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COMPARISON OF PREDICTIVE ACCURACY OF TRANSCEREBELLAR DIAMETER TO ABDOMINAL CIRCUMFERENCE RATIO (TCD/AC) VERSUS HEAD CIRCUMFERENCE TO ABDOMINAL CIRCUMFERENCE RATIO (HC/AC) IN INTRAUTERINE GROWTH RESTRICTION ON ULTRASONOGRAPHY

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ABSTRACT

Background: Intrauterine growth restriction (IUGR) is considered as serious complication relating to the female reproductive system. Condition if unattended may lead to the infertility in the group of patients. Primary aim of the current study is to compare the predictive accuracy in between trans-cerebellar diameter/abdominal circumference and head circumference/ abdominal circumference in patients with intrauterine growth restriction (IUGR). **Methodology:** For the present study two hundred (n=200) pregnant females with gestational age between 18-35 weeks and no other congenital anomaly and hundred (n=100) controls were substituted. Samples were obtained after getting informed consent at Bahria International Hospital Lahore-Pakistan. Ultra-sonographic determination of BPD, FL, TCD, AC, HC and EFW were carried out and were then subjected to statistical analysis for the findings. **Results:** Results of the study suggest ratio of

TCD/AC as the most accurate and significant measure in the early determination of gestational age and IUGR in patients. ROC curve findings also suggest maximum area under curve (AUC) such as, (0.911) in case of TCD/AC as compared to HC/AC where it restricts to (0.652). Furthermore, specificity and sensitivity in TCD/AC remains to (88%, 69%) respectively which is greater than that to compared with all other gynecological measures performed. Findings show that the best cut-off value of TCD/AC ratio is 14.3%. **Conclusion:** On the basis of findings of all the analytical and gynaelogical measures performed it concludes ratioof TCD/AC performed over the pregnant females was most accurate compared to HC/AC, BPD, EFW etc. Thus, the findings help to state that the said ratio is far more helpful in the determination of IUGR in early trimesters of pregnancies.

Keywords: Intrauterine growth restriction (IUGR), Trans-cerebellar Diameter (TCD), Femur Length (FL), Biparietal Diameter (BPD)

INTRODUCTION

Intrauterine growth restriction (IUGR) condition is believed to affect a large number of population worldwide especially in developing countries **[1]**. Fetuses suffering from IUGR are at higher risk to develop conditions such as cardiovascular diseases (CVDs), diabetes and hypertension as compared healthy fetuses **[2]**. IUGR is placenta-based vascular disorder that starts with the abnormal tertiary villous vessels and leads to the fetal multi-vessel cardiovascular manifestations. The condition can be well understood with the help of Doppler ultrasound examination that includes study of different vessels i.e., maternal uterine arteries and fetal umbilical arteries for placenta, percordial veins for the cardiac effects of placental dysfunction and middle cerebral artery (MCA) for the preferential brain perfusion **[3]**. Gestation period can be defined as the time period the infant has spent fetus or precisely it can be termed as the measurement of weeks during the pregnancy of females. Time period is calculated from the last menstrual period (LMP) to the date of examination. Time period for the full term pregnancy can last up to 42 weeks. During the period of gestation fetal growth is monitored that helps in planning of delivery and overcoming the complications that one can come across during the pregnancy **[4]**. Accurate assessments of the gestational age is another very crucial identifier of preterm labor and for post-dated deliveries. Standard method for such determinations includes antenatal

ultrasound assessment based upon the different fetal parameters. Gestational age can be measured and can be compared with the reference ranges to look for the fetal growth. The accuracy in the measurement of the gestational age decreases as the fetal age advances from second to third trimester. Accuracy in the measurement of the fetal age is thus maximum in the first trimester **[4]**. One of the most common problem number of obstetricians go through the medical practice includes assessment of fetal maturity for the persisting and prolonging problems in pregnancy. Complications such as, pregnancy induced hypertension (PIH), diabetes, fetal distress and Rh incompatibility may lead to the development of intrauterine growth restriction (IUGR). Methods employed for the prediction of gestational age and expected delivery date includes clinical examination, history of menstrual cycle, perception of fetal movement and calculation of biparietal diameter (BPD), femur length (FL), LMP, EDD etc. Apart from the fact that history of menstrual cycle and LMP is quite misleading in the determination of gestational age. Ultrasonography (USG) helps in the evaluation of the duration of pregnancy based on the measurement of fetus where size is the indicator of menstrual age. Various parameters that are employed for such determination includes biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femur length (FL) **[5]**. Whereas, increased variability in the parameters is observed with increasing gestational age. Measurement of another parameter like transverse cerebellar diameter (TCD) is becoming more accurate in the assessment of gestational age especially in the cases where the last menstrual cycle is not known. Thus, it is kept essential to determine the fetal growth restriction antenatally as it remains associated with the increased perinatal mortality and morbidity. Similarly, biparietal diameter (BPD), head circumference/ abdominal circumference (HC/AC) ratio is determined for the fetal maturity if the exact gestational age is known. TCD emerges to be one effective parameter in the fetal growth retardation. The IUGR fetuses demonstrate a temporally related, consistent pattern of abnormal Doppler velocimetry changes in a number of vessels for the weeks preceding delivery. Worsening of the pattern of flow in the UA, identified by the AEDF (absent end diastolic flow), and a persistent dilatation of the MCA is usually observed. These represent an early stage of progressive placental disease. Abnormal central

circulatory changes consisting of changes in the ductusvenosus wave form and in the outflow tract of the aorta and pulmonary artery are also observed but are seen in late stages of uteroplacental insufficiency **[6]**.

MATERIALS AND METHODS

Current study substituted two hundred (n=200) pregnant females with gestational age between 18-35 weeks and no other congenital anomaly and hundred (n=100) controls were substituted. Samples were obtained after getting informed consent at Jinnah Hospital Lahore-Pakistan in the period of 9 months.

STUDY DESIGN

It is a Cross-sectional analytical study.

INCLUSION CRITERIA

- Gestational age between 18-35 weeks determined by first trimester scan
- Pregnant females with singleton pregnancy
- No congenital anomaly
- Favourable lie which facilitates posterior fossa visualization and TCD measurement

EXCLUSION CRITERIA

- Females with gestational diabetes mellitus
- Mothers with history of fever in first trimester
- Females having history of irregular cycles
- Females having history of preterm birth

STATISTICAL ANALYSIS

Descriptive statistics, Independent T test and ROC curve of the samples were performed to find out the specificity and sensitivity of the said markers with the help of SPSS v.21. Results of the findings were stated as Mean±S.D where $p<0.05$ shows the significance of the results. While specificity and sensitivity was explained in the terms of area under curve (AUC). Greater the AUC relates higher the specificity and sensitivity of the performed parameters.

SCANNING TECHNIQUE

Xario-100 ultrasound machine will be used for Trans abdominal obstetrical scan using convex probe (3.5 MHz), ultrasound will be done in a dimly lit room at a comfortable temperature (22^{o}c – 25^{o}c). Informed consent is obtained from patient and the patient is requested to lie supine on the examination table and her ultrasound is done. Following USG parameters were determined BPD, FL, TCD, AC, HC and EFW and were then subjected to statistical analysis for the findings.

RESULTS

Results of the following study show significant changes in the gynaecological

parameters that were estimated in the group of controls and females with IUGR. Sonographic measures i.e., BPD, FL, HC, AC, TCD, TCD/AC and HC/AC of the samples show TCD/AC as one of the significant measure in the determination of IUGR. Results of the findings suggest the area under curve (AUC) for the performed variables by the determination of ROC curve. Findings suggest TCD/AC to be the most specific and sensitive marker for the determination of IUGR. TCD/AC shows the AUC of 0.921 that remains the maximum as compared to all other performed parameters [TCD (0.684), AC (0.662), HC (0.755), HC/AC (0.701), EFW (0.687), FL (0.741), BPD (0.691) and GA (0.70)] as shown in table 01. Area under curve for the transverse cerebellar diameter (TCD) is also quite significant which is almost to 0.684. Rest of the gynecological variables have expressed the significance in determining the IUGR in early trimesters whereas, they may fail to signify the mainstream causes of the condition while, ratio of TCD/AC has served as prime significant marker in the determination of IUGR in early trimesters of pregnant females and therefore, the accuracy of the said ratio withstands over all the other markers that have been served to determine the condition with the help of ultrasonography (USG).Mean level of femur length (FL) in the controls were observed as (57.17±11 mm) that observed to be significantly decreased in the groups of patients with IUGR as (44.41±9.7 mm). Levels of transverse cerebellar diameter (TCD) the patients with IUGR (24.12±2.31 mm) as compared to healthy controls (32.31±6.41 mm). Current findings demonstrate significant differences in the ratio of TCD/AC as ratio remained (14.77±1.02) in controls while in the patients were (11.12±0.98). The mean biparietal diameter of IUGR cases is 59.81±12.14 mm which is lower as compared to 67.66±11.8 mm. The mean value of head circumference and abdominal circumference were shown to be decreased in IUGR patients [HC (231.7±37 mm); AC (221.12±44 mm)] in comparison with the control group [HC (270.95±31 mm); AC (255±8.7 mm)] as shown in table 02. The estimated fetal weight (EFW) of IUGR patients mean value is 613.96±7.41 g which is reduced as compared to non-IUGR patients mean value 690.07±4.71 g. Most of the pregnancies GA lie between 34 to 36th week.

Table 01: Area Under The Curve Obtained By The Roc Curve Analysis Of The Parameters

AREA UNDER THE CURVE	
TEST RESULT VARIABLE(S)	**AREA**
TCDmm	**0.684**
ACmm	**0.662**
HCmm	**0.755**
TCD/AC	**0.921**
HC/AC	**0.701**
EFWgrams	**0.687**
FLmm	**0.741**
BPDmm	**0.691**
Gestational Age	**0.70**

Table 02: Gynaecological Parameters Obtained In The Group Of Pregnant Females

Sr.#	Parameters	IUGR	Non-IUGR	P value
1.	**Trans-cerebellar Diameter**	**24.12±2.31**	**32.31±6.41**	**0.035**
2.	**Biparietal Diameter**	**59.81±12.14**	**67.66±11.8**	**0.022**
3.	**Femur Length**	**44.41±9.7**	**57.17±11**	**0.041**
4.	**Abdominal Circumference**	**221.12±44**	**255±8.7**	**0.033**
5.	**Head Circumference**	**231.7±37**	**270.95±31**	**0.034**
6.	**TCD/AC**	**11.12±0.98**	**14.77±1.02**	**0.044**
7.	**HC/AC**	**1.34±0.06**	**1.27±0.05**	**0.038**
8.	**EFW**	**613.96±7.41**	**690.07±4.71**	**0.040**

DISCUSSION

Intrauterine growth restriction is a major neonatal health issue. The term IUGR generally should be assigned only to those infants with birth weight or birth length below the 10^{th} percentile for GA with a pathologic restriction of fetal growth. Infants with intrauterine Growth Restriction (IUGR) or Small for gestational age (SGA) are at increased risk of perinatal morbidity and mortality. IUGR is a type of fetal growth which is less than the growth potential of specific infants as per the race and gender of the fetus. IUGR is a deprived fetal growth pattern and it is the outcome of innate reduced growth potential or due to multiple adverse effects on the fetus. In medical literature, IUGR and small for gestational age (SGA) usually use correspondently but slight difference exists between them. IUGR is a common cause of perinatal morbidity and impaired growth during childhood. SGA are neonates whose birth weight is less than the 10^{th} percentile for gestational age as per the population growth charts. SGA can be moderate or severe if it is moderate than birth weight would be from 3^{rd} or 10^{th} percentile and if it is severe then birth weight would be less than the 3^{rd} percentile. IUGR or SGA are at increased risk of perinatal morbidity and mortality. The term IUGR usually implies to neonates born with clinical features of malnutrition and in-utero growth retardation, irrespective of their birth weight percentile. It is important to be noted here that neonates with birth weight less than the 10^{th} percentile

will be called as SGA but not an IUGR unless there are no features of malnutrition and if the neonate with a birth weight greater than the 10th percentile will be an IUGR **[7]**.

IUGR is found to be the communal outcome of maternal, placental, fetal or genetic factors. Besides an assessment of maternal factors for IUGR, SGA subgroups were also investigated for possible risk factors in this study. IUGR can also be caused by the combination of any of these factors. Symmetric IUGR fetuses may present at an earlier stage in gestation and incidence of total Symmetric IUGR are 20 to 30%. The antenatal scan head circumference, Abdominal circumference, Biparietal diameter and Femur length are observed to be proportionally reduced on the other hand cell number are reduced and cell size is normal. Difference between the head and chest circumference would be less than 3cm. In Symmetrical IUGR features of malnutrition are less pronounced and prognosis will be poor. On the other hand, Asymmetrical IUGR present at the later gestational stages and incidence of Asymmetric IUGR are 70 to 80%. Abdominal circumference decreased Biperietal diameter while Head circumference and femur length will be normal. Cell number remains normal while cell size get reduced. The difference between the head and chest circumference will be more than 3cm. The features of malnutrition will be more pronounced and prognosis will be good. Maternal malnutrition and uteroplacental inadequacy causes asymmetric IUGR while congenital infections encounter early in pregnancy cause symmetric IUGR **[8]**.

Various maternal factors such as maternal age less than 16 years and more than 35 years, inter-pregnancy interval (less than 6 months or 120 months or more), pregnancy induced hypertension, maternal health, maternal infection affect the growth of the fetus **[9]**, previous IUGR and placenta previa usually contribute to the subtypes Symmetric and Asymmetric IUGR babies. Maternal malnutrition, poverty and anaemia contributed to the asymmetric IUGR babies. Maternal causative agents for IUGR may also include previous delivery of SGA, maternal substance abuse (smoking both active and passive, alcohol, illicit drugs like marijuana or cocaine), maternal medication (warfarin, steroids, anticonvulsants, antineoplastic, anti-metabolite and folic acid antagonists, moderate to heavy physical work, maternal pre-pregnancy height and weight (BMI less than 20, weight less than 45 kg and more than 75 kg), parity (non or

more than 5 birth), pregnancy poor medical care, pregnancy severe maternal starvation, pregnancy poor weight gain, pathological conditions in pregnancy like preeclampsia and diabetes associated with vasculopathy, maternal Bronchial asthma, cyanotic congenital heart diseases, maternal medical disorder (hypertensive disorder chronic renal disease, antiphospholipid syndrome, sickle cell disease, maternal infection and parasite infestations including malaria, tuberculosis, urinary tract infection and bacterial vaginosis. Insufficiant supply of nutrients to the fetus by placenta is also the leading cause of IUGR. Factors cause the malfunctioning of placental nutrient supply include placental weight less than 350 grams, avascular villi, multiple infractions, abnormal uteroplacental vasculature, syncytial knots, chronic inflammatory lesions, decidual or spiral artery arteritis, single umbilical artery, placental hemangioma, multiple gestation, infectious villitis, placental infections (placental malaria), confined placental mosaicism (CPM), partial molar pregnancy, reduced expression of enzymes for redox regulation (thioredoxin, glutaredoxin) **[9]**.

Many studies suggest fetal deformity may also lead to IUGR. Fetal deformities cause inborn error of metabolism (including agenesis of pancreas, congenital absence of islets of Langerhans, congenital lipodystrophy, galactosemia, hypo-phosphatasia, transient neonatal diabetes mellitus, Leprechaunism), chromosomal abnormalities (including trisomies 13, 18, 21, autosomal deletions, ring chromosomes, uniparentaldisomy), 50-70% of SGA fetuses with fetal growth appropriate for maternal size, multiple gestation, congenital infections (TORCH, Malaria, congenital HIV infection, syphilis), major congenital anomalies (trachea-esophageal fistula, congenital heart disease, congenital diaphragmatic hernia, anorectal malformation), genetic syndrome (bloom syndrome, Russell-Silver syndrome, Brachmann-de Lange syndrome) **[9]**. With the recent advancement in the field of molecular biology and genetics, role of various maternal, fetal and placental genes polymorphism has become important and has now been implicated as a cause of IUGR **[10]**.

CONCLUSION

Current study concludes that one of the most important complications come across during pregnancy is intrauterine fetal growth restriction. The growth-restricted fetus is at menace for adverse perinatal morbidity and mortality. Sonographic fetal parameters are regularly examined for gestational age prediction as well as to cope

with fetal growth disturbances pregnancies. Now-a-days, Fetal ultrasonic biometry is used for evaluating growth of fetus. Numerous diameters and circumferences included biparietal diameter (BPD), femur length (FL), head circumference (HC) and abdominal circumference (AC) have been deliberated regarding their association with the gestational age but these all are gestational age dependent. Two morphometric ratios, TCD/AC and HC/AC, are considered to be independent gestational age parameters and can be used in predicting intrauterine growth retardation (IUGR) with better diagnostic precision. The current study has revealed a strong significant correlation between TCD and AC throughout the pregnancy time with constant TCD/AC with a cut off value of 14.38 could be used as a growth factor for IUGR detection. And also evident that TCD/AC ratio had a better diagnostic legitimacy and accuracy compared to HC/AC ratio in detecting asymmetric IUGR.

CONFLICT OF INTERESTS

Author declare no conflict of interests

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