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PLACENTAL AND NEONATAL MORPHOMETRY INCLUDING DOPPLER INDICES IN HIGH-RISK VERSUS NORMAL PREGNANCIES

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Abstract

Background: High-risk pregnancies, encompassing Pregnancy-Induced Hypertension (PIH), Gestational Diabetes Mellitus (GDM), Preeclampsia Toxaemia (PET), and Intrauterine Growth Restriction (IUGR), represent intricate medical challenges with potential repercussions for maternal and fetal health. This research undertakes a comprehensive comparative investigation into the variations of Doppler indices and placental parameters within the context of these high-risk conditions when juxtaposed against pregnancies characterized as normal. **Method:** Employing a rigorous cross-sectional study design, a diverse cohort of pregnant individuals with gestational diabetes, IUGR, PIH, and preeclampsia is meticulously assembled. Additionally, a group of normal pregnant women serves as the comparative reference. Doppler ultrasound assessments viz Pulsatilityindexare carefully performed to estimate blood flow velocities within critical maternal and fetal vessels, while placental parameters are meticulously quantified, encompassing dimensions, vascular architecture, and morphological features. **Results:** Except in the GDM group, all high-risk groups had reduced estimated placental weight actual birth weight, thickness, placental diameter, and placental cotyledon count than normal pregnant women. All the high-risk groups showed a highly significant elevation of the Pulsatility index of the Umbilical artery (PI of UA) and Pulsatility index of the Middle cerebral artery (PI of MCA) than normal but the PI of MCA was significantly reduced in the PET group individuals than in normal. The Cerebroplacental Ratio in the GDM and IUGR groups revealed markedly greater values, whereas PET showed lower values. IUGR and PIH groups showed a substantial reduction in the fetal birth weight. All the high-risk groups (GDM, IUGR, PIH, and PET) showed a highly significant reduction in Luminal Area Umbilical artery 1than the normal pregnant women. In IUGR marginal placental insertion was very high, followed by GDM and PET groups. **Conclusion:** This study reveals that Doppler indices, placental parameters, newborn weight, and their related ratios may be utilized to anticipate gestation difficulties and also to gain insight into the pathophysiology of problematic conceptions.

Keywords: High-Risk Pregnancies, Gestational Diabetes, Hypertension, Doppler Indices, Preeclampsia Toxaemia, Intrauterine Growth Restriction, Placenta.

INTRODUCTION

Due to the several neurophysiological, and social alterations that occur during gestation, the pregnancy is a critical instant in the life of women. They face rigorous problems because of failing to cope with these alterations. Despite the fact that pregnancy is a physiological phenomenon, some situations can put maternal or fetal health in jeopardy, making it a high-risk pregnancy (HRP) and adding to the stress that women must endure. Approximately 22% of women suffer from HRP during their pregnancy (1). Preeclampsia, GDM, and small for gestational age (SGA) are frequent issues with pregnancy. For SGA, the frequency of problematic conceptions has progressively elevated by 5% to 10% v(2), 2% to 5% for Preeclampsia(3), and 2% to 13% for gestational diabetes mellitus (4) globally. Recent research has demonstrated that fetal development abnormalities and placental disorders can both complicate pregnancies. This has been noted that the placenta, a transitory structure for regulating nourishment from the mother to offspring, affects birth weight(5), Recent research has indicated a clear correlation between its weight and fetal birth weight (6,7). According to several research, factors related to the placenta have a significant influence on fetal development limitation, and all macroscopic and microscopic pathological abnormalities indicate that vascular injury is the root cause of the restricted flow of blood(2). Unfavorable prenatal outcomes can be predicted by placental weight independently. However, it is not well understood what variables increase and decrease placental weight(8). When compared to individuals born with normal development, intrauterine growth restriction (IUGR) is an indication of a perinatal risk that leads to morbidity and death. The occurrence of IUGR differs significantly between various groups of people. Its frequency is close to 33% in newborns who weigh less than 2500 g at delivery. Economic growth is also correlated with the occurrence of IUGR, which is substantially lower in wealthy nations (4–8%) than in poor ones (6%–30%) (9). In the general population, intrauterine growth retardation occurrence averages close to 8%. Certain established indicators of the possibility of IUGR such as infections, preeclampsia, hypertension, diabetes mellitus, cardiovascular disorders, low socio-economic position, and placental insufficiency (10).

According to reports, of all the arteries examined by Doppler ultrasonography, the middle cerebral artery, and umbilical artery are the most accessible as well as repeatable. The middle cerebral artery of the fetuses was carefully inspected in order to determine placental damage and fetal anemia (11). The PI of the MCA and UA ratio, often called as cerebro-placental ratio (CP ratio), is a valuable indicator of the health of the fetus. The lower CP ratio, as opposed to MCA or UA Doppler indices alone, shows relative redistribution of the flow of blood to cerebral irrigation and is thought to increase precision in forecasting challenges and adverse outcomes (12). This proportion is now being used more frequently in monitoring the conceptus of danger by repeating the Doppler exams frequently. Despite the fact that these Doppler indices have reference ranges in the literature from the West, there aren't many studies of a comparable nature conducted among the Indian population (13,14). The peripheral resistance of the blood arteries is measured by the PI. A rise in resistance in distal segments of the vessels may be indicated by higher PI, which denotes hypoperfusion in the area (15).

An independent indicator of unfavorable perinatal outcomes is the weight of the placenta. The causes of both increased as well as decreased placental weight, still are inadequately known. The current study intended to determine placental and umbilical cord parameters were taken into consideration. Very little information was observed in relation to Doppler indices in association with placental morphometry and luminal diameter of umbilical vessels hence this study. This research undertakes a thorough investigation into the interplay between these high-risk conditions and their impact on Doppler indices and placental parameters. By examining a diverse cohort of pregnant individuals afflicted by these complications, this study aims to uncover potential associations that could advance the understanding of their underlying mechanisms and clinical implications.

METHODOLOGY

Study design: The observational cross-sectional research was conducted from 20-10-2021, and 12 -05-2023, in the Anatomy Department, with the collaboration of the Departments of Radiology, Obstetrics and Gynaecology, and Paediatrics at tertiary care and teaching hospitals. At different phases of pregnancy, participants underwent a series of ultrasound/Doppler scans for research purposes. Both the patients and the researcher were unaware of the scan results. The study scan findings were made accessible after delivery. Placental and neonatal parameters were taken after the posturition.

Study Population:

The study will include pregnant women from different clinical groups - GDM, IUGR, PIH, PET, and a control group of normal pregnancies. Women who participated in all planned prenatal investigation scans and gave birth to a live child following thirty-six weeks of conception met the inclusion criteria for the current research among those with high-risk pregnancies. Women who left the study early or whose fetuses were found to have abnormalities were excluded.

Sample Size: The sample size was assessed depending on power analysis to ensure sufficient statistical significance. It should account for the number of clinical groups, anticipated dropout rates, and the desired level of statistical power.

Doppler assessment:

All individuals who met the criteria for inclusion were recruited in this investigation. Parameters were made utilizing the LOGIQ P5 duplex Doppler ultrasound equipment, which has a curvilinear low-frequency transducer. Many technical features were spectral frequency, frequency, filter medium, sample volume, and PRF-4-5MH (16).

MCA PI and RI, UA PI, and CP ratio

All participants were assessed by employing a 3.5-MHz curvilinear transducer for duplex Doppler once the biometry results were confirmed. Doppler waveforms from UA and the fetal MCA were recorded across 3 successive cardiac cycles. The fetus was asleep and apneic while the patients were evaluated while they were laying semi-recumbent. Spectral waveforms were created with the use of a medium filter and a 4 mm sample volume (16).

Pulsatility index of middle cerebral artery:

The MCA is closest to the probe and was found using the color Doppler each time. A 4 mm sample volume was used to get a spectral trace from the MCA immediately after it was formed. Every time, it was made sure that the angle of insonation was between 0 and 60. Both human and automated PI evaluations were performed throughout 3 successive cardiac cycles. The parameters were repeated, and two interpretations that had similar findings were recorded for this research (16).

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Pulsatility index Umbilical artery:

The umbilical artery was located in every instance employing color Doppler. A spectral trace was created utilizing a 4 mm sample volume from the UC's free loop. If it was not able to locate the free loop of the UC, the placental implantation of the chord was tracked. From 0 to 60, the angle of insonation was maintained constant. The PI was computed both automatically and manually across 3 successive cardiac cycles. The measurements were repeated, and the final 2 interpretations from the research that gave similar findings were recorded (16).

MCA PI / UA PI ratio:

Cerebro-placental ratio, a computation comparing the MCA PI to UA PI, was performed in each patient after confirming the technical accuracy of the examination and measurements.

Follow-up studies:

Neonatal and Placental and Morphometry:

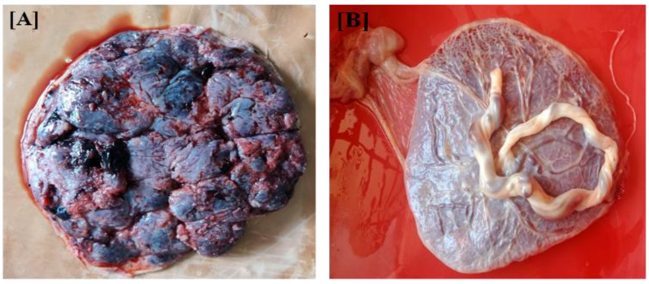

Figure 8: Placenta A) Maternal surface showing cotyledons B) Fetal surface along with amnion

Neonatal measurements will include birth weight collected immediately after birth. Placental measurements include estimated weight, actual weight, diameter, thickness, number of cotyledons, fetoplacental ratio, placental coefficient, placental shape, and cord insertion (Figure 8). Followed by The length of the umbilical cord was measured and umbilical cord samples were collected for histopathological examination of umbilical vessels. Data was simultaneously submitted to properly set up Microsoft Excel worksheets.

Histopathology

The tissue of the umbilical cord was fixed in a ten percent formalin solution and then sectioned at 4μ thick. Employing hematoxylin and eosin, sections of tissue were stained, and observed for histopathological alterations and measured luminal area (17).

Statistical analysis:

The statistical evaluations were carried out utilizing the package SPSS, version 21. The mean ± SD was used to describe quantitative data having a normal distribution. The Student's t-test was performed for statistical comparisons between two categories, and with respect to statistics, a value of $P < 0.05$ was considered significant. One-way ANOVA was employed to evaluate variations among the groups, followed by Tukey's Honestly Significant Difference (HSD) test.

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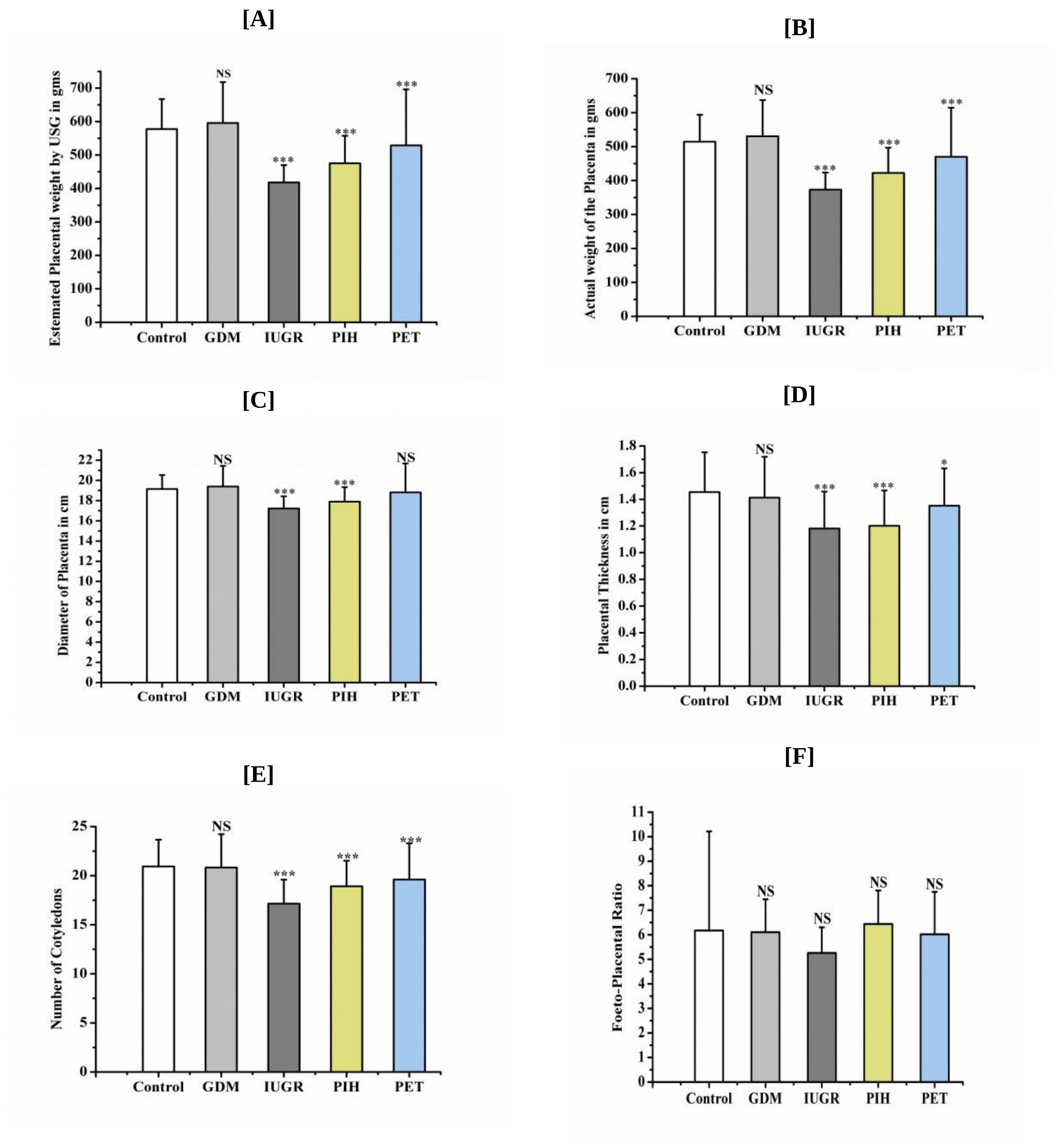
RESULTS

Estimated placental weight by USG:

This study's findings exhibited considerable variation among the groups (F4, 395 = 27.25, *P* = 0.00001), it was found in one-way ANOVA. Except the gestational diabetes mellitus group all groups (IUGR, PIH, and PET) showed highly significant (t= 8.87, *P* = 0.00001, t= 7.94, *P* = 0.00001, and t= 2.45, *P* = 0.007464 respectively) reduction in estimated placental weight than the normal pregnant women. Using Tukey's HSD post hoc analysis, the major variation was further evaluated and determined to be considerable (*P* ≤0.05). The estimated placental weight was examined between the groups.



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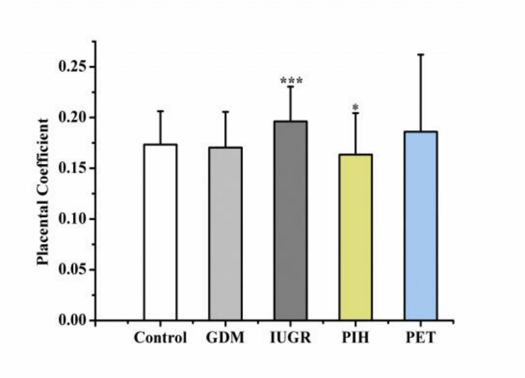

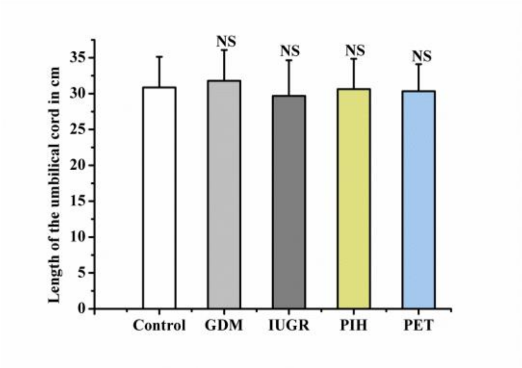

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Figure 1: Parameters of Placenta and umbilical cord in high-risk groups in comparison with control: A) Estimated placental weight by USG, B) actual placental weight, C) Diameter of the placenta, D) Placental thickness, E) Number of cotyledons, F) fetoplacental ratio, G) Placental Coefficient, H) length of umbilical cord

The data is indicated as mean ± standard deviation. The statistical significance is shown by the superscripted stars (*). NS- Non-significant, ***p0.001, **p0.01, *p0.05.

It was significantly less in IUGR, PIH, and PET groups than in GDM (t=7.134, p=0.00001, t= 6.38. p=0.00001 and t= 2.18. p=0.015888 respectively). The IUGR group showed the least estimated placental weight than the rest of the groups, followed by the PIH and PET groups. The GDM vs. IUGR, GDM vs. PIH, GDM vs. PET, IUGR vs. PIH, IUGR vs. PET, and PIH vs. PET showed statistically significant difference (t= 7.13, P = 0.00001, t= 6.38, P = 0.00001, t= 2.18, P = 0.015888, t= 3.30, P = 0.000699, t= 3.24, P= 0.001013and t= 2.04, P= 0.022133 respectively) (Figure 1A).

Actual placental weight

The findings of the one-way ANOVA showed a noteworthy (F4, 395 = 27.85, P = 0.00001) difference among the groups in the actual weight of the placenta. Except for gestational diabetes mellitus group rest, all group groups (IUGR, PIH, and PET) showed highly significant (t= 8.81, P = 0.00001, t= 8.02, P = 0.00001, and t= 2.53, P = 0.00587 respectively) reduction in actual placental weight than the normal pregnant women. The actual placental weight was examined between the groups. It was significantly less in IUGR, PIH, and PET groups than in GDM (t=7.134, p=0.00001, t= 6.38. p=0.00001 and t= 2.18. p=0.015888 respectively). The IUGR group showed the least actual placental weight than the rest of the groups, followed by the PIH and PET groups. The GDM vs. IUGR, GDM vs. PIH, GDM vs. PET, IUGR vs. PIH, IUGR vs. PET, and PIH vs. PET showed statistically significant differences (t= 7.18, P = 0.00001, t= 6.50, P = 0.00001, t= 2.28, P = 0.012412, t= 3.08, P = 0.001389, t= 3.23P= 0.001029 and t= 2.06, P= 0.021054 respectively) (Figure 1B).

Diameter of Placenta

A considerable variation in Placental diameter was noticed among the groups using one one-way ANOVA test (F4, 395 = 14.91, P = 0.00001). When compared between the groups t-test results exhibited no difference in GDM and PET group than control. Whereas PIH and PET groups showed significantly lower placental diameter when compared with normal (t=6.82, P = 0.00001, and t= 6.18, P = 0.00001 respectively).

The least placental diameter was found in IUGR followed by PIH group individuals. The GDM vs. IUGR, GDM vs. PIH, IUGR vs. PIH, IUGR vs. PET, and PIH vs. PET showed substantial differences (t= 5.07, P = 0.00001, t= 4.70, P = 0.00001, t= 2.08, P = 0.019825, t= 2.62, P = 0.005592and t= 2.01P= 0.023265 respectively), whereas GDM vs. PET was not showed any difference (Figure 1C).

Placental thickness

The findings of the ANOVA examination showed a considerable variation in the thickness of the placenta among the groups (F4, 395 = 12.38, P = 0.00001). The placental thickness was examined between the groups. Except for the gestational diabetes mellitus group rest, all group groups (IUGR, PIH, and PET) showed highly significant (t= 4.44, P = 0.00001, t= 5.94, P = 0.00001, and t= 1.77, P = 0.038 respectively) reduction in placental thickness than the normal pregnant women. The IUGR group showed the least placental thickness than the rest of the groups, followed by the PIH and PET groups. The GDM vs. IUGR, GDM vs. PIH, IUGR vs. PET, and PIH vs. PET exhibited statistically considerable differences (t= 3.33, P = 0.000622, t= 4.09, P = 0.000038, t= 2.28, P = 0.013118 and t= 2.49, P = 0.007312 respectively), whereas GDM vs. PET, IUGR vs. PIH was not showed difference (Figure 1D).

Number of cotyledons

The one-way ANOVA test results showed a significant difference in placental cotyledon count among the groups (F4, 395 = 14.93, P = 0.00001). The placental cotyledon count was examined between the groups. Except for the gestational diabetes mellitus group rest, all group groups (IUGR, PIH, and PET) showed highly significant (t= 6.76, P = 0.00001, t= 5.14, P = 0.00001, and t=2.40, P= 0.008464 respectively) reduction in number of cotyledons than the normal pregnant women. The IUGR group showed the least placental cotyledon count than the rest of the groups, followed by the PIH and PET groups. The GDM vs. IUGR, GDM vs. PIH, IUGR vs. PIH, and IUGR vs. PET were ‘shown to be statistically significant (t= 5.00, P = 0.00001, t= 3.50, P = 0.00032, t= 2.94, P = 0.002089, t= 2.86, P = 0.002929 respectively) whereas GDM vs. PET and PIH vs. PET was not exhibited considerable difference (Figure 1E).

Foeto-Placental Ratio

The difference in the Foeto-Placental Ratio among the groups was not significant (F4, 395 = 0.65, P = 0.620537), it was determined by one-way ANOVA. No high-risk group showed a significant difference when compared with normal. However, GDM vs. IUGR, IUGR vs. PIH, and IUGR vs. PET exhibited statistical differences (t= 2.87, P = 0.002546, t= 3.91, P = 0.000091, t= 1.93, P = 0.029023 respectively), whereas GDM vs. PIH, GDM vs PET and PIH vs. PET was showed significant difference (Figure 1F).

Placental Coefficient

A statistically considerable difference in the Placental Coefficient was observed among the groups using a one-way ANOVA test (F4, 395 = 3.97, P = 0.003567). When compared between the groups t-test results exhibited no difference in the GDM and PET cohort than the normal. Whereas PIH and PET groups showed significantly higher Placental coefficients when compared with normal (t=3.33, P = 0.000498, and t= 1.93, P = 0.026725 respectively). The least placental coefficient was found in PIH group individuals. The GDM vs. IUGR, IUGR vs. PIH, and PIH vs. PET showed considerable differences (t=3.15, P = 0.001082,t=3.56, P = 0.000307and t= 1.82922, *P* = 0.035377 respectively) whereas GDM vs. PIH, GDM vs. PET and IUGR vs. PET was not exhibited considerable difference (Figure 1G).

Length umbilical cord

The difference in the Length umbilical cord among the groups was not significant (F4, 395 = 1.37, *P* = 0.24038), it was determined by one-way ANOVA. No high-risk group showed a significant difference when compared with normal. However, the IUGR group showed the least Length umbilical cord but it was not significant statistically. The GDM vs. IUGR demonstrated a statistically noteworthy distinction (t= 1.99, *P* = 024588) rest did not show any difference statistically (Figure 1H).

Umbilical artery pulsatility index

The findings of the ANOVA investigation showed that there was a considerable variation in the Umbilical artery pulsatility index among the groups (F4, 395 = 27.25, *P* = 0.00001). All the high-risk groups (GDM, IUGR, PIH, and PET) showed highly significant (t= 10.32, *P* = 0.00001, t= 8.41, *P* = 0.00001, t= 11.39, *P* = 0.00001, and t= 7.66, *P* = 0.00001 respectively) elevation in UA PI than control (Figure 2A). The UA PI was examined between the cohorts. There was no considerable distinction between the high-risk clusters.

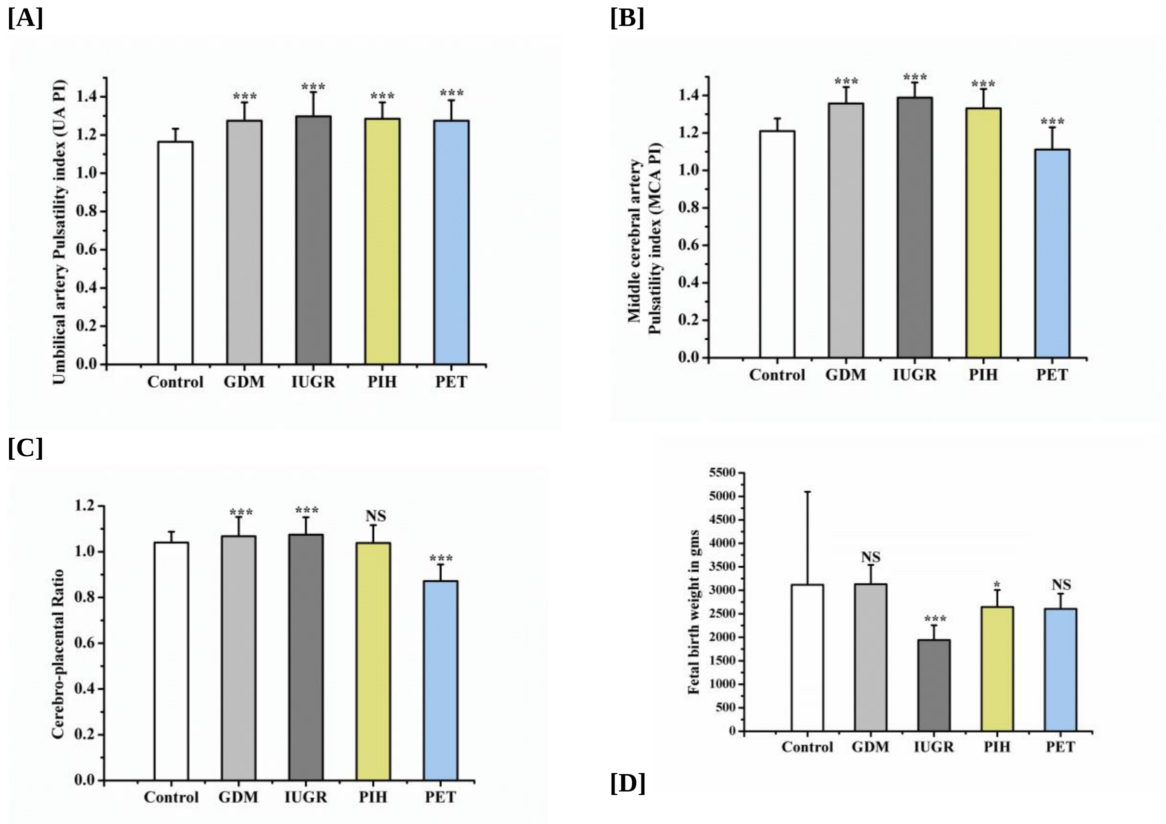

Figure 2: Doppler indices and birth weight in high-risk groups in comparison with control: A) Umbilical artery pulsatility index, B) middle cerebral artery pulsatility index, C) Cerebro placental ratio. D) Fetal birth weight

The data is indicated as mean ± standard deviation. The statistical significance is shown by the superscripted stars (*). NS- Non-significant, ***p0.001, **p0.01, *p0.05.

Middle cerebral artery pulsatility index

There was an extremely considerable distinction in the MCA PI among the groups (F4, 395 = 93.23, *P* = 0.00001), which was observed by using the ANOVA test. The high-risk groups including GDM, IUGR, and PIH showed highly significant (t= 14.24, *P* = 0.00001, t= 12.40, *P* = 0.00001, and t= 10.87, *P* = 0.00001respectively) elevation in Middle cerebral artery pulsatility index than the normal pregnant women but it was significantly (t= 6.670, *P* = 0.00001) reduced in PET group individuals than normal. The MCA PI was observed in between the high-risk cohorts. There was no significant difference between the high-risk groups. GDM vs. PET, IUGR vs. PIH, IUGR vs. PET, and PIH vs. PET showed statically significant differences (t=11.26, *P*= 0.00001, t= 2.48, *P* = 0.007489, t= 10.052, *P* = 0.00001 and t= 9.055, *P* = 0.00001 respectively), rest did not show a significant difference (Figure 2B).

Cerebroplacental Ratio

The one-way ANOVA test results showed a significant difference in Cerebroplacental ratio among the groups (F4, 395 = 56.94, *P* = 0.00001). The Cerebroplacental Ratiowas examined between the groups. GDM and IUGR groups showed substantially higher Cerebroplacental Ratio than normal (t= 3.35, *P* = 0.000448, t= 3.27, *P* = 0.000609 respectively) whereas PET exhibited lower Cerebroplacental Ratio than the control (t= 17.15, *P* = 0.00001). However, PIH showed no difference when compared with the control. The GDM vs. IUGR was not significant (t= 0.36, p=0.358216) whereas GDM vs. PIH, GDM vs. PET, IUGR vs. PIH, IUGR vs. PET, and PIH vs. PET were exhibited significant difference (t=2.01, *P*= 0.022949, t= 10.94, *P* = 0.00001, t= 2.00, *P* = 0.024091, t=10.20, *P*= 0.00001, and t= 9.75, *P* = 0.00001 respectively) (Figure 2C).

Fetal birth weight

The one-way ANOVA test results showed a significant difference in Foetal birth weight among the groups (F4, 395 = 4.92, *P* = 0.000692). The Foetal birth weight was examined between the groups. IUGR and PIH groups showed substantially lower Foetal birth weight than normal (t= 3.02, *P* = 0.001367, t=1.84, *P* = 0.032781 respectively) whereas GDM and PET did not demonstrate considerable distinction statistically (t= 0.04, *P*=0.480263, t=1.41, *P*=0.07882). The PIH vs. PET was not significant (t= 0.49, p=0.310449) whereas GDM vs. IUGR, GDN vs. PIH, GDM vs. PET, IUGR vs. PIH, and IUGR vs. PET were exhibited statistically considerable variation (t=13.28, *P*= 0.00001, t= 7.00, *P* = 0.00001, t= 6.17, *P* = 0.00001, t=8.59, *P*= 0.00001, and t= 7.74, *P* = 0.00001 respectively) (Figure 2D).

Luminal Area Umbilical vessels

Luminal Area UmbilicalArtery 1

There was a highly significant variation in Luminal Area Umbilical artery 1 among the groups (F4, 395 = 10.63, *P* = 0.00001), it was tested by ANOVA test. All the high-risk groups (GDM, IUGR, PIH, and PET) showed highly significant (t= 4.50, *P* = 0.000013,t= 3.15, *P* = 0.001246, t= 4.06, *P* = 0.000063 and t= 3.37, *P* = 0.000624 respectively) reduction in luminal area of umbilical artery 1than the normal pregnant women. The luminal area umbilical artery 1 was observed in between the high-risk groups and detected no significant difference (Figure 3A& Figure 4).

Luminal Area Umbilical Artery 2

There was no significant variation in Luminal Area Umbilical artery 2 among the groups (F4, 395 = 1.58, *P* = 0.184392), it was tested by the results of the ANOVA test. All the high-risk groups (GDM, IUGR, PIH, and PET) showed a relative reduction in Luminal Area Umbilical artery 2 than the normal pregnant women but it was not statistically significant because of the high standard deviation of means. The Luminal Area Umbilical artery 2 was observed in between the high-risk groups and found no significant difference (Figure 3B& Figure 4).

Luminal Area Umbilical vein

There was no significant variation in the Luminal Area Umbilical vein among the groups (F4, 395 = 0.32, *P* = 0.858187), it was tested by the results of the ANOVA test. All the high-risk groups (GDM, IUGR, PIH, and PET) showed relatively equalLuminal Area Umbilical veins than the normal pregnant women, except the IUGR group which showed higher Luminal Area Umbilical vein but it was not statistically significant because of the high standard deviation of means. The Luminal Area Umbilical vein was observed in between the high-risk groups and found no significant difference (Figure 3C& Figure 4).

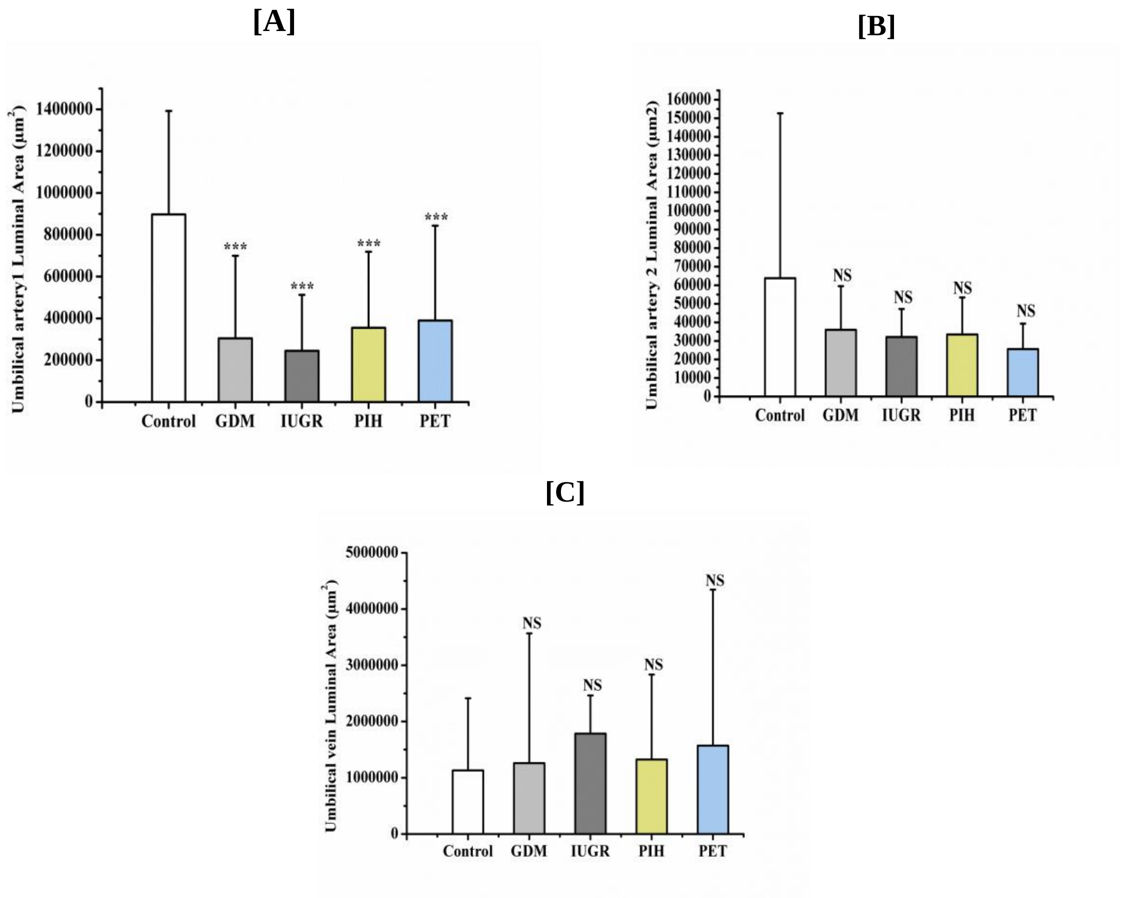

Figure 3: The luminal diameter of umbilical vessels in different high-risk groups in comparison with control: A) Umbilical artery 1 lumenal area, B) Umbilical artery 2 lumenal area, C) Umbilical vein lumenal area

The data is indicated as mean ± standard deviation. The statistical significance is shown by the superscripted stars (*). NS- Non-significant, ***p0.001, **p0.01, *p0.05.

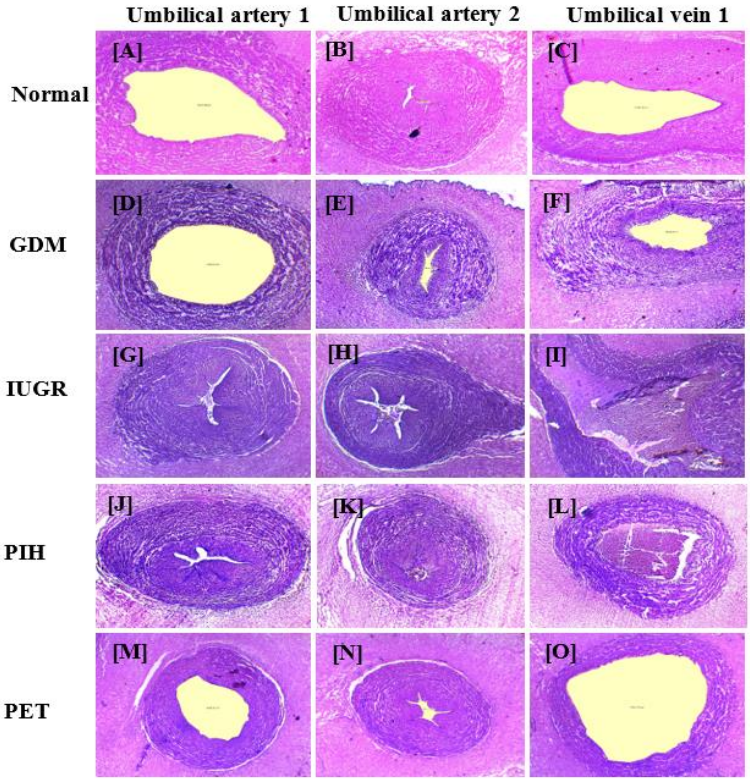

Figure 4: Representative photomicrographs of umbilical vessel sections of different high-risk groups and control stained with H&E

DISCUSSION

The placenta is an essential structure for nutrients and metabolite exchange between the mother and coceptus, the placenta is a vital organ. Normal umbilical cord attachment occurs in the middle of the fetal aspect of the placenta. The length of the stem villi decides the thickness of the placenta. Hyperplasia and hypertrophy are the two stages of the placenta's growth and development(18). Current study results exhibited that except for the gestational diabetes mellitus group rest of the groups (IUGR, PIH, and PET) showed a highly significant reduction in estimated placental weight and actual placental weight than normal pregnant women. It is in line with an earlier study conducted by Helen McNamara et al., 2014, who advocated that reduced weight of the placenta was linked to persistent hypertension, but pre-eclampsia was only linked to low placenta weight prior to birthweight adjustment. High placental weight was associated with anemia and gestational diabetes both before and after birthweight correction(8). Placental volume weight of the baby and placenta were all reduced in the groups with PET, and gestational diabetes mellitus, and smaller for gestational age (SAG) than control cohort (2).

The present study results demonstrated that placental thickness was reduced in all high-risk groups except the gestational diabetes mellitus group and very little difference was shown in the Preecalmsia group. According to the research that has been published by Sun et al., 2021, the elevated thickness of the placenta might be a strong prognosticator of high-risk pregnancies, particularly those with PET, hydrops fetalis, and gestational diabetes mellitus (19), it is in line with the current study findings there was a rise in the number of blood vessels per placental villous in diabetes individuals. It is because of increased neoangiogenesis in diabetic individuals. All of these blood arteries had thicker walls despite being young and several of them had fibrinoid thrombi. Some of the villous blood arteries in the diabetic placentae were found in the center of the villi. As a result, the placental barrier's thickness was raised in the placentae of diabetics (20). While IUGR exhibited a drastic reduction in placental thickness followed by PIH. Generally speaking, the placental thickness should be 10 mm, or about equivalent to the fetal age in weeks, as the thickness of the placenta rises throughout pregnancy (21). The prevalence of both SGA and large-for-gestational-age fetuses (LGA), hydrops fetalis, and greater perinatal death have all been linked to the thickness of the placenta (21,22). The present research results showed no distinction in the thickness of the placenta in the gestational diabetes mellitus, Preeclampsia toxaemia group than the normal pregnant women. Whereas PIH and PET groups showed significantly lower placental diameter. The least placental diameter was found in IUGR followed by PIH group individuals.

According to previous investigations, the number of cotyledons is much larger in the placentas of GDM women than in non-GDM moms. In contrast to the non-GDM group, the GDM group placentas simultaneously increased in width and weight, which may have been an adaptive response(23). Current study results supporting aforesaid research findings, the placental cotyledon count except for the gestational diabetes mellitus group was higher but did not show statistical significance, the rest of all group groups (IUGR, PIH, and PET) showed a reduction in the number of cotyledons than the normal pregnant women it is in line with existing literature stated that Preeclampsia caused an inadequate blood supply, which was reflected in the preeclampsia group's smaller placentae's diameter, thickness, number of cotyledons, and volume(24). Pre-eclamptic pregnancies had considerably lower fetal birth weights and placental weights, diameters, and cotyledon counts than normotensive pregnancies(25). The IUGR group showed the least placental cotyledon count than the rest of the groups, followed by the PIH and PET groups. As a result of their increased risk of hypoxemia, IUGR infants with placental insufficiency are less likely to withstand labor and are more likely to give birth through cesarean section. Infants with IUGR have lower APGAR scores than controls and almost half of them develop intrapartum hypoxia. Additionally, it has been shown that these babies have a greater incidence of meconium aspiration (26).

In a healthy pregnancy, placental weight (PW), fetal weight (FW), and the F/P weight ratio all increase gradually with preceding gestational age, with the FW increasing more quickly than the weight gain of the placenta. After the fetus outgrows the placenta at 42 weeks of gestational age, the F/P ratio rises gradually at first before rising suddenly at 43 weeks of gestational age. Gestational age greatly influences FW, PW, and F/P ratios(27). The fetoplacental ratio rise in the group of normal pregnant women(27) but in this study, we did not find any significant alteration in high-risk groups when compared with control.

In contrast to the non-GDM group, the umbilical cord length was shorter in the GDM cohort(28), Gestational hypertension was linked to umbilical cord anomalies, such as aberrant length, diameter, insertion, entanglements, knots, and coils (29), but this study's results did not show any significant difference in high-risk groups when compared to the control.

The fetal circulatory alterations that result from hypoxia include elevated impedance in umbilical veins and decreased impedance in cerebral arteries. Less maternal cardiac output and greater peripheral vascular resistance are related to these modifications. When umbilical Doppler results are seriously aberrant, this becomes especially clear. To ameliorate pathologically aberrant uteroplacental function and, therefore, fetal state, this link opens the possibility of therapeutic treatment of maternal cardiovascular function(30).

The current study result revealed that all the high-risk groups including GDM, IUGR, PIH, and PET showed a highly significant elevation in Umbilical artery pulsatility index than normal pregnant women. The high-risk groups including GDM, IUGR, and PIH showed a highly significant elevation in the Middle cerebral artery pulsatility index than normal pregnant women but it was significantly reduced in PET group individuals than normal. According to Leung et al., neither UA-PI nor MCA-PI was helpful for identifying an aberrant pregnancy outcome in GDM(31). While Niromanesh et al. claimed that faulty UA Doppler evaluation is associated with poor newborn outcomes(32). Additionally, Shabani et al. emphasized that individuals with GDM had higher MCA PI values(33). Further, earlier research did not assess standardized color Doppler ultrasound (CDUS) characteristics; for instance, certain investigations assessed only PI values, while others focused on the CP ratio, etc. Besides, the majority of the investigations that were published in the scientific literature used CDUS data that were collected during third-trimester assessments. Moreover, Niromanesh et al. 2017 emphasized the usefulness of UA and MCA CDUS alterations in prognosticating poor infant outcomes in GDM cohort. They used a different approach and assessed how CDUS alterations affected the course of the pregnancy. Instead of defining CDUS characteristics separately, they simply characterised UA and MCA exams as normal or abnormal. They also did not provide a certain timing for CDUS evaluation (32).

The values of mean PI, RI, and SD were substantially greater in umbilical artery IUGR patients than in non-IUGR instances, whereas the values of MCA PI, RI, and SD were considerably less in IUGR cases than in non-IUGR individuals (34). According to earlier investigations, cases with severe PIH had a considerably higher mean UA-PI than individuals with moderate PIH(35), which is similar to the current study. However, the PI values of fetal MCA were considerably lower among PIH patients (35), which is in contrast with current study results. Similar fluctuation in Doppler indicators with the severity of the disorders was also seen in research on pre-eclampsia and prenatal hypertension individuals. As gestational age increased, the normal ratios of MCA/uterine artery PI dropped. 30% of moderate instances and 46% of severe cases of pre-eclampsia exhibited fetal circulation, as evidenced by a low ratio of MCA/uterine artery PI (36).

In comparison to healthy fetuses, Shivani Singh et al. (2013) found that intrauterine growth restriction fetuses had higher Doppler indices (37). According to Sattar MA et al., 2011in comparison to the normal group, the intrauterine growth restriction suspected fetuses group had higher values of Doppler PI (38). Their conclusions of Doppler’s findings are akin to the current investigation.

Low CPR and the perinatal outcomes of pregnancies affected by a hypertension condition are related. Compared to other forms of hypertension diseases, this association seemed to be greater in PET (39), these findings are in line with our observation. In comparison to the control groups, the Cerebroplacental Ratio in the

GDM and IUGR groups revealed markedly greater values, whereas PET showed lower values. However, due to fetal discomfort and a composite unfavorable perinatal outcome, lower CPR is linked to a greater probability of obstetric intervention(40), this change we observed only in the PET group.

While the GDM and PET groups did not show statistical significance in the birth weight of newborns compared with control. However, the IUGR and PIH groups showed a substantial reduction in fetal birth weight. The GDM group did demonstrate a greater fetal weight, which is consistent with past results. The risk of LGA and greater birth weight were both significantly enhanced by GDM. Post-load glucose levels had more of an impact on fetal development than FBG. Additionally, the birth weight, likelihood of LGA, and macrosomia were all significantly affected by the blood glucose levels at various time points(41). A decrease in birth weight was correlated with preeclampsia(42). Low birth weight and IUGR are both made more likely by preeclampsia (43). Preterm births were more common in preeclamptic women (26.7%). Preeclamptic mothers gave birth to babies with lower birth weights, lengths, and head circumferences. Significant statistical contributions to SGA were made by severe preeclampsia. The hypoperfusion model was utilized to explain the pathophysiology of preeclampsia in PIH mothers who had LBW babies. When uteroplacental perfusion decreased owing to preeclamptic women's condition, LGA children were delivered as a result of compensating illnesses such as gestational diabetes mellitus or obesity in mothers(44).

Infants with IUGR or SGA status at delivery are more likely to die during pregnancy and have birth-related complications, such as acidosis during the perinatal period, hypothermia, coagulation abnormalities, hypoglycemia, and specific immunologic issues. Along with chronic lung disorders as well as necrotizing enterocolitis, babies with IUGR appear to be more vulnerable to other prematurity-related problems. The effects of IUGR on children include a small but considerable rise in the risk of neurological problems such as cerebral palsy as well as an increased risk of short stature, cognitive delays, and compromised performance in school(45). A newborn with a low birth weight is born at full term weighing less than 2500Gms (46). It may be the result of premature delivery or IUGR is frequently a comorbidity of preterm birth and is correlated with both the aided and unassisted induction of preterm delivery (47,48). All the high-risk groups (GDM, IUGR, PIH, and PET) showed a highly significant reduction in the Luminal Area Umbilical artery 1than the normal pregnant women. Luminal Area Umbilical artery 2 is also lower in high-risk groups than control but it was not statistically significant because of the high standard deviation of means. All the high-risk groups showed relatively equal luminal area umbilical veins than the normal pregnant women, except the IUGR group which showed a higher Luminal Area Umbilical vein but it was not statistically significant because of the high standard deviation of means. We couldn’t find any earlier research data related to the luminal area of umbilical vessels.

The study aims to offer a comprehensive understanding of the relationships between Doppler indices and placental/neonatal morphometry in various pregnancy complications and normal pregnancies. The findings from this study could have implications for better understanding the pathophysiology of pregnancy complications and for potentially improving clinical management strategies. Limitations, such as the cross-sectional design and potential confounding variables, will be acknowledged. The

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study will consider subgroup analyses based on the severity and timing of pregnancy complications if feasible.

Conclusion: This research enriches the understanding of the interrelationships among Doppler indices, placental parameters, and high-risk pregnancies, offering a comparative lens by including normotensive pregnancies. By shedding light on the intricate dynamics at play, the study paves the way for improved maternal and fetal care, providing a foundation for evidence-based clinical decisions within the realm of high-risk obstetrics.

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