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Association Between Cerebroplacental Uterine Ratio With Fetal Gender In Normal And Intrauterine Growth Restricted Pregnancies

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Abstract

Background: Antenatal ultrasound plays a vital role in monitoring fetal and maternal wellbeing during pregnancy. Doppler ultrasound is widely used for assessing fetoplacental circulation, and cerebroplacental uterine ratio (CPUR) is considered an important marker for detecting uteroplacental insufficiency, fetal growth restriction (FGR), and adverse perinatal outcomes. The relationship between CPUR and fetal gender remains insufficiently explored, particularly in South Asian populations.

Methodology: This prospective case-control study was conducted on 144 pregnant women attending Shervon London Healthcare, Model Town Lahore. Participants were aged 18–40 years with gestational age between 15–40 weeks. Doppler ultrasound was performed to measure pulsatility indices of the middle cerebral artery (MCA), uterine artery (UTA), and umbilical artery (UMB A), and CPUR was calculated. Fetal gender was determined using ultrasonographic assessment. Data were analyzed using SPSS version 25.

Results: A total of 144 fetuses were included in this study, with 76 (52.8%) males and 68 (47.2%) females. The average maternal age was 28.38 ± 4.33 years. Fetal measurements showed mean values of 69.42 mm for biparietal diameter (BPD), 260.17 mm for head circumference (HC), 236.13 mm for abdominal circumference (AC), and 50.09 mm for femur length (FL), with an average estimated fetal weight of 1406.40 grams. Doppler findings showed mean values of 1.05 for umbilical artery pulsatility index (UA PI), 0.65 for resistance index (RI), 3.16 for S/D ratio, and 1.98 for middle cerebral artery pulsatility index (MCA PI). Most placentas were located in the fundoposterior region (50.6%), and Grade 2 placenta was the most common (51.4%).

The majority of fetuses had normal CPUR and CPR values. Only 12 fetuses had abnormal CPUR, including 5 females and 7 males, while abnormal CPR was found in only 2 male fetuses. Statistical analysis showed no significant relationship between fetal gender and CPUR ($p = 0.68$) or CPR ($p > 0.05$). This means that fetal gender does not affect CPUR or CPR values.
Conclusion: CPUR is a useful Doppler metric for fetoplacental and uteroplacental assessment, but fetal gender showed no significant association with CPUR or CPR in normal or IUGR pregnancies. Most fetuses had normal values, and abnormal findings were similarly rare in both genders. Thus, gender does not affect these indices, which remain reliable markers of fetal well-being without need for gender-specific interpretation.

Introduction

Antenatal ultrasound is a pivotal, non-invasive, and safe imaging modality for assessing maternal and fetal well-being. It evaluates fetal anomalies, number, gestational age, placental location, amniotic fluid, and conditions like placenta previa. First-trimester high-resolution ultrasound is essential for viability and nuchal translucency screening. Doppler ultrasound in the third trimester detects placental insufficiency by assessing blood flow in fetal and placental vessels, with early diagnosis significantly reducing perinatal and maternal morbidity and mortality. Umbilical artery Doppler, supported by Cochrane reviews of over 10,000 pregnancies, reduces perinatal mortality by ~30% and decreases labor induction and cesarean delivery rates, though long-term outcome data remains moderate(1).

The cerebroplacental ratio (CPR) = MCA PI / Umbilical artery PI, reflecting fetal blood flow redistribution (brain-sparing effect) in response to hypoxia. A low CPR near term is linked to slower growth, operative delivery for fetal distress, and NICU admissions. The cerebroplacental uterine ratio (CPUR) combines MCA, umbilical artery (UA), and uterine artery (UtA) pulsatility indices (PI). CPUR is calculated as (MCA PI / UtA PI) / mean UA PI. CPUR MoM is a stronger indicator of placental insufficiency and FGR than either mean UtA PI MoM or CPR MoM alone. Low CPUR predicts stillbirth even after adjusting for fetal size (2).

In high-risk pregnancies, increased UA and UtA resistance indices (RI) occur alongside cerebral vasodilation (reduced MCA PI). Increased UtA PI in the third trimester indicates placental insufficiency. FGR (failure to achieve fetal biometry, EFW <10th percentile) is a major contributor to adverse outcomes and is associated with a 3-4 fold increased stillbirth risk. FGR is divided into early (<32 weeks) and late (>32 weeks) onset. Ultrasound and Doppler are essential to distinguish true FGR due to placental insufficiency from SGA without placental involvement. In a Karachi study, impaired intrauterine fetal growth incidence was 10%. Maternal factors affecting FGR include hypertension, diabetes, smoking, anemia, cardiopulmonary disease; fetal causes include aneuploidy, congenital malformations, multiple pregnancies, infection; placental causes include insufficiency, infarction, mosaicism (3).

Fetal gender is routinely determined via ultrasound in the second/third trimester (male: scrotum/penis, "turtle sign"; female: labia/three parallel lines, "burger sign") and increasingly in the first trimester (genital tubercle angle: >30° male, <10° female).

Sexual dimorphism in placental function and Doppler indices is documented:Female fetuses may show lower CPR and higher umbilical-to-cerebral ratio (UCR) than males. Some studies report UA PI 2-8% higher in females from 20-36 weeks, with higher fetal heart rates (4).

Other studies show higher placental weight and birth weight in males, with increased UA resistance in males. However, opposing results exist, including lower UA PI in males (28-34 weeks), indicating sex-specific differences in placental perfusion and cardiac function. Critically, male fetuses have higher chances of FGR, placental

insufficiency, preeclampsia, and placental abruption. Female perinatal survival is recognized as superior (5).
This study aims to assess the association between CPUR and fetal gender in both normal and IUGR pregnancies using non-invasive ultrasound in the Pakistani population, addressing a gap in literature regarding sex-based physiological differences in CPUR and their relation to adverse perinatal outcomes.

METHODOLOGY

This prospective case-control study was conducted at Shervon London Healthcare, Model Town, Lahore, over a duration of four months following synopsis approval. A sample size of 144 participants was calculated using a 95% confidence level, a 10% prevalence based on prior literature, and a 5% margin of error. Convenient sampling technique was employed. Inclusion criteria comprised patients aged 18 to 40 years with either normal pregnancy or intrauterine growth restriction (IUGR), gestational age between 15 and 40 weeks, documented complete CPUR measurement including pulsatility indices of the middle cerebral artery (MCA), uterine artery (UtA), and umbilical artery (UmA), and those providing informed consent. Exclusion criteria included multiple pregnancies, congenital anomalies, gestational diabetes, hypertension, patients with incomplete Doppler data, ambiguous fetal gender, and those refusing consent.

RESULTS

The study included a total of 144 fetuses, consisting of 76 (52.8%) males and 68 (47.2%) females, indicating a slightly higher proportion of male fetuses in the study population. The mean maternal age was 28.38 ± 4.33 years, with a range from 19 to 38 years, based on 143 valid observations. Fetal biometric assessment showed a mean biparietal diameter (BPD) of 69.42 ± 16.66 mm, head circumference (HC) of 260.17 ± 56.46 mm, abdominal circumference (AC) of 236.13 ± 62.49 mm, and femur length (FL) of 50.09 ± 13.49 mm. The mean estimated fetal weight (EFW) was 1406.40 ± 879.90 grams, reflecting variability in fetal growth, including both appropriately grown and potentially growth-restricted fetuses.
Doppler ultrasound evaluation of fetoplacental circulation demonstrated a mean umbilical artery pulsatility index (UA PI) of 1.05 ± 0.59, umbilical artery resistance index (RI) of 0.65 ± 0.09, and systolic/diastolic (S/D) ratio of 3.16 ± 1.11. The mean middle cerebral artery pulsatility index (MCA PI) was 1.98 ± 0.60. These parameters reflect the status of placental resistance and fetal cerebral circulation. Placental assessment revealed that the most common location was fundoposterior (50.6%), followed by anterior (31.8%), posterior (16.5%), and fundal (1.2%) positions. In terms of placental maturity, Grade 2 placenta was most frequently observed (51.4%), followed by Grade 1 (43.1%) and Grade 0 (5.6%), while no cases of Grade 3 placenta were detected, suggesting that most pregnancies were in a normal to moderately advanced gestational stage.
Analysis of cerebroplacental uterine ratio (CPUR) showed that the majority of fetuses had normal values (≥1.0), indicating adequate balance between uteroplacental and fetoplacental circulation. Only 12 fetuses (8.3%) had abnormal CPUR values (<1.0), including 5 (7.4%) females and 7 (9.2%) males. Similarly, evaluation of cerebroplacental ratio (CPR) demonstrated that only 2 male fetuses (2.6%) had abnormal values (<1.0), while none of the female fetuses were affected. The remaining fetuses in both groups showed normal CPR values, suggesting preserved fetal cerebral adaptation and placental function.

Statistical analysis revealed no significant association between fetal gender and CPUR category ($\chi^2 = 0.17$, $p = 0.68$). Likewise, no statistically significant association was observed between fetal gender and CPR category ($p > 0.05$, Fisher's exact test). These findings indicate that fetal gender does not have a measurable impact on CPUR or CPR values. Therefore, both indices appear to be independent of fetal sex and can be reliably used in the assessment of fetal well-being in both normal and intrauterine growth-restricted pregnancies.

Table 4.1:
Distribution of Fetal Gender Among Study Participants (n = 144).

Fetal Gender		
	Frequency	Percent
Female	68	47.2
Male	76	52.8
Total	144	100.0

Table 4.1 presents the frequency distribution of fetal gender in the study population. Out of 144 fetuses, 76 (52.8%) were male and 68 (47.2%) were female. The distribution shows a slightly higher proportion of male fetuses compared to female fetuses as shown in the graph below as well.

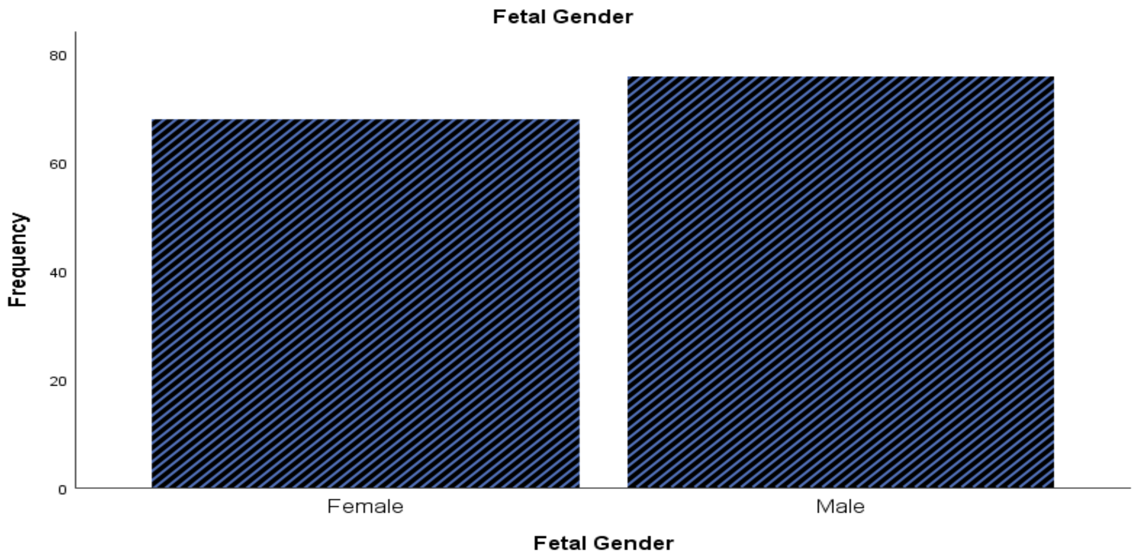


Figure- 4.1; Graph representing the gender groups of patients

Table 4.2: Descriptive Statistics of Maternal Age

Descriptive Statistics					
	N	Minimum	Maximum	Mean	Std. Deviation
Age	143	19	38	28.38	4.328

Table 4.2 summarizes the descriptive statistics for maternal age. The mean maternal age was 28.38 ± 4.33 years, with a minimum age of 19 years and a maximum age of 38 years. A total of 143 valid observations were included in the analysis.

Table 4.3: Descriptive Statistics of Fetal Biometric Parameters

Fetal Biometric Parameters					
	N	Minimum	Maximum	Mean	Std. Deviation
Age	143	19	38	28.38	4.328
BPD in mm	144	34.90	93.30	69.4181	16.66068
HC in mm	144	149.50	341.70	260.1715	56.46408
AC in mm	144	126.1	334.5	236.128	62.4894
FL in mm	144	24.40	69.00	50.0903	13.49435
EFW in grams	144	182.00	2946.00	1406.4028	879.89931
Valid N (listwise)	143				

Table 4.3 presents the descriptive statistics of fetal biometric measurements. The mean biparietal diameter (BPD) was 69.42 ± 16.66 mm, head circumference (HC) was 260.17 ± 56.46 mm, abdominal circumference (AC) was 236.13 ± 62.49 mm, and femur length (FL) was 50.09 ± 13.49 mm. The mean estimated fetal weight (EFW) was 1406.40 ± 879.90 grams. These measurements reflect the growth profile of fetuses included in the study.

Table 4.4: Descriptive Statistics of Doppler Indices

Doppler Indices					
	N	Minimum	Maximum	Mean	Std. Deviation
UA PI	144	.43	4.44	1.0522	.58588
UMB PI	144	.64	1.79	1.0634	.24995
UMB RI	144	.47	.89	.6506	.09020
UMB S/D Ratio	144	2.01	8.79	3.1613	1.11282
MCA PI	144	.80	4.06	1.9759	.59822
MCA RI	144	.7	5.1	1.052	.8417
MEAN UTA PI	0				
Valid N (listwise)	0				

Table 4.4 demonstrates the descriptive statistics of Doppler indices. The mean umbilical artery pulsatility index (UA PI) was 1.05 ± 0.59. The mean umbilical artery resistance index (UMB RI) was 0.65 ± 0.09, and the mean S/D ratio was 3.16 ± 1.11. The mean middle cerebral artery pulsatility index (MCA PI) was 1.98 ± 0.60. These Doppler parameters were used to assess fetoplacental circulation.

Table 4.5: Distribution of Placental Location

Placental Location			
	Frequency		Percent
Anterior	27	31.8	31.8

Posterior	14	16.5	16.5
Fundoposterior	43	50.6	50.6
Fundal	1	1.2	1.2
Total	85	100	100.0
Total	144		100.0

Table 4.5 shows the distribution of placental location among study participants. Fundoposterior placenta was the most common location (50.6%), followed by anterior placenta (31.8%), posterior placenta (16.5%), and fundal placenta (1.2%) as shown in the graph below

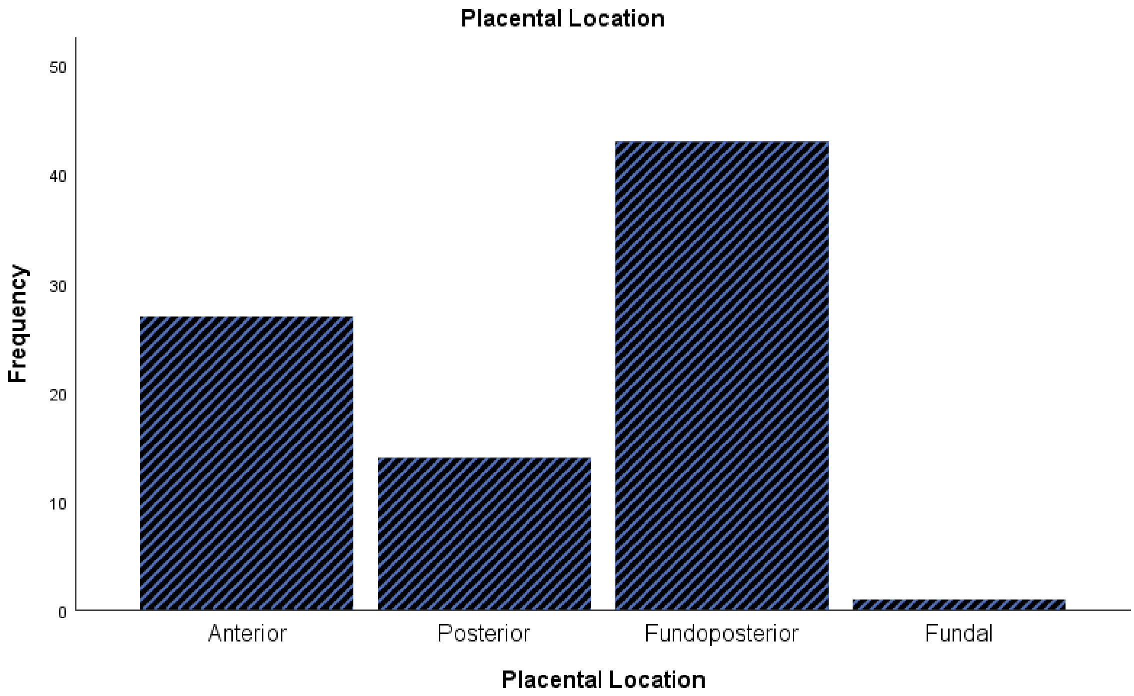


Figure- 4.2; Graph representing the placental locations

Table 4.6: Distribution of Placental Grading

Placental grading		
	Frequency	Percent
Grade 0	8	5.6
Grade 1	62	43.1
Grade 2	74	51.4
Total	144	100.0

Table 4.6 presents the distribution of placental grading. Grade 2 placenta was observed in 74 (51.4%) cases, followed by Grade 1 in 62 (43.1%) cases and Grade 0 in 8 (5.6%) cases. No cases of Grade 3 placenta were reported in this study.

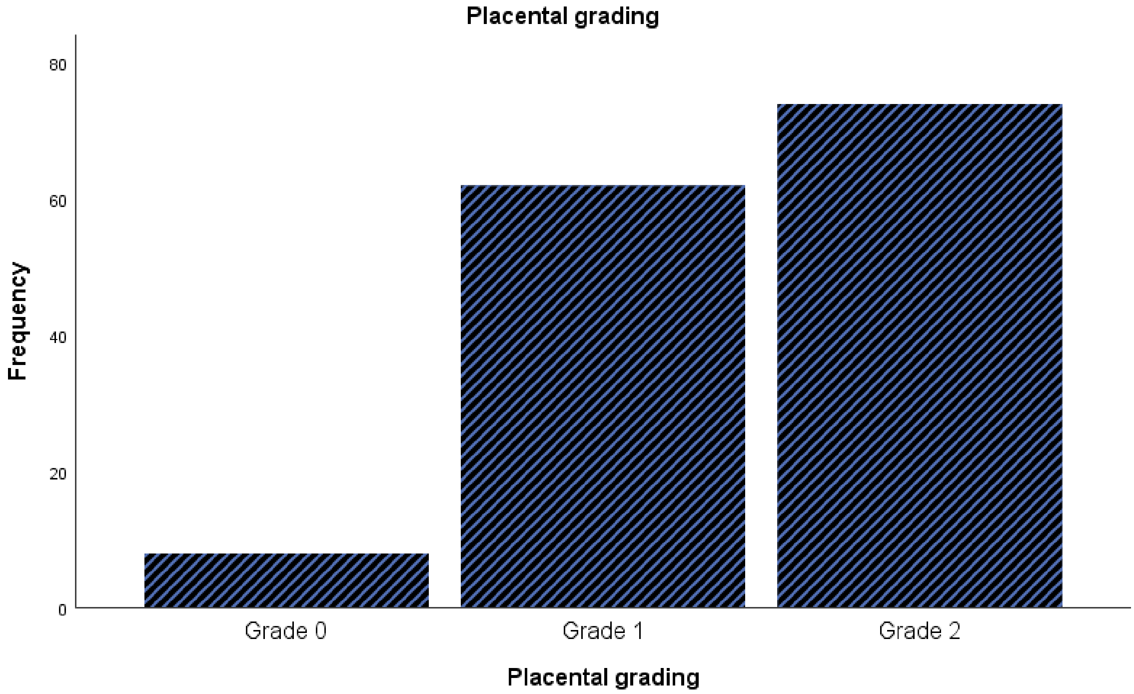


Table 4.7: Association Between Fetal Gender and CPUR Category
(CPUR categorized as Abnormal <1.0 and Normal ≥1.0)

Fetal Gender	**Abnormal**	**Normal**	**Total**
Female	5	63	68
Male	7	69	76
Total	12	132	144

Table 4.7 illustrates the association between fetal gender and CPUR category. Among female fetuses, 5 (7.4%) had abnormal CPUR values, while 7 (9.2%) male fetuses had abnormal CPUR. The majority of both female (92.6%) and male (90.8%) fetuses demonstrated normal CPUR values. Chi-square test showed no statistically significant association between fetal gender and CPUR category ($\chi^2(1) = 0.17$, $p = 0.68$).

Table 4.8: Association Between Fetal Gender and CPR Category
(CPR categorized as Abnormal <1.0 and Normal ≥1.0)

Fetal Gender	**Abnormal CPR (<1.0)**	**Normal CPR (≥1.0)**	**Total**
Female	0	68	68
Male	2	74	76
Total	2	142	144

Table 4.8 presents the association between fetal gender and CPR category. Only 2 (2.6%) male fetuses demonstrated abnormal CPR values (<1.0), whereas none of the female fetuses had abnormal CPR. The majority of both female (100%) and male

(97.4%) fetuses had normal CPR values (≥1.0). Fisher's Exact test indicated no statistically significant association between fetal gender and CPR category ($p > 0.05$). CPUR categorized as:

Abnormal (<1.0)
Normal (≥1.0)

DISCUSSION

Fetal growth restriction (FGR) remains a major contributor to perinatal morbidity and mortality worldwide. Doppler ultrasonography has become an essential non-invasive tool for evaluating fetoplacental circulation and identifying pregnancies at risk. Among Doppler parameters, the Cerebroplacental Uterine Ratio (CPUR) integrates maternal and fetal vascular resistance, providing a comprehensive assessment of uteroplacental and fetal hemodynamics (8). Understanding its relationship with fetal gender may improve risk stratification and individualized obstetric management (9).

In the present study, 144 pregnant women were evaluated to determine the association between CPUR and fetal gender. The distribution of fetal gender showed a slight male predominance (52.8% males vs. 47.2% females). Most fetuses demonstrated normal CPUR values (≥1.0), with only 12 cases (8.3%) categorized as abnormal (<1.0). Statistical analysis revealed no significant association between fetal gender and CPUR category ($\chi^2 = 0.17$, $p = 0.68$). Similarly, no significant association was observed between fetal gender and CPR values ($p > 0.05$) (10).

These findings suggest that although sex-specific physiological differences in placental circulation have been described in previous literature, CPUR may not significantly vary according to fetal gender in low-risk and IUGR pregnancies within this population. Several studies have reported sexual dimorphism in Doppler indices, indicating higher umbilical artery resistance in female fetuses and altered middle cerebral artery (MCA) indices in males. However, our results did not demonstrate statistically significant gender-based variation in CPUR (11).

Previous literature highlights that reduced cerebroplacental ratio (CPR) is associated with adverse perinatal outcomes such as operative delivery, neonatal intensive care admission, and fetal compromise, even in appropriately grown fetuses. Low CPUR values reflect increased uterine and umbilical artery resistance combined with cerebral vasodilation, indicating placental insufficiency. Despite this established association with adverse outcomes, the current study did not find a gender-specific predisposition to abnormal CPUR (12).

The mean Doppler indices observed in this study (UA PI: 1.05 ± 0.59; MCA PI: 1.98 ± 0.60) were within acceptable reference ranges for the studied gestational ages. The majority of cases showed normal placental grading (Grade I and II), and abnormal Doppler findings were limited (13). This may explain the lack of statistically significant correlation between fetal gender and CPUR. Literature suggests that male fetuses may have a higher risk of placental insufficiency and FGR, whereas female fetuses are often reported to have better perinatal survival. However, our findings indicate that CPUR alone may not demonstrate a significant sex-based difference in predicting adverse outcomes. This could be due to sample size limitations, population characteristics, or inclusion of both normal and IUGR pregnancies without subgroup stratification (14).

The strength of this study lies in its prospective design and standardized Doppler assessment using high-resolution ultrasound equipment. However, limitations include the relatively small sample size, single-center setting, and absence of long-term neonatal outcome assessment. Further multicenter studies with larger populations are recommended to validate these findings and explore whether CPUR has prognostic value when analyzed separately in normal versus IUGR pregnancies according to fetal gender (15).

CONCLUSION

This study evaluated the association between cerebroplacental ratio (CPR), cerebroplacental uterine ratio (CPUR), and fetal gender in normal and suspected IUGR pregnancies. Although slight variations were observed, no statistically significant association was found between fetal gender and abnormal CPR or CPUR values ($p > 0.05$). The findings suggest that fetal gender does not significantly influence fetoplacental Doppler indices in the studied population. CPR and CPUR remain important indicators of fetal well-being irrespective of gender.

LIMITATIONS:

The study was limited to 144 participants, which may not fully represent the broader population. A larger cohort would improve the statistical power and generalizability of the findings.

The research was conducted at a single medical center, which may introduce selection bias and limit the external validity of the results.

The study did not include long-term neonatal follow-up to assess postnatal growth, neurodevelopmental outcomes, or long-term perinatal complications.

The number of abnormal CPUR and CPR cases was relatively small, which may have reduced the ability to detect subtle gender-based differences.

Doppler measurements may vary depending on operator expertise and ultrasound machine specifications, which could influence the consistency and reproducibility of CPUR values.

RECOMMENDATIONS:

Future research should include a larger sample size across multiple institutions to enhance the validity and applicability of the findings.

Longitudinal studies with postnatal follow-up should be conducted to evaluate the long-term neonatal outcomes associated with abnormal CPUR values.

Subgroup analysis of normal and IUGR pregnancies should be performed separately to better understand gender-specific hemodynamic differences.

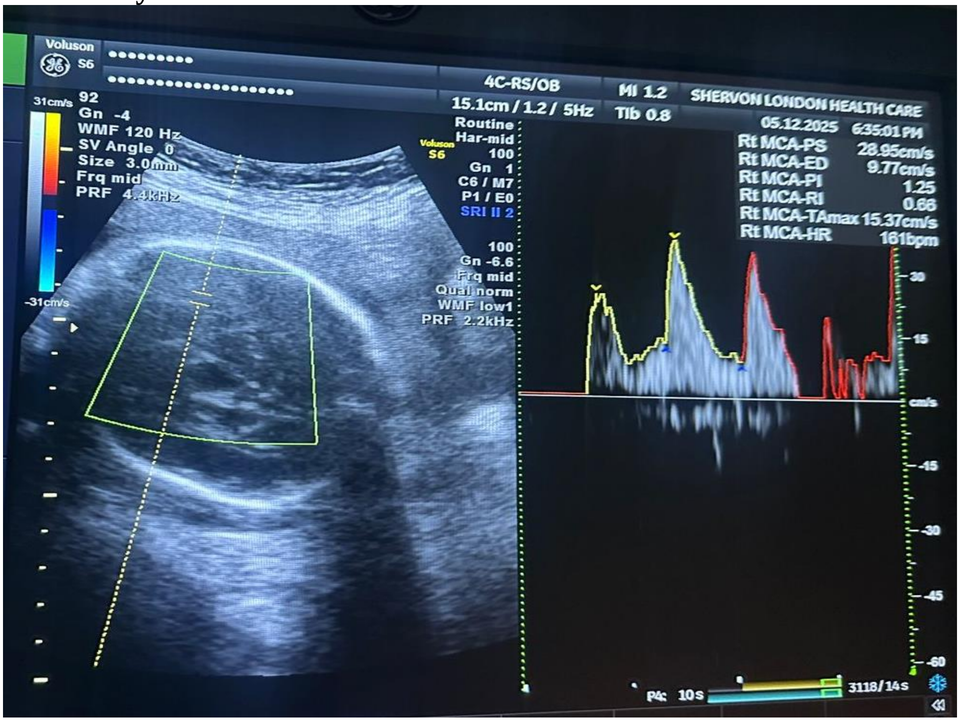
Correlation of CPUR findings with additional Doppler parameters such as ductus venosus and uterine artery indices may improve prediction of adverse perinatal outcomes.

Development of population-specific reference ranges for CPUR in the Pakistani population is recommended to improve clinical decision-making

Case study

This obstetric ultrasound image shows the fetal profile within the uterine cavity during the late second to early third trimester of pregnancy. The fetal head and facial structures are clearly visualized, and a linear measurement is being performed between two anatomical points for assessment. Biometric parameters such as BPD, HC, FL, and estimated fetal weight are displayed on the monitor to evaluate fetal growth and development.

Case study



This obstetric Doppler ultrasound image shows the fetal head in axial view with assessment of the right middle cerebral artery (MCA). Color Doppler and spectral waveform analysis are used to evaluate blood flow velocity and resistance within the MCA. Parameters such as peak systolic velocity, pulsatility index, and resistive index are displayed to assess fetal cerebral circulation and well-being.

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