal weight, the comparison was made after collecting the birth weights of the fetuses delivered within 72 hours of the last ultrasound scan.

### 4.3: SAMPLE SIZE AND SAMPLING TECHNIQUE

#### 4.3a: SAMPLE SIZE AND SAMPLING TECHNIQUE TO PREPARE NOMOGRAMS:

Healthy gravid women, who met the criteria, were included in the study. The data was collected irrespective of age and socio-economic status. The patients were referred by obstetricians from hospitals, clinics and from private practice settings. This study and the statistical analysis were carried out on a cross section of consecutively scanned women. Every member of the society therefore had an equal chance of being represented.

By following the standard sample size estimation formula, the sample size for this study came to 768.

We considered growth restricted among the study population was 50%.

That is, p (prevalence rate) = 0.5. We also considered the level of significance 5% at 95% confidence limit and then the value of d (standard error) = 0.05

Using the standard sample size estimation formula  $n = \frac{z^2 p q}{d^2}$

where n = number (sample size),

z = the standard normal deviate, usually set at 1.96 at 5% level which corresponds to 95% confidence level.

p = prevalence rate or assumed target proportion = 0.5

d = the degree of accuracy level considered as 5% = 0.05

q = 1 - p = 1 - 0.5 = 0.5

$$n = \frac{(1.96)^2 \times 0.5 \times 0.5}{(0.05)^2}$$

= 0.9604 ÷ 0.0025

= 384.16

So the sample size (n) = 384.

To cover the design effect, the sample can be doubled, so the sample size in this study

= 384 x 2 = 768

Since this was a population study to create normative charts the study sample was increased.

In order to get extremes of percentiles greater size of sample gives better result and more



accuracy. The larger the sample size the greater precision the resulting centiles will have. Because attention is concentrated on the tails of the distribution (the extreme values), several hundred observations are necessary to get reasonable estimates of extreme centiles. But time constraint is also to be considered.

#### 4.3b: SAMPLE SIZE AND SAMPLING TECHNIQUE TO DETERMINE THE ACCURACY OF ESTIMATED FETAL WEIGHT BY ULTRASOUND:

The sample size has been determined to measure a given proportion with a given degree of accuracy at a given level of statistical significance by using the following formula.

To determine the sample size, the formula used was;  $n = \frac{z^2 pq}{d^2}$

Where,

n= The desired sample size.

Z= The standard normal deviate, usually set at 1.96 at 5% level which corresponds to 95% confidence level;

The assumed target proportion is p to have a particular characteristics and q = 1-p, Here p = 0.05

Suppose,  $\frac{|\hat{p} - P|}{\hat{p}}$  is the relative error of estimate, p is to be tolerated with P, as proportion in

the population and d is the degree of accuracy level considered as 5%. The degree of accuracy d, which was assumed = 0.05

Putting the values in the above equation the sample size n is estimated as

$$\frac{3.84 \times 0.05 \times 0.95}{0.05^2} = 72.99$$

So the sample size (n) = 73

#### 4.4: SAMPLE SELECTION

Only one scan of each fetus was included in the study. When a patient was scanned more than once between 13 to 40 weeks of her pregnancy, her first scan was only included.

All study subjects were Bengalis, residing in Dhaka and the adjoining areas but belonging to different districts of Bangladesh. Caucasians, Mongols (Chinese, Japanese and tribal people) and other ethnic groups were excluded.

#### I. INCLUSION CRITERIA:

1. Subjects, who were sure of their last menstrual period (LMP) dates, had regular  $28 \pm 2$  days menstrual cycles and no unusual bleeding.
2. Patients who reported here with a previous ultrasound scan done before 20 weeks gestational age which confirmed the gestational age within 2 standard deviations (7 to 10days).
3. Singleton pregnancy.
4. No oral contraceptive taken 3 months prior to conception.

#### II. EXCLUSION CRITERIA:

1. Maternal malnutrition with a BMI of less than 18.5.
2. Any major maternal systemic disease which is likely to affect the growth of the fetus, like hypertension requiring treatment, diabetes mellitus, gestational diabetes, impaired glucose tolerance, and cardiac or renal disease.
3. History of tobacco or substance abuse.
4. Ethnic groups like foreigners and tribal people.
5. Uterine anomaly or large fibroids.
6. Bad obstetric history.
7. Congenital fetal anomalies.
8. Rhesus (Rh) incompatibility.
9. Oligo and polyhydramnios.
10. When the head shape was not optimum.
11. Ultrasonic evaluation was considered inadequate if any of the fetal measurements could not be obtained and the patient was excluded from the study.

## **4.5: ETHICAL CONSIDERATION**

### **4.5a: APPROVAL**

The research protocol was approved by the Independent Review Board (IRB) and by the Institutional Ethical Research Committee (ERC) of BIRDEM.

### **4.5b: CONSENT**

Well informed written consent was obtained from the patients before scan. for including in the study. A copy of it is attached in the appendix, page xiii.

### **4.5c: SAFETY**

Although ultrasonography is in use for a long time no adverse affect has been found on the patient or the fetus. So it is now considered safe for clinical use with the modern machines.

## **4.6: SOCIAL CLASS**

The social class system used in this study was prepared by the department of Epidemiology and Biostatistics of BIRDEM. It divides the population in four classes as follows:

Poor or destitute: Family earning is marginally low and starvation is avoided by loan or others help (relative, neighbour, government, NGO).

Lower: Family earning is adequate for food but not for other primary expenses (house, clothes, health) and are forced to sell articles for them.

Middle: Family earning exceeds the primary expenses and saving enables to buy land.

Upper: Family earning is at least more than double the primary expenses.

## **4.7: METHODOLOGY**

**4.7a:** On entry, all patients underwent a complete fetal sonographic examination including measurements of the fetal biparietal diameter (BPD), head circumference (HC), femur length (FL), and abdominal circumference (AC), using standard methodology. Measurements were made by electronic calipers. Only one measurement was taken of each variable. Measurements were recorded on specifically designed data sheets and entered into a computer at a later date. At the time of data analysis any outlying values were rechecked for

transcription errors. The few remaining outliers were not excluded from the analysis. Using measurements from poor images or images that depicted fetal anomalies was avoided. The estimated fetal weight (EFW) was computed by using Hadlock and colleague's formula (1985), in grams. All the fetal biometric measurements were taken by the student herself.

#### **4.7b: DESCRIPTION OF THE INSTRUMENT & TRANSDUCER**

All Sonographic measurements were made by using real-time Ultrasonography and electronic calipers. Ultrasound system employed was Toshiba (Tosbee) of Japan. A 3.5 megahertz (MHz) curvilinear transducer was used. Electronic trackball calipers capable of measuring up to 1 mm were used for all linear and circumferential measurements. Circumference measurements were made by calipers that open to outline the circumference. The formula is built into the ultrasound machine. It is an approximation to the circumference of an ellipse.

Birth weights of infants were measured in grams by an analogue 'Baby scale' of Japan.

#### **4.7c: PATIENT'S PREPARATION & EXAMINATION PROCEDURE**

##### **I. PATIENT'S PREPARATION:**

- No preparation was needed except optimally full bladder in early pregnancies.

##### **II. EXAMINATION PROCEDURE:**

- **POSITION OF PATIENT-**

Patient was laid in a supine position on a firm bed. Her abdomen was exposed up to the symphysis pubis and gel was applied on the lower part of her abdomen which was to be scanned. The transducer was thus coupled to the abdomen by a coating of gel.

- **GAIN SETTING -**

Gain was adjusted to get the best possible images.

#### **4.7d: RECORD**

The findings were recorded in predesigned Case Record Forms (CRF). A copy of it is attached in the appendix.

#### 4.7e: TEST FOR HYPOTHESIS

##### CORRELATION CO-EFFICIENT (R) TEST:

This test was done to see the degree of relationship between two variables, when one variable was dependent on the other, such as gestational age and BPD. The quality of the fit of the equation was measured by the coefficient of multiple correlation,  $R$ , or by the square of this value (the coefficient of determination,  $R^2$ ). The better the correlation, the closer these coefficients were to 1. Parameters that correlated very well had  $R^2$  values in the 0.90 to 0.99 range. Among the curves with a high  $R$  value, the most appropriate one was the curve with the lowest order. Accuracy of estimated fetal weight (EFW) was determined by using a t-test for paired two-sample means between Hadlock's weight standards and the birth weights.

#### 4.8: OUT-COME VARIABLES/ STUDY PARAMETERS

The variables that were studied included fetal biometric measurements of BPD, HC, FL and AC. All measurements were obtained in millimeters (mm). Fetal weight was estimated from HC, FL and AC measurements. Data were presented as mean with 2 standard deviations ( $\pm 2$  SD) and 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles of the observed values and estimated values. This gives a 95% Confidence Interval (CI). The data was analyzed by polynomial regression analysis to give it the form of a graph or a curve. The fitted models were superimposed on scatter diagrams to see their goodness of fit. The size charts derived from these measurements refer to exact postmenstrual age in weeks and days. The charts are based on cross sectional data and should be used only for assessing size. Serial measurements may show increasing or decreasing centiles for a fetus over time.

##### I. DEMOGRAPHIC VARIABLES:

Age, location, socio economic strata, parity, height, weight, BMI, hemoglobin.

##### II. INDEPENDENT VARIABLES:

- Gestational age.
- Birth weight of the infants.

The gestational age for each fetus was calculated to the nearest 10<sup>th</sup> of a week on the basis of the patients last normal menstrual period. For example, if the fetal age calculated on the basis of the last menstrual period was 39 weeks 3 days, it was recorded as 39.4 weeks.

### III. DEPENDENT VARIABLES:

Ultrasonographic measurements of BPD, HC, FL, AC and estimated fetal weight (EFW), also FL/AC, HC/AC, FL/ BPD, BPD/AC and FL/HC ratios.

#### 4.8a: BIPARIETAL DIAMETER

First, the lie of the fetus was determined and then the longitudinal axis found. A strong midline echo in the fetal head was demonstrated. Then the transducer was rotated through 90° until a transverse axial section of the fetal head was obtained. The correct plane of section demonstrated the following features:

- a) Oval shaped head. The calvaria was smooth and symmetric bilaterally
- b) Falx cerebri anteriorly and posteriorly only.
- c) The cavum septum pellucidum, anteriorly in the midline (It is an anechoic fluid filled box like structure, located anterior to thalamus in the midline).
- d) Choroid plexus in the atrium of each lateral ventricle.
- e) Paired Thalamic nuclei (A diamond shaped structure, which is divided equally by a hyperechoic line or slit, the third ventricle) (Campbell and Thomas, 1977).

BPD is the widest fetal head diameter at right angles to the mid-line. It was easier to get this section in occipito-transverse position of fetal head, not possible in direct occipito-anterior or posterior position. After freezing the image, the calipers were positioned in outer edge of near calvarial wall to inner edge of far calvarial wall (outer to inner) or from leading-edge to leading-edge. The transducer was perpendicular to the parietal bones. The instrument was set at medium gain so the parietal bones were not more than 3 mm in thickness (Hadlock, 1994). Soft tissue over the skull was not included. If the fetus was early for BPD measurement with proper landmarks, BPD was obtained by including: A smooth symmetrical head, visible choroid plexus and a well defined midline echo that was equal distance from both parietal bones (Jeanty & Romero, 1984).

The ultrasound image of the plane of measurement of BPD is given in the appendix, Fig. 2.

#### 4.8b: HEAD CIRCUMFERENCE

The aim of the technique was to obtain a horizontal section of fetal head which included both the biparietal diameter (coronal plane) and the occipital- frontal diameter (sagittal plane).

The procedure was identical to that described for the measurement of fetal BPD. Transverse scans were made so that a horizontal section of the fetal head was obtained; this was recognized by the appearance of the mid-line echo. The transducer was rotated until the head was ovoid and third ventricle was detected in the mid-line, one-third of the distance from the synciput. This ensured that the occipito-frontal HC section had been achieved.

The correct plane of section was through the third ventricle and thalami in the central position of the brain (as with the BPD), and the cavum septi pellucidi was visible in the anterior portion of the brain (Campbell and Thomas, 1977). The calvarium was smooth and symmetric bilaterally. After the proper plane of section was obtained, the calipers were positioned at the outer edges of the near and far calvarial walls. The equipment then allowed a computer- generated ellipse to fit to the calvarial margins or open to the outline of the fetal head. The ellipse adequately estimated the head perimeter even when it was not entirely imaged. To obtain an accurate HC measurement, 60% to 70% of the skull outline should be displayed on the screen (Hobbins et al, 1983). It was made certain that the ellipse fitted to the calvarium and not to the skin of the scalp.

Fig. 3 in the appendix gives ultrasound image plane for the measurement of HC.

#### 4.8c: FEMUR LENGTH

First the lie of the fetus was determined. The transducer was then placed at right angles to the fetal spine and passed down the fetus to the caudal end. When the femur was located, the transducer was rotated through 30 to 45 degrees towards fetal abdomen until the full length of the femoral diaphysis was obtained. Both ends of the femur were clearly visualized and the gain was reduced. The transducer was then aligned along the long axis of the bone, with the beam exactly perpendicular to the shaft. The measured ends of the bone were blunt and not pointed. Both the soft tissues of the buttock and knee joint should be seen, which avoids tangential section of the bone. When a clear image of the femur was obtained, the image was frozen and with multidirectional electronic calipers, the calcified portion was measured. Under estimation may result from a tangential section or incorrect plane orientation and not

obtaining the full length of the bone. Over measurement could be caused by superimposition of the ossification centers of the ileum or ischium or if the knee was semi-flexed by tibio-fibular complex, or if the head or distal epiphysis was included or by high gain setting, when the bone got thickened. The aim was a femur which was finely outlined and had clear-cut ends. Diagnostic ultrasound images, the calcified portion of the bone (primary ossification centers) from the proximal to distal metaphysis. Only the ossified portions of the diaphyses and metaphysis were measured. The cartilaginous ends of the femur were excluded (O'Brien et al, 1981). After 32 weeks, the distal femoral epiphysis was visualized but not included in the measurement. The measurements also did not include artifactual echoes such as the 'distal femoral point', which were echoes from cartilaginous material beyond the ends of the diaphyses. Including it significantly over measured the femur. Femur was measured from the major trochanter; femoral head was not taken into account even when it was visible. Only the length of diaphysis, which cast acoustic shadow, was measured. Mild bowing of the femur was observed from about 18 weeks gestation (Queenan et al, 1980). A straight measurement from one end of the diaphyses to the other was made, disregarding the curvature.

Fig. 4, in the appendix, gives ultrasound image plane for the measurement of FL.

#### 4.8d: ABDOMINAL CIRCUMFERENCE

Fetal abdominal circumference (AC) was measured at the position where the transverse diameter of the liver was the greatest. This was determined sonographically as the position where the right and left portal veins were continuous with one another. Some refer to this anatomic confluence of the intrahepatic portal veins as 'the hockey stick', or J-shape. Second, the appearance of the lower ribs was symmetric. Finally, the shortest length of the umbilical segment of the left portal vein was depicted, with the fetal stomach representing a secondary landmark (Hadlock, 1994). After this plane of section was frozen on the screen, the ellipse was fitted to the outer skin edge. If the ellipse margin was mistakenly fitted to the rib, it would significantly under measure the AC and have an effect on the weight estimate. Excessive pressure with the transducer was avoided because it distorted the shape of the abdomen. The fetal AC was measured on a transverse section through the fetal abdomen as described by Campbell and Wilkin (1975). A section which was as close as possible to circular was obtained, taking care to identify the spine and descending aorta posteriorly and



the stomach bubble in the same plane. If the kidneys were present, the section was too low or angled improperly (Sanders, 1984), so it was corrected.

This circumference could be traced along its outer margin with a map measurer or electronic digitizer, or by using the antero-posterior and transverse diameters measured outer to outer. In this study the later method was used, in which electronic ellipse calipers that opened to the outline, measured the perimeter of the fetal abdomen. Most of the modern generation of ultrasound machines use this method. With this facility the circumference was derived from the two maximum diameters of the ellipse.

Fig 5, in the appendix, gives ultrasound image plane for the measurement of AC.

#### 4.7e: ESTIMATED FETAL WEIGHT

The fetal weight was estimated at different stages of gestation, and a chart was prepared to obtain growth profile of the prenatal stage. The estimated fetal weight was computed at the time of ultrasound scan by using the formula based on measurements of head circumference, femur length and abdominal circumference in combination (Hadlock et al, 1985).

The data thus collected was analyzed by regression analysis to construct predictive curves for fetal weight. The model was superimposed on a scatter diagram to see its goodness of fit.

#### 4.8f: RATIOS DETERMINED

Tables and graphs of the mean and 95 percent confidence limits of the following fetal ratios were prepared.

- a. Femur length/ Abdominal circumference (FL/AC).
- b. Head circumference/ Abdominal circumference (HC/AC).
- c. Femur length/ Biparietal diameter (FL/ BPD).
- d. Biparietal diameter/ Abdominal circumference (BPD/AC).
- e. Femur length/ Head circumference (FL/HC).

#### 4.8g: ESTIMATED FETAL WEIGHT ACCURACY

Estimated fetal weights (EFW) were expressed in grams. Calculated estimated fetal weights were compared with birth weights of the infants to determine the accuracy of this method of estimation. EFW were derived from measurements of HC, FL and AC. Once included in the

study, no patient was excluded later on. After collecting the birth weights of the fetuses delivered within 72 hours of the last ultrasound scan, the comparison was made. Adjustment for days was not made. The infants' birth weights were obtained within half hour of delivery and were measured on an analogue scale. The birth weights were collected from the labor room of Obstetrics & Gynecology department of BIRDEM Hospital. Paired *t* test was used for comparison of the mean EFW and birth weight in the population examined.

#### **4.9: PROCEDURE OF DATA COLLECTION**

##### **DATA COLLECTION INSTRUMENT:**

a. Questionnaires:

Pre-designed structured questionnaire were used. It had sections on- history, socioeconomic strata and clinical information.

b. Case record forms (CRF)/ Obstetric Ultrasound report.

These forms were filled up after all the four basic measurements were taken by ultrasound scan and the fetal weights were deduced by the machine.

Questionnaires and CRF were used to collect information and for recording the findings. To determine the nutritional state of the patient, Body mass index (BMI) was calculated by dividing maternal weight in the first trimester in kg by square of her height in meter. A BMI of 18.5 was taken as the cut-off point of chronic energy deficiency (WHO, 2003). Fetuses were excluded if the pregnancy was exposed to factors known to influence fetal growth pathologically. History was taken and physical examination was done by the student herself. Then informed consent was obtained and ultrasound scan was done. Fetal Biometry and fetal weights were determined by Ultrasonographic measurements. The following measurements were carried out: biparietal diameter, head circumference, femur length and abdominal circumference. The measurements were taken according to standard techniques and were carried out by the student herself.

#### 4.10: PROCEDURE OF DATA ANALYSIS (STATISTICAL ANALYSIS)

Statistical analysis was carried out with Statistical package for Social Science (SPSS) for Windows (version 12, SPSS Inc.); Excel (Office premium 2000, Microsoft Corporation) was used to fit second order curves through the selected data points and to plot graphs.

The mean and centiles were estimated after polynomial regression (cubic or quadratic) models were fitted for mean and standard deviation (SD) separately as functions of gestational age in exact weeks from last menstrual period. Reference centiles should change smoothly with gestation, and they should be a good fit to the data. Here in almost all cases the linear-cubic model gave an excellent fit to the mean. For all simple measurements the SD increased in a linear fashion. The percentiles, mean and the 2SD were calculated for BPD, HC, FL and AC from 13 to 40 weeks of gestation based on the assumption that at each gestational age the measurements had a normal distribution. The relationship between the mean of each measurement and gestational age was modeled by fractional polynomial. The statistical methods used were as described by Altman and gave proper attention to the changing variability with increasing gestational age and the goodness of fit of the models obtained was carefully assessed (Altman and Chitty 1994). The correlation coefficient between a dependent variable, here BPD, HC, FL and AC, its estimate was calculated from polynomial or curvilinear regression. This coefficient of correlation is known as the coefficient of multiple correlations, denoted by  $R^2$ . The larger value of  $R^2$  indicates a closer agreement or relationship between the dependent and independent variable. The variability was expressed as  $\pm 2SD$ , which should be applicable to 95% of the fetuses in a normal population. 5% of the time estimates were outside this range.

##### 1. Modeling the mean:

The mean was modeled by fitting a polynomial regression model to the raw data. A quadratic or cubic curve gave a good fit to the data. The linear-cubic model, given by,

$Y = b_0 + b_1 X + b_2 X^3$ , where  $X$  is gestational age and  $Y$  is the measurement, seemed to work well. The model chosen was the simplest that gave a good fit to the data.

2. Calculating residuals: The differences or residuals between the observed values and the fitted line were calculated. The residuals were plotted against gestational age to show if and how the variability changes with gestation.

### 3. Modeling the variability:

The standard deviation was also modeled as a function of gestation. Polynomial regression was used to model the SD as a function of gestation. SD was used for each completed week of gestation, which was regressed on the mean age in each group. The values  $\pm 2SD$  were superimposed on the residual plot to see how well the SD has been modeled. The regression analysis to estimate the mean strictly took into account of any increase in SD with gestation.

### 4. Checking the goodness of fit of the models:

The standard approach to assessing the goodness of fit of a regression model is to calculate the statistic  $R^2$ , which represents the proportion of variability in the data explained by the model.

### 5. Deriving the centiles:

After the required centiles have been calculated they were superimposed on a scatter diagram of the observations as a final check of the fit. 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles were derived for the measurements. Statistical methods were used which gave proper attention to the changing variability with increasing gestation (Altman and Chitty, 1994).

### 6. Estimated fetal weight:

Regression analysis was used to evaluate the relationship between EFW in grams and menstrual age in weeks. The models tested included both log and non-log functions of EFW on menstrual age, menstrual age squared, and menstrual age cubed. To be included in the equation, the coefficient for each variable had to be statistically significant at the 0.5 level. The optimal model was chosen on the basis of the largest coefficient of determination ( $R^2$ ) and the smallest SD and by inspection of the residuals for uniformity of variance. This model was used to calculate predicted normal weight values between 13 and 40w. A log transformation reduced heteroselasticity of the EFW. An additional advantage of the log transformation was that the slope coefficient measured the elasticity of dependent with respect to independent, that is, the percentage change in dependent for a percentage change in independent. Difference were considered statistically significant if  $p < 0.05$  and  $p < 0.001$ .

### 7. Comparison study of EFW with Birth weight:

Paired t- test was used to compare EFW and birth weight to determine the accuracy of EFW. Mean values and  $\pm SD$  were calculated. (Multiple) regression analysis and Student's paired  $t$  test was used for statistical analysis.

## CHAPTER 5

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### *OBSERVATIONS AND RESULTS*

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COMPILED RESULTS	...	...	52-53
FETAL MEASUREMENTS:			
5.1: BPD TABLES & GRAPHS	...	...	55-58
5.2: HC TABLES & GRAPHS	...	...	59-62
5.3: FL TABLES & GRAPHS	...	...	63-66
5.4: AC TABLES & GRAPHS	...	...	67-70
5.5: EFW TABLES & GRAPHS	...	...	71-74
5.6: RATIOS:			
5.6a: FL/AC TABLES & GRAPHS	...	...	75-78
5.6b: HC/AC TABLES & GRAPHS	...	...	79-82
5.6c: FL/BPD TABLES & GRAPHS	...	...	83-86
5.6d: BPD/AC TABLES & GRAPHS	...	...	87-90
5.6e: FL/HC TABLES & GRAPHS	...	...	91-94
5.7: ACCURACY OF EFW	...	...	95-96

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## OBSERVATIONS AND RESULTS

In 1223 gravid women all the sonographic measurements were possible and the criteria satisfied, to be included in the study. 73 infants were also included for accuracy study of estimated fetal weight. The demographic characteristics of the study population were as follows. Variables are shown as 95% confidence interval (CI).

Mean maternal age was 26.95 ( $\pm 4.49$ ) with a minimum age of 17 and maximum age of 40 years; 93.9% patients were between 20 to 35 years age. It was predominantly a middle class population, as poor/ destitute patients do not go to the doctors or hospitals for antenatal care in our country. 96.9% were from middle class, 0.8% belonged to lower class and 2.3% were from upper class. 93.6% were from urban and 6.4% from rural areas. 54.7% were primipara and 45.3% were multipara. Mean parity was 0.6 ( $\pm 0.78$ ). 32.8 % were para one, 10.9% were of para two, 1% were of para three, 0.3% were of para four and 0.3 % were of para five. Body mass index (BMI) was used to determine the nutritional status. 18.5 was taken as the cutoff value (WHO, 2003). Mean BMI was found to be 23.67 ( $\pm 3.4$ ) (95% CI of 18.7-31.2). Mean maternal height was 156.73 ( $\pm 5.1$ )cm (95% CI of 148-167) and mean maternal weight in the first trimester was 57.92 ( $\pm 9.2$ )kg (95% CI of 43.8-78). Mean hemoglobin percent was 11.13 ( $\pm 1.08$ )g/dl (95% CI of 9-13).

Parameters	Mean	SD	Range	95%CI
Maternal age(yr)	26.95	4.49	17-40	20-36
Mat. Height (cm)	155.3	5.11	146-173	148-167
Mat. Weight (Kg)	56.2	9.2	40-90	43.8-78
BMI	23.67	3.40	18.5-37	18.7- 31.2
Hemoglobin(g/dl)	11.13	1.079	8-14.1	9-13
Parity	0.6	0.78	0-5	0-2

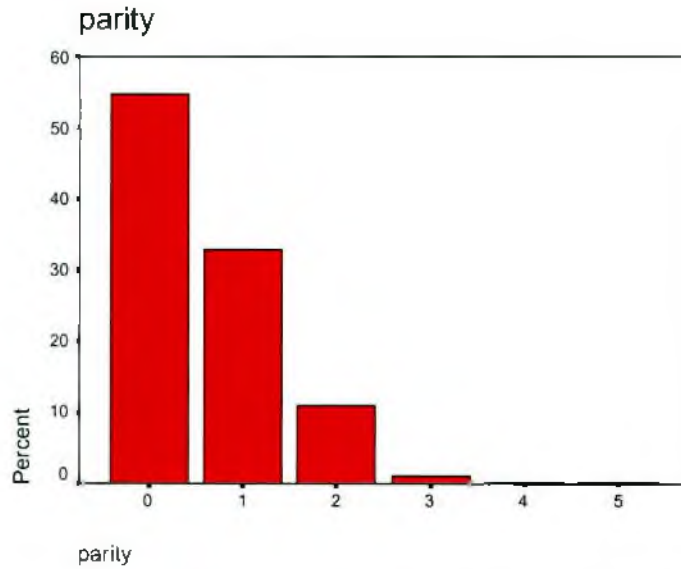
Nomograms comprising the third, tenth, fiftieth, ninetieth and ninety-seventh centiles, covering the period of gestation from 13 to 40 weeks, were constructed from all of the measurements data for each of the 5 individual parameters: biparietal diameter (BPD), head circumference (HC), femur length (FL), abdominal circumference (AC), and estimated fetal weight (EFW). It covered 95% of the population. Graph 1, gives the parity of the patients and Graph 2, gives the sample size and its distribution in each week from 13 to 40 weeks gestational age. In the present study the sex of the fetus was not considered.

### PERCENTILES FOR SIZE

Results were expressed as 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles, mean and 2 standard deviations (SD) of observed data. Then the mean was estimated by regression analysis and linear, quadratic or cubic models were fitted based on  $R^2$ . Polynomial regression models were fitted separately to the mean and SD as a function of gestational age. Linear cubic and quadratic models gave excellent fit to the mean.

Scatter diagrams with standard deviations were used to compare between observed and fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles plotted in graph. For BPD, HC, FL, and AC measurements linear- cubic and quadratic models were fitted to the mean and linear models to the SD. All the models were excellent fits to the data. The observed mean, 2SD and centiles for exact weeks of gestation are shown in Tables I, III, V, VII, IX and the estimated mean, 2SD and centiles for exact weeks of gestation are shown in Tables II, IV, VI, VIII, X. Models that were fitted are given in the appendix.

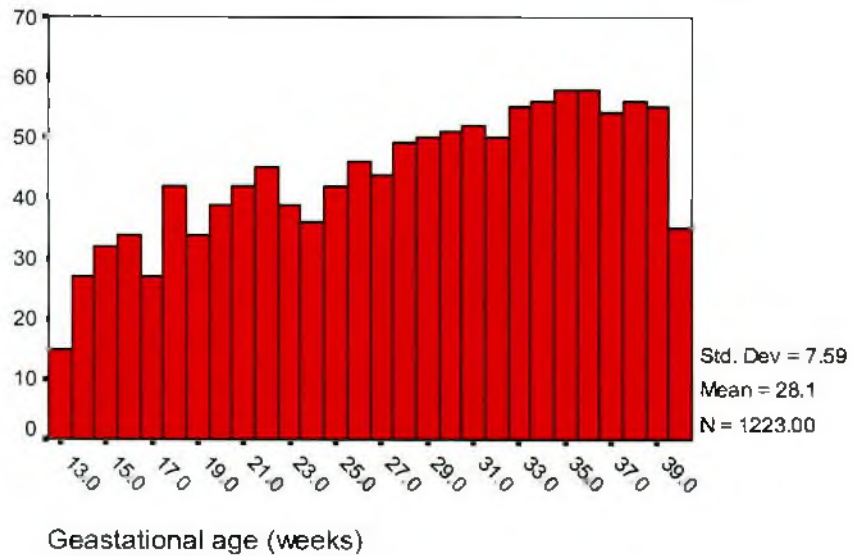
Graphs 3, 5, 7, 9, 11 show the raw data for each parameter's measurements with the 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves superimposed. Graphs 4, 6, 8, 10, 12, show the plots of the standardized residuals against gestation. The plots show that the data meets the assumptions well. Similarly Tables XI, XIII, XV, XVII, XIX give observed centile values of the 5 ratios and Tables XII, XIV, XVI, XVIII, XX give estimated 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles, mean and 2SD prepared by regression analysis of the 5 ratios. Graphs 13 to 22 were constructed to show the percentile curves fitted on the scatter diagram of the raw data of the 5 ratios and standard deviation scores. Finally tables XXI, XXII and graph 23, are presented to show the accuracy of EFW. All the regression equations are given in the Appendix.



Graph 1: Parity of patients in percentage. Range 0 to 5

### Sample size

#### Distribution of observations in each week



Graph 2: Distribution of data in each week of gestation.



## 5.1: BIPARIETAL DIAMETER

Table I shows summary of measurements of fetal biparietal diameter (BPD) (mm) as a function of gestational age. It gives the observed values. Total number of patients was 1223. The table gives the number of observations in each week, from 13 to 40 weeks gestational age and 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles of biparietal diameter at each week of gestation. It also gives the mean and 2 standard deviations ( $\pm 2SD$ ) of the observed values. At 13 weeks gestational age mean BPD was 23mm ( $\pm 3$ mm) (2SD), at 36 weeks it was 86.8mm (8.3mm) and at 40 weeks it was 91mm ( $\pm 6$ mm). Table II shows the fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles of fetal biparietal diameter (mm) with 95% confidence interval (CI). It also gives estimated mean and 2 standard deviations (2SD) of the data. At 13 weeks gestational age mean BPD was 24mm ( $\pm 4$ mm) (2SD), at 36 weeks it was 88.1mm ( $\pm 7$ mm) and at 40 weeks it was 92mm ( $\pm 8$ mm). The coefficient of multiple correlation  $R^2 = 0.977$  ( $p < .001$ ), which indicates a good correlation between the two variables.

There was gradual increase of 2 standard deviations towards term, from 4mm to 8mm.

Graph 3 shows raw data for biparietal diameter with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centile curves superimposed on it and in Graph 4, the values  $\pm 2$  standard deviations are superimposed on the residual plot to see how well the standard deviation has been modeled. Plot of standard deviation score (standardized residuals) against gestational age for biparietal diameter, shows expected 2 standard deviations.

## Summary of measurement of Fetal Biparietal diameter (observed)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean (mm)	2SD (mm)
13	15	20.3	21.3	23.3	25.3	26.3	23.3	3.2
14	27	22.9	24.1	26.6	29.1	30.3	26.6	3.9
15	32	25.8	27.1	30.0	32.9	34.2	30.0	4.5
16	34	28.3	30.1	34.0	37.9	39.7	34.0	6.1
17	27	33.3	34.6	37.4	40.2	41.5	37.4	4.4
18	42	36.4	37.9	41.1	44.3	45.8	41.1	5.0
19	34	39.7	41.1	44.1	47.1	48.5	44.1	4.7
20	38	42.6	44.0	47.1	50.2	51.6	47.1	4.8
21	43	45.3	46.7	49.8	52.9	54.3	49.8	4.8
22	45	48.5	49.9	52.8	55.7	57.1	52.8	4.6
23	39	51.5	52.9	56.0	59.1	60.5	56.0	4.8
24	36	53.1	55.0	59.1	63.2	65.1	59.1	6.4
25	42	57.0	58.6	62.1	65.6	67.2	62.1	5.4
26	46	59.6	61.3	65.1	68.9	70.6	65.1	5.9
27	44	61.2	63.1	67.3	71.5	73.4	67.3	6.5
28	49	64.2	66.1	70.2	74.3	76.2	70.2	6.4
29	50	67.5	69.3	73.0	76.7	78.5	73.0	5.8
30	51	69.9	71.7	75.6	79.5	81.3	75.6	6.1
31	52	70.9	73.1	77.6	82.1	84.3	77.6	7.1
32	50	73.5	75.5	79.8	84.1	86.1	79.8	6.7
33	55	77.3	78.9	82.4	85.9	87.5	82.4	5.4
34	56	79.4	81.2	84.9	88.6	90.4	84.9	5.8
35	59	79.7	81.7	86.1	90.5	92.5	86.1	6.8
36	57	79.0	81.5	86.8	92.1	94.6	86.8	8.3
37	54	81.4	83.7	88.6	93.5	95.8	88.6	7.7
38	56	82.5	84.6	89.0	93.4	95.5	89.0	6.9
39	55	82.4	84.8	89.9	95.0	97.4	89.9	8.0
40	35	84.9	86.7	90.7	94.7	96.5	90.7	6.2

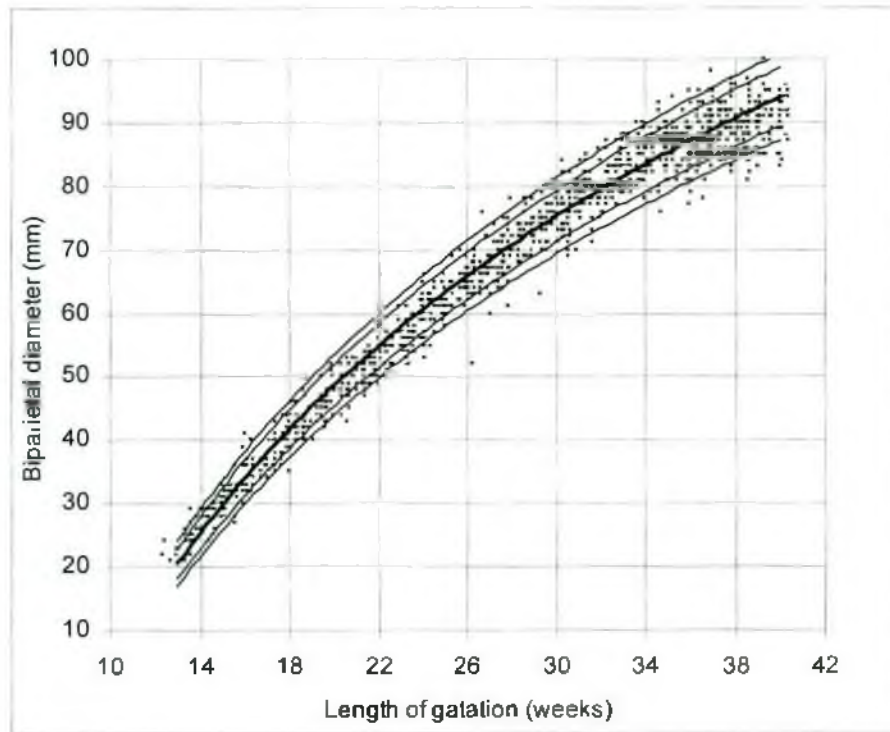
Table I: Summary of measurements of fetal biparietal diameter (mm). Observed values.

Total (n) = 1223.

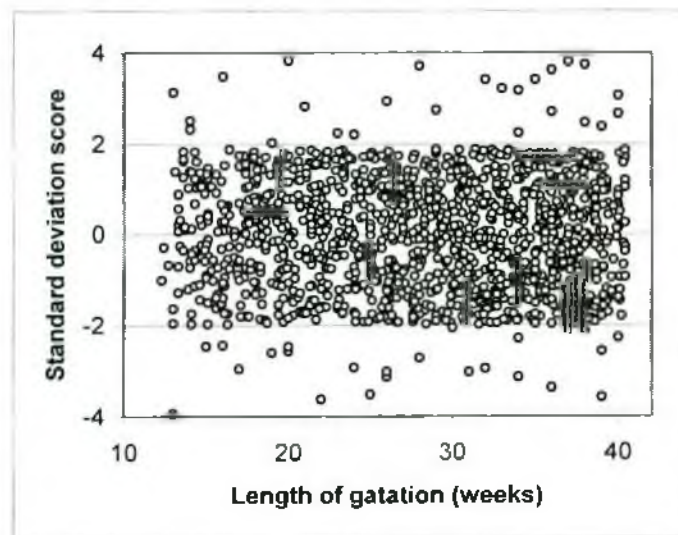
## Fitted Centiles of Fetal Biparietal diameter (estimated)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean (mm)	2SD (mm)
13	15	21.2	22.2	24.2	26.2	27.2	24.2	4.1
14	27	23.5	24.7	27.2	29.7	30.9	27.2	4.2
15	32	26.1	27.4	30.3	33.2	34.5	30.3	4.3
16	34	28.1	29.9	33.8	37.7	39.5	33.8	4.5
17	27	33.4	34.7	37.5	40.3	41.6	37.5	4.6
18	42	35.6	37.1	40.3	43.5	45.0	40.3	4.7
19	34	39.3	40.7	43.7	46.7	48.1	43.7	4.9
20	38	42.1	43.5	46.6	49.7	51.1	46.6	5.0
21	43	45.7	47.1	50.2	53.3	54.7	50.2	5.1
22	45	49.0	50.4	53.3	56.2	57.6	53.3	5.2
23	39	52.2	53.6	56.7	59.8	61.2	56.7	5.4
24	36	53.6	55.5	59.6	63.7	65.6	59.6	5.5
25	42	57.5	59.1	62.6	66.1	67.7	62.6	5.6
26	46	60.1	61.8	65.6	69.4	71.1	65.6	5.7
27	44	62.1	64.0	68.2	72.4	74.3	68.2	5.9
28	49	64.9	66.8	70.9	75.0	76.9	70.9	6.0
29	50	68.2	70.0	73.7	77.4	79.2	73.7	6.1
30	51	70.6	72.4	76.3	80.2	82.0	76.3	6.3
31	52	71.8	74.0	78.5	83.0	85.2	78.5	6.4
32	50	74.5	76.5	80.8	85.1	87.1	80.8	6.5
33	55	77.6	79.2	82.7	86.2	87.8	82.7	6.6
34	56	79.4	81.2	84.9	88.6	90.4	84.9	6.8
35	59	80.2	82.2	86.6	91.0	93.0	86.6	6.9
36	57	80.3	82.8	88.1	93.4	95.9	88.1	7.0
37	54	82.2	84.5	89.4	94.3	96.6	89.4	7.1
38	56	84.0	86.1	90.5	94.9	97.0	90.5	7.3
39	55	84.0	86.4	91.5	96.6	99.0	91.5	7.4
40	35	86.5	88.3	92.3	96.3	98.1	92.3	7.5

Table II: Fitted percentiles of fetal biparietal diameter (mm). Estimated values.



Graph 3: Raw data for biparietal diameter with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles.



Graph 4: Assessment of goodness of fit of model for fetal biparietal diameter. Plot of standard deviation score against gestational age, showing expected 2SD.

## 5.2: HEAD CIRCUMFERENCE

Table III shows summary of measurements of fetal head circumference (HC) (mm). It gives the observed values. A total of 1223 observations were made. 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles and the mean and  $\pm 2$  standard deviations (2SD) of head circumference at each week of gestation were calculated from the raw data. At 13 weeks gestational age mean head circumference was 86.1mm ( $\pm 12$ mm) (2SD), at 36 weeks it was 317.0mm (25.3mm) and at 40 weeks it was 330.2mm ( $\pm 23.3$ mm). Table IV shows fitted centiles of fetal head circumference measurements. The fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles of fetal head circumference, that is, 95% confidence interval (CI) are given. It also gives estimated mean and 2 standard deviations of the data. At 13 weeks gestational age mean HC was 89.5mm ( $\pm 12.1$ mm) (2SD), at 36 weeks it was 320.6mm (23.2mm) and at 40 weeks it was 334.6mm ( $\pm 25.1$ mm). The coefficient of multiple correlation,  $R^2 = 0.981$  ( $p < .001$ ), which indicates a good correlation between the two variables.

There was gradual increase of 2 standard deviations towards term, from 12.1 to 25.1mm.

Graph 5 shows raw data for fetal head circumference with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves superimposed on it. It gives 95% confidence interval and Graph 6 shows assessment of goodness of fit of model for standard deviation of head circumference. Plot of standard deviation score against gestational age for head circumference, shows expected 2 standard deviations.

**Summary of measurement of Fetal Head Circumference (observed)**

<b>Weeks of gestation (w)</b>	<b>No. of fetuses</b>	<b>3rd</b>	<b>10th</b>	<b>50th</b>	<b>90<sup>th</sup></b>	<b>97th</b>	<b>Mean (mm)</b>	<b>2SD (mm)</b>
13	15	77	79	84	97		86.1	12.0
14	27	83	89	100	106		98.5	14.0
15	32	97	101	110	122		111.0	14.3
16	34	98	115	124	136	144	124.4	17.8
17	27	131	132	138	149		138.7	13.3
18	42	136	140	152	163	168	151.8	16.1
19	34	144	150	164	175	185	163.1	17.8
20	38	156	163	174	187	188	174.4	16.1
21	43	167	175	185	194	196	183.9	14.1
22	45	183	187	196	207	208	196.7	14.2
23	39	194	198	208	219	222	208.4	15.8
24	36	200	207	218	231	237	218.7	18.6
25	42	214	221	229	241	246	229.8	16.4
26	46	208	232	241	250	257	240.1	19.0
27	44	229	238	249	264	271	249.1	19.3
28	49	233	246	258	270	276	258.7	19.8
29	50	243	250	266	281	283	266.9	21.1
30	51	261	265	276	291	299	277.8	19.9
31	52	263	270	285	300	310	284.7	22.3
32	50	267	276	292	311	317	293.1	25.1
33	55	284	289	300	315	322	301.3	19.0
34	56	288	295	309	322	327	308.5	19.9
35	59	286	300	315	329	332	313.6	22.3
36	57	294	304	316	333	351	317.0	25.3
37	54	303	310	323	338	345	322.7	21.4
38	56	301	306	325	339	347	324.1	23.3
39	55	296	306	325	343	356	325.7	28.3
40	35	298	313	333	344	346	330.2	23.3

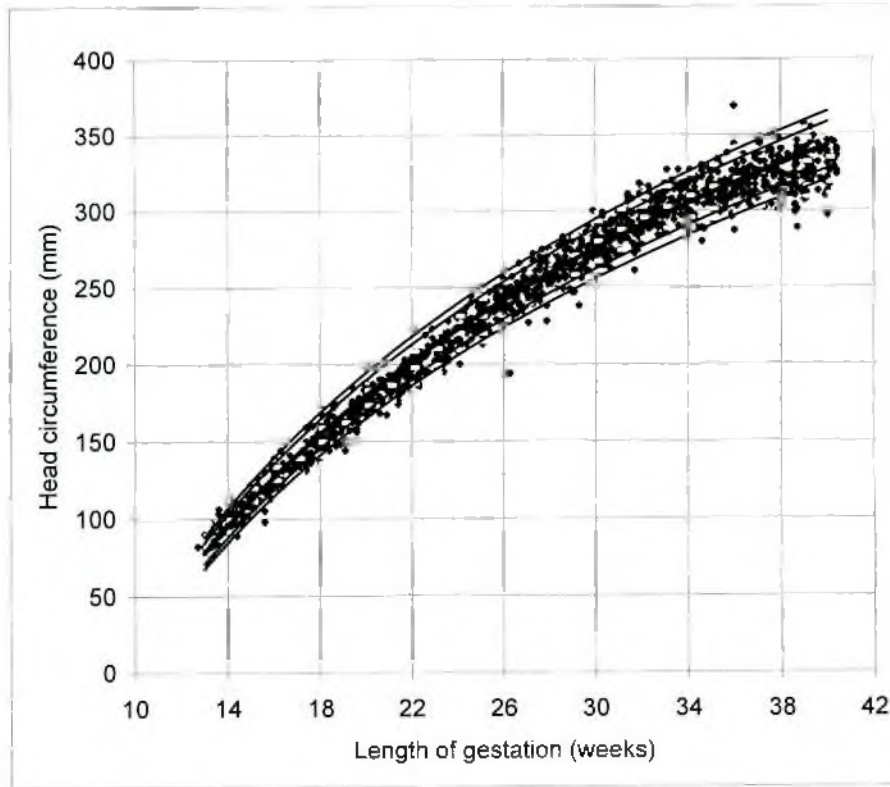
Table III: Summary of measurements of fetal head circumference (mm). Observed values.

Total = 1223.

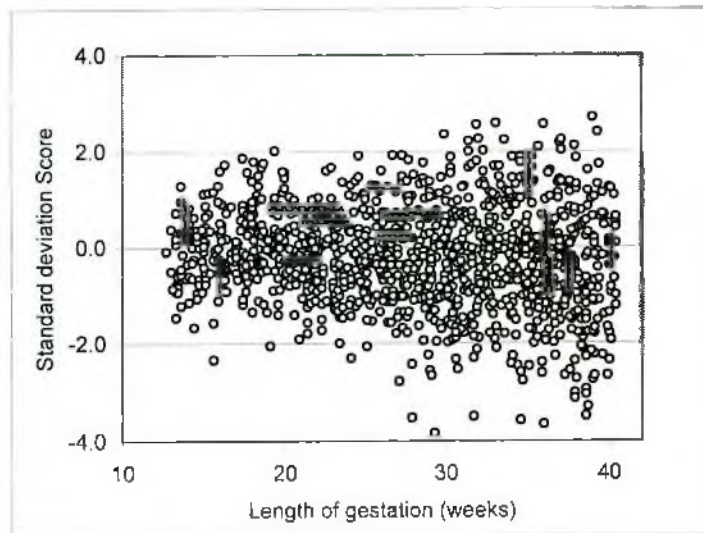
**Fitted Centiles of Fetal Head Circumference (estimated)**

<b>Weeks of gestation(w)</b>	<b>No. of fetuses</b>	<b>3rd</b>	<b>10th</b>	<b>50th</b>	<b>90th</b>	<b>97th</b>	<b>Mean (mm)</b>	<b>2SD (mm)</b>
13	15	78.1	81.8	89.5	97.2	100.9	89.5	12.1
14	27	87.7	91.4	99.4	107.4	111.2	99.4	12.5
15	32	99.2	103.0	111.3	119.6	123.4	111.3	12.9
16	34	112.0	116.1	124.7	133.3	137.4	124.7	13.5
17	27	125.7	129.9	138.9	147.9	152.1	138.9	14.0
18	42	135.9	140.2	149.4	158.6	162.9	149.4	14.4
19	34	148.1	152.6	162.1	171.6	176.1	162.1	14.9
20	38	158.6	163.2	173.0	182.8	187.4	173.0	15.3
21	43	171.3	176.0	186.2	196.4	201.1	186.2	15.9
22	45	182.2	187.1	197.6	208.1	213.0	197.6	16.4
23	39	194.1	199.2	210.0	220.8	225.9	210.0	16.9
24	36	203.8	209.0	220.1	231.2	236.4	220.1	17.3
25	42	214.4	219.7	231.1	242.5	247.8	231.1	17.8
26	46	224.7	230.2	241.9	253.6	259.1	241.9	18.3
27	44	233.5	239.2	251.2	263.2	268.9	251.2	18.8
28	49	242.7	248.4	260.8	273.2	278.9	260.8	19.3
29	50	252.0	257.9	270.5	283.1	289.0	270.5	19.7
30	51	260.8	266.9	279.9	292.9	299.0	279.9	20.3
31	52	267.9	274.2	287.4	300.6	306.9	287.4	20.7
32	50	275.4	281.7	295.3	308.9	315.2	295.3	21.2
33	55	281.8	288.3	302.1	315.9	322.4	302.1	21.6
34	56	288.6	295.3	309.5	323.7	330.4	309.5	22.2
35	59	294.1	300.9	315.4	329.9	336.7	315.4	22.7
36	57	298.8	305.8	320.6	335.4	342.4	320.6	23.2
37	54	302.8	309.9	325.0	340.1	347.2	325.0	23.6
38	56	306.0	313.3	328.7	344.1	351.4	328.7	24.1
39	55	308.8	316.2	331.9	347.6	355.0	331.9	24.6
40	35	311.0	318.5	334.6	350.7	358.2	334.6	25.1

Table IV: Fitted percentiles of fetal head circumference (mm). Estimated values.



Graph 5: Raw data of fetal head circumference with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles.



Graph 6: Assessment of fit of model for fetal head circumference: Plot of standard deviation score against gestational age, showing expected 2SD.



### 5.3: FEMUR LENGTH

Table V shows summary of measurements of observed values of fetal femur length (FL) (mm), as a function of gestational age. Total number of patients was 1223. It shows the number of observations in each week of gestation and the 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles, mean and  $\pm 2$  standard deviations (2SD) of femur length at each week. At 13 weeks gestational age mean FL was 11.3mm ( $\pm 1.6$ ) (2SD), at 36 weeks it was 67.3mm (5.2mm) and at 40 weeks it was 73.2mm ( $\pm 5.1$ mm).

Table VI gives fitted estimated values of 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles of fetal femur length at each week of gestation and also the mean and 2 standard deviations of the data. At 13 weeks gestational age mean femur length was 10.6mm ( $\pm 3.4$ mm) (2SD), at 36 weeks it was 67.8mm (5.4mm) and at 40 weeks it was 73.2 mm ( $\pm 5.8$ mm). The coefficient of multiple correlation,  $R^2 = 0.982$  ( $p < .001$ ), which indicates a good correlation between the two variables.

There was gradual increase of 2 standard deviations towards term, from 3.4mm to 5.8mm.

Graph 7 shows raw data of femur length with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves superimposed on it. It shows 95% confidence level and Graph 8 shows assessment of goodness of fit of model for standard deviations of femur length. Plot of standard deviation score against gestational age for femur length, shows expected 2 standard deviations.

## Summary of measurement of Fetal Femur length (observed)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean (mm)	2SD (mm)
13	15	10.0	10.0	12.0	12.0		11.3	1.6
14	27	11.0	11.8	14.0	16.0		14.0	3.5
15	32	11.0	13.3	17.0	18.7		16.5	4.3
16	34	14.1	16.5	20.0	23.0	25.0	20.1	4.9
17	27	20.0	22.0	24.0	27.2		24.2	3.8
18	42	23.3	24.0	26.0	29.0	30.7	26.5	3.6
19	34	26.0	26.5	30.0	32.0	34.0	30.0	3.8
20	38	28.2	29.9	32.0	35.1	37.8	32.1	4.4
21	43	29.3	32.0	35.0	38.6	39.7	35.4	4.7
22	45	33.4	35.0	38.0	40.0	41.0	37.8	4.0
23	39	38.2	39.0	41.0	43.0	46.6	41.2	3.5
24	36	40.0	40.0	43.0	45.0	45.9	42.8	3.6
25	42	42.0	43.0	46.5	49.0	49.0	46.2	4.0
26	46	38.8	45.0	48.0	51.3	53.6	48.0	5.7
27	44	44.7	47.5	50.0	53.0	54.0	50.3	4.0
28	49	48.0	51.0	53.0	56.0	57.0	53.0	4.2
29	50	50.1	52.0	54.5	58.0	60.0	54.9	4.9
30	51	51.8	54.2	57.0	59.0	61.3	57.0	4.4
31	52	51.8	55.3	59.5	63.0	64.8	59.3	6.4
32	50	54.5	58.0	60.5	65.0	66.0	60.9	5.4
33	55	57.0	60.0	63.0	66.4	69.0	63.0	5.1
34	56	57.7	62.0	65.0	68.0	70.0	65.2	5.2
35	59	59.4	62.0	67.0	69.0	71.0	66.4	5.6
36	57	61.0	64.8	67.0	71.0	72.3	67.3	5.2
37	54	63.0	65.0	70.0	73.0	74.0	69.5	5.7
38	56	64.7	66.0	71.0	74.3	77.0	70.7	5.8
39	55	64.7	67.0	72.0	74.4	76.0	71.0	5.6
40	35	68.1	69.6	73.0	76.0	77.9	73.2	5.1

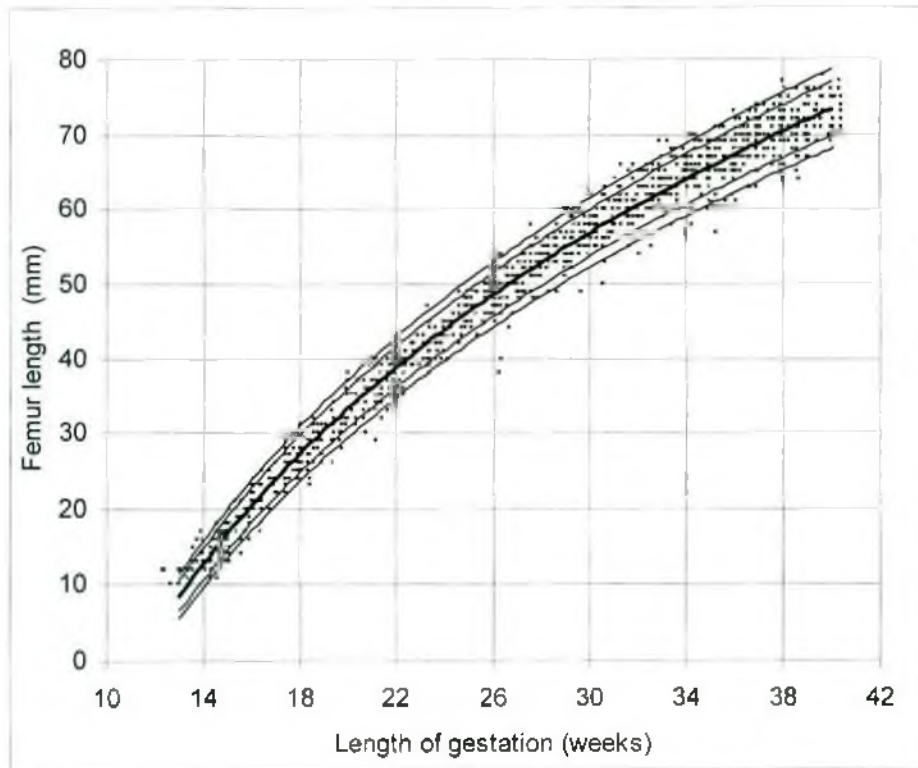
TableV: Summary of measurements of fetal femur length (mm). Observed values.

Total = 1223.

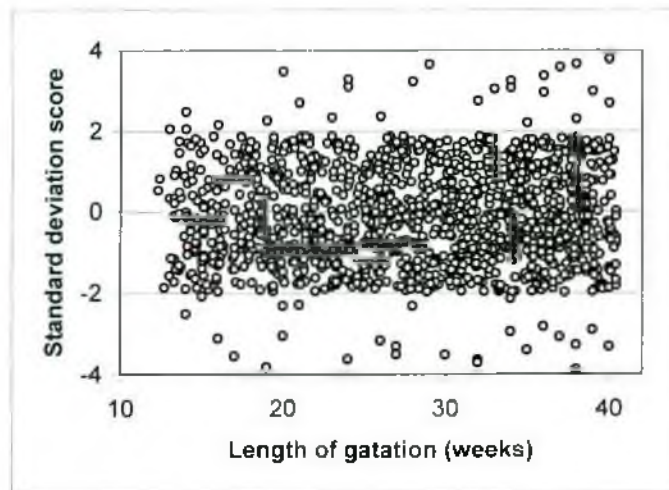
**Fitted Centiles of Femur length (estimated)**

<b>Weeks of gestation(w)</b>	<b>No. of fetuses</b>	<b>3rd</b>	<b>10th</b>	<b>50th</b>	<b>90th</b>	<b>97th</b>	<b>Mean (mm)</b>	<b>2SD (mm)</b>
13	15	7.4	8.4	10.6	12.8	13.8	10.6	3.4
14	27	10.4	11.5	13.7	15.9	17.0	13.7	3.5
15	32	13.6	14.7	16.9	19.1	20.2	16.9	3.5
16	34	17.0	18.1	20.4	22.7	23.8	20.4	3.6
17	27	20.4	21.6	24	26.4	27.6	24.0	3.8
18	42	23.0	24.2	26.6	29.0	30.2	26.6	3.8
19	34	26.0	27.2	29.7	32.2	33.4	29.7	3.9
20	38	28.5	29.7	32.3	34.9	36.1	32.3	4.0
21	43	31.5	32.8	35.4	38.0	39.3	35.4	4.1
22	45	34.3	35.5	38.2	40.9	42.1	38.2	4.2
23	39	37.0	38.2	41	43.8	45.0	41.0	4.3
24	36	39.3	40.6	43.4	46.2	47.5	43.4	4.4
25	42	41.8	43.1	45.9	48.7	50.0	45.9	4.4
26	46	44.2	45.5	48.4	51.3	52.6	48.4	4.5
27	44	46.2	47.6	50.5	53.4	54.8	50.5	4.6
28	49	48.3	49.7	52.7	55.7	57.1	52.7	4.7
29	50	50.5	51.9	55	58.1	59.5	55.0	4.8
30	51	52.6	54.1	57.2	60.3	61.8	57.2	4.9
31	52	54.3	55.8	59	62.2	63.7	59.0	5.0
32	50	56.2	57.7	61	64.3	65.8	61.0	5.1
33	55	57.8	59.4	62.7	66.0	67.6	62.7	5.2
34	56	59.6	61.2	64.6	68.0	69.6	64.6	5.3
35	59	61.3	62.9	66.3	69.7	71.3	66.3	5.3
36	57	62.7	64.3	67.8	71.3	72.9	67.8	5.4
37	54	64.0	65.7	69.2	72.7	74.4	69.2	5.5
38	56	65.2	66.9	70.5	74.1	75.8	70.5	5.6
39	55	66.4	68.2	71.8	75.4	77.2	71.8	5.7
40	35	67.7	69.5	73.2	76.9	78.7	73.2	5.8

Table VI: Fitted percentiles of fetal femur length (mm). Estimated values.



Graph 7: Raw data for fetal femur length with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles.



Graph 8: Assessment of goodness of fit of models for fetal femur length. Plot of standard deviation score against gestational age, showing expected 2SD.

## 5.4: ABDOMINAL CIRCUMFERENCE

Table VII shows summary of measurements of the observed values of fetal abdominal circumference (AC) (mm). Total number of subjects was 1223. It gives the number of observations and the centiles, mean and 2 standard deviations (2SD) of abdominal circumference at each week of gestation. At 13 weeks gestational age mean abdominal circumference was 66mm ( $\pm 6.5$ mm), at 36 weeks it was 305.7mm (37.0mm) and at 40 weeks it was 327.2mm ( $\pm 33.8$ mm).

Table VIII gives fitted percentiles of estimated values of fetal abdominal circumference. It also gives estimated mean and 2 standard deviations of the data. At 13 weeks gestational age mean abdominal circumference was 71.7mm ( $\pm 8.5$ mm), at 36 w it was 304.6mm (31.5mm) and at 40w it was 331.9mm ( $\pm 35.5$ mm). These are the estimated values after fitting the model. The coefficient of multiple correlation,  $R^2 = 0.970$ , ( $p < .001$ ), which indicates a good correlation between the two variables.

There was gradual increase of standard deviations towards term, from 8.5mm to 35.5mm. The body parameter is approximately twice as variable as those of the head. Graph 9 shows raw data of abdominal circumference with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles superimposed on it. It covers 95% of the population, therefore in 5% of cases the values will be outside this range and Graph 10 shows assessment of goodness of fit of models for fetal abdominal circumference. Plot of standard deviation score against gestational age, shows expected 2 standard deviations.

## Summary of measurement of Fetal Abdominal circumference (observed)

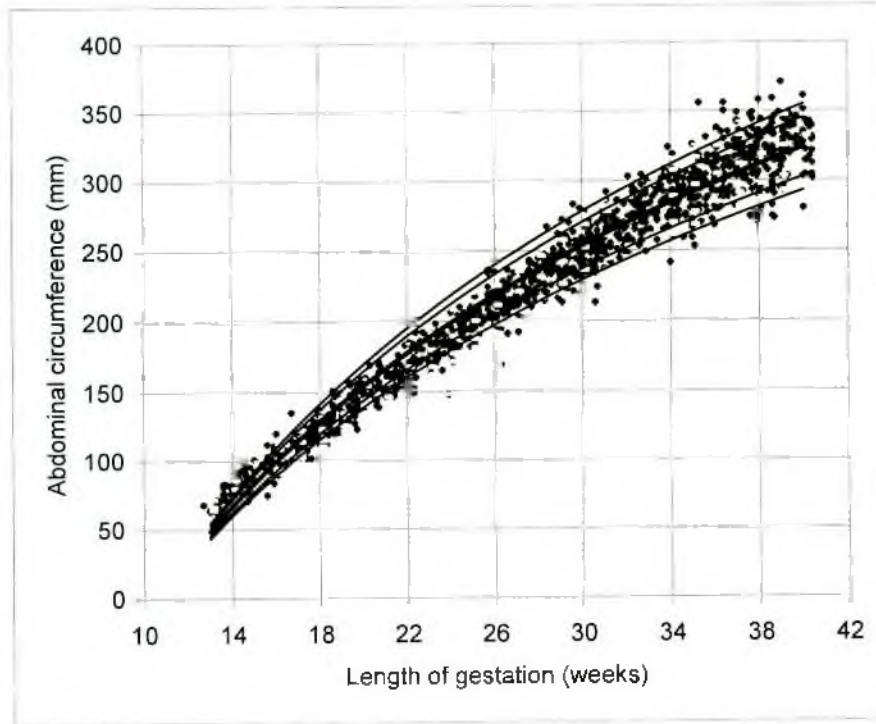
Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean (mm)	2SD (mm)
13	15	62	62	65	71	.	66.0	6.5
14	27	70	72	81	89	.	80.9	11.5
15	32	71	79	89	97	.	89.2	13.8
16	34	75	88	102	111	120	100.9	18.0
17	27	101	103	114	125	.	114.9	15.6
18	42	105	112	125	134	137	123.8	16.0
19	34	120	122	138	150	157	137.3	19.7
20	38	124	136	149	158	167	147.2	18.5
21	43	139	146	158	167	171	156.8	16.4
22	45	150	153	165	183	189	166.9	20.9
23	39	164	169	179	192	197	179.7	17.0
24	36	150	172	184	200	210	185.0	22.6
25	42	182	186	200	208	216	198.7	16.0
26	46	179	200	213	226	236	212.3	23.7
27	44	191	207	217	233	235	217.9	20.5
28	49	210	214	231	244	257	230.1	24.3
29	50	215	225	243	260	271	241.6	25.1
30	51	222	232	251	270	281	250.5	29.0
31	52	219	237	258	276	288	257.5	30.8
32	50	246	251	268	289	299	269.9	27.8
33	55	252	259	277	295	302	277.7	26.2
34	56	254	271	292	307	320	289.8	30.7
35	59	258	270	294	314	332	293.2	33.9
36	57	271	281	307	332	352	305.7	37.0
37	54	286	291	314	335	345	313.7	31.0
38	56	274	290	320	343	352	317.3	38.2
39	55	274	293	322	347	363	321.7	43.2
40	35	282	303	329	345	360	327.2	33.8

TableVII: Summary of measurements of fetal abdominal circumference (mm). Observed values. Total = 1223.

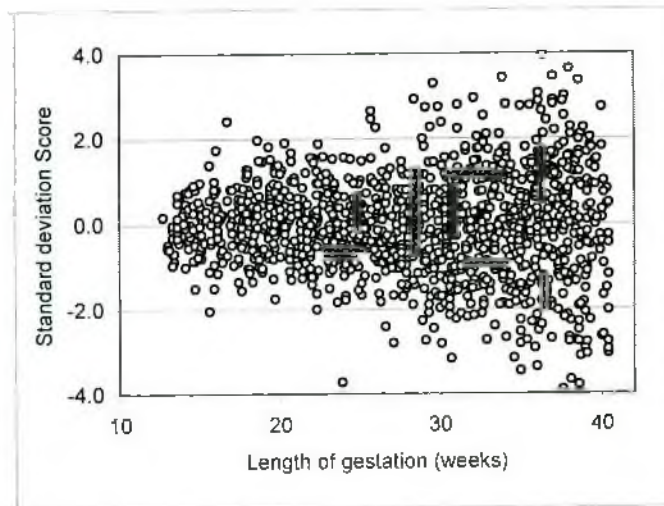
## Fitted Centiles of Fetal Abdominal Circumference (estimated)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean (mm)	2SD (mm)
13	15	63.7	66.3	71.7	77.1	79.7	71.7	8.5
14	27	71.3	74.0	80.0	86.0	88.7	80.0	9.3
15	32	80.3	83.4	90.0	96.6	99.7	90.0	10.3
16	34	90.9	94.3	101.5	108.7	112.1	101.5	11.3
17	27	102.3	106.0	114.0	122.0	125.8	114.0	12.5
18	42	110.7	114.7	123.2	131.7	135.7	123.2	13.3
19	34	121.3	125.5	134.7	143.9	148.1	134.7	14.3
20	38	130.2	134.8	144.5	154.2	158.8	144.5	15.2
21	43	141.5	146.4	156.8	167.2	172.1	156.8	16.3
22	45	151.3	156.5	167.6	178.7	183.9	167.6	17.3
23	39	162.1	167.6	179.4	191.2	196.7	179.4	18.4
24	36	171.2	176.9	189.3	201.7	207.4	189.3	19.3
25	42	181.1	187.2	200.2	213.2	219.3	200.2	20.3
26	46	191.1	197.5	211.2	224.9	231.3	211.2	21.4
27	44	199.8	206.5	220.8	235.1	241.8	220.8	22.3
28	49	209.0	216.0	231.0	246.0	253.0	231.0	23.4
29	50	218.8	226.1	241.7	257.3	264.6	241.7	24.4
30	51	228.1	235.8	252.1	268.4	276.1	252.1	25.5
31	52	236.0	243.9	260.8	277.7	285.6	260.8	26.4
32	50	244.6	252.9	270.4	287.9	296.2	270.4	27.4
33	55	252.1	260.6	278.8	297.0	305.5	278.8	28.4
34	56	260.8	269.6	288.5	307.4	316.2	288.5	29.5
35	59	268.1	277.3	296.8	316.3	325.5	296.8	30.5
36	57	275.0	284.4	304.6	324.8	334.2	304.6	31.5
37	54	281.2	291.0	311.7	332.4	342.2	311.7	32.4
38	56	287.1	297.1	318.4	339.7	349.7	318.4	33.3
39	55	292.7	302.9	324.9	346.9	357.1	324.9	34.3
40	35	298.5	309.2	331.9	354.6	365.3	331.9	35.5

Table VIII: Fitted percentiles of fetal abdominal circumference (mm). Estimated values.



Graph 9: Raw data for fetal abdominal circumference with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles.



Graph 10: Assessment of fit of model for AC plotted: Plot of standard deviation score against gestational age, showing expected 2SD.



## 5.5: ESTIMATED FETAL WEIGHT

Table IX shows summary of measurements of observed values of estimated fetal weight (EFW) (g). Total number of subjects was 1223. At 13 weeks gestational age mean estimated fetal weight was 72.3g ( $\pm 6.6$ g) (2SD), at 36 weeks it was 2509.8g (687g) and at 40 weeks it was 3095.0g ( $\pm 702.8$ g). These are the observed values of the raw data. It gives the number of observations and the percentiles, mean and 2 standard deviations (2SD) at each week of gestation from 13 to 40 weeks. The increase of EFW at 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles was slow up to 26<sup>th</sup> week of gestation. Thereafter a linear growth rate was observed up to term or 40 weeks gestational age. There was gradual increase of standard deviations towards term showing increasing dispersion of data towards term.

Table X gives fitted percentiles of estimated values of estimated fetal weight (g). It also gives estimated mean and 2 standard deviations of the data. The optimal model for estimated fetal weight was a natural log model of weight in grams on menstrual age (in weeks) and menstrual age squared. At 13 weeks gestational age mean estimated fetal weight was 76.9g ( $\pm 18.7$ g), at 36 weeks it was 2515g (431.3g) and at 40 weeks it was 3131.5g ( $\pm 749.1$ g). The coefficient of multiple correlation,  $R^2 = 0.988$ , ( $p < .001$ ), which indicates a good correlation between the two variables.

There was gradual increase of 2 standard deviations towards term, from 18.7g to 749.1g.

Graph 11 shows raw data of estimated fetal weight with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves superimposed on it. It gives 95% confidence level and in Graph 12 the values  $\pm 2$  standard deviations is superimposed on the residual plot to see how well the standard deviation has been modeled. Plot of standard deviation scores (standardized residuals) against gestational age for estimated fetal weight, shows expected 2 standard deviations.

**Summary of measurement of Estimated Fetal Weight (observed)**

<b>Weeks of gestation (w)</b>	<b>No. of fetuses</b>	<b>3rd</b>	<b>10th</b>	<b>50th</b>	<b>90th</b>	<b>97th</b>	<b>Mean (gm)</b>	<b>2SD (gm)</b>
13	15	68	69	71	78	.	72.3	6.6
14	27	77	81	94	107	.	93.4	18.8
15	32	81	98	113	132	.	112.7	26.6
16	34	90	112	150	166	186	143.4	40.8
17	27	144	157	185	208	.	183.7	35.6
18	42	176	195	215	255	273	221.3	46.7
19	34	216	227	278	320	337	279.2	69.3
20	38	235	270	330	393	411	326.7	83.8
21	43	310	326	387	450	468	389.6	85.8
22	45	385	399	445	545	583	459.6	112.2
23	39	480	496	560	635	713	560.8	105.8
24	36	446	531	615	722	794	618.1	140.9
25	42	624	673	752	842	894	749.3	130.8
26	46	572	764	876	1005	1043	878.5	200.5
27	44	783	816	962	1118	1153	968.0	192.8
28	49	861	975	1123	1274	1392	1127.9	245.0
29	50	1033	1096	1296	1489	1595	1276.8	281.2
30	51	1081	1227	1438	1641	1899	1440.1	362.4
31	52	1042	1283	1602	1876	2058	1590.2	451.3
32	50	1398	1496	1749	2064	2253	1781.1	432.2
33	55	1578	1670	1958	2240	2380	1958.4	407.7
34	56	1605	1889	2186	2499	2703	2198.4	487.4
35	59	1671	1891	2328	2575	2933	2305.4	598.4
36	57	1952	2065	2454	3040	3304	2509.8	687.0
37	54	2159	2379	2695	3144	3353	2729.3	589.4
38	56	2039	2295	2848	3198	3557	2824.6	710.7
39	55	2091	2395	2966	3406	3611	2912.1	798.4
40	35	2200	2596	3079	3536	3762	3095.0	702.8

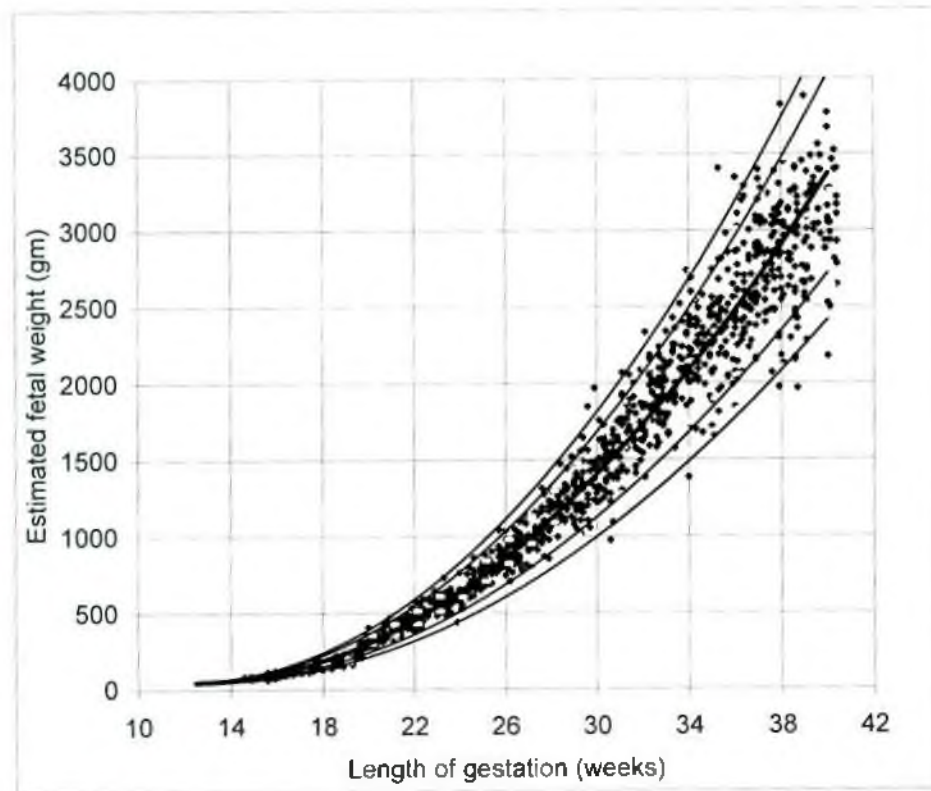
Table IX: Summary of estimated fetal weight (gm). Observed values.

Total = 1223.

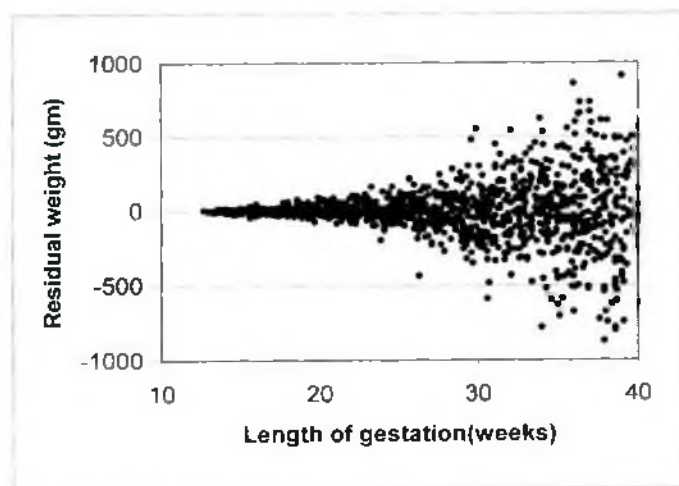
## Fitted Centiles of Estimated Fetal Weight (estimated)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90 <sup>th</sup>	97 <sup>th</sup>	Mean (gm)	2SD (gm)
13	15	68.1	70.9	76.9	82.9	85.7	76.9	18.7
14	27	82.3	85.5	92.2	98.9	102.1	92.2	21.0
15	32	103.2	106.7	114.3	121.9	125.4	114.3	23.6
16	34	131.1	135.2	144	152.8	156.9	144.0	27.4
17	27	168.7	173.5	183.7	193.9	198.7	183.7	32.0
18	42	201.3	206.7	218.1	229.5	234.9	218.1	35.7
19	34	248.6	254.8	268	281.2	287.4	268.0	41.3
20	38	296.1	303.1	318.1	333.1	340.1	318.1	46.8
21	43	363.9	372.1	389.5	406.9	415.1	389.5	54.4
22	45	432.9	442.3	462.3	482.3	491.7	462.3	62.5
23	39	520.9	531.7	554.8	577.9	588.7	554.8	72.2
24	36	603.2	615.6	641.9	668.2	680.6	641.9	82.3
25	42	705.0	719.1	749.3	779.5	793.6	749.3	94.3
26	46	821.0	837.3	872.1	906.9	923.2	872.1	108.8
27	44	932.9	951.4	991	1030.6	1049.1	991.0	123.6
28	49	1063.0	1084.2	1129.4	1174.6	1195.8	1129.4	141.3
29	50	1210.2	1234.7	1287	1339.3	1363.8	1287.0	163.3
30	51	1279.5	1336.3	1457.6	1578.9	1635.7	1457.6	189.5
31	52	1408.1	1472.4	1609.7	1747.0	1811.3	1609.7	214.5
32	50	1557.4	1631.5	1789.6	1947.7	2021.8	1789.6	247.0
33	55	1692.9	1777.2	1957.2	2137.2	2221.5	1957.2	281.2
34	56	1851.4	1949.7	2159.6	2369.5	2467.8	2159.6	327.9
35	59	1985.4	2098.2	2338.8	2579.4	2692.2	2338.8	376.0
36	57	2109.6	2239.0	2515	2791.0	2920.4	2515.0	431.3
37	54	2214.9	2362.2	2676.3	2990.4	3137.7	2676.3	490.8
38	56	2303.6	2471.2	2828.7	3186.2	3353.8	2828.7	558.6
39	55	2376.3	2568.6	2978.7	3388.8	3581.1	2978.7	640.8
40	35	2427.3	2652.1	3131.5	3610.9	3835.7	3131.5	749.1

Table X: Fitted percentiles of estimated fetal weight (gm). Estimated values.



Graph 11: Raw data of estimated fetal weight with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> & 97<sup>th</sup> centiles.



Graph 12: Assessment of fit of model for estimated fetal weight plotted: Plot of standard deviation score against gestational age.

## Summary of measurement of FL/AC ratio (observed)

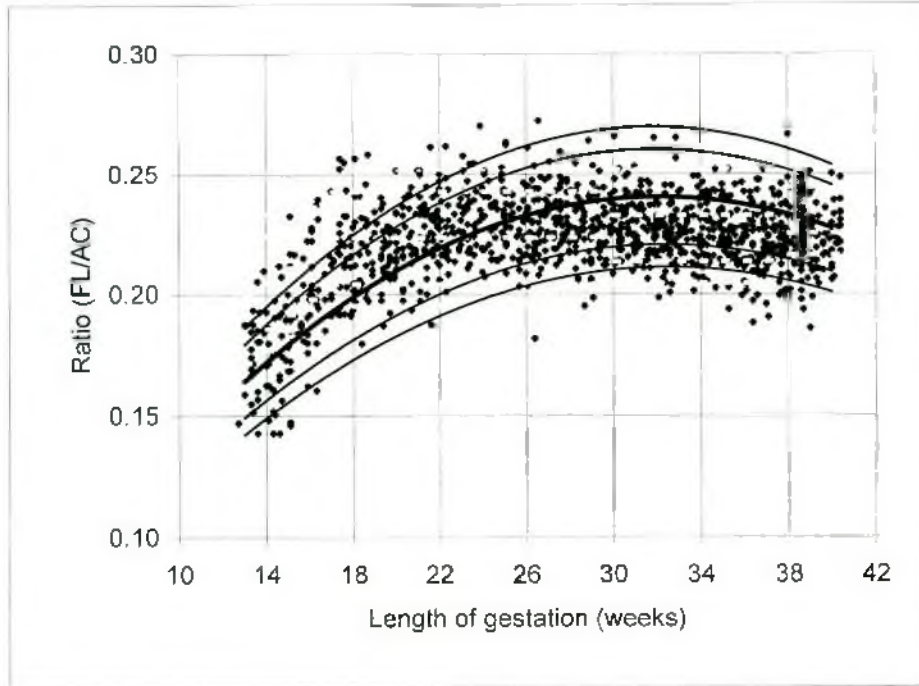
Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	0.15	0.15	0.17	0.19	.	0.17	0.03
14	27	0.14	0.15	0.17	0.20	.	0.17	0.04
15	32	0.14	0.15	0.19	0.22	.	0.18	0.04
16	34	0.16	0.18	0.20	0.23	0.24	0.20	0.04
17	27	0.19	0.19	0.21	0.24	.	0.21	0.04
18	42	0.18	0.19	0.21	0.24	0.26	0.21	0.03
19	34	0.19	0.20	0.22	0.24	0.26	0.22	0.03
20	38	0.19	0.20	0.22	0.23	0.25	0.22	0.02
21	43	0.19	0.20	0.23	0.24	0.25	0.23	0.03
22	45	0.19	0.21	0.23	0.25	0.26	0.23	0.03
23	39	0.21	0.22	0.23	0.25	0.26	0.23	0.02
24	36	0.21	0.21	0.23	0.25	0.27	0.23	0.03
25	42	0.21	0.22	0.23	0.25	0.26	0.23	0.02
26	46	0.19	0.21	0.22	0.25	0.26	0.23	0.03
27	44	0.21	0.21	0.23	0.25	0.27	0.23	0.03
28	49	0.21	0.22	0.23	0.25	0.26	0.23	0.02
29	50	0.20	0.21	0.23	0.24	0.26	0.23	0.03
30	51	0.21	0.21	0.23	0.24	0.26	0.23	0.02
31	52	0.21	0.22	0.23	0.24	0.25	0.23	0.02
32	50	0.20	0.21	0.23	0.24	0.26	0.23	0.02
33	55	0.20	0.21	0.23	0.24	0.26	0.23	0.02
34	56	0.20	0.21	0.22	0.24	0.25	0.23	0.03
35	59	0.20	0.21	0.23	0.24	0.25	0.23	0.02
36	57	0.19	0.20	0.22	0.24	0.25	0.22	0.02
37	54	0.19	0.21	0.22	0.24	0.25	0.22	0.03
38	56	0.20	0.21	0.22	0.24	0.25	0.22	0.03
39	55	0.19	0.20	0.22	0.24	0.25	0.22	0.03
40	35	0.21	0.21	0.22	0.24	0.25	0.22	0.02

Table XI: Summary of measurement of femur length/abdominal circumference (FL/AC) ratio. Observed values. Total = 1223.

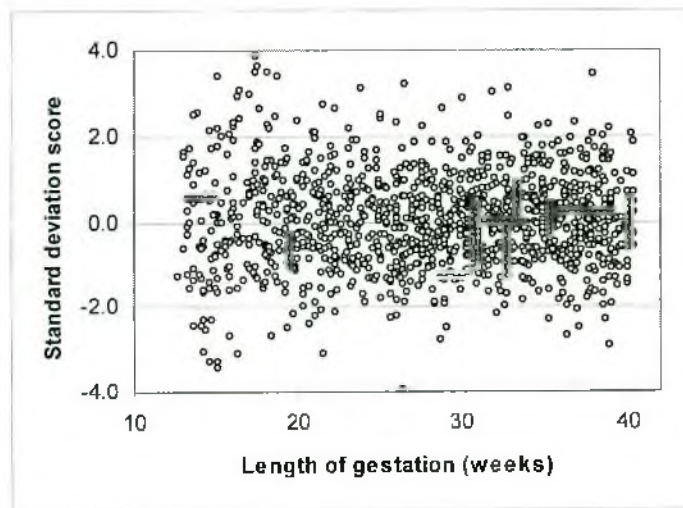
## Fitted Centiles of FL/AC ratio (estimated)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	0.17	0.18	0.20	0.22	0.23	0.20	0.03
14	27	0.18	0.19	0.20	0.22	0.23	0.20	0.03
15	32	0.18	0.19	0.21	0.23	0.24	0.21	0.03
16	34	0.19	0.20	0.22	0.24	0.25	0.22	0.03
17	27	0.20	0.20	0.22	0.24	0.25	0.22	0.03
18	42	0.20	0.20	0.22	0.24	0.25	0.22	0.03
19	34	0.20	0.20	0.22	0.24	0.25	0.22	0.03
20	38	0.20	0.20	0.22	0.24	0.25	0.22	0.03
21	43	0.20	0.20	0.22	0.24	0.25	0.22	0.03
22	45	0.20	0.20	0.22	0.24	0.25	0.22	0.03
23	39	0.20	0.20	0.22	0.24	0.25	0.22	0.03
24	36	0.20	0.20	0.22	0.24	0.25	0.22	0.03
25	42	0.20	0.20	0.22	0.24	0.25	0.22	0.03
26	46	0.20	0.20	0.22	0.24	0.25	0.22	0.03
27	44	0.20	0.20	0.22	0.24	0.25	0.22	0.03
28	49	0.20	0.20	0.22	0.24	0.25	0.22	0.03
29	50	0.20	0.20	0.22	0.24	0.25	0.22	0.03
30	51	0.20	0.21	0.23	0.25	0.26	0.23	0.03
31	52	0.20	0.21	0.23	0.25	0.26	0.23	0.03
32	50	0.21	0.22	0.23	0.25	0.25	0.23	0.02
33	55	0.21	0.22	0.23	0.25	0.25	0.23	0.02
34	56	0.21	0.22	0.23	0.25	0.25	0.23	0.02
35	59	0.21	0.22	0.23	0.25	0.25	0.23	0.02
36	57	0.21	0.22	0.23	0.25	0.25	0.23	0.02
37	54	0.21	0.22	0.23	0.25	0.25	0.23	0.02
38	56	0.22	0.23	0.24	0.26	0.26	0.24	0.02
39	55	0.22	0.23	0.24	0.26	0.26	0.24	0.02
40	35	0.22	0.23	0.24	0.26	0.26	0.24	0.02

Table XII: Fitted centiles of femur length/abdominal circumference (FL/AC) ratio. Estimated values.



Graph 13: Raw data for femur length/abdominal circumference (FL/AC) ratio with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles.



Graph 14: Assessment of fit of model for FL/AC plotted: Plot of standard deviation score against gestational age, showing expected 2SD.

## 5.6b: HEAD CIRCUMFERENCE/ABDOMINAL CIRCUMFERENCE (HC/AC) RATIO

Table XIII gives summary of measurements of head circumference/abdominal circumference (HC/AC) ratio. It gives the number of cases in each week of gestation, percentiles, mean and 2 standard deviations (2SD) of the observed values. At 13 weeks gestational age mean HC/AC was 1.31 ( $\pm 0.20$ ), at 36 weeks it was 1.04 ( $\pm 0.10$ ) and at 40 weeks it was 1.01 ( $\pm 0.08$ ).

Table XIV gives fitted percentiles of head circumference/abdominal circumference ratio. It gives the estimated values of 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles and the mean with 2 standard deviations of the data. At 13 weeks gestational age mean head circumference/abdominal circumference ratio was 1.25 ( $\pm 0.15$ ), at 36 weeks it was 1.03 ( $\pm 0.09$ ) and at 40 weeks it was 0.99 ( $\pm 0.08$ ). The coefficient of multiple correlation  $R^2 = 0.598$ , ( $p < .001$ ). Range of the ratio was 1.3 to 1.

2 standard deviations of the ratio ranged from  $\pm 0.15$  to  $\pm 0.08$ .

Graph 15 shows the raw data for head circumference/abdominal circumference with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile boundaries superimposed on it. Head circumference/abdominal circumference ratio shows higher values in the early stage of gestation and later the values come down as the pregnancy progresses. In the table the mean ratio is in 1:1 relationship at 39 weeks of gestation. It covers 95% of the population.

Graph 16 shows assessment of goodness of fit of model for standard deviations of head circumference/abdominal circumference ratio. It gives a plot of standard deviation score against gestational age, and shows expected 2 standard deviations.



## Summary of measurement of HC/AC ratio (observed)

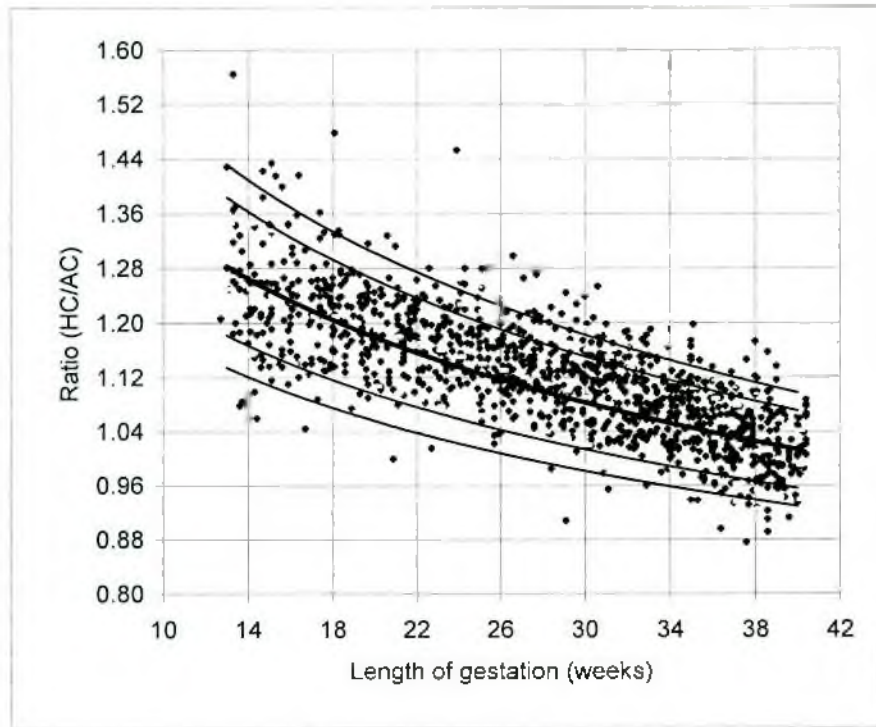
Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	1.18	1.19	1.28	1.48	.	1.31	0.20
14	27	1.06	1.08	1.25	1.31	.	1.22	0.15
15	32	1.12	1.14	1.24	1.41	.	1.25	0.18
16	34	1.11	1.14	1.23	1.35	1.42	1.24	0.16
17	27	1.04	1.12	1.22	1.31	.	1.21	0.14
18	42	1.13	1.14	1.23	1.33	1.44	1.23	0.14
19	34	1.07	1.11	1.19	1.27	1.28	1.19	0.11
20	38	1.09	1.11	1.18	1.25	1.31	1.19	0.11
21	43	1.03	1.11	1.17	1.25	1.32	1.18	0.12
22	45	1.08	1.11	1.19	1.24	1.26	1.18	0.10
23	39	1.03	1.09	1.16	1.23	1.28	1.16	0.11
24	36	1.10	1.11	1.18	1.26	1.43	1.18	0.13
25	42	1.06	1.09	1.16	1.22	1.27	1.16	0.10
26	46	1.03	1.05	1.13	1.21	1.23	1.13	0.10
27	44	1.06	1.08	1.14	1.20	1.29	1.14	0.10
28	49	1.01	1.05	1.13	1.21	1.25	1.13	0.12
29	50	0.97	1.05	1.10	1.17	1.23	1.11	0.11
30	51	1.01	1.04	1.12	1.19	1.23	1.11	0.11
31	52	0.97	1.03	1.12	1.17	1.22	1.11	0.11
32	50	1.02	1.02	1.09	1.15	1.19	1.09	0.10
33	55	0.99	1.03	1.08	1.15	1.18	1.09	0.10
34	56	0.98	1.01	1.07	1.12	1.17	1.07	0.09
35	59	0.94	1.01	1.08	1.14	1.18	1.07	0.11
36	57	0.93	0.97	1.03	1.11	1.12	1.04	0.10
37	54	0.94	0.97	1.03	1.09	1.12	1.03	0.09
38	56	0.91	0.96	1.02	1.10	1.15	1.02	0.11
39	55	0.90	0.96	1.00	1.10	1.14	1.02	0.11
40	35	0.91	0.94	1.01	1.07	1.09	1.01	0.08

Table XIII: Summary of measurement of head circumference/abdominal circumference (HC/AC) ratio. Observed values. Total = 1223.

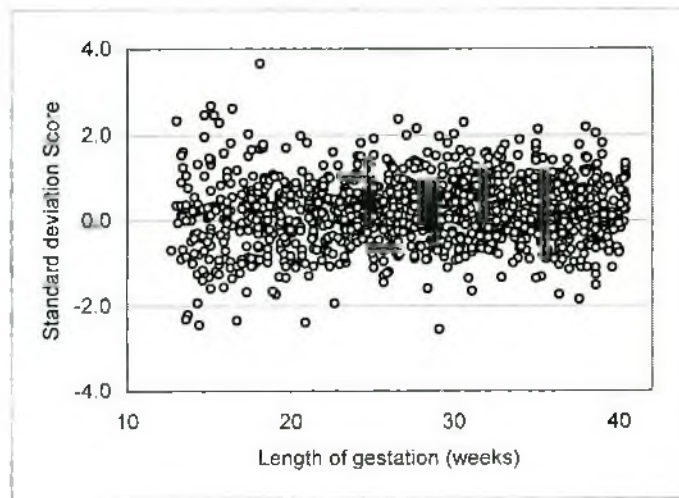
## Fitted Centiles of HC/AC ratio (estimated)

Weeks of gestation(w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	1.11	1.15	1.25	1.35	1.39	1.25	0.15
14	27	1.11	1.15	1.25	1.35	1.39	1.25	0.15
15	32	1.10	1.14	1.24	1.34	1.38	1.24	0.15
16	34	1.10	1.14	1.23	1.32	1.36	1.23	0.14
17	27	1.08	1.12	1.21	1.30	1.34	1.21	0.14
18	42	1.08	1.12	1.21	1.30	1.34	1.21	0.14
19	34	1.07	1.11	1.20	1.29	1.33	1.20	0.14
20	38	1.07	1.11	1.19	1.27	1.31	1.19	0.13
21	43	1.06	1.10	1.18	1.26	1.30	1.18	0.13
22	45	1.05	1.09	1.17	1.25	1.29	1.17	0.13
23	39	1.04	1.08	1.16	1.24	1.28	1.16	0.13
24	36	1.04	1.07	1.15	1.23	1.26	1.15	0.12
25	42	1.03	1.06	1.14	1.22	1.25	1.14	0.12
26	46	1.02	1.05	1.13	1.21	1.24	1.13	0.12
27	44	1.01	1.04	1.12	1.20	1.23	1.12	0.12
28	49	1.01	1.04	1.11	1.18	1.21	1.11	0.11
29	50	1.00	1.03	1.10	1.17	1.20	1.10	0.11
30	51	0.99	1.02	1.09	1.16	1.19	1.09	0.11
31	52	0.98	1.01	1.08	1.15	1.18	1.08	0.11
32	50	0.98	1.01	1.07	1.13	1.16	1.07	0.10
33	55	0.97	1.00	1.06	1.12	1.15	1.06	0.10
34	56	0.96	0.99	1.05	1.11	1.14	1.05	0.10
35	59	0.95	0.98	1.04	1.10	1.13	1.04	0.10
36	57	0.95	0.97	1.03	1.09	1.11	1.03	0.09
37	54	0.94	0.96	1.02	1.08	1.10	1.02	0.09
38	56	0.93	0.95	1.01	1.07	1.09	1.01	0.09
39	55	0.92	0.94	1.00	1.06	1.08	1.00	0.09
40	35	0.91	0.94	0.99	1.04	1.07	0.99	0.08

Table XIV: Fitted percentiles of head circumference/abdominal circumference (HC/AC) ratio. Estimated values.



Graph 15: Raw data for head circumference/abdominal circumference (HC/AC) with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles.



Graph 16: Assessment of fit of model for HC/AC: Plot of standard deviation score against gestational age, showing expected 2SD.

### 5.6c: FEMUR LENGTH/ BIPARIETAL DIAMETER (FL/BPD) RATIO

Table XV gives summary of measurement of femur length/biparietal diameter (FL/BPD) ratio. It gives the number of cases in each week of gestation, and percentiles, mean and 2 standard deviations (2SD) of the observed values. At 13 weeks gestational age mean FL/BPD was 0.49 ( $\pm 0.08$ ), at 36 weeks it was 0.78 ( $\pm 0.07$ ) and at 40 weeks it was 0.81 ( $\pm 0.06$ ).

Table XVI gives fitted percentiles of femur length/biparietal diameter ratio. It gives the estimated values of 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles and the mean with 2 standard deviations of the data. At 13 weeks gestational age mean FL/BPD was 0.50 ( $\pm 0.10$ ), at 36w it was 0.79 ( $\pm 0.07$ ) and at 40 weeks it was 0.83 ( $\pm 0.06$ ). The coefficient of multiple correlation  $R^2 = 0.736$ , ( $p < .001$ ). The range of the ratio is 5 to 8 and 2 standard deviations of the ratio ranged from  $\pm 0.10$  to  $\pm 0.06$ .

At 13 weeks it is 5 and at 40 weeks it is 8 (Table XVI). Graph 17 shows the raw data for femur length/biparietal diameter with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile lines superimposed on it and Graph 18 shows the values  $\pm 2$  standard deviations superimposed on the residual plot to see how well the standard deviations has been modeled.

The values of the ratio are lower in the early part of gestation and later they gradually increase. It covers 95% of the population.

## Summary of measurement of FL/ BPD ratio (observed)

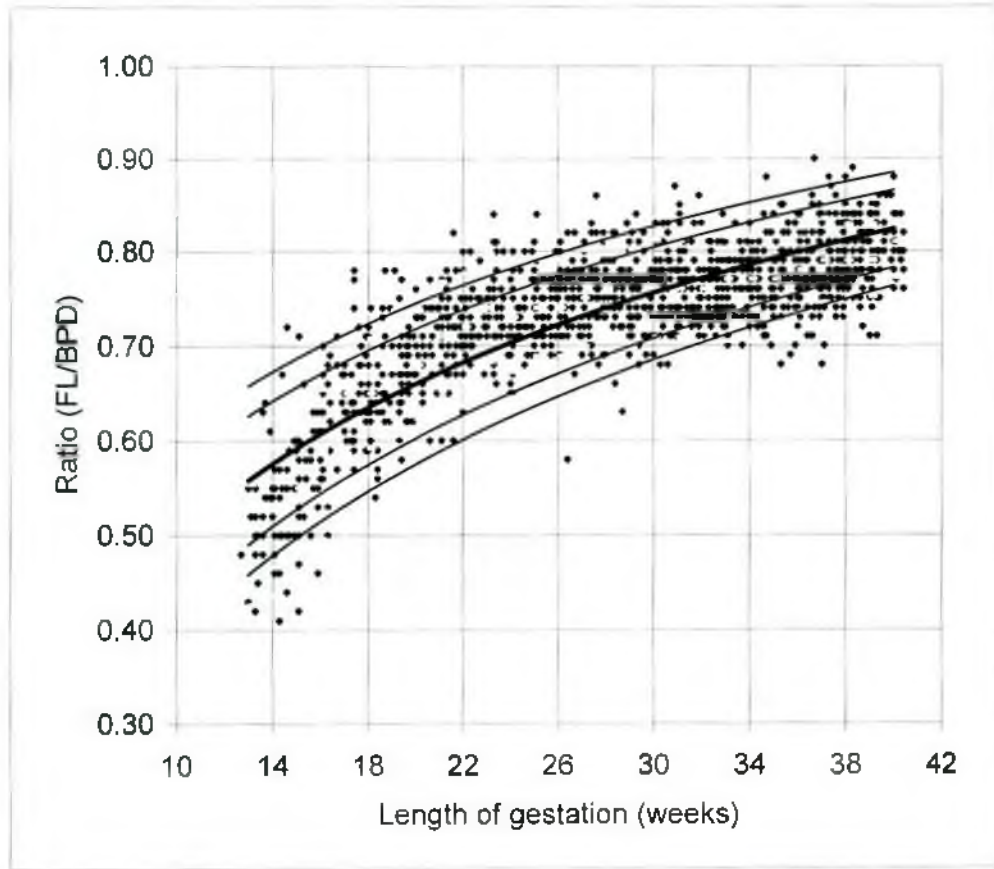
Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	0.42	0.42	0.50	0.55		0.49	0.08
14	27	0.41	0.45	0.52	0.63		0.53	0.12
15	32	0.42	0.48	0.55	0.64		0.55	0.13
16	34	0.46	0.51	0.59	0.67	0.70	0.59	0.11
17	27	0.57	0.59	0.64	0.74		0.65	0.11
18	42	0.55	0.59	0.64	0.71	0.74	0.65	0.09
19	34	0.58	0.62	0.67	0.76	0.78	0.68	0.10
20	38	0.62	0.64	0.68	0.73	0.76	0.68	0.07
21	43	0.60	0.65	0.72	0.77	0.77	0.71	0.09
22	45	0.61	0.68	0.72	0.78	0.81	0.72	0.08
23	39	0.66	0.67	0.74	0.80	0.83	0.74	0.08
24	36	0.65	0.67	0.72	0.78	0.80	0.73	0.07
25	42	0.68	0.69	0.74	0.80	0.83	0.74	0.07
26	46	0.62	0.70	0.74	0.79	0.81	0.74	0.08
27	44	0.67	0.70	0.75	0.80	0.82	0.75	0.08
28	49	0.67	0.72	0.75	0.82	0.84	0.76	0.08
29	50	0.66	0.71	0.76	0.81	0.83	0.75	0.08
30	51	0.69	0.71	0.75	0.81	0.83	0.76	0.07
31	52	0.70	0.71	0.77	0.82	0.86	0.76	0.08
32	50	0.71	0.72	0.76	0.81	0.84	0.76	0.07
33	55	0.70	0.72	0.77	0.81	0.83	0.77	0.06
34	56	0.70	0.73	0.77	0.81	0.82	0.77	0.06
35	59	0.69	0.73	0.77	0.82	0.86	0.77	0.08
36	57	0.70	0.73	0.77	0.83	0.84	0.78	0.07
37	54	0.70	0.73	0.78	0.85	0.89	0.79	0.09
38	56	0.73	0.75	0.79	0.84	0.88	0.79	0.07
39	55	0.71	0.74	0.79	0.84	0.85	0.79	0.07
40	35	0.76	0.77	0.81	0.85	0.88	0.81	0.06

Table XV: Summary of measurement of femur length/biparietal diameter (FL/BPD) ratio. Observed values. Total= 1223.

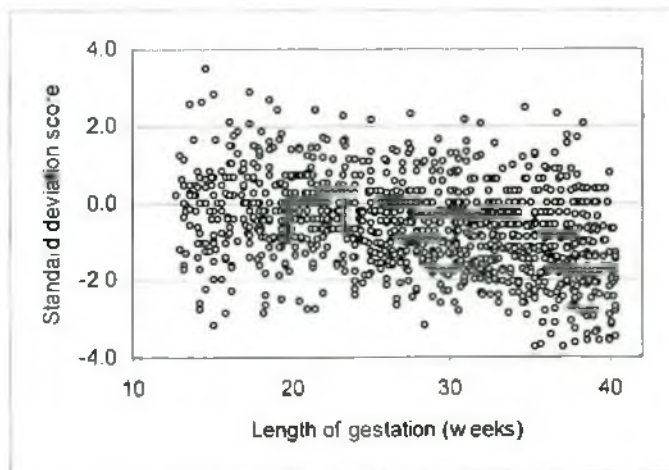
## Fitted Centiles of FL/BPD ratio (estimated)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90 <sup>th</sup>	97 <sup>th</sup>	Mean	2SD
13	15	0.40	0.43	0.50	0.56	0.59	0.50	0.10
14	27	0.43	0.46	0.53	0.59	0.62	0.53	0.10
15	32	0.47	0.50	0.56	0.63	0.66	0.56	0.10
16	34	0.51	0.54	0.60	0.66	0.69	0.60	0.10
17	27	0.54	0.57	0.63	0.70	0.73	0.63	0.10
18	42	0.57	0.60	0.65	0.71	0.74	0.65	0.09
19	34	0.59	0.62	0.68	0.73	0.76	0.68	0.09
20	38	0.61	0.64	0.69	0.75	0.78	0.69	0.09
21	43	0.63	0.65	0.71	0.77	0.80	0.71	0.09
22	45	0.64	0.67	0.72	0.78	0.81	0.72	0.09
23	39	0.65	0.68	0.74	0.79	0.82	0.74	0.09
24	36	0.66	0.69	0.74	0.80	0.83	0.74	0.09
25	42	0.68	0.70	0.75	0.80	0.83	0.75	0.08
26	46	0.68	0.71	0.76	0.81	0.83	0.76	0.08
27	44	0.69	0.71	0.76	0.81	0.84	0.76	0.08
28	49	0.69	0.71	0.76	0.82	0.84	0.76	0.08
29	50	0.69	0.72	0.77	0.82	0.84	0.77	0.08
30	51	0.69	0.72	0.77	0.82	0.85	0.77	0.08
31	52	0.70	0.72	0.77	0.82	0.85	0.77	0.08
32	50	0.71	0.73	0.77	0.82	0.84	0.77	0.07
33	55	0.71	0.73	0.78	0.82	0.84	0.78	0.07
34	56	0.71	0.74	0.78	0.82	0.85	0.78	0.07
35	59	0.72	0.74	0.78	0.83	0.85	0.78	0.07
36	57	0.72	0.74	0.79	0.83	0.85	0.79	0.07
37	54	0.73	0.75	0.80	0.84	0.86	0.80	0.07
38	56	0.75	0.76	0.80	0.84	0.86	0.80	0.06
39	55	0.76	0.77	0.81	0.85	0.87	0.81	0.06
40	35	0.77	0.79	0.83	0.87	0.88	0.83	0.06

Table XVI: Fitted percentiles of femur length/biparietal diameter (FL/BPD) ratio. Estimated values.



Graph 17: Raw data for femur length/ biparietal diameter (FL/BPD) ratio with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles.



Graph 18: Assessment of fit of model for estimated FL/BPD plotted: Plot of standard deviation score against gestational age, showing expected 2SD.

## 5.6d: BIPARIETAL DIAMETER/ABDOMINAL CIRCUMFERENCE (BPD/AC) RATIO

Table XVII gives summary of measurement of biparietal diameter/abdominal circumference (BPD/AC) ratio. It gives the number of cases in each week of gestation, and percentiles, mean and 2 standard deviations (2SD) of the observed values. At 13 weeks gestational age mean BPD/AC was 0.35 ( $\pm 0.05$ mm), at 36 weeks it was 0.28 ( $\pm 0.03$ ) and at 40w it was 0.28 ( $\pm 0.03$ ), these are observed values of the raw data.

Table XVIII gives fitted percentiles of biparietal diameter/abdominal circumference ratio. It gives the estimated values of 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles and the mean with 2 standard deviations of the data. At 13 weeks gestational age mean BPD/AC was 0.34mm ( $\pm 0.04$ mm), at 36 weeks it was 0.29 ( $\pm 0.03$ ) and at 40w it was 0.28 ( $\pm 0.02$ ), estimated values after fitting the model. The coefficient of multiple correlation  $R^2 = 0.519$ , ( $p < .001$ ). Range of the ratio is 34 to 28 or  $31 \pm 3$  and 2 standard deviations of the ratio ranged from  $\pm 0.04$  to  $\pm 0.02$ .

Graph 19 shows the raw data for biparietal diameter/abdominal circumference with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile limits superimposed on it. The values are higher in the early part of gestation and then gradually decrease in the later part. It is of 95% confidence level and Graph 20 shows assessment of goodness of fit of model for standard deviations of biparietal diameter/ abdominal circumference: Plot of standard deviation score against gestational age, showing expected 2 standard deviations.



## Summary of measurement of BPD/AC ratio (observed)

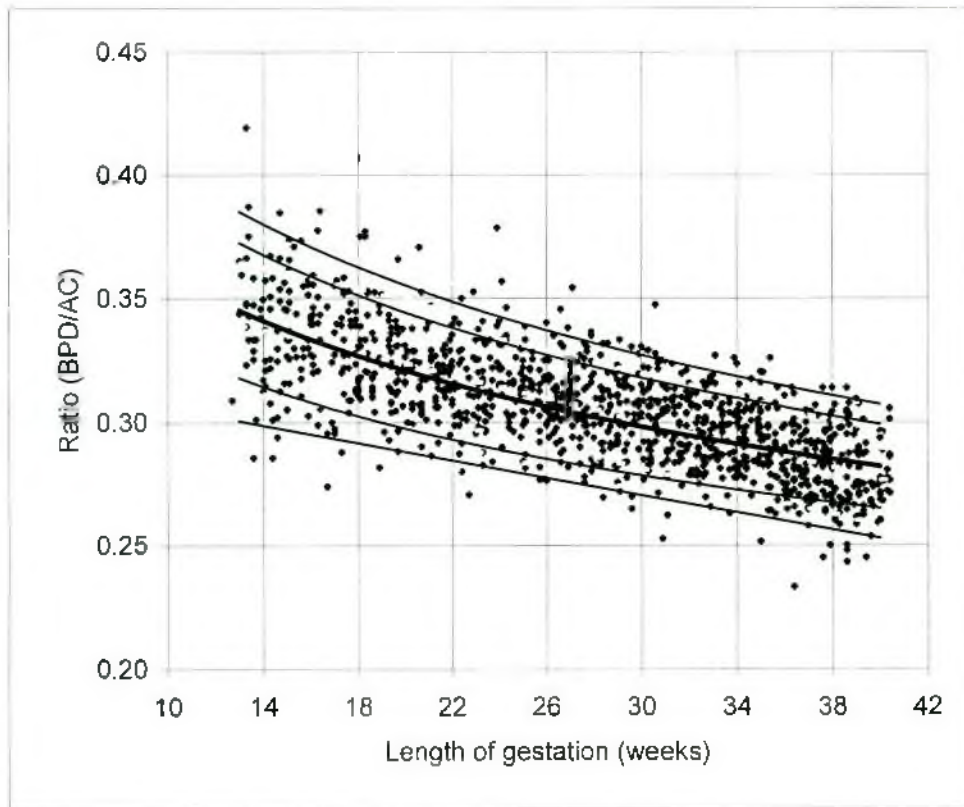
Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	0.31	0.32	0.35	0.40		0.35	0.05
14	27	0.29	0.30	0.33	0.36		0.33	0.04
15	32	0.29	0.31	0.34	0.37		0.34	0.05
16	34	0.30	0.31	0.34	0.37	0.39	0.34	0.04
17	27	0.27	0.29	0.33	0.36		0.33	0.05
18	42	0.31	0.31	0.33	0.37	0.40	0.33	0.04
19	34	0.28	0.30	0.32	0.35	0.35	0.32	0.03
20	38	0.29	0.30	0.32	0.34	0.36	0.32	0.03
21	43	0.29	0.30	0.32	0.34	0.36	0.32	0.03
22	45	0.28	0.30	0.32	0.34	0.35	0.32	0.03
23	39	0.27	0.30	0.31	0.34	0.35	0.31	0.03
24	36	0.28	0.30	0.32	0.34	0.38	0.32	0.04
25	42	0.28	0.29	0.31	0.33	0.34	0.31	0.03
26	46	0.28	0.29	0.31	0.33	0.34	0.31	0.03
27	44	0.28	0.29	0.31	0.33	0.35	0.31	0.03
28	49	0.27	0.28	0.30	0.33	0.34	0.31	0.03
29	50	0.27	0.28	0.30	0.32	0.33	0.30	0.03
30	51	0.27	0.28	0.30	0.33	0.33	0.30	0.03
31	52	0.26	0.28	0.30	0.32	0.34	0.30	0.03
32	50	0.27	0.28	0.30	0.31	0.32	0.30	0.02
33	55	0.27	0.28	0.30	0.32	0.32	0.30	0.03
34	56	0.27	0.28	0.29	0.31	0.32	0.29	0.03
35	59	0.26	0.27	0.30	0.32	0.32	0.29	0.03
36	57	0.26	0.27	0.28	0.31	0.31	0.28	0.03
37	54	0.26	0.27	0.28	0.30	0.31	0.28	0.02
38	56	0.25	0.26	0.28	0.30	0.31	0.28	0.03
39	55	0.24	0.26	0.28	0.30	0.31	0.28	0.04
40	35	0.25	0.26	0.28	0.30	0.31	0.28	0.03

Table XVII: Summary of measurement of biparietal diameter/abdominal circumference (BPD/AC) ratio. Observed values.

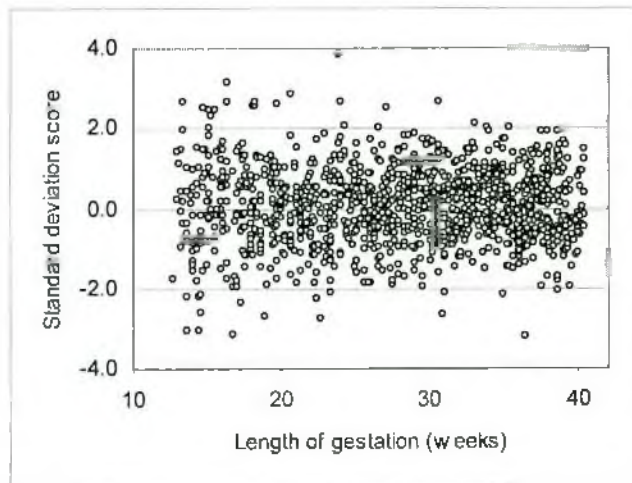
## Fitted Centiles of BPD/AC ratio (estimated)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	0.30	0.31	0.34	0.36	0.38	0.34	0.04
14	27	0.30	0.31	0.34	0.36	0.37	0.34	0.04
15	32	0.30	0.31	0.33	0.36	0.37	0.33	0.04
16	34	0.29	0.31	0.33	0.36	0.37	0.33	0.04
17	27	0.29	0.30	0.33	0.36	0.37	0.33	0.04
18	42	0.29	0.30	0.33	0.35	0.37	0.33	0.04
19	34	0.29	0.30	0.33	0.35	0.36	0.33	0.04
20	38	0.29	0.30	0.32	0.35	0.36	0.32	0.04
21	43	0.28	0.30	0.32	0.35	0.36	0.32	0.04
22	45	0.28	0.29	0.32	0.34	0.36	0.32	0.04
23	39	0.29	0.30	0.32	0.34	0.34	0.32	0.03
24	36	0.29	0.29	0.31	0.33	0.34	0.31	0.03
25	42	0.28	0.29	0.31	0.33	0.34	0.31	0.03
26	46	0.28	0.29	0.31	0.33	0.34	0.31	0.03
27	44	0.28	0.29	0.31	0.33	0.34	0.31	0.03
28	49	0.28	0.29	0.30	0.32	0.33	0.30	0.03
29	50	0.27	0.28	0.30	0.32	0.33	0.30	0.03
30	51	0.27	0.28	0.30	0.32	0.33	0.30	0.03
31	52	0.27	0.28	0.30	0.32	0.33	0.30	0.03
32	50	0.27	0.28	0.30	0.31	0.32	0.30	0.03
33	55	0.27	0.27	0.29	0.31	0.32	0.29	0.03
34	56	0.26	0.27	0.29	0.31	0.32	0.29	0.03
35	59	0.26	0.27	0.29	0.31	0.32	0.29	0.03
36	57	0.26	0.27	0.29	0.31	0.31	0.29	0.03
37	54	0.26	0.26	0.28	0.30	0.31	0.28	0.03
38	56	0.25	0.26	0.28	0.30	0.31	0.28	0.03
39	55	0.25	0.26	0.28	0.30	0.31	0.28	0.03
40	35	0.26	0.26	0.28	0.29	0.30	0.28	0.02

Table XVIII: Fitted percentiles of biparietal diameter/abdominal circumference (BPD/AC) ratio. Estimated values.



Graph 19: Raw data for biparietal diameter/abdominal circumference (BPD/AC) ratio with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles.



Graph 20: Assessment of fit of model for BPD/AC plotted: Plot of standard deviation score against gestational age, showing expected 2SD.

### 5.6e: FEMUR LENGTH/ HEAD CIRCUMFERENCE (FL/HC) RATIO

Table XIX gives summary of measurements of femur length/head circumference (FL/HC) ratio. It gives the total number of cases in each week of gestation, percentiles, mean and 2 standard deviations (2SD) of the observed values. At 13 weeks gestational age mean femur length/head circumference ratio was  $0.13 (\pm 0.03)$ , at 36 weeks it was  $0.21 (\pm 0.02)$  and at 40 weeks it was  $0.22 (\pm 0.01)$ .

Table XX gives fitted percentiles of femur length/head circumference ratio. It gives the estimated values of 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles and the mean with 2 standard deviations of the data. At 13 weeks gestational age mean femur length/head circumference ratio was  $0.14 (\pm 0.03)$ , at 36 weeks it was  $0.22 (\pm 0.02)$  and at 40 weeks it was  $0.23 (\pm 0.02)$ . Range of ratio was from 14 to 23. The coefficient of multiple correlations  $R^2 = 0.776$ , ( $p < .001$ ).

2 standard deviations of the fitted table ranged from  $\pm 0.03$  to  $\pm 0.02$ .

Graph 21 shows the raw data for femur length/head circumference ratio with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves superimposed on it. The values of the ratio increase as the pregnancy progresses. It gives 95% confidence interval (95% CI).

Graph 22 shows assessment of goodness of fit of model for standard deviations of femur length/head circumference ratio. It gives a plot of standard deviation score against gestational age, and shows expected 2 standard deviations.

## Summary of measurement of FL/HC ratio (observed)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	0.11	0.11	0.13	0.15		0.13	0.03
14	27	0.11	0.12	0.14	0.17		0.14	0.04
15	32	0.11	0.13	0.15	0.17		0.15	0.03
16	34	0.13	0.14	0.17	0.18	0.19	0.16	0.03
17	27	0.15	0.16	0.17	0.20		0.17	0.03
18	42	0.15	0.16	0.18	0.19	0.20	0.17	0.02
19	34	0.16	0.17	0.18	0.20	0.22	0.18	0.03
20	38	0.17	0.17	0.18	0.20	0.20	0.18	0.02
21	43	0.16	0.18	0.19	0.20	0.23	0.19	0.02
22	45	0.17	0.18	0.19	0.20	0.22	0.19	0.02
23	39	0.18	0.18	0.20	0.21	0.22	0.20	0.02
24	36	0.18	0.18	0.20	0.21	0.21	0.20	0.02
25	42	0.19	0.19	0.20	0.21	0.22	0.20	0.02
26	46	0.17	0.19	0.20	0.21	0.22	0.20	0.02
27	44	0.18	0.19	0.20	0.21	0.22	0.20	0.02
28	49	0.18	0.20	0.20	0.22	0.23	0.20	0.02
29	50	0.19	0.19	0.21	0.22	0.23	0.21	0.02
30	51	0.19	0.19	0.21	0.22	0.22	0.21	0.02
31	52	0.19	0.20	0.21	0.22	0.23	0.21	0.02
32	50	0.19	0.19	0.21	0.22	0.23	0.21	0.02
33	55	0.19	0.20	0.21	0.22	0.23	0.21	0.02
34	56	0.19	0.20	0.21	0.22	0.23	0.21	0.02
35	59	0.19	0.20	0.21	0.23	0.23	0.21	0.02
36	57	0.19	0.20	0.21	0.22	0.23	0.21	0.02
37	54	0.20	0.20	0.21	0.23	0.24	0.22	0.02
38	56	0.20	0.21	0.22	0.23	0.24	0.22	0.02
39	55	0.20	0.21	0.22	0.23	0.23	0.22	0.02
40	35	0.21	0.21	0.22	0.23	0.24	0.22	0.01

Table XIX: Summary of measurement of femur length/head circumference (FL/HC) ratio. Observed values. Total = 1223.

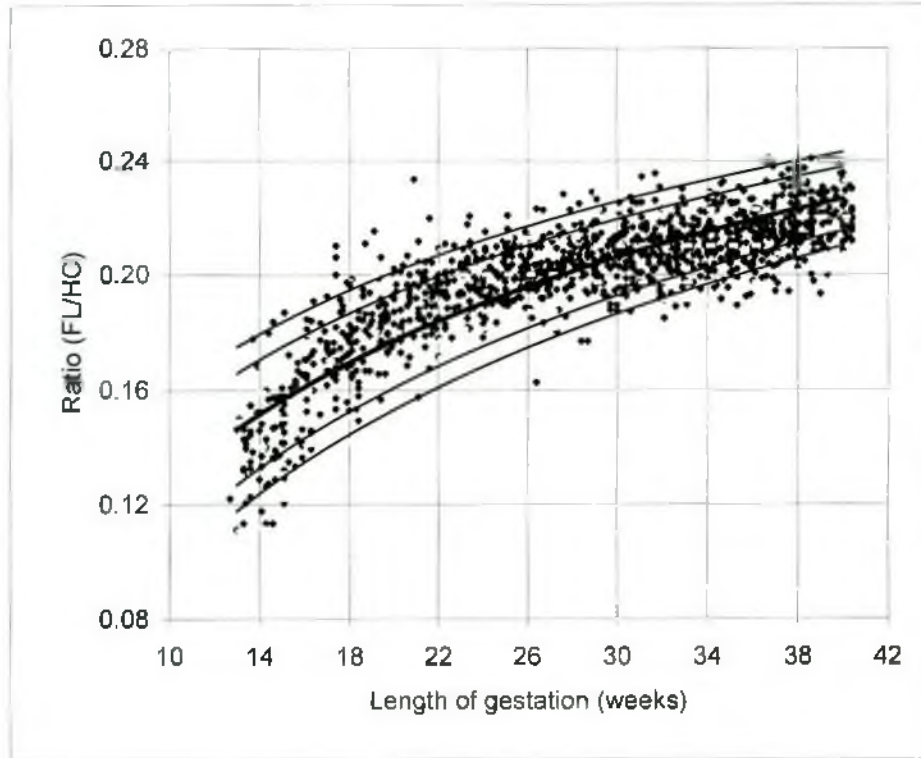
## Fitted Centiles of FL/HC ratio (estimated)

Weeks of gestation (w)	No. of fetuses	3rd	10th	50th	90th	97th	Mean	2SD
13	15	0.11	0.12	0.14	0.16	0.17	0.14	0.03
14	27	0.12	0.13	0.15	0.17	0.18	0.15	0.03
15	32	0.13	0.14	0.16	0.18	0.19	0.16	0.03
16	34	0.14	0.15	0.17	0.19	0.20	0.17	0.03
17	27	0.15	0.16	0.18	0.20	0.21	0.18	0.03
18	42	0.15	0.16	0.18	0.20	0.21	0.18	0.03
19	34	0.16	0.17	0.19	0.21	0.22	0.19	0.03
20	38	0.16	0.17	0.19	0.21	0.22	0.19	0.03
21	43	0.18	0.19	0.2	0.21	0.22	0.20	0.02
22	45	0.18	0.19	0.2	0.21	0.22	0.20	0.02
23	39	0.19	0.20	0.21	0.22	0.23	0.21	0.02
24	36	0.19	0.20	0.21	0.22	0.23	0.21	0.02
25	42	0.19	0.20	0.21	0.22	0.23	0.21	0.02
26	46	0.19	0.20	0.21	0.22	0.23	0.21	0.02
27	44	0.20	0.21	0.22	0.23	0.24	0.22	0.02
28	49	0.20	0.21	0.22	0.23	0.24	0.22	0.02
29	50	0.20	0.21	0.22	0.23	0.24	0.22	0.02
30	51	0.20	0.21	0.22	0.23	0.24	0.22	0.02
31	52	0.20	0.21	0.22	0.23	0.24	0.22	0.02
32	50	0.20	0.21	0.22	0.23	0.24	0.22	0.02
33	55	0.20	0.21	0.22	0.23	0.24	0.22	0.02
34	56	0.20	0.21	0.22	0.23	0.24	0.22	0.02
35	59	0.20	0.21	0.22	0.23	0.24	0.22	0.02
36	57	0.20	0.21	0.22	0.23	0.24	0.22	0.02
37	54	0.21	0.22	0.23	0.24	0.25	0.23	0.02
38	56	0.21	0.22	0.23	0.24	0.25	0.23	0.02
39	55	0.21	0.22	0.23	0.24	0.25	0.23	0.02
40	35	0.21	0.22	0.23	0.24	0.25	0.23	0.02

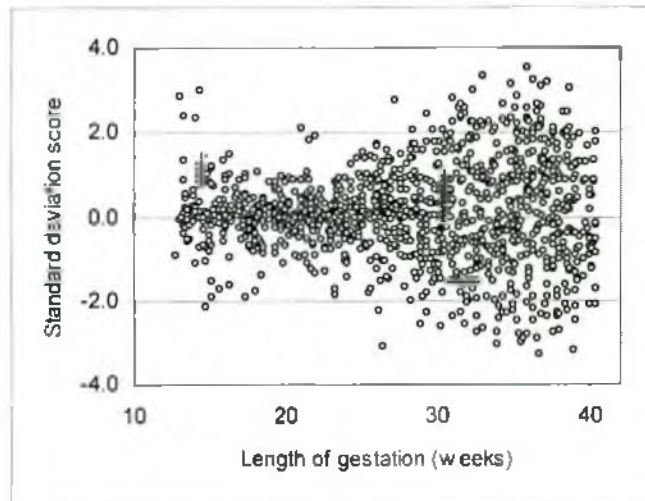
Table XX: Fitted percentiles of femur length/head circumference (FL/HC) ratio. Estimated values.

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Graph 21: Raw data for femur length/head circumference (FL/HC) ratio with fitted 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles.



Graph 22: Assessment of fit of model for FL/HC plotted: Plot of standard deviation score against gestational age, showing expected 2SD.

## 5.7: ACCURACY OF ESTIMATED FETAL WEIGHT

A total of 73 infants were included in the analysis to determine the accuracy of estimated fetal weight (EFW). The mean interval from ultrasound examination to delivery was 1.59 (1SD= 1.15) days, with a range of 0 to 3 days. Fetal weight estimation was done by Hadlock et al's formula of HC/FL/AC (1985). With this method, there was a good correlation between EFW and birth weight (BW) over the full range of birth weights. Mean gestational age at estimation of fetal weight was 37.4 (SD= 1.98) weeks and range was 32 to 41 weeks (Table XXII). The regression line in Graph 23, represented by  $EFW = 0.8796 \times BW + 274.86g$  ( $R^2 = 0.9243$ ), was not significantly different from the line of identity.

With Hadlock's formula, the mean EFW was 2753.4 ( $\pm 716.4$ )g, and range was 1200- 4184g. It was not significantly different from the mean actual birth weight of 2817.9 ( $\pm 783.0$ )g. The actual birth weights ranged from 1200 to 4500g. The mean EFW was 65g less than the mean birth weight. A good correlation was found between estimated fetal weight using HC/FL/AC formula and actual birth weight ( $r = 0.961$ ).

The mean absolute difference between EFW and birth weight was, -64.5 ( $\pm 218.5$ ) (95% CI of the difference was -116.19 to -12.7g) and the mean relative difference or the mean percentage error of fetal weight estimation [ $100 (EFW - BW) / BW$ ] was -1.4 ( $\pm 7.6$ ) % (Table XXI).

Graph 23, shows correlation between estimated fetal weight and birth weight, by the method of Hadlock and colleagues (circles and dashed lines). The unbroken line represents identity. Null hypothesis considered EFW and BW as equal. Paired t-test was performed to compare the EFW and BW. The calculated  $p$  value was  $>.05$ , hence the difference was not significant. The hypothesis may be accepted at 95% CI. In other words there was no statistically significant difference between estimated fetal weight and the actual birth weight.

### ACCURACY

Using Student's t-test for paired two-sample means, between estimated fetal weight and the birth weight no significant difference was found between the two ( $r = 0.961$ ,  $n = 73$ ).

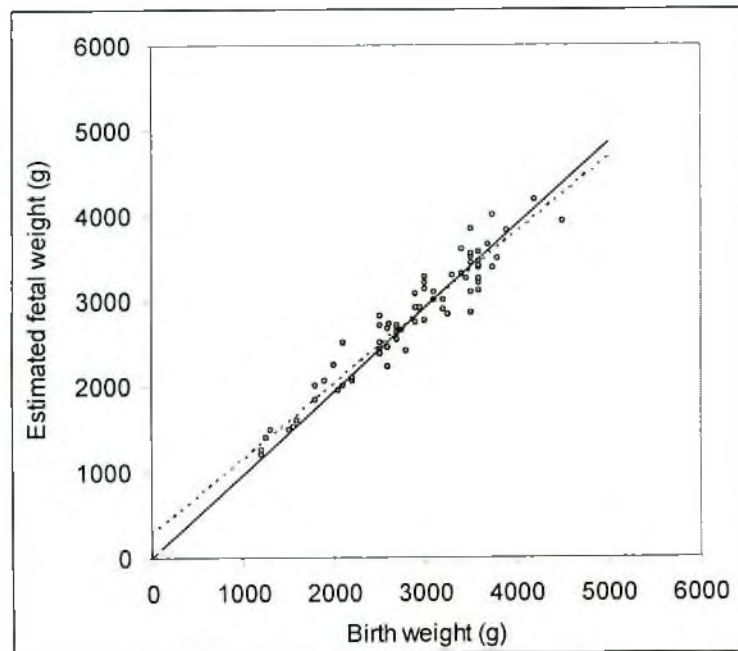


VARIABLES	FINDINGS	
Total number of infants (n)	73	
Gestational age (weeks)	37.4 ± 2.0	
Birth weight (g)	2817.9 ± 783.0	
Estimated fetal weight (g)	2753.4 ± 716.4	
EFW – BW (g)	-64.5 ± 218.5	$p > 0.05$
100(EFW- BW)/BW (%)	-1.4 ± 7.6	
Correlation coefficient (r)	0.961	$p < 0.001$

Table XXI: Differences between estimated fetal weight (EFW) and birth weight (BW). Values are mean and Standard deviation (± SD).

Variables	n	Minimum	Max	Mean	SD
Estimated fetal weight (g)	73	1200	4184	2753.42	716.4
Birth weight (g)		1200	4500	2817.89	783.04
Gestational age (weeks)		32	41	37.42	1.98
Growth percentile		3	97	50.19	22.80
Gap of days		0	3	1.59	1.15

Table XXII: Descriptive Statistics.



Graph 23: Correlation between estimated fetal weight and birth weight, by the method of Hadlock and colleagues (circles and dashed lines). The unbroken line represents identity.

$n = 73$ .

## CHAPTER 6

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### *DISCUSSION*

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6.1: DISCUSSION	...	...	97
6.2: LIMITATIONS	...	...	121

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## DISCUSSION

### 6.1: DISCUSSION

Accurate assessment of fetal size and growth is of utmost clinical importance, both in normal and abnormal pregnancies. The effects of maternal diseases on fetal development and the problems associated with prematurity and growth restriction are being more clearly understood now and so the precise measurement of fetal size in relation to menstrual age is gaining more importance.

Diagnostic ultrasound has been used in obstetrics for nearly 35 years. It is generally considered safe but still there is continuous study and research to confirm this. It is a very important technique for examining pregnant women and can be used when clinically indicated at any time during pregnancy (Palmer 1995).

Literature is fraught with nomograms of different fetal parameters, but they have all been generated by studies on western population. Caucasians are different from us not only in their size and stature but also in their socio-economic condition. Therefore studies were conducted to see if those charts were suitable for us or not and it was found that they were not (Quddus, 2006, 2005, 2004, 2002, 2000, 1999; Quddus and Khatun, 2001; Moslem et al, 1996; Bala, 1991). In this study fetal growth charts were therefore constructed from our own population. This study produced for the first time in Bangladesh, fetal size charts which changed smoothly with gestational age. Tables of measurements and percentile charts for BPD, HC, FL, AC, EFW and their ratios derived from a sample of 1223 patients were presented here. SPSS program in computer software was used for data entry and analysis.

Until recently it was difficult to monitor the development of fetus during pregnancy. Real time ultrasonography is a non invasive method which has made this possible. Lei and Wen sought to construct ultrasonography– based growth curves in Chinese population. They found

that all fetal growth measures increased with gestational age, whereas the ratios either decreased or remained constant. BPD and cerebral hemispheric width were higher at early gestational ages, whereas FL, thoracic circumference and AC were lower in later gestations, in their study than in previous studies. They concluded that a different standard of ultrasonography-based fetal growth is needed for different populations (Lei and Wen, 1998). In the last 10 years the quality of the ultrasound has improved remarkably regarding its resolution and measurement techniques. Improvement of methodologies and statistical analysis and consideration of change in variability with gestation and presentation of scatter diagrams of the data with fitted centiles superimposed contributed in development of good quality fetal size charts.

As the reference fetal size charts presented here are for the normal fetuses, exclusion of fetuses with congenital abnormality was justified. Fetuses found to be large for date and small for date (SFD) were not excluded in this study. As maternal diseases (diabetes mellitus, gestational diabetes, hypertension and renal diseases) may influence fetal growth, these were reasonable exclusion criteria. Non-pathological determinants of fetal size are gestational duration, fetal gender, and maternal height, weight, age and parity. Fetuses were excluded only if the pregnancy was exposed to factors known to influence fetal growth pathologically. All observations were collected prospectively from a cross-sectional population. Statistical methods were used which gave proper attention to the changing variability with increasing gestation, and the goodness of fit of the models obtained, were carefully assessed as Altman and Chitty (1994) described in their study.

First, the observed 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles and the mean and standard deviations (SD) at each week of gestation for all five parameters (BPD, HC, FL, AC and EFW) and their ratios were prepared from the raw data. To construct fetal size charts with smooth lines, models were then fitted. The mean and 2SD were estimated at each gestational age and the 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles were calculated. It covered 95% of the population. In 5% of cases the values were outside this range i.e. it is of 95% confidence interval (CI).

The mean were estimated by polynomial regression, linear, cubic or quadratic models. This approach was based on the strong assumption that at each gestational age the data came from a population with a normal distribution. After the required centiles were calculated they were superimposed on scatter diagrams of the observations as a final check of the fit. The

coefficient of multiple correlations ( $R^2$ ) of all parameters showed high value. High value indicates a good correlation between the two variables, the independent and the dependent. Although these results have some similarity with western published data, a comparatively lower rate of fetal growth after 37 weeks of gestation in cases of BPD, HC, FL, and AC was revealed. Western studies found lower rate of only BPD and HC growth after 38 weeks, but not in FL and AC growth.

Near term all the parameters were found to be smaller than the western ones as was assumed. Therefore population specific nomograms constructed in this study are more appropriate for Bangladeshi fetuses.

Linear, quadratic and cubic models gave good fit to the data. Goodness of fit of SD and standardized residuals were given in Graphs. There was a gradual increase of variability as pregnancy advanced. Chitty and Altman's study also showed similar pattern of increase of these parameters with increasing gestational age (Chitty et al, 1994). But the pattern of changes in measurements were different from Hadlock et al, their centiles were much wider apart in early pregnancy and narrower at term (Hadlock et al, 1982).

In this study, there was one outlier at 28<sup>th</sup> week of gestation, but it was not excluded from the study. It was a transitory growth restriction phase, as in subsequent scans of the same fetus the growth was normal. This was therefore the result of instability in the control system regulating fetal growth (Deter et al, 1983).

As fetal biometry and fetal weight charts obtained from this study were different from the industrialized countries it should be more appropriate to use fetal charts originated from our own population with its characteristic socioeconomic and genetic background and growth potential. A large number of unexplained intrauterine fetal deaths in Bangladesh may be associated with SFD and intrauterine growth restriction (IUGR) which remained undiagnosed. Fetal biometry for monitoring fetal growth can prevent both perinatal mortality and morbidity by timely diagnosis of IUGR and SFD fetuses. Further study with a larger sample size is also necessary covering the low risk population to construct charts of fetal size (Ashrafunnesa et al, 2003).

Normal ranges of BPD, HC, FL and AC were established from longitudinal data of singleton pregnancies of Arabian mothers. It is suggested that a normogram of "fetal growth" is of less

variance than absolute measurements and could be more useful in the early identification of growth abnormalities than absolute fetal measurements (Nasrat, 1997).

One study in Singapore found that though Hadlock's formula was originally derived from an American population, it was equally useful in south-east Asian population (Venkat et al, 2001). Altitude influences ultrasonic fetal biometric measurements as seen in a study in Peru which suggested that at high altitude, all fetal biometry measurements follow a lower trajectory than at sea level. Specific biometry charts should therefore be used for obstetric ultrasound at high altitude (Krampfl et al, 2000). Overall 74% of 3 dimensional (3D) BPD measurements were within 1mm of the 2 dimensional (2D) measurements, and 64% of 3D FL measurements were within 1mm of the 2D measurements (Benacerraf et al, 2006).

### **6.1a: BIPARIETAL DIAMETER**

In the present study first the observed values were determined by analysis of the raw data. At 13 weeks (w) gestational age, mean biparietal diameter (BPD) (outer-inner) was 23mm ( $\pm 3$ mm) (2SD) and at 40w it was 91mm ( $\pm 6$ mm). Then estimated values were derived after fitting the model, and at 13w gestational age, mean BPD was found to be 24mm ( $\pm 4$ mm) and at 40w it was 92mm ( $\pm 8$ mm), with a 95% CI of 87 to 98 mm. The coefficient of multiple correlation  $R^2 = 0.977$ , indicated a good correlation between the two variables, gestational age and BPD. The head exhibited a greater increase in variability after approximately 29 weeks. There was gradual increase of 2SD towards term, from 4mm to 8mm, showing increasing dispersion of BPD towards term.

First the values  $\pm 2$ SD were superimposed on the residual plot to see how well the SD had been modeled. Plot of standard deviation scores (standardized residuals) against gestational age for BPD, showed expected 2SD. Linear model was fitted to the SD. It was similar to Chitty and co-worker's study (1994). Then 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves derived by fitting a model were superimposed on the raw data of 1223 subjects. There was a gradual increase of BPD centiles up to 37<sup>th</sup> week of gestation; thereafter a slower growth rate was noted. The polynomial regression linear- cubic model showed a good fit to the mean. It also showed that there was increased dispersion of data and the centile curves as the pregnancy progressed. This was not found in the studies which did not follow the proper methodology (Chitty et al, 1994).

One Bangladeshi study found that at 28w gestational age mean BPD was 72mm and at 40w it was 95mm (Biswas, et al, 2006). In another study with gestational age as the dependent variable 23mm indicated 13w ( $\pm 7d$ ) (2SD) and 92mm indicated 40w ( $\pm 21d$ ) (Quddus, 2005). A study here found that at 18w mean BPD was 41mm ( $\pm 3mm$ ) and at 40w it was 90mm ( $\pm 4mm$ ). Lower growth rates were found in BPD measurements after 38w of gestation. (Ashrafunnessa, et al, 2003). In yet another study at 13w gestational age mean BPD was 23mm ( $\pm 2mm$ ) and at 40w it was 91mm ( $\pm 3mm$ ) (Quddus, 2002).

A study here, found BPD of 93mm ( $\pm 11mm$ ) at 38w (Moslem, et al, 1996) whereas Campbell and Newman reported 96mm (1971). Another study here, found that the fetal BPD was 1 to 2w smaller for the date in comparison to fetus from developed countries. At 15w gestational age BPD was 24mm ( $\pm 2mm$ ) and at 40w it was 93mm ( $\pm 8mm$ ) (Bala, 1991).

A study in our country found that BPD measurements increased gradually from 13 to 28w at the rate of 3mm/w, then from 28 to 33 weeks it increased by about 2mm/w, thereafter up to 40w the increase was about 1mm/w. It was 92mm at 40 and 41w (Quddus and Chowdhury, 2004). In this study also the rate of increase tailed off as pregnancy advanced.

In an Indian study at 13w gestational age mean BPD was 23mm ( $\pm 3mm$ ) and at 40w it was 90mm ( $\pm 3mm$ ) (Observed values) and after fitting a model, at 13w gestational age mean BPD was 23mm and at 40w it was 95mm (Estimated values) (Rajan, et al, 2001).

In two Japanese studies, at 12w mean BPD was 21mm ( $\pm 4mm$ ) (2SD) and at 40 w it was 94mm ( $\pm 8mm$ ) (Osaka University) and in the other study 20mm indicated 12w ( $\pm 7d$ ) (2SD) and 95mm indicated 40w ( $\pm 25d$ ) (Tokyo University).

In a Western study, at 13w gestation mean BPD was 22mm ( $\pm 3mm$ ) (2SD) and at 40w it was 95mm ( $\pm 9mm$ ) (Observed values), and by fitting model, at 13w BPD was 22mm ( $\pm 4mm$ ) and at 40w it was 95mm ( $\pm 8mm$ ) (Estimated values) (Chitty et al, 1994). In another study 24mm predicted 13w ( $\pm 8d$ ) (2SD) and 99mm predicted 40w ( $\pm 30d$ ) (Hansmann et al, 1985).

A study found that at 14w gestational age mean BPD was 27mm and at 40w it was 95mm (Observed values) and by taking gestational age as dependent variable 20mm predicted 12w ( $\pm 6d$ ) (2SD) and 96mm predicted 40w ( $\pm 25d$ ) (Hadlock et al, 1982). In Shepard and Filly's study (1982) at 14w gestational age mean BPD was 28mm and at 40w it was 97mm, and in another study at 14w mean BPD was 26mm and at 40w it was 95mm (Kurtz et al, 1980). In

one of the earliest studies 24mm indicated 13w ( $\pm 7d$ ) (2SD) and 100mm indicated 40w ( $\pm 21d$ ) (Campbell et al, 1977).

Various studies showed that in the early 2<sup>nd</sup> trimester all the Bangladeshi, Indian, Japanese and Western measurements were the same but as pregnancy progressed there was discrepancy between different races. At term the BPD values of the present study was similar to other Bangladeshi studies except from Biswas, et al whose finding was similar to the Japanese studies. It could be due to measurement or methodology error. The observed value of Indian study was similar to this study at term. At term, Japanese BPD was a little bigger by 2 to 3mm but western values were much bigger than ours by 4 to 8mm.

Moslem et al, excluded fetuses whose growth fell below 10<sup>th</sup> percentile and Hadlock, et al excluded from their analysis all fetuses outside mean  $\pm 2SD$ . Altman and Chitty (1994) do not consider such exclusions justified. Campbell and Newman (1971) used a diasonograph static B-scanner and outer-outer BPD measurements, they excluded babies delivered before 39w and those whose weight was less than 5<sup>th</sup> percentile for 40w gestation. Also their study included multiple measurements on many fetuses. All these factors can affect the resulting mean and SD. This and Chitty et al's (1994) data showed a widening towards term because of the increase in variability with increasing gestation.

A study in Australia did not show any statistical or clinically important difference in BPD, AC and FL of Aboriginal and Caucasian fetuses. They concluded that there is no reason to use separate fetal growth charts when examining Aboriginal fetal growth (Humphrey and Holzheimer, 2000). But other studies show that ethnicity influences ultrasonic fetal biometric measurements. A prospective study in Tehran in Iran showed that Iranian fetuses had smaller BPD and shorter FL measurements in comparison with Western studies ( $p < 0.05$ ) (Beigi and Zarrin, 2000). A study in Tanzania denotes that tables from industrialized countries relating gestational age to sonographically measured BPD are not applicable for pregnancies in developing countries (Gutknecht, 1998).

### **6.1b: HEAD CIRCUMFERENCE**

First, analysis of the raw data of fetal head circumference (HC) measurements was done to determine the observed values. At 13w gestational age mean HC was 86mm ( $\pm 12mm$ ) (2SD) and at 40w it was 330mm ( $\pm 23mm$ ). Then the estimated values were derived after fitting the



model and at 13w gestational age mean HC was 90mm ( $\pm 12$ mm) (2SD) and at 40w it was 335mm ( $\pm 25$ mm), with a 95% CI of 311 to 358mm. The coefficient of multiple correlation,  $R^2 = 0.981$ , was statistically significant.

Assessment of goodness of fit of the model for SD of fetal HC was shown in a graph. It was similar to Chitty and co-worker's study (1994). The 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves derived by fitting the model were superimposed on the scatter diagram of the raw data. Polynomial regression cubic model showed a good fit to the data. There was a gradual increase of the HC measurements up to 37<sup>th</sup> w of gestation thereafter the growth was slower. It also showed that there was increased dispersion of data and the outer centiles as the pregnancy advanced. This was not found in the studies which did not follow the proper methodology and study design (Chitty et al, 1994).

In one Bangladeshi study at 14w gestation HC was found to be 98mm ( $\pm 5$ mm) and at 40w it was 333mm ( $\pm 13$ mm) (Quddus, 2006). In another study at 13w HC was 87mm ( $\pm 13$ mm) (2SD) and at 40w it was 330 mm ( $\pm 23$ mm) (Estimated values),  $R^2 = 0.980$ . In the same study with gestational age as dependent variable 85mm predicted 14w ( $\pm 0.4$ w) (2SD) and 340mm predicted 40w ( $\pm 3$ w) (Estimated values),  $R^2 = 0.966$  (Quddus and Rashid, 2006). In a third study at 13w HC was 86mm ( $\pm 5$ mm) and at 40w it was 333mm ( $\pm 13$ mm) (Quddus, 2004).

In a study in Bangladesh, the HC gradually increased with menstrual age at the rate of 13mm/w to 3mm/w at term. The 2SD also increased from  $\pm 10$ mm to  $\pm 26$ mm at term. At 13w the HC was 86mm ( $\pm 10$ mm), at 20w it was 175mm ( $\pm 15$ mm), at 38w it was 327mm ( $\pm 26$ mm) and at 40w it was 333mm ( $\pm 26$ mm) (Quddus, 2004). A western study also found that the growth rate of HC tapered off as the gestational age increased. At 12-13w it is 1.6 ( $\pm 0.2$ ) (2SD) cm/w and at 39- 40w it is 0.4 ( $\pm 0.3$ ) cm/w (Deter et al, 1982). This shows that the rate of increase in both Bangladeshi and Western studies declines as the pregnancy advances.

In an Indian study, at 13w gestational age HC was 91mm ( $\pm 8$ mm) and at 40w it was 329mm ( $\pm 20$ mm) (Observed values) and after fitting model, at 13w HC was 84mm and at 40w it was 343mm (Estimated values) (Rajan et al, 2001).

In different Western studies, at 13w HC was 84mm ( $\pm 14$ mm) (2SD) and at 40w it was 342 mm ( $\pm 38$ mm) (Observed values) and by estimating values, at 13w mean HC was 82mm ( $\pm 14$ mm) and at 40w it was 344mm ( $\pm 26$ mm) (Chitty et al, 1994). In another series at 14w mean HC was 97mm ( $\pm 6$ mm) and at 40w it was 346mm ( $\pm 20$ mm) (Hadlock et al, 1984). In

a study with gestational age as dependent variable, 106mm predicted 14w ( $\pm 8d$ ) (2SD) and 349mm predicted 40w ( $\pm 35d$ ) (Hansmann et al, 1985).

At 13w gestational age HC was 89mm ( $\pm 19mm$ ) (2SD) and at 40w it was 345mm ( $\pm 19mm$ ), and by estimated values and taking gestational age as dependent variable, 80mm predicted 12w.3d ( $\pm 9d$ ) (2SD) and 350mm indicated 40w ( $\pm 24d$ ) (Hadlock et al, 1982). In Deter's study, at 13w HC was 87mm ( $\pm 15mm$ ) (2SD) and at 40w it was 359mm ( $\pm 25mm$ ) (Deter et al, 1982) and in a very early study 115mm predicted 14w ( $\pm 10d$ ) (2SD) and 345mm indicated 40w ( $\pm 35d$ ) (Campbell et al, 1977).

Here also like BPD, all studies showed that at in the early 2<sup>nd</sup> trimester all the local, Indian, and western measurements were similar but as pregnancy progressed there was discrepancy between different races. The observed values of the other Bangladeshi and Indian studies were similar to this study at term but western values of HC were much bigger than ours with a difference of 16 to 24mm at term. This was because of the difference in size and stature between the sub-continental people and the western people. The socio-economic conditions of these groups are also very different to make an impact on the fetal size.

The technique is important in the measurement of HC. The measurements obtained by direct measurement around the circumference were consistently (by about 1%) more than those obtained by derivation from the BPD (outer-outer) and occipito-frontal diameters (Chitty et al, 1994). When using a nomogram same method should be used as the author did.

Predicted reduction in birth weight at an increase of exposure to fine particles from 10-50  $\mu\text{g}/\text{m}^3$  was 140.3g. The corresponding predicted reduction of birth length would be 1cm, and of HC, 0.5cm. The study provides new and convincing epidemiologic evidence that high personal exposure to fine particles is associated with adverse effects on developing fetus (Jedrychowski et al, 2004). Three years of growth hormone treatment induced a growth resulting in a normalization of height and other anthropometric measurements, including HC, in contrast to untreated SFD control subjects (Arends et al, 2004).

### **6.1c: FEMUR LENGTH**

In this study first the summary of the raw data was given. At 13w gestational age mean FL was 11mm ( $\pm 2mm$ ) (2SD) and at 40w it was 73mm ( $\pm 5mm$ ) (Observed values). Then another table of estimated values was prepared after fitting the model and at 13w gestational

age mean FL was 11mm ( $\pm 3$ mm) (2SD) and at 40w it was 73 mm ( $\pm 6$ mm), with 95% CI of 68 to 79mm and  $R^2 = 0.982$ . There was a gradual increase of the FL measurements up to 37<sup>th</sup> week of gestation, and then there was a slower increase till term. There was also gradual increase of 2SD towards term, from 3.4 to 5.8mm.

Plot of standard deviation scores against gestational age, showed expected 2SD. It was similar to a western study (Chitty et al, 1994). Fitted curves describing 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles were superimposed on the scattered raw data. The polynomial regression quadratic model showed a good fit to the data. It also showed that there was increased dispersion of data and the fitted curves as the pregnancy progressed.

In other Bangladeshi studies at 28w FL was 52mm and at 40w it was 75mm (Biswas et al, 2006), by taking gestational age as dependent variable 18mm predicted 15w ( $\pm 7$ d) (2SD) and 73mm indicated 40w ( $\pm 21$ d) (Quddus and Begum, 2004), at 18w FL was 26mm ( $\pm 3$ mm) and at 40w it was 71mm ( $\pm 3$ mm) (Ashrafunnessa et al, 2003) and in another study at 16w, FL was 19mm ( $\pm 2.6$ mm) and at 40w it was 72mm ( $\pm 3.2$ mm) (Quddus, 2002).

In an Indian study, at 13w gestational age FL was 11mm ( $\pm 2$ mm) and at 40w it was 72mm ( $\pm 4$ mm) (Observed values), and after fitting model, at 13w FL was 11mm and at 40w it was 76mm (Estimated values) (Rajan et al, 2001).

In two Japanese studies, at 13w mean FL was 9mm ( $\pm 2$ mm) and at 40w it was 71mm ( $\pm 3$ mm) (Osaka University), and in the other study with gestational age as dependent variable 32mm predicted 20w ( $\pm 17$ d) (2SD) and 70mm predicted 40w ( $\pm 64$ d) (Tokyo University).

In Western studies, at 13w gestational age FL was 11mm ( $\pm 2$ mm) and at 40w it was 75mm ( $\pm 4$ mm) (Observed values) and after fitting model, at 13w FL was 11mm ( $\pm 2$ mm) and at 40w it was 74mm ( $\pm 3$ mm) (Chitty et al, 1994). With gestational age as dependent variable, 10mm predicted 13w ( $\pm 7$ d) (2SD) and 75mm predicted 40w ( $\pm 23$ d) (Hansmann et al, 1985). In other studies at 14w FL was 14mm ( $\pm 1$ mm) and at 40w it was 77mm ( $\pm 2$ mm) (Hadlock et al, 1984); at 13w FL was 12mm ( $\pm 7$ mm) (2SD) and at 40w it was 75mm ( $\pm 9$ mm) (Jeanty, 1983); at 14w FL was 17mm ( $\pm 3$ mm) (2SD) and at 40w it was 75mm ( $\pm 6$ mm) (O'Brien et al, 1981). With gestational age as dependent variable 10mm predicted 13w ( $\pm 10$ d) (2SD) and 78mm predicted 40w ( $\pm 22$ d) (Hadlock et al, 1982) and in one of the earliest studies 18mm indicated 15w ( $\pm 6$ d) (2SD) and 75mm indicated 40w ( $\pm 22$ d) (Campbell et al, 1977).

In case of FL also, as in BPD and HC, all studies showed that in the early second trimester Bangladeshi, Indian, Japanese and Western measurements were similar but as pregnancy progressed there was discrepancy between different races. The observed values of FL measurement of other local studies were similar to this one except Biswas' study (2006) which was similar to western study probably due to some methodological error. Indian study was similar to this study at term, Japanese measurements were 2 to 3mm smaller than ours, whereas western values of FL were much bigger than ours at term, by 2 to 5mm.

Several authors have evaluated the measurement of the femur for the prediction of gestational age and fetal size, and in the detection of fetal abnormalities (Kurtz and Goldberg 1988). FL should be measured routinely and recorded after the 14<sup>th</sup> w of gestation. As with BPD considerable biological variation is present late in pregnancy (Leopold, 1986).

The ultrasonic measurement of the fetal FL is a sensitive and precise variable for estimation of fetal growth and development. Previous normal ultrasonic fetal FL curves for another population may underestimate or overestimate normal fetal weight for the Iranian population (Honarvar et al, 2001).

There was a statistically significant difference in FL in the Asian group compared with all other groups, as well as the white group compared with the black and Asian groups ( $p < .05$ ). The Asian group had the largest variation, with the measured FL being less than the expected FL. Using ethnic-specific formulas for expected FL can have a considerable impact on the use of sonographic risk factors for Down's syndrome screening. Further data are required for use of FL as a screening tool in the genetic sonogram (Kovac et al, 2002).

New fetal measurement charts were prepared for FL and BPD from the Israeli population and those were found to be similar to those published for other Caucasian populations (Shohat and Romano, 2001).

#### **6.1d: ABDOMINAL CIRCUMFERENCE**

For abdominal circumference (AC) also, first the summary of the raw data was presented as observed values. At 13w gestational age mean AC was 66mm ( $\pm 7$ mm) (2SD) and at 40w it was 327mm ( $\pm 34$ mm). Another table was constructed of the estimated values in which, at 13w gestational age mean AC was 72mm ( $\pm 9$ mm) (2SD) and at 40w it was 332mm ( $\pm 36$ mm), with a 95% CI of 299 to 365mm.  $R^2 = 0.970$ , with a  $p$  value of  $< .001$ .

Residuals from model describing mean with 2SD was shown. It was similar to a western study (Chitty et al, 1994). The 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves were superimposed on the scatter chart. Polynomial regression cubic model showed a good fit to the data. It also showed that there was increased dispersion of data as the pregnancy advanced. This was not found in the studies which did not follow the proper methodology (Chitty et al, 1994).

In the other Bangladeshi studies, at 28w gestational age mean AC was 240mm and at 40w it was 370-375mm (Biswas et al, 2006), at 18w AC was 133mm ( $\pm 13$ mm) and at 40w it was 330mm ( $\pm 19$ mm) (Ashrafunnessa et al, 2003), at 16w gestational age AC was found to be 110mm ( $\pm 11$ mm) and at 40w it was found to be 328mm ( $\pm 22$ mm) (Quddus, 2002).

In an Indian study at 13w gestational age AC was 74mm ( $\pm 16$ mm) and at 40w it was 334mm ( $\pm 25$ mm) (Observed values), and after estimating values at 13w AC was 69mm and at 40w it was 354mm (Rajan et al, 2001).

In a Western study at 13w gestational age mean AC was 69mm ( $\pm 6$ mm) (2SD) and at 40w it was 344mm ( $\pm 23$ mm) (Observed values) and after fitting a model at 13w AC was 67mm ( $\pm 5$ mm) and at 40w it was 340mm ( $\pm 21$ mm) (Estimated values) (Chitty et al, 1994). In another study, at 14w AC was 73mm ( $\pm 6$ mm) (2SD) and at 40w 353mm ( $\pm 29$ mm) (Hadlock et al, 1984), and with gestational age as dependent variable 63 mm indicated 13w gestational age and 320mm predicated 40w (Hansmann et al, 1985). At 13w AC was 69mm ( $\pm 3$ mm) (2SD) and at 40w it was 354mm ( $\pm 3$ mm) and in the same study with gestational age as dependent variable and fitting model, 100mm indicated 15w.4d ( $\pm 13$ d) gestational age and 360mm predicated 40w ( $\pm 18$ d) (Hadlock et al, 1982). In Deter's series at 13w age AC was 74mm ( $\pm 1$ mm) (2SD) and at 40w it was 370mm ( $\pm 5$ mm) (Deter et al, 1982). In one of the earliest studies 90mm indicated 14w ( $\pm 14$ d) (2SD) gestational age and 350mm predicated 40w ( $\pm 30$ d) (Campbell et al, 1977).

In the evaluation of AC also, like BPD, HC and FL, all studies showed that in the early second trimester the local, Indian, and western measurements were similar but as pregnancy advanced there was variation between different races. The findings of this study were similar to other local studies except from Biswas' study where AC was bigger than even the western studies. Methodological error could be a reason. The observed values of AC measurement of

Indian study was similar to ours at term, whereas western values of AC were much bigger at term than ours, by 21 to 28mm.

The measurement of fetal AC was first described in 1975 as a useful measure for estimating fetal weight (Campbell and Wilkin 1975). It is now widely used to monitor normal fetal growth, to detect IUGR (Campbell and Thomas 1977) or macrosomia, and in the estimation of fetal weight (Hadlock et al, 1985).

In a study here, in cases of BPD and AC, after 38w of gestation the percentiles showed a slower growth rate. So the new charts constructed for these parameters are different after 38w from those published for Caucasian populations. This may be a characteristic of the fetal size chart for Bengali population (Ashrafunnesa et al, 2003). Fetal abdominal size charts were constructed which should have several applications in clinical practice. Comparison of this cross sectional data with that of other authors might be explained by difference of study population. In this study after 37w of gestation the percentiles showed a slower growth rate in case of AC but in western studies the AC continued to grow linearly till term.

In a study in Bangladesh, gestational age obtained by ultrasonography from the measurement of AC and using Hadlock et al's table (1982), was found to be constantly smaller after 24w. At 40w the AC age was 37w ( $\pm 3w$ ) by using the western table. At 40w AC was 359mm by Hadlock's table but 330mm by Bangladeshi table. Therefore a table was prepared to give the mean AC measurements of our fetuses, so that in one glance the obstetricians can get an accurate idea of the fetal nourishment at a particular gestational age (Quddus, 2000).

Hadlock et al (1982) did not model the SD to take into account the increasing variation with gestation. So their centiles were much wider apart in early pregnancy and narrower at term. Difference in sampling may have been more influential. They studied 400 unselected women, but 101 of these were seen at 38 to 40w of gestation.

To establish reference charts for the population of Nigeria by ultrasound scanning, 736 fetuses were examined at the Pondriere Hospital in Niamey. Transverse abdominal fetal diameter in Nigeria appeared to be below normal (Vangeenderhuysen and Nono, 1998).

Growth restriction was diagnosed when there was no growth in fetal AC between two consecutive examinations. There was a dramatic increase in false-positive rates as the time interval between exams was reduced. There was a significant increase in the false-positive

rate as the gestational age of initial ultrasound was increased. At 28w, the false-positive rate with a 2w interval was 11.8%, increasing to 24.1% at 38w (Mongelli et al, 1998).

Reduced AC was the best single parameter in discriminating between IUGR and non-IUGR fetuses with the highest sensitivity among the proposed parameters in the both Iranian and Australian sample. Its positive predictive value is low. The parameters obtained to evaluate their diagnostic accuracy in predicting IUGR babies, were BPD, FL, HC, AC, AFI and Doppler from umbilical arteries (Systolic/Diastolic ratio) (Niknafs and Sibbald, 2001).

Institution-specific nomograms of fetal AC measurements are important to avoid incorrect categorization of outer centiles. Comparison with other published nomograms indicated that the false-negative rates for classifying our population as <10<sup>th</sup> centile or >90<sup>th</sup> centile ranged from 11.3% to 90.5% and from 0 to 66.4%, respectively (Smulian et al, 2001).

## **6.2e: ESTIMATED FETAL WEIGHT**

Fetal weight is one of the most important and most often sought parameters of fetal growth. In the present study first, a table was prepared showing observed values of the raw data of 1223 subjects. At 13w gestational age mean estimated fetal weight (EFW) was 72g ( $\pm 7$ g) (2SD) and at 40w it was 3095g ( $\pm 703$ g). Next a table of estimated values was constructed after fitting a model, at 13w gestational age mean EFW was 77g ( $\pm 19$ g) (2SD) and at 40w it was 3131.5g ( $\pm 749$ g), with 95% CI of 2427 to 3836g. The coefficient of multiple correlation,  $R^2 = 0.988$ , ( $p < .001$ ), indicated a good correlation between the two variables.

Assessment of goodness of fit of model for SD of EFW was done. Plot of standard deviation score against gestational age showed expected 2SD. The graph demonstrated the raw residuals across gestational ages. It was similar to a study on Caucasian population (Hadlock et al, 1991).

The 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves derived by fitting a model were superimposed on the observed raw data. Regression analysis was used and the model showed a good fit to the data, as shown in the graph. It also showed that there was increased dispersion of data and percentile curves as the gestational age increased. This was also found in a Caucasian study which followed the same methodology (Hadlock et al, 1991). In this study the growth was slow up to 26w and then it increased linearly up to 40w of gestation, similar to Hadlock's study of 1991.

In a study in Bangladesh, at 16w gestational age EFW was 0.2 ( $\pm 0$ )kg and at 40w it was 3 ( $\pm 0.4$ )kg. The EFW were found to be less than the Caucasian population (Hadlock et al, 1991) at the same gestational ages in the third trimester. From 29w the difference increased gradually from 0.1 kg to 0.6 kg at 40w. This was most likely due to racial factor, as very poor and malnourished patients were not included in this study and majority of patients belonged to the middle class (Quddus, 2002).

In another series here mean (SD) were 2.86 ( $\pm 0.34$ )kg at 38w, which rose to 3.1 ( $\pm 0.4$ )kg at 40w but did not increase after that. The curve showed a linear trend upwards from 22w, with the increase of fetal age, but with a flattening from 40 to 42w gestational age. At 22w gestational age EFW was 0.5 ( $\pm 0.06$ )kg (Quddus and Khatun, 2001). The mean EFW reported in one study here at 38w was 2998g, but they used Hansmann's formula that is based on BPD and antero-posterior body diameter and not AC (Miah et al, 1998).

In an Indian study, at 24w gestational age EFW was 595 ( $\pm 180$ )g and at 40w it was 3076 ( $\pm 565$ )g (Observed values), and after fitting a model, at 24w gestational age EFW was found to be 640g and at 40w it was found to be 3280g (Estimated values) (Rajan et al, 2001).

In a Japanese study, at 16w gestational age mean EFW was 137 ( $\pm 29$ )g and at 40w it was 3220 ( $\pm 387$ )g (Osaka University). In a Brazilian study, at 20w gestational age mean EFW was 368g and at 42w it was 3417g. There was a mean increase of 200g/w from 27 to 38<sup>th</sup> week, when the gain decreased (Cecatti et al, 2000).

In studies generated in Western countries, at 26w mean EFW was 860g and at 40w it was 3280g (Doubilet et al, 1997), at 13w gestational age mean EFW was 73 (55-91)g (95%CI), and at 40w it was 3619 (2714-4524)g (Hadlock et al, 1991), at 14w mean EFW was 93g and at 40w it was 3788g (Ott et al, 1988), at 21w gestational age mean EFW was 0.41 (0.28-0.86)kg and at 40w it was 3.28 (2.75-3.87)kg (Hadlock et al, 1983), at 14w mean EFW was 82g and at 40w it was 3863g (Deter et al, 1982), at 21w gestational age mean EFW was 410g and at 40w it was 3280g (Brenner et al, 1976).

At term different Bangladeshi studies were 0.2 to 0.8kg smaller than Western studies, but similar to Indian and Japanese studies. In early second trimester all studies were comparable.

In Postnatal weight studies, at 22w gestational age mean EFW was 513 ( $\pm 30$ )g and at term it was 3462 ( $\pm 13$ )g (Williams et al, 1982), and in Babson's study at 28w mean EFW was 1118 ( $\pm 30$ )g, and at 40w it was 3448 ( $\pm 13$ )g (Babson et al, 1970).



Extremes in fetal weight are associated with poor perinatal outcomes (Kurtz and Goldberg, 1988). For this reason, reliable estimates of fetal weight can be valuable in the management of pregnancy. Fetal weight gain as measured by ultrasound is subject to pathological deviation, as well as physiological variations due to maternal height, weight, ethnic group and parity (De Jong et al, 1998). Sex, race and parity differences have also been found. These results document the need for selecting a set of normal ranges, which is appropriate for the specific population being studied (Deter et al, 1983).

Birth weight correlates negatively with maternal hemoglobin concentration. This is consistent with well-known effect of high-altitude exposure during pregnancy, which increases both hematocrit and blood viscosity and lowers birth weight. Term birth weight was reduced by 89g for each 1.0g/dL increase in hemoglobin concentration ( $P < .01$ ) (Nahum and Stanislaw, 2004).

Adjustable standards reduce false- positive assessments of abnormal intrauterine growth. Prospective studies are now needed to evaluate whether an improved detection of growth abnormality can be translated into improvements in perinatal outcome (De Jong et al, 1999). Perinatal mortality is inversely related to gestational age and birthweight (Fanaroff et al, 1995). Whereas gestational age is generally known, fetal weight can only be estimated. Clinical variables including fundal height measurements are rather inaccurate predictors of fetal weight, especially in preterm and small-for-gestational-age fetuses in which weight estimates are the most relevant (Guidetti et al, 1990).

Fetal weight estimates derived from biometric data have been reported as accurate. Hadlock and colleagues method is based on longitudinally measured normal fetuses. The reported standard deviation of this method is 7.3%, which implies that 95% of infants have a measured birthweight within 15% of the EFW (Hadlock et al, 1985). In another of his study 95% confidence range was  $\pm 16\%$  (Hadlock et al, 1985). In Vintzileo's study 95% confidence range was  $\pm 17.6\%$  (Vintzileo et al, 1987). In Shepard's study it was  $\pm 18.2\%$  (Shepard et al, 1982) and in Warsof's study it was  $\pm 17.4\%$  (Warsof et al, 1977).

Whereas in the present study which was a cross-sectional study, the 2SD was found to be  $\pm 16\%$ , which implies that 95% of infants have a measured birth weight within  $\pm 16\%$  of the EFW. In a post-natal weight study, there was a uniform variance of approximately  $\pm 16\%$  at

the 10<sup>th</sup> and 90<sup>th</sup> percentiles (Secher et al, 1986), which is very similar to the variance observed in Hadlock's pre-natal weight study,  $\pm 17\%$  (Hadlock et al, 1991) and this study.

Recent studies have documented increased perinatal morbidity and mortality rates in the growth restricted post-term fetus. Ultrasonographic estimation of fetal weight is a useful test for predicting fetal growth restriction in prolonged pregnancies (O'Reilly-Green and Divon, 1999).

In a Japanese study, Sonographic determination of fetal growth from 20w of gestation onwards correlated with birth weight deviation, and this emphasized the clinical value of evaluating fetal growth during the later half of pregnancy (Youshida et al, 2001). The Osaka University determined mean fetal weight to be 2.9kg at 38w and 3.2kg at 40w.

The ultrasonography-based growth curve generated in China provided an additional tool for the evaluation of fetal growth and development in Chinese population (Lei and Wen, 1998).

In a study on Arabian mothers it was suggested that a nomogram of "fetal growth" is of less variance than absolute measurements and could be more useful in the early identification of growth abnormalities than absolute fetal measurements (Nasrat, 1997). In a population of small fetuses, Hadlock's estimates of fetal weight correlated well with measured birth weight, whereas Scott's method tended to overestimate (Kaaij et al, 1999).

Fetal BPD, HC, AC, FL and fetal thigh soft tissue thickness (FTSTT) were measured by ultrasonography and found that there was significant correlation between FTSTT and birth weight,  $R^2 = 0.8601$ . They concluded that, FTSTT is a simple, accurate and valuable index in estimation of fetal weight (Han et al, 1998).

Another study confirmed the usefulness of measurement of fetal thigh circumference for the small for date fetuses and arm circumference for the other groups. It concluded that the use of 3D ultrasound could facilitate the accurate prediction of fetal weight (Favre et al, 1995). 3D volumetric measurements of the fetal thigh, upper arm and abdomen were performed together with conventional 2D biometry. 3D sonography allows superior fetal weight estimation by including soft tissue volume (Schild et al, 2000).

Mean clinical estimate of fetal weight was equal to ultrasound for the estimation of fetal weight in their population. This has important implications for developing countries where there is a lack of technologically advanced ultrasound machines capable of performing sophisticated functions like fetal weight estimation (Mehdizadeh et al, 2000).

## 6.2f: FETAL GROWTH

Ultrasound scanning to confirm fetal growth is an essential part of maternal antenatal screening and depends on comparison with biometric reference charts. Impaired fetal weight gain prior to birth is associated with adverse perinatal events suggestive of growth failure (De Jong et al, 1999). Fetal growth and birth weight are subject to a variety of influences, which include physiological and pathological factors (Villar et al, 1990). Although there is some variation in growth rate at different gestations, as shown by the polynomial model, the normal curve for fetal weight gain in the third trimester is nearly linear (Mongelli and Gardosi, 1995).

In the current study too fetal weight gain is nearly linear in the third trimester. A study based on ultrasound data, describing fetal growth velocities in low risk pregnancies, also showed little variation in the late third trimester, with a mean increment in EFW of 24-26g/day (Owen et al, 1996).

Intrauterine growth restriction is associated with significantly increased perinatal morbidity and mortality as well as cardiovascular disease and glucose intolerance in adult life. A number of disorders from genetic to metabolic, vascular, coagulative, autoimmune, as well as infectious, can influence fetal growth by damaging the placenta, leading to IUGR as a result of many possible fetal, placental and maternal disorders (Cetin et al, 2004).

Infant measurements were recorded soon after birth. Indian babies were on average 795g lighter, had 5.5 days shorter mean length of gestation and slower growth of BPD and AC when compared to Fijian babies. Ethnicity of the mother was significantly associated with the difference in growth even after adjusting for other factors known to influence fetal growth. It would be appropriate to use ethnicity specific standards for perinatal care (Mathi et al, 2004).

52% of unexplained stillbirths were growth restricted, with a mean gestational age at death of 35w. IUGR is an important risk factor of sudden intrauterine unexplained death. Concurrent maternal overweight or obesity, high age, and low education further increase the risk. Overweight and obesity increase the risk irrespective of fetal growth, and high maternal age increases the risk of normal weight fetus (Froen et al, 2004).

Maternal malaria at delivery and primiparity were associated with reduced newborn weight and length but not with disproportionate growth. Maternal HIV infection was associated only with reduced birth weight (Kalanda et al, 2005).

The major non-genetic factor determining the size of the fetus at term is maternal constraint. It refers to a set of processes by which maternal and uteroplacental factors act to limit the growth of the fetus, presumably by limiting nutrient availability and/or the metabolic-hormonal derive to grow. It can be divided into supply-limited constraint (maternal size) and demand driven constraint (twinning). Maternal constraint is greater in young maternal age, small maternal size, nulliparous and multiple pregnancies. It is a physiological cause of the variation in birth size, but is not without longer-term consequences. It is an important factor in determining the increased risk of adult diseases in those who have poor fetal growth (Gluckman and Hanson, 2004).

Infants of smoking mothers were 126g lighter compared with non-smokers (95% CI, -198 to -54). On average, birthweight decreased 27g per cigarette smoked during pregnancy. Living in shared apartments, in crowded housing, and perceived stress were associated significantly with birthweight loss: -89g, -82g, and -61g, respectively. A positive association between maternal alcohol consumption and birthweight was found. Living with parents was associated positively with both birthweight and ponderal index. Infants whose fathers consumed more than 100ml/week of absolute alcohol were thinner at birth compared with those of non-drinking and moderate drinking fathers (Grjibovski et al, 2004).

Adjusting for confounders, pregravid oral contraceptive use, increased birth weight (mean difference, +207.3g) and placental weight (mean difference, +64.9g) compared with never use. This effect may be mediated through oestriol and progesterone (Mucci et al, 2004).

Maternal glucose levels correlate with fetal birth weights and a glucose level of 7.8mmol/l or more at the initial screening is predictive of macrosomia in Chinese gravidas regardless of gestational diabetes mellitus states (Yang et al, 2004).

It was found that prenatally known males had the highest mean birth weights as compared with females. It is proposed that these differences could be attributed to behavioral factors related to son preference (Al-Qutob et al, 2004).

## 6.1g: RATIOS DETERMINED

Ratio can be a powerful method of comparing two parameters, as long as one of the parameters can be determined to be normal. The most useful parameters are those that remain constant through some period, thus making them easier to remember. Ratios of the cranium are constant throughout the second and third trimesters. Many ratios become relatively constant after mid-pregnancy (DuBose, 1996).

No regional or Bangladeshi study was available on ratios, to compare with this study. Therefore comparisons were made with western studies only.

### 1. FEMUR LENGTH/ ABDOMINAL CIRCUMFERENCE RATIO:

First the observed values of the raw data was calculated, at 13w gestational age mean femur length/abdominal circumference (FL/AC) ratio was 0.17 ( $\pm 0.03$ ) (2SD) and at 40w it was 0.22 ( $\pm 0.02$ ) and then the estimated values after fitting the model were deduced. At 13w gestational age mean FL/AC was 0.20 ( $\pm 0.03$ ) and at 40w it was 0.24 ( $\pm 0.02$ ) with 95 % confidence interval (CI) of 0.22 to 0.26. The coefficient of multiple correlation  $R^2 = 0.454$ , with a  $p$  value of  $< .001$ .

The ratio in this study was more or less constant. At 13w it was 20 and at 40w it was 24. That is, from 13 to 40w the ratio was 20-24 or  $22 \pm 2$ . Residuals from model describing mean with 2SD were shown. The 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves derived by fitting the model were superimposed on the observed raw data of 1223 subjects. Regression analysis was used and the quadratic model showed a good fit to the data. In 5% of cases the values will be outside this range. That is, it was of 95% confidence range.

This was similar to a western study where, at 21w gestational age FL/AC was 0.20- 0.24 and at 40w it was 0.20- 0.24 (Hadlock et al, 1983), i.e. it was constant at  $22 \pm 2$ .

Femur length/abdominal circumference ratio is a time-independent body proportionality ratio. Fetuses with FL/AC values less than 10<sup>th</sup> centile and newborns with birth weights above 90<sup>th</sup> centile were classified as macrosomic, both prenatally and postnatally (Hadlock, et al, 1985). It was suggested that these parameters might better be applied in diabetic pregnancies where asymmetric macrosomia is more likely (Modanlou et al, 1982).

Sonographic criteria for large for gestational age (LGA) in Diabetic mothers: performance characteristics of Low FL/AC– Sensitivity is 58-79%, specificity 75-80%, Positive predictive value 68-83%, Negative predictive value 75-76% (Bracero et al, 1985).

## 2. HEAD CIRCUMFERENCE/ ABDOMINAL CIRCUMFERENCE RATIO:

Summary of the observed values was first given in a table. At 13w gestational age mean head circumference/abdominal circumference (HC/AC) was 1.31 ( $\pm 0.2$ ) (2SD) and at 40w it was 1.01 ( $\pm 0.08$ ). The next table gave estimated values after fitting the model. At 13w mean HC/AC was 1.25 ( $\pm 0.15$ ) and at 40w it was 0.99 ( $\pm 0.08$ ) with 95% CI of 0.91 to 1.07.  $R^2 = 0.598$ , ( $p < .001$ ). Residuals from model describing mean with 2SD was shown. The percentile curves were superimposed on the scatter plot. The linear model gave a good fit to the data.

The ratio in this study was high in the beginning and gradually decreased up to term. At 39w the ratio was 1:1, which meant that the two variables were equal at that gestational age. In one Caucasian study also the ratio was 1:1 at 39w (Deter et al, 1982), in another study at 38w (Hadlock, et al, 1982), in a third study the ratio was 1:1 at 37w (Campbell and Thomas, 1977) and at 36w in a fourth study (Patricia and Pearce, 1992). In this study the curve is similar to Campbell's study only mathematical smoothing was not done in their study (Campbell and Thomas, 1977).

In various studies conducted on western population, at 13w, gestational age HC/AC was 1.14- 1.31 and at 40w it was 0.87- 1.06 (Campbell and Thomas, 1977), at 13w HC/AC was 1.28 ( $\pm 0.12$ ) and at 40w it was 0.99 ( $\pm 0.12$ ) (Deter et al, 1982) and in a third study at 13w HC/AC was 1.21( $\pm 0.1$ ) and at 40w it was 0.98 ( $\pm 0.1$ ) (Hadlock et al, 1982).

Measurement of both HC and AC allow the independent assessment of head and abdominal growth which tends to differ under circumstances of vascular or placental failure such that head growth is maintained for some time while abdominal growth slows or even ceases. These changes cause the HC/AC ratio to rise making it possible to identify the truly growth retarded fetus from a single study. The sensitivity of the ratio for SFD babies is about 70% (Campbell and Thomas, 1977). HC/AC ratio can also be used to distinguish between symmetric and asymmetric IUGR (Chervenak et al, 1983). It is a highly sensitive predictor of IUGR (Crane and Kopta, 1979).

## 3. FEMUR LENGTH/ BIPARIETAL DIAMETER RATIO:

Summary of the observed values was given first; at 13w gestational age mean femur length/biparietal diameter (FL/BPD) was 0.49 ( $\pm 0.08$ ) (2SD) and at 40w it was 0.81 ( $\pm 0.06$ ). Then estimated values after fitting the model were given; at 13w gestational age mean FL/BPD was 0.50 ( $\pm 0.10$ ) and at 40w it was 0.83 ( $\pm 0.06$ ), with 95 % CI of 0.77 to 0.88. The

coefficient of multiple correlation  $R^2 = 0.736$ , ( $p < .001$ ). The ratio was low in the beginning and gradually increased till term. At 13w it was 5 and at 40 w it was 8. It was of 95% CI.

Assessment of goodness of fit of model for SD of fetal FL/BPD ratio was shown. Plot of standard deviation scores against gestational age, showed expected 2SD. Fitted curves describing 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles were superimposed on the scattered raw data. The model was prepared by Regression analysis and the cubic model showed a good fit.

In a Western study the ratio remained constant. At 23w gestational age FL/BPD ratio was 0.71- 0.87 and at 40w it was also 0.71- 0.87 (Hohler and Quetel, 1981). BPD/FL ratio should be  $0.79 \pm 0.03$  (Sanders, 1984). So the present study was similar to the western at term only.

#### 4. BIPARIETAL DIAMETER/ ABDOMINAL CIRCUMFERENCE RATIO:

Observed values of the raw data were presented first. At 13w gestational age mean biparietal diameter/abdominal circumference (BPD/AC) ratio was  $0.35 (\pm 0.05\text{mm})$  (2SD) and at 40w it was  $0.28 (\pm 0.03)$ . Then Estimated values were derived, at 13w mean BPD/AC was  $0.34\text{mm}$  ( $\pm 0.04\text{mm}$ ) and at 40w it was  $0.28 (\pm 0.02)$ , with 95% CI of 0.26 to 0.30.  $R^2 = 0.519$ , ( $p < .001$ ). The ratio in this study was slightly high in the beginning and gradually decreased till term. At 13w it was  $34 (\pm 4)$  and at 40w it was  $28 (\pm 2)$ . It covered 95% of the population.

Assessment of goodness of fit of model for SD of fetal BPD/AC ratio was done. The percentile curves derived by fitting the model were superimposed on the scatter diagram. The boundaries were at 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> centiles. By Regression analysis the quadratic model gave a good fit to the data.

Sonographic criteria for large for gestational age in Diabetic mothers: performance characteristics of low BPD/AC– Sensitivity is 83%, Specificity 60%, Positive predictive value 71%, Negative predictive value 75% (Bracero et al, 1985).

#### 5. FEMUR LENGTH/ HEAD CIRCUMFERENCE RATIO:

The present study first presented observed values of the raw data, at 13w gestational age mean femur length/head circumference (FL/HC) ratio was  $0.13 (\pm 0.03)$  (2SD) and at 40w it was  $0.22 (\pm 0.01)$ . Next, a model was fitted and estimated values were presented, and at 13w gestational age mean FL/HC was  $0.14 (\pm 0.03)$  and at 40w it was  $0.23 (\pm 0.02)$ , with 95 % CI of 0.21 to 0.25.  $R^2 = 0.776$ , ( $p < .001$ ). Plot of standard deviation scores against gestational age, showed expected 2SD. The 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentile curves derived by

fitting a model were superimposed on the scatter chart of the study population and the cubic model gave a good fit to the data. It covered 95% of the population.

The ratio in this study was low in the beginning and gradually increased till term. At 13w it was 14 ( $\pm 3$ ) and at 40w it was 23 ( $\pm 2$ ). In a Western study at 15w the ratio was 16 ( $\pm 2$ ) and at 40w, it was 21 ( $\pm 2$ ) (Hadlock et al, 1984). So it is more or less similar to the present study.

### **6.1h: ACCURACY OF ESTIMATED FETAL WEIGHT**

Accurate estimation of fetal weight is the goal of all Sonologists. In the current study fetal weight estimation was done by Hadlock and colleagues' formula based on HC, FL and AC (1985). The mean gestational age at delivery was 37.4 ( $\pm 2$ ) weeks and the mean time interval between ultrasound examination and delivery was 1.59 ( $\pm 1.15$ ) days. No adjustments were made for days. A good correlation was found between EFW using this formula and the actual birth weights. The correlation coefficient,  $r = 0.961$  ( $p = <.001$ ). The difference between ultrasonographic fetal weight estimation and actual birth weight (absolute percent error) was analyzed. The mean percentage error (PE) of EFW using this formula was  $-1.4 \pm 7.6\%$ . This was close to the PE of the better examiners of the study mentioned below (Kurmanavicius et al, 2004). EFW was underestimated in this study, and Meyer also found that predicted fetal weights were significantly underestimated with each of the formulas (Meyer et al, 1995).

In the present study mean EFW was 2753 ( $\pm 716$ )g, which was not significantly different from the mean birth weight of 2818 ( $\pm 783$ )g and SD was 7.6% nearly same as reported by Hadlock, on normal population, 7.3% (Hadlock et al, 1985). The graph shows that the two lines completely overlap at about 3000g, which is the 50<sup>th</sup> percentile weight in this study. The further the EFW is from this value the less it coincides with the birth weight. This indicates that the EFW is most accurate at 3000g or the 50th centile weight in our population.

In another study here mean EFW was 3.07 ( $\pm 0.47$ )kg by BPD and AC formula of Shepard. Birth weights ranged from 2.2kg to 4.1kg and mean was 3.15 ( $\pm 0.43$ ) kg. The mean EFW was 0.08kg less than mean birth weight. The percentage error was -2.5%. This study concluded that USG is a reliable tool to estimate fetal weight (Quddus and Khatun, 2001).

With Hadlock and Campbell's formulae and Shepard and Merz formulae the percent errors of EFW varied from  $-4.0 \pm 8.5\%$  to  $1.3 \pm 8.5\%$  between examiners (Kurmanavicius et al, 2004).



To compare the accuracy of eight sonographic formulae for predicting fetal birth weight at term in a multiethnic population, pregnant women at term were included. Patients were from the Indian subcontinent, from Africa, from the Arabian Peninsula and from other ethnic groups. The mean absolute error ranged from a minimum of 0.3% ( $\pm 11.3$ ) for Hadlock (BPD, HC, AC, FL) to a maximum of 37.5% ( $\pm 10.0$ ) for Warsof (FL only). The correlation of EFW with birth weight ranged from a minimum of  $r = 0.09$  with Warsof (FL) to a maximum of  $r = 0.77$  with Shepard and Warsof (BPD, AC) and Hadlock (BPD, HC, AC, FL). The combination of AC with BPD measurements rather than FL achieves a high level of accuracy (Mirghani et al, 2005).

A good correlation was found between EFW using the BPD/AC formula and the actual birth weight ( $r = 0.96$ ), between EFW by the FL/AC formula and the birth weight ( $r = 0.95$ ), and between EFW using BPD/AC/FL formula and actual birth weight ( $r = 0.96$ ). The mean percentage error of EFW using the BPD/AC formula was  $-0.99\%$  ( $\pm 8.17\%$ ); for the FL/AC,  $-3.82\%$  ( $\pm 9.13\%$ ); and for the BPD/AC/FL,  $2.43$  ( $\pm 8.29\%$ ) (Yarkoni et al, 1986).

With Hadlock's method, there was a good correlation between EFW and birth weights of small infants. Mean EFW was  $736$  ( $\pm 186$ )g, which was not significantly different from the mean birth weight of  $742$  ( $\pm 173$ )g. Mean EFW error was  $0.8$  ( $\pm 12.7$ )%. With Scott's method, mean EFW was  $780$  ( $\pm 185$ )g, which was significantly higher than the mean birth weight ( $p < 0.001$ ), the mean EFW error was  $5.7$  ( $\pm 12.5$ )%. SD of the EFW error of  $12.7\%$  on high risk population was markedly larger than the  $7.3\%$  reported by Hadlock on normal population (Hadlock, et al, 1985). The standard deviations of the mean EFW errors were similar for Hadlock's and Scott's methods on high-risk population with values of  $12.7$  and  $12.5\%$ , respectively (Kaaij et al, 1999).

Clinical estimation of birth weight in early labor is as accurate as routine ultrasonic estimation obtained in the preceding week. In the lower range of birth-weight ( $< 2500$ g), ultrasonic estimation is more accurate; in the  $2500$ - $4000$ g range, clinical estimation is more accurate. In the higher range of birth weight ( $> 4000$ g), both methods have similar accuracy (Sherman et al, 1998).

The accuracy of intrapartum ultrasonographic fetal weight estimation was similar among diabetic and non-diabetic women. Birth weights  $\geq 4500$  gm rather than maternal diabetes seem to be associated with less accurate ultrasonographic fetal weight estimates. The mean

(SD) absolute percent error of fetal weight estimates among subjects with macrosomic fetuses (birth weight  $\geq 4500$  gm) was significantly greater than that observed in fetuses with birth weights  $< 4500$  gm ( $12.6 \pm 8.4\%$  vs  $8.4 \pm 6.5\%$ ,  $p = 0.001$ ) (Alsulyman et al, 1997).

Retrospective analysis was undertaken of ultrasound data of all fetuses who underwent an examination within one week of delivery. It was concluded that EFW is as accurate in twins and triplets as it is in singletons (Lynch et al, 1995). When more than one ultrasound estimation of fetal weight are available, prediction of birth weight in relation of gestational age should be based on the last ultrasound examination only (Larsen et al, 1995).

The accuracy of sonographic fetal weight estimation was independent of amniotic fluid index (AFI) across all gestational ages and birth weights. Each of the five formulas had similar error percentages, and no significant differences were detected. Predicted fetal weight was significantly underestimated with each of the formulas, a finding that was also independent of birth weight and AFI. Ultrasonography can be therefore used reliably to estimate fetal weight in patients with altered amniotic fluid volumes (Meyer et al, 1995).

In a study in Thailand, the accuracy of clinical and US estimation of fetal weight was compared. It was found that accuracy of clinical estimation of fetal weight by second year resident physicians was comparable to that of US estimation. However, when the clinical estimate of fetal weight is less than 2500g, ultrasound examination should be performed for more accurate results. Careful attention should be paid to infants with birth weight of more than 4000g since no method can correctly estimate the weight (Titapant et al, 2001).

Thigh volume measurement using three cross-sectional images of femur by 3D ultrasound was simple, and there was better accuracy ( $R^2 = 0.921$ ,  $p < .001$ ) with this method than with 2D ultrasound methods (BPD, FL and AC), for predicting fetal weight during the third trimester of pregnancy (Song et al, 2000).

Ultrasound based estimations of fetal weight showed a correlation rate of  $R^2 = 0.77$  with the actual birth weights, while volume determinations based on magnetic resonance imaging (MRI) showed a significantly better correlation rate of  $R^2 = 0.95$ . Diabetic women did not differ from the normal pregnancy group with regard to birth weight or the accuracy of weight estimations. High resolution MRI combined with semi-automatic segmentation software was found to be accurate in determining fetal volume and, consequently, better than conventional ultrasound in estimating fetal weight. The use of MRI in fetal weight estimation may be

recommended for clinical situations where an accurate weight estimate is considered essential (Uotila et al, 2000).

Ultrasound fetal weight estimation is a key element of obstetric management in pregnancy complicated with diabetes. Ultrasound estimates based on formulae utilizing AC measurements only, appear more accurate in this group of women. However they are still associated with errors of up to 25% of true birth weight (Farrell et al, 2004).

Gender-related fetal weight calculation allows optimized prediction of fetal weight at birth. Inclusion criteria were a singleton live fetus, gestational age above 25 weeks, birth weight between 1000g and 4500g and fetal biometry within 8 days of delivery (Schild et al, 2004).

## **6.2: LIMITATIONS**

The sample size could not be further increased because of time constraint, so in a couple of early weeks the data of at least 30 cases in each week, could not be attained. Another limitation was that this study was conducted in only the capital city of Dhaka, as it was conducted by one person only.

Fetal biometric studies and nomograms were prepared in the western countries about two decades before this study so most of the references are of that time, because of historical importance. Recent studies in the west are not on the normal biometry but affects of different things on it e.g. drugs, alcohol, smoking, geographic location, environment, ethnicity, etc.

More comparisons of fetal biometry, with regional studies could not be made as those could not be obtained by browsing Medline or internet, at the time of this research work and also those were not found in the libraries of BIRDEM, BSMMU, BCPS, ICDDR, Dhaka University and National library that were visited and searched. Reason being either the neighboring countries have not conducted research in this field yet or those were not published in international journals.

The weighing machine for the new born infants used in the hospital was an analogue machine. But the EFW was measured digitally by the ultrasound machine. Correlation between the two would have been more accurate if the neonatal birth weights could also be taken by a digital machine.

## CHAPTER 7

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### *SUMMARY AND CONCLUSION*

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7.1: SUMMARY	...	...	122
7.2: CONCLUSION	...	...	122
7.3: RECOMMENDATIONS	...	...	123

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## SUMMARY AND CONCLUSION

### 7.1: SUMMARY

Ultrasonography has played a revolutionary role in the management of pregnant patients. Fetal biometry is crucial for monitoring fetal well being. To make fetal growth assessment more accurate and reliable by ultrasonography we need charts generated by studies on Bangladeshi population. This aim and objective has been attained in this study.

This study was conducted in BIRDEM. Ultrasonography scans were performed by a 3.5 MHz curvilinear transducer. Standard methods were used to measure fetal biparietal diameter (BPD), head circumference (HC), femur length (FL), and abdominal circumference (AC). Fetal weight was estimated from HC, FL and AC by using Hadlock et al's formula (1985).

Growth profile tables and graphs of fetal BPD, HC, FL, AC and estimated fetal weight (EFW) showing 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles were obtained from a cross-sectional study sample of 1223 subjects. Mean, two standard deviations (2SD) and 95% confidence interval were derived after fitting models. Tables and graphs of mean, 2SD and percentiles of the ratios of these parameters were also prepared. The ratios studied were FL/AC, HC/AC, FL/BPD, BPD/AC and FL/HC. Accuracy chart and graph of the EFW were prepared from the birth weights of 73 neonates included in the study for this purpose.

### 7.2: CONCLUSION

Prenatal ultrasound studies can enable accurate determination of the boundaries of normal fetal growth. These nomograms are unique for Bangladeshi population and will therefore help the sonologists and obstetricians to accurately monitor the fetal size and growth. Growth deviations as well as fetal skeletal anomalies can now be precisely diagnosed so that the fetus

can be taken care of in the best possible way. This will be of much benefit as a healthy, normal, well grown, fetus means a healthy, intelligent, well grown adult.

### **7.3: RECOMMENDATIONS**

Though the sample size used in this study is enough for a good result, still the sample size can be further increased, but it is known that after a point further increase in sample size does not improve result. A multi-centre based study can be conducted with data from all over Bangladesh, to prepare a National standard of fetal nomograms.

If the computer expertise is available in Bangladesh the nomograms derived in this study can be installed into the ultrasound machine's software in the clinics and hospitals. This way the tables and graphs can promptly be used while scanning the patients. The growth percentile of different parameters can be acquired and accurate report based on these population specific nomograms can be given to the patient, to improve the growth rate of fetus with growth deviation.

Normal predicted values and 95% confidence limits for fetal parameters, BPD, HC, FL, AC and EFW, were given in this study. Proper use of these data will lead to earlier recognition of abnormal growth patterns such as growth restriction and growth acceleration, as well as fetal skeletal anomalies from the nomograms of live fetal ratios presented here. In view of the distribution of the normal data on these curves, 3<sup>rd</sup> and 97<sup>th</sup> percentile boundaries can be used as confidence limits for normal growth, as these cover 95% of the population. It is imperative that gestational age be known and verified by an early ultrasound before these data are used to diagnose abnormal fetal growth. Minor errors in assignment of fetal age may lead to false diagnosis of altered fetal growth and may result in errors of management.

These growth curves presented herein should also be applicable to populations of nearby regions of similar racial and socioeconomic origins, till they prepare their own nomograms. These nomograms and others like these of different investigators of Bangladesh and the neighboring and developing countries should be published in the Medline and internet so that these can be accessed easily in different research and clinical works. Doctors in western countries can also avail it when needed for their south Asian patients. This will then be of benefit to the maximum number of people, which is the aim of all research work.

## CHAPTER 8

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### *REFERENCES*

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... .. 124 -141

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## *APPENDICES*

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QUESTIONNAIRE	...	...	xi, xii
CONSENT FORM	...	...	xiii
OBST REPORT SHEET/ CASE RECORD FORMS	...	...	xiv
PHOTOGRAPHIC PLATES OF U/S IMAGES	...	...	xv-xvi
Plane for measurement of BPD (Image)	...	...	xv
Plane for measurement of HC (Image)	...	...	xv
Plane for measurement of FL (Image)	...	...	xvi
Plane for measurement of AC (Image)	...	...	xvi
OPERATIONAL DEFINITIONS	...	...	xvii
STATISTICAL PROCEDURE	...	...	xviii
FORMULAE	...	...	xix-xx

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# GROWTH PROFILE OF FETUS IN OUR POPULATION.

Supervisors: Prof. T. A. Chowdhury & Prof. Akhtaruddin Ahmed.

Investigator: Dr. Sabrina Quddus.

## Questionnaire Form

ID No:

\* For Yes = ✓

\* For No = ✗

Name: .....

Age:

Address:.....

.....

Location:    Urban                       Rural

SOCIOECONOMIC STRATA:

                  Upper                       Middle                       Lower

PRESENTING COMPLAINTS:

Antenatal Checkup:

Menstrual History:            Regular :     Irregular :

LNMP .....            Sure :     Not sure :

History of complicated pregnancy:

Lactating at the time of conception:

Para:                                      Primi :     Multi :

Any complication of pregnancy: Hypertension:  Diabetes :

Per vaginal bleeding:  Leaking membrane:

History of congenitally deformed baby:

DRUG HISTORY: Oral Contraceptive:  When stopped:

Fertility Medication :  Any other drug :

Smoking habit / Tobacco chewing:

#### EXAMINATION:

B.P:

Height:

Weight in 1<sup>st</sup> trimester : ..... BMI : .....

Heart : NAD

Lungs: NAD

#### INVESTIGATIONS

1. Blood for TC, DC, ESR, Hb%, Grouping and Rh factor.

2. Blood Sugar, VDRL.

3. Urine R/E.

4. Ultrasonography:

- a) Biparietal diameter
- b) Head circumference
- c) Femoral length
- d) Abdominal circumference
- e) Estimated fetal weight

-----  
Dr. Sabrina Quddus.

## CONSENT FORM

I, Mrs..... hereby give my well informed consent to participate in the study conducted by Dr. Sabrina Quddus, in which my fetus (baby in my womb) will be scanned by Ultrasonography. I fully understand that implication of the study may be useful for the benefit of other patients.

I am convinced that during participation in the study, I shall not be exposed to any serious health hazards. If any injury does occur I will be treated properly. My privacy and confidentiality will be safeguarded and my anonymity will be protected. I understand that I can withdraw from the study at any time I wish.

Signature of the Investigator

Signature of the Subject

Date:.....

## অনুমতি পত্র

আমি, ..... সম্পূর্ণরূপে অবগত হইয়া বজ্ঞানে ডাঃ সাবরিনা কুদ্দুস কর্তৃক পরীক্ষা ও গবেষণার জন্য অনুমতি প্রদান করিতেছি। এই গবেষণায় আমার গর্ভস্থ শিশুর আলট্রাসোনোগ্রাফী করা হইবে। এই গবেষণায় প্রাপ্ত তথ্যাদি দ্বারা অন্যদের উপকার হইতে পারে।

আমি আশ্বস্ত হইলাম যে এই পরীক্ষায় আমার ও আমার গর্ভস্থ শিশুর কোন ক্ষতিব্দ সন্ভাবনা নাই। তবে কোন দুর্ঘটনা ঘটিলে হাসপাতাল কর্তৃপক্ষ উপযুক্ত চিকিৎসার ব্যবস্থা করিবে। এই পরীক্ষা ও গবেষণায় আমার অংশগ্রহণ ও এ বিষয়ের গোপনীয়তা রক্ষা করা হইবে। গবেষণা থেকে আমার অংশ গ্রহণ যেচছায় যে কোন সময় প্রত্যাহার করার সুযোগ আছে।

গবেষকের স্বাক্ষর

রোগীর / স্বাক্ষর বা টিপ সহি

**OBS. ULTRASOUND REPORT**

Patient's Name ..... Age ..... Sex .....

Refd. by Prof./Dr. ....

Indication for U/S. .... L. M. P. .... G A by L. M. P. ....

Gestation ..... Single ..... Multiple  
Presentation ..... Ceph ..... Breech  
Lie ..... Long ..... Oblique ..... Transverse  
Foetal Movement :  
Cardiac Activity ..... Present ..... Absent  
Foetal Measurements :  
B.P.D.  
F.L.  
A. C.  
H.C.  
C. R. L.  
Estimated Foetal Age :  
Placental Location :  
Grade :  
Uterus & Adnexa :  
Foetal Anatomy :  
Amniotic Fluid Volume :  
..... Normal ..... Increased ..... Decreased  
Estimated Foetal Weight :  
Foetal Growth :  
**COMMENTS**

Presentation ..... Ceph ..... Breech  
Lie ..... Long ..... Oblique ..... Transverse  
Foetal Movement :  
Cardiac Activity ..... Present ..... Absent  
Foetal Measurements :  
B.P.D.  
F.L.  
A. C.  
H.C.  
C. R. L.  
Estimated Foetal Age :  
Placental Location :  
Grade :  
Uterus & Adnexa :  
Foetal Anatomy :  
Amniotic Fluid Volume :  
..... Normal ..... Increased ..... Decreased  
Estimated Foetal Weight :  
Foetal Growth :  
**COMMENTS**

Date : .....

Date : .....

Signature



Image of the plane for measurement of fetal biparietal diameter  
Figure 2



Image of the plane for measurement of fetal head circumference  
Figure 3



Image of the plane for measurement of fetal femur length  
Figure 4



Image of the plane for measurement of fetal abdominal circumference  
Figure 5



## OPERATIONAL DEFINITIONS

**Gestational age (menstrual age)** = Conceptual age + 2 weeks.

**Dolichocephaly:** The head is shortened in the transverse plane, biparietal diameter (BPD) and elongated in antero-posterior (fronto-occipital diameter) plane.

**Brachycephaly:** The head is elongated in the transverse plane and shortened in antero-posterior diameter.

**Ratio** = numerator/ denominator. **Percentage** = 100x (numerator/ denominator)

**Small for date (SFD) or small for gestational age (SGA):** Are babies with birth weights below the 10<sup>th</sup> percentile for the gestational age. Ideally, the chart used to decide that they are small should be derived from the population being studied.

**Appropriate for gestational age:** Are babies with birth weights between the 10<sup>th</sup> and the 90<sup>th</sup> percentile for gestational age.

**Intrauterine growth retardation/ restriction (IUGR):** The term is applied to a fetus whose growth velocity is less than expected due to some pathological process. Not all the SFD fetuses are IUGR. Most cases of symmetrical SFD have no demonstrable cause and represent the lower end of the normal range.

**Low birth weight infants (LBW):** Are those that are born with a birth weight of under 2.5 kg. This includes both preterm and small for date. This term is still used in the third world countries where many patients are unsure of their LMP. In countries where routine ultrasound confirmation of gestational age is practiced this term is replaced by SFD or SGA.

**Macrosomia:** Has classically been defined as a birth weight of 4000g or greater or above the 90<sup>th</sup> percentile for its estimated gestational age. With respect to delivery, however, any fetus that is too large for the pelvis through which it must pass is macrosomic.

**Large for gestational age (LGA):** Is defined as a weight above the 90<sup>th</sup> percentile for gestational age.

**The cephalic index:** Calculated from the BPD and the fronto-occipital diameter (FOD) measured from the outer edge of the calvaria to the outer edge of the calvaria:

Cephalic index (CI) = BPD/FOD X 100.

**Circumference** =  $\pi \sqrt{[(d_1^2 + d_2^2)/ 2]}$ . Where  $d_1$  and  $d_2$  are the two maximum diameters of the ellipse.

## STATISTICAL PROCEDURE AND FORMULAE

Both nonparametric and parametric methods can be used to calculate reference centiles. The nonparametric approach involves calculating, say, the observed 5<sup>th</sup> and 95<sup>th</sup> centiles at each week of gestation. Lines joining these values will not be smooth, although smooth curves can be obtained. This approach requires a large number of observations (several hundred) at each week of gestation in order to get reasonable estimate of extreme centiles. This is therefore not a suitable method for the derivation of fetal size charts. In the most common parametric method, the mean and standard deviation (SD) at each gestational age are estimated, and the 5<sup>th</sup> and 95<sup>th</sup> centiles are calculated as mean  $\pm$  1.645 SD, the value of 1.645 coming from the theoretical normal distribution. Other centiles are calculated in a similar way. The mean is estimated by polynomial regression, usually linear or quadratic/cubic. This approach is based on the strong assumption that at each gestational age the data comes from a population with a normal distribution (Altman and Chitty, 1994).

Nonparametric approach was used to calculate the observed 3<sup>rd</sup>, 10<sup>th</sup>, 50<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles and the mean and 2 standard deviations (2SD) at each week of gestation for all five parameters (BPD, HC, FL, AC and EFW) and their ratios. Lines joining these results were not smooth. So to construct fetal size charts with smooth lines parametric method was also used in this study. With the SPSS program in computer software, the mean, 2SD and percentiles were estimated at each gestational age, of the 5 parameters and their ratios by fitting polynomial regression, linear or quadratic/cubic models to them. The SD was estimated by linear models. After the required percentiles were calculated they were superimposed on a scatter diagram of the observations as a final check of the fit. The coefficient of multiple correlations ( $R^2$ ) was used to choose the models. Assessment of goodness of fit of models for SD of fetal measurements and their ratios were shown by plots of standard deviation scores against gestational age, showing expected 2SD. Estimated fetal weight was determined by Hadlock, et al's formula (1985) based on HC, FL and AC and its accuracy was assessed by Student's *t*-test.

## FORMULAE

The regression equations used to generate the charts and tables are as follows, where  $w$  is exact gestational age in weeks:

### 1. BIPARIETAL DIAMETER

#### Fitted model of biparietal diameter (BPD)

$$\text{Mean} = -10.707 + 1.8240w + 0.0865w^2 - 0.0017w^3$$

$$\text{SD} = 2.4434 + 0.1271w$$

$$R^2 = 0.977 (p < 0.001)$$

### 2. HEAD CIRCUMFERENCE

#### Fitted model of head Circumference (HC)

$$\text{Mean} = -63.89 + 9.6667w + 0.2141w^2 - 0.00517w^3$$

$$\text{SD} = 5.6845 + 0.4850w$$

$$R^2 = 0.981 (p < 0.001)$$

### 3. FEMUR LENGTH

#### Fitted model of femur length (FL)

$$\text{Mean} = -42.083 + 4.5764w - 0.0424w^2$$

$$\text{SD} = 2.1964 + 0.09w$$

$$R^2 = 0.982 (p < 0.001)$$

### 4. ABDOMINAL CIRCUMFERENCE

#### Fitted model of abdominal circumference (AC)

$$\text{Mean} = -41.694 + 5.9220w + 0.2572w^2 - 0.0043w^3$$

$$\text{SD} = -4.7877 + 1.0051w$$

$$R^2 = 0.970 (p < 0.001)$$

### 5. ESTIMATED FETAL WEIGHT

#### Fitted model of estimated fetal weight (EFW)

$$\text{Log (weight)}g = 0.2467 + 0.1448w - 0.00159w^2$$

$$\text{SD} = 0.4782 + 0.0598w$$

$$R^2 = 0.988 (p < 0.001)$$

**6. FL/AC RATIO**

**Fitted model of FL/AC**

$$\text{Mean} = 0.0747 + 0.0121w - 0.0002w^2$$

$$\text{SD} = 0.0407 - .0005w$$

$$R^2 = 0.454 (p < 0.001)$$

**7. HC/AC RATIO**

**Fitted model of HC/AC**

$$\text{Mean} = 1.3828 - 0.0093w$$

$$\text{SD} = 0.1841 - 0.0025w$$

$$R^2 = 0.598 (p < 0.001)$$

**8. FL/BPD RATIO**

**Fitted model of FL/BPD**

$$\text{Mean} = - 0.5818 + 0.128w - 0.0041w^2 + 0.0000445w^3$$

$$\text{SD} = 0.1217 - 0.0015 w$$

$$R^2 = 0.736 (p < 0.001)$$

**9. BPD/AC RATIO**

**Fitted model of BPD/AC**

$$\text{Mean} = - 0.368 - 0.0022w - 0.000002w^2$$

$$\text{SD} = 0.0487 - 0.0006w$$

$$R^2 = 0.519 (p < 0.001)$$

**10. FL/HC RATIO**

**Fitted model of FL/ HC**

$$\text{Mean} = - 0.1399 + 0.0325w - 0.001w^2 + 0.0000105w^3$$

$$\text{SD} = 0.0353 - 0.0005w$$

$$R^2 = 0.776 (p < 0.001)$$

**11. ESTIMATED FETAL WEIGHT ( g ) =**

$$10 \exp (1.326 - 0.00326 \times \text{AC} \times \text{FL} + 0.0107 \times \text{HC} + 0.0438 \times \text{AC} + 0.158 \times \text{FL}).$$

The regression line in Graph 23, for accuracy of EFW is represented by

$$\text{EFW} = 0.8796 \times \text{BW} = 274.86\text{g}, \quad R^2 = 0.9243 (p < 0.001).$$

**12. Percentage error of EFW =  $\frac{\text{Estimated fetal weight} - \text{birth weight}}{\text{Birth weight}} \times 100$**

Birth weight