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Correlation of Placental and Fetal Liver Morphometry in 2nd and 3rd Trimester Ultrasound Findings

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Abstract: ***Background: The global prevalence of Low Birth Weight (LBW) is 14.6% accounting for 25 million LBW infants born every year. More than 50% of LBW infants born in India are attributed to Intrauterine Growth Retardation (IUGR). Liver is the severely affected organ in the IUGR fetus. Evaluating placental dimensions and grading is of importance as it has an association with the growth of fetal liver. Limited consummate nomograms have been computed by making an inter-relational study between placental morphometry and fetal liver dimensions. Aim: The purpose of the study was to identify whether association between placental morphometry and fetal liver dimensions be used as an application in the evaluation of fetal growth in cases of intrauterine growth restriction. Methods: A prospective observational study was done on 70 normal ultrasonographic findings at 2nd and 3rd trimester primigravida and multigravida pregnancies. Placental thickness, position of the placenta, cord attachment, placental grading(cotyledons) and fetal liver dimensions. The normal morphology and the variations observed were recorded. Results: The mean values of variables with Standard deviation were computed for gestational age from 15 weeks to 40weeks. Multiple linear regression analysis was applied to establish relationship between gestational age, liver length and placental morphometry. Predictive values for 5th,50th,90th percentile ranges of placental thickness, placental grading and fetal liver length were constructed. P values less than 0.05 was considered as statistically significant. Conclusions: The placental thickness less than 25 mm in the third trimester indicated IUGR. Placental thickness greater than 45 mm was associated with maternal comorbidities like diabetes, hypertension or fetal anomalies such as hydrops fetalis. Also, cases with abnormal placental thickness were associated with reduced fetal liver length less than fifth percentile indicating IUGR. Placentas that were less than 29 mm thick and associated with fetal liver length less than 3.7cm were related to higher morbidity.***

Keywords: Fetal Liver length, Placental Thickness, Intrauterine Growth Retardation

1. Background

The World Health Organization states that the global prevalence of Low Birth Weight (LBW) is 14.6% (with a range of 12.4-17.1) accounting for 25 million LBW infants born each year, of which 95% occur in LMICs (Lower-Middle-Income Countries) with South Asia accounting for nearly 52% of the global burden [1]. The frequency of LBW in India estimated from nationally representative survey data decreased from 22% (National Family Health Survey [NFHS-3], 2005-6) to 17.5% (NFHS-4, 2015-16). However, the country is still not on track towards achieving the targeted 30% reduction in LBW burden by 2025 [2]. More than 50% of LBW infants born in India are attributed to Intrauterine Growth Restriction (IUGR); indicating a significant burden of IUGR in India [3].

Intrauterine growth restriction (IUGR) is defined as the velocity of fetal growth less than the normal fetus growth potential for a specific neonate or it is the failure of the fetus to achieve its growth potential [4].

Symmetrical (early onset) Fetal Growth Restriction Infants (FGR) face more complications and have got poor prognosis compared to asymmetrical (late onset) ones. The Liver is said to be the most severely affected organ in the IUGR fetus. Evaluating placental dimensions and grading is of huge importance as it has an association with the growth of fetal liver. The flow of nutrient-rich blood from the placenta divides as it enters the fetus, either to perfuse fetal liver or to bypass it via the ductus venosus[5]. Also, Ultrasound examination of fetal liver dimensions can be helpful in the diagnosis of several pathological conditions associated with changes in fetal liver size. For example, a decrease in liver size is associated with intrauterine growth restriction. Till date, no consummate nomograms have been computed by considering an interrelational study between placental morphometry and fetal liver dimensions. This study also paves the way for the International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) and the Fetal Medicine Foundation (FMF) which are dedicated to improve the knowledge and performance of the clinicians, sonographers leading to advancements in clinical practice [6].

The purpose of the study is therefore to investigate whether there is a correlation between placental morphometry and fetal liver dimensions, with the potential to be used as an application in evaluation of fetal growth in cases of intrauterine growth restriction.

2. Methods

The present study was carried out on 70 primigravida and multigravida antenatal mothers visiting the Akash hospital for ultrasound examination as a part of their routine antenatal health checkups. The ethical approval from the Institutional Review Committee was obtained before starting the work. Informed consent was taken from the antenatal mothers visiting the radiology department for ultrasound examination. Exclusion criteria were: age less than 18 years, gestational age

less than 15 weeks, pregnancy induced hypertension, diabetes mellitus, severe anemia that complicates pregnancy, disorders such as cardiovascular and/or renal diseases, Rh-isoimmunization, abruptio placenta, intrauterine death. Patient information including name and age was documented. Gestational age was confirmed using previous ultrasonography reports from the first trimester.

The grey scale real-time ultrasonographic examinations of 2nd and 3rd trimester pregnancy, in the period of Aug 2023 to Sept 2023, were performed by the radiologist using a Samsung UGEO 60 and GE Voulson machines at the Department of Radiology of Akash Institute of Medical Sciences and Research Centre.

Placental thickness was measured at the level of the cord insertion site, from the echogenic chorionic plate to the placental myometrial surface. All placental measurements were taken during the relaxed phase of the uterus as contractions can deceptively increase the placental thickness. The Ultrasonographies were therefore examined looking for placental thickness, position of the placenta, cord attachment, placental grading and fetal liver dimensions. The fetal weight was calculated with the guidance of a junior resident working in the department of radiology, using the Hadlock's formula. The normal morphology and the variations observed were recorded.

3. Sampling Method

The sample size was calculated using the following formula:
n= Z^ 2 * p(1-p)/e^2
= 1.96^2 * (0.045*0.935)/0.05^2
= 65
n = minimum required sample size
p = prevalence taken as 4.5% from an educated guess Z = 1.96 for a 95% confidence interval (CI)
e = margin of error, 5%
Hence, the minimum required sample size is 65. However, a sample size of 70 is taken. The collected data will be compiled, entered and analyzed in Microsoft Excel 2018. A point estimate and 95% CI will be calculated.

Grading of maturity of placenta:

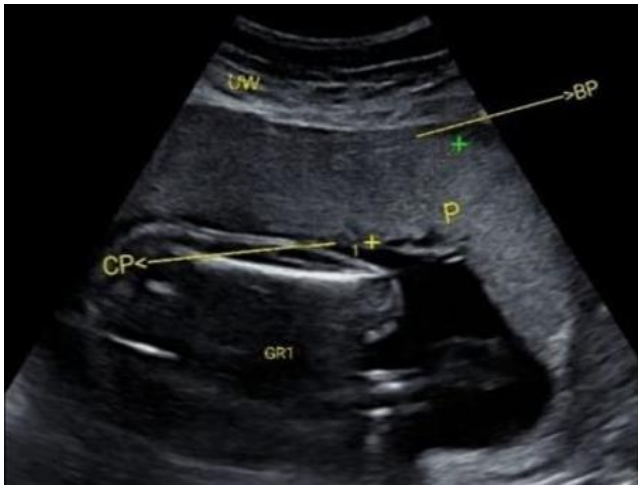


Figure 1: Gestational age: 23 weeks, Grade 1, Placental thickness: 3.3cm,
Estimated fetal weight: 615gms

Figure 2: Gestational age: 30 weeks, Grade 2, Placental thickness: 3.5cm,
Estimated fetal weight: 1748gm

Figure 3: Gestational age: 36 weeks, Grade 3, Placental thickness: 3.9cm,
Estimated fetal weight: 2871gms
UW: Uterine Wall; BP: Basal Plate; CP: Chorionic Plate; P: Placenta; G: Grade; AF: Amniotic Fluid

Figure 4: Fetal liver length measured at mid clavicular line

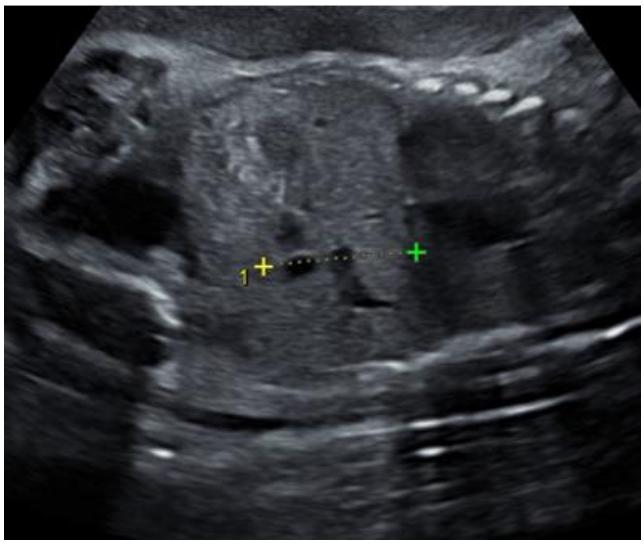


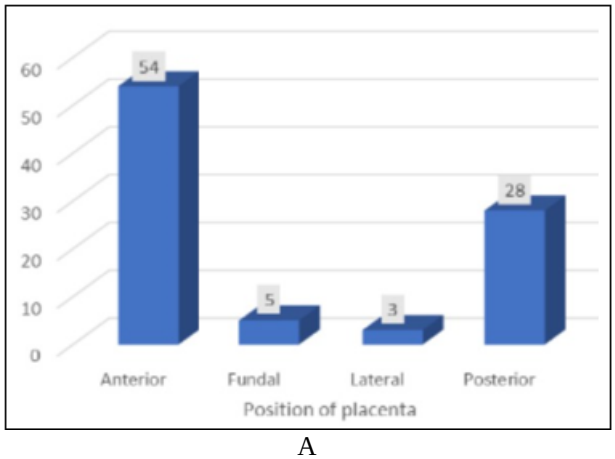
Figure 5: Fetal liver transverse diameter

Statistical Analysis

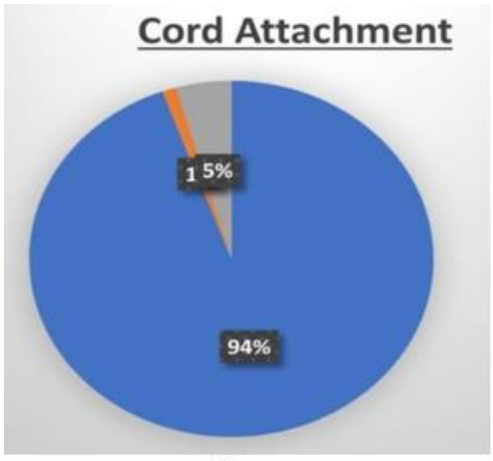
Gestational Age is an independent variable; liver length and placental morphometry as a dependent variable were used to generate the linear regression equation using the SPSS software version 10.0. The resulting residuals were tested for the normality distribution. The mean values of above parameters along with respective Standard deviation were computed for each Gestational age from 15 weeks-40weeks.

The 95% Confidence Interval was calculated. The correlation between placental parameters and fetal liver length at each different Gestational Age was computed. The respective data are plotted on the scattered diagrams and the best fit are shown with a straight line. Predictive values for 5th,50th 90th percentile ranges of placental thickness, placental grading and fetal liver length are constructed. P values less than 0.5 are assumed as statistically significant.

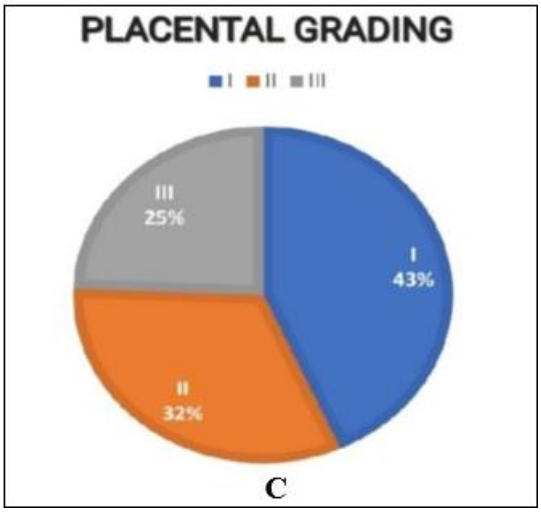
4. Results



A



B



C

Figure 6: Representative graphs by data analysis. (A) Histogram depicting number of patients with different positions of placenta **(B)** Pie chart illustrating the various proportions of population having different cord attachment **(C)**Pie chart depicting the percentage of women with varying placental grades.

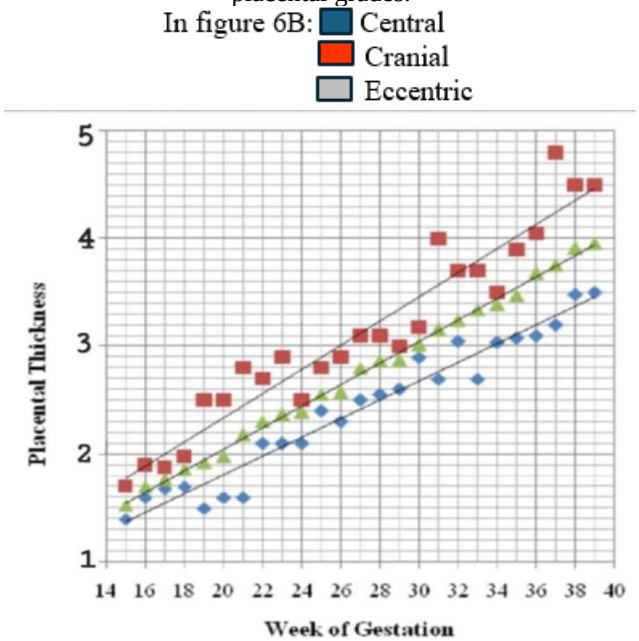


Figure 7: Line graph illustrating the relationship between placental thickness and gestational weeks

Table 1: Association of Fetal Liver Length with Placental Thickness

Statistics								
		PT	FLB	FLL	FLP	AFW	GA	AGE
n	**Valid**	90	90	90	90	90	90	90
	Missing	0	0	0	0	0	0	0
Mean		3.4676	3.94	3.1202	12.9732	1284.92	27.3000	24.6444
Std. Deviation		.77869	1.235	1.60231	8.02889	979.680	6.96774	3.69728
Minimum		1.90	2	1.20	1.80	103	16.00	18.00
Maximum		5.60	7	14.00	31.80	3471	40.00	35.00

PT: Placental thickness, FLB: Fetal liver breadth, FLL: Fetal liver length, FLP: Fetal liver product, EFW: Estimated fetal weight, GA: Gestational age.

Table 1 (a): Independent Samples Test

	Mean Difference	Std. Error Difference	t	df	Sig. (2-tailed)
Equal variances assumed	-.340	.187	-1.817	178.000	.071
Equal variances not assumed	-.340	.187	-1.817	128.126	.072

Hartley test for equal variance: F = 4.318, Sig. = 0.0000, df: degrees of freedom

Table 2: Association of Fetal Liver Length, Placental Thickness with Fetal Weight

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
FLL	Between Groups	224.943	82	2.743	5.399	.012
PT	Within Groups	3.557	7	.508		
	Total	228.500	89			
	Between Groups	52.009	82	.634	2.269	.126
	Within Groups	1.956	7	.279		
	Total	53.966	89			

5. Discussion

Standring. S reported that the full-term human placenta is a flattened discoidal mass with an approximately circular or oval outline [7]. In 90% of individuals a discoid or oval-shaped placenta is seen. Similar finding of 94% circular and 6% oval shape of placenta has also been reported [8]. Meanwhile, 48% placentas with oval and 36% with circular shape has been reported in a study [9].

Yadav.SK conducted a study in Nepal and reported that there was no abnormality regarding the attachment of cord [8]. In 2% of individuals, marginal attachment of the cord has been reported. Other studies have reported 7%, 8.97%, 25% marginally attached umbilical cord[10,11,12]. These variations in placental morphology has been looked upon as being correlated to any predisposing conditions such as placenta previa, vaginal bleeding, and premature delivery[13]. Kumar SM conducted a study in rural population in Eastern India and reported that 15 (30%) had central type insertion, 16 (32%) had medial, 3 (6%) had lateral type, and 16 (32%) had marginal type of cord insertion [14].

Hassan Mumtaz (2021) reported that the mean placenta thickness at 24 gestation weeks was 24.55 ± 0.79 mm, at 32 gestation weeks was 31.84 ± 1.34 mm, and at 36 gestation weeks was 35.54 ± 2.78. They concluded that placental thickness less than 25 mm in the third trimester could indicate IUGR. In contrast, thickness greater than 45 mm could show maternal comorbidities like diabetes or hypertension or fetal anomalies such as hydrops fetalis. Placentas that were less than 29 mm thick at 32 weeks and 31 mm thick at 36 weeks were related to higher morbidity.
They concluded that the earliest symptom of fetal growth restriction can be a decline in placental thickness for gestational age [15].

Shumaila Zia (2013) studied that Anterior placenta was found to have a relation with a greater risk of pregnancy-induced hypertension, gestational diabetes mellitus and placental abruption, while posterior placenta had a significant association with preterm labour.

Regarding fetal outcome, an anterior placenta was significantly associated with intrauterine growth retardation and intrauterine fetal death. The majority (54%) of women with an anterior placenta were O-positive blood group, while 46% of women in the posterior placenta group were A-positive blood group[16].

Sapna Jain (2000) conducted a study where, in hypertensive and IUGR cases, placental maturity accelerates due to compromised utero-placental circulation. But, in diabetic women lower grades of placenta were more common indicating tendency towards delayed maturation. It was reported that women with grade III placenta before 37 weeks showed maternal complications in 8 cases and fetal complications in 16 cases in the form of IUGR, Functional

Dyspepsia (FD) and neonatal death. It was concluded that detection of higher grades early in 3rd trimester can alert the obstetrician for closer observation regarding development of Pregnancy Induced Hypertension (PIH), IUGR, Abruptio placentae and Fetal Distress. There is definite correlation of early maturation of placentae with fetal complications. It primarily affects the extent of calcification and cotyledons found [17].

Tongprasert, (2010) reported that in the study conducted, gestational Age (GA) of 18 weeks (<5th percentile) had liver length on an average of 16.4mm, GA 24 weeks (<50th percentile) = 31.9mm, GA 36 weeks (<50th percentile) = 51.3mm. The liver length was found to increase in a linear fashion throughout the second and third trimesters. The liver length had normal distribution at all GAs. The interobserver

mean difference for the measurement of liver length was 4.6% [18].

6. Conclusions

The thickness of placenta did not vary relative to the placental location. These data show that fetal liver can be used as an additional determinant for early detection of fetus suffering from IUGR.

This study provides contribution towards organizations including **International Society of Ultrasound in Obstetrics and Gynaecology (ISUOG) and the Fetal Medicine Foundation (FMF)** which are dedicated to improve the knowledge and performance of clinicians, sonographers leading to advances in the clinical practice.

Competing interests
The authors declare that they have no competing interests.

Authors' Contributions
The SD carried out experimental analysis and interpretation of the data. VK contributed to the concept, design and supervision of the study.SS carried out the experimental ultrasounds and interpretation of data. All the authors read and appproved the final version of the manuscript.

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