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Relationship between Placental Pulsatility Index and Umbilical Venous Blood Flow

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ABSTRACT

The Placental Pulsatility Index (PPI) and umbilical venous blood flow are critical parameters in assessing fetal well-being during pregnancy. This study investigates the relationship between PPI, a measure of placental vascular resistance, and umbilical venous blood flow, a key indicator of fetal oxygen and nutrient supply. Through a comprehensive analysis of prenatal ultrasound data from a cohort of pregnant women, we explore how variations in PPI correlate with changes in umbilical venous blood flow. Our findings reveal a significant association between these two parameters, shedding light on their interplay and potential implications for fetal development and health. Understanding this relationship may provide valuable insights for clinicians in monitoring and managing pregnancies, particularly in cases of compromised fetal well-being. This research contributes to the broader knowledge of fetal physiology and the assessment of fetal health during gestation.

Keywords: Placental pulsatility index; Umbilical vein; Umbilical venous blood flow; Crown rump length; Resistance index

INTRODUCTION

A importance organ in the womb called the placenta transmits oxygen and nutrients between the mother and the fetus *via* the umbilical vein in pregnancy [1,2]. The circulation of the placenta plays an essential role in many fetal or maternal conditions. Placental vascular remodelling failure in the 1st trimester results in placental insufficiency and is strongly associated with the risk of perinatology morbidity and mortality, including fetal growth reduced velocity or restriction, prematurity, fetal central nervous system damage, hypoxia, and stillbirth. Furthermore, it increases the obstetrical complications of pre-eclampsia [3-7]. Due to this, ultrasound assessment of placental insufficiency became increasingly important during pregnancy. The most common methods for evaluating placental impedance in the previous studies were uterine artery Doppler and umbilical artery Doppler. Umbilical artery flow may be indicative of fetal side placental resistance. Uterine artery flow determines may be reflected in the placenta of maternal upstream blood flow resistance [8-13]. In recent years, Gudmundsson S, et al. developed a new index for determining the impedance of both the maternal and fetal sides of the placenta simultaneously: The placental Pulsatility Index (PPI) [14]. Compared with the conventional Doppler method of UA and UtA alone, it was more sensitive to predict unfavourable outcomes when used with PPI. Todumrong N, et al. analyse the relationship between the Placental Pulsatility Index (PPI) and adverse pregnancy outcomes in the 2nd trimester of high-risk pregnancies. The results showed that a higher value of PPI has relevance to Small for Gestational Age (SGA), FGR, and adverse perinatal outcomes [15].

Fetal growth development maturation in the womb depends on 2 important parameters: Genetic factors and blood flow. One of the most common causes of poor growth development during perinatology is placental insufficiency [1,16,17].

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Placental malperfusion reduction in the blood supply from the mother can lead to fetal hypo-oxygenation and poor nutrition. A measure of placental perfusion and function may be provided by the volume of blood flowing in the Umbilical Vein (UV), which indicates oxygen and nutrients reaching the fetus. In this situation, blood flow in the umbilical vein plays a crucial role in assessing the placental blood supply to the fetus [18]. During the past few years, the measurement of Umbilical Venous Blood Flow (UVBF) has become easy and possible with newer ultrasound equipment and software. With UBVF, it is possible to conduct a more comprehensive evaluation of prenatal Doppler ultrasounds [17,19-23]. Nonetheless, as far as we are aware, no previous study has investigated the relationship between blood flow in the umbilical veins and PPI in the human fetus. The present study aims to determine the relevance of UVBF and PPI, to construct a new reference chart for UVBF according to the Placental Pulsatility Index (PPI), due to PPI could be an index declared to be at fault for the combined placental resistance which includes either side in maternal and fetal. Therefore, our information could provide a theoretical foundation for predicting fetal intrauterine growth and development and thus assist clinical prediction and intense surveillance of fetuses with adverse pregnancy outcomes.

MATERIALS AND METHODS

Settings

Our study data collected from 792 women with singleton pregnancies during 21^{+1} ~ 40^{+6} weeks between January 2022 and December 2022 were used for cross sectional analyses. Our research was approval by the Medical Research Ethics Review Committee of Fujian Medical University affiliated Mindong Hospital Ningde (Issued: 2022083101K). All our research procedures followed the guidelines of our institutional medical research ethics committee. With the exception of pregnancies with Assisted Reproductive Technology (ART), fetal Gestational Age (GA) was determined from the time of delivery using fetal Crown-Rump Length (CRL) at ultrasonography at 8 weeks-14 weeks. Exclusion criteria were chromosomal abnormalities in the history, fetal structural abnormalities, and maternal complications. According to the ISUOG and AIUM practice guidelines, the CRL, fetal biometry, Umbilical Artery Doppler Pulsatility Index (Um A PI), Umbilical Artery Resistance Index (Um A RI), Uterine Artery Doppler Pulsatility Index (Ut A PI), Uterine Artery Resistance Index (Ut A RI), Time-Averaged Maximum Velocity (TAMXV), and Time-Averaged Intensity-weighted mean velocity (TAV) of the umbilical vein (UV) [24-28]. After tracing the accuracy Doppler waveform was confirmed, the ultrasound equipment's built-in calculation software can handle most of the Doppler index calculations automatically. In all cases, fetal examinations were performed with a Voluson E10 ultrasound platform (General Electric Medical Systems, Milwaukee, WI, USA) with C2-9-D multifrequency transabdominal transducers (XD Clear Wide Band Convex Probe). To ensure fetal safety, all prenatal sonographic procedures are performed according to the ALARA (as low as reasonably achievable) principle. All scans and fetal measurements were performed by a single licensed physician who had more than 10 years of experience in obstetric ultrasonography. To evaluate repeatability among observers, reliability statistics were used to assess interobserver agreement in repeated fetal biometric measurements by the same examiner.

Fetal Doppler Flow Index Quantitative Setting

The adequate size of the color box and suitable PRF and gain were optimized for color flow mapping and Doppler index acquisition. To avoid the Doppler velocities and waveforms being misclassified as absent or abnormal. The angle of insonation was kept at 0° as much as possible, or stability was maintained at less than 20°. The Doppler spectrum was recorded during fetal moving at rest and during breathing resting intermitted. The Doppler exposure time was always kept as short as possible (not longer than 5 minutes) [27]. All the Doppler index obtained was calculated by the software of the ultrasound system automatically. For the Umbilical Artery (Um A) flow measurement, the umbilical artery Doppler waveforms were obtained in a free cord loop transabdominal. The Doppler index of the umbilical artery in our study included the Systolic-to-Diastolic Ratio (S/D), Pulsatility Index (PI), and Resistance Index (RI). For the Uterine Artery (Ut A) flow measurement, the uterine artery Doppler waveforms were obtained through transabdominal examination. The probe is placed Trans abdominally, angled medially in the parasagittal plane, and placed longitudinally in the lower lateral quadrant of the abdomen. The point of 1 cm which downstream of the external iliac artery crosses the uterine artery, which can be identified using color flow mapping. Depending on the orientation of the uterine artery, the probe position should be adjusted to achieve the best insonation angle. The Doppler index of the uterine artery in our study included the Systolic-to-Diastolic Ratio (S/D), Pulsatility Index (PI), and Resistance Index (RI).

The PPI calculated according to the formula [14]:

PPI=(Um A PI+mean of the left and right Ut A PI)/2.

For measurement of Umbilical Venous Blood Flow (UV), the site of the umbilical artery was chosen to be at the same location as the free loop of the umbilical vein.

Assessment of Umbilical Venous Diameter (UV_d): For the measurement of UVd, the UV vessel wall is perpendicular to the direction in which the ultrasound beam travels. The corresponding magnified grayscale image with clearly visible UV vascular wall line followed by UV diameter was measured [29].

The equation of UV blood flow (UVBF) (mL/min):

UVBF=Cross-section area of UV (mm^2) × mean velocity (mm/s) × 60

Data Analysis

We performed statistical analysis using the Statistical Package for the Social Sciences (SPSS, Ver. 25.0 for Windows; Chicago, IL, USA). Statistical significance was determined by a probability value of $p<0.05$. Mean, Standard Deviation (SD), and percentiles of the GA, fetal biometry, and estimated fetal body weight, PIs of Um A, Ut A and UV flow were determined.

RESULTS

Our study included 492 pregnant women who met the inclusion criteria finally. The median maternal age was 30.00 years old (range, 18 years-44 years old); the median maternal gravidity was 2 (range, 1-9) and the median maternal parity was 0 (range, 0-4). The median gestation age in ultrasound examination was 27^{+1} weeks (range, 21^{+0}-40^{+0} weeks). Maternal and perinatal hemodynamics of the study population are shown in **Table 1**. The average fetal UVBF and PPI were 151.95 ml/min ± 80.69 ml/min and 0.93 ml/min ± 0.20 ml/min, respectively. Regression analysis revealed a negative relationship between the UVBF and PPI. The correlation coefficient of PPI and UVBF, as calculated using the Pearson correlation, was -0.555 (p=0.000). Using regression analysis, the best-fit regression equation was the Exponential function model, which explains the value of UVBF parameters based on PPI. The scatterplots of Umbilical Vein Blood Flow (UVBF) based on Placental Pulsatility Index (PPI) in 492 singleton pregnancies are shown in **Figure 1** with the best-fit regression equation line was the exponential function mode:

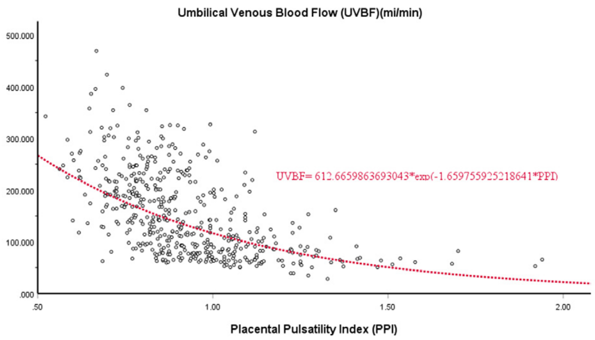

Figure 1: Scatterplots of Umbilical Vein Blood Flow (UVBF) based on placental Pulsatility Index (PPI) in 492 singleton pregnancies. The best-fit regression equation was the exponential function mode (red dashed line)

Table 1: Maternal characteristics and fetal hemodynamics of 492 low-risk singleton pregnancies included in the study population

Parameter	Median	Minimum	Maximum
Maternal age (years)	30	18	44
Gravidity	2	1	9
Parity	0	0	4
GA at measurement (weeks)	27.14	21+0	40+0
UVBF (ml/min)	132.07	21.84	468.9
UV_d (mm)	5.8	3.3	3.9
UV TA_{max} (cm/s)	16.88	8.35	32.71
UA PI	1.03	0.54	1.76
UA RI	0.65	0.42	0.97
mUt A PI	0.75	0.39	2.38
mUt A RI	0.5	0.31	0.86
MCA PI	1.92	0.98	4.41
MCA RI	0.84	0.6	1.85
PPI	0.89	0.52	1.94
CPR	1.87	0.78	5.65

(GA) Gestational Age; (UVBF) Umbilical Vein Blood Flow; (UV_d) Umbilical Vein Diameter; (UV TA_{max}) Umbilical Vein Time-Averaged Maximum Velocity; (UA PI) Umbilical Artery Doppler Pulsatility Index; (UA RI) Umbilical Artery Resistance Index; (mUt A PI) Mean Uterine Artery Pulsatility Index of Bilateral; (mUt A RI) Mean Uterine Artery Resistance Index of Bilateral; (PPI) Placental Pulsatility Index; (CPR) Cerebroplacental Ratio

UVBF=612.6659863693043*exp (-1.659755925218641*PPI).

Based on the PPI values, we categorized them into 8 classes (0.4 to 2.0), and **Table 2** presents the number of cases, mean ± standard deviation, 10^{th} percentile, and 90^{th} percentile UVBF values per class. As the PPI class increased, UVBF proportions decreased.

Table 2: Reference range of UVBF with based on the PPI (N=492)

PPI	n	UV flow (ml/min)		
		Mean (SD)	10^{th} percentiles	90^{th} percentiles
0.41-0.60	7	251.95 (62.94)	141.16	NA
0.61-0.80	126	210.53 (76.80)	117.44	311.91
0.81-1.00	218	150.53 (72.96)	70.62	263.47
1.01-1.20	98	103.85 (51.27)	58.27	188.48
1.21-1.40	31	78.94 (32.97)	39.2	134.72
1.41-1.60	8	65.83 (12.10)	50.7	NA
1.61-1.80	2	69.68 (17.53)	57.29	NA
1.81-2.00	2	59.28 (9.00)	52.92	NA

(UVBF) Umbilical Venous Blood Flow; (PPI) Placental Pulsatility Index

Table 3 showed the Cronbach's Alpha coefficients for the UVBF and PPI with current mean data versus the previous study's mean data. Our observed data have similar mean UVBF values within various GAs as the 50^{th} percentile UVBF in the systematic review by Barbieri M, et al. the Cronbach's alpha of 0.991 was obtained when comparing ours and the study of Barbieri M, et al. [18]. The similar result of the current study is the distribution of PPI throughout the trimester comparison with the reference range by Gudmundsson S, et al. the PPI was decreased with GA in both studies [14]. Comparing the reliability of PPI between ours and previous studies, showed good consistency (Cronbach's alpha: 0.861).

DISCUSSION

A crux strength of our advance is that the UVBF charts were created using PPI, which is particularly foremost for this type of data due to we seriously consider UVBF to be a highly correlated relationship with PPI. We found that UVBF was significantly decreased across PPI increased in the present study. The UVBF and PPI showed a negative exponential correlation in our cross-sectional data. We established the reference ranges for fetal UVBF of normal Chinese fetuses in the function of PPI and formulas to calculate the 10^{th} percentile values of these UVBF parameters to use as the lower normal limits. Nevertheless, ultra-sonographers usually focus on a qualitative assessment of the UV Doppler pattern within pulsations or not. Unfortunately, it usually indicates fetal hypoxia in the late sign. UV pulsation signs usually indicate fetal hypoxia. As a result, this is not an early indication. Compared to UV pulsations, a decrease in UVBF may reflect the pathophysiology of placental insufficiency at an early stage sign. In a previous study, Wang L, et al. descript longitudinal references for 907 fetuses and reported that mean UV blood flow increased from 32.66 ml/min to 381.88 ml/min during weeks 22 to 39 of gestation [22]. DeVore, G. R. and Epstein, A. illustrated 240 fetuses with elevated UV blood flow at weeks 20 to 42 of gestation age [30]. Barbieri, M, et al. performed a systematic review of available reference ranges for UVBF in the human fetus, showing that mean FUV blood flow increased with gestation age [19]. In the present study, we examined the UVBF of 492 normal fetuses (21 weeks-40 weeks) and found that UVBF increased with the progression of pregnancy, UVBF increased from 62.31 ml/min to 305.45 ml/min. Our observed data have similar mean UVBF values within various GAs as the 50^{th} percentile UVBF in the systematic review by Barbieri M, et al. the Cronbach's alpha of 0.991 was obtained when comparing ours and the study of Barbieri M, et al. (Table 3) [19].

Table 3: Cronbach's Alpha coefficients for the UVBF and PPI with current mean data vs the previous study mean data

Item	Cronbach's Alpha coefficients	
	Ccurrent vs Barbieri M	Current vs Gudmundsson S
UVBF	0.991	NA
PPI	NA	0.861

(UVBF) Umbilical Venous Blood Flow; (PPI) Placental Pulsatility Index

Another major key point of the current study is the distribution of PPI throughout the trimester. Our data in comparison with the reference range by Gudmundsson S, et al. which do collate from 53 low-risk pregnancies (248 observations) during 20 weeks-40 weeks of gestation. The PPI was decreased with GA in both studies [14]. Comparing the reliability of PPI between ours and previous studies, showed good consistency (Cronbach's alpha: 0.861). A key strength of our data is that the UVBF and PPI charts were high consistency with the previous research. Utilize high-reliability data to create UVBF using PPI, which is particularly important for this type of data, as UVBF is a highly correlated relationship with PPI. As a consequence, our analysis result would be highly associated with increased reliability of quality high related to our collected data. Finally, our analyses revealed that UVBF and PPI are strongly associated with a negative correlation. With the possibility of converting a PPI value into a UVBF value, we have developed a clinically useful tool for evaluating the placental perfusion situation in fetal-related diseases and for appraising pregnancy prognosis. An important component of a high-risk placental insufficiency fetal ultrasound report should be these values and nomogram for a more exact assessment of UVBF by fetal medicine departments. In conclusion, current study verifies PPI and UVBF showing an inverse relationship in value. We propose a sonographic screening model combining PPI and UVBF in prenatal assessment care plan. In the high risk of placental insufficiency pregnancy, it might be useful for prenatal counselling and even faster critical evaluation in emergency status.

Limitations of the Study

There are 4 limitations in our present study should be considered. 1^{st}, because of the current study was an analysis based on obstetric sonographic reports and clinical data within the limited sample size. 2^{nd}, our study is limited to data from a local tertiary hospital, and the results cannot be extrapolated to other regional hospitals. 3^{rd}, we included only normal fetuses, which do not include pregnancy complications, fetal anomalies, and genetic cases. 4^{th}, placental pathology in placental insufficiency was not performed because of Chinese culture. Our current study was still not comprehensive enough, further research would consider assessing both healthy children and a spectrum of conditions into further research, and test the validity of cut-offs derived from them.

CONCLUSION

In conclusion, current study verifies PPI and UVBF showing an inverse relationship in value. We propose a sonographic screening model combining PPI and UVBF in prenatal assessment care plan. In the high risk of placental insufficiency pregnancy, it might be useful for prenatal counselling and even faster critical evaluation in emergency status.

AUTHORS CONTRIBUTION

Wei-Hsiu Chiu: Conceptualization, methodology, formal analysis, investigation, resources, data curation, writing-original draft, project administration.

Xiu-Qin Wu: Methodology, formal analysis, investigation, resources, data curation, project administration.

Lin Ye: Investigation, resources, data curation.

Xiao-Bin Zhang: Conceptualization, methodology, investigation, resources, data curation

Xiao-Feng Yang: Conceptualization, methodology, investigation, resources, data curation.

Yong-Qiang Hong: Conceptualization, methodology, formal analysis, investigation, resources, data curation, project administration.

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CONFLICT OF INTEREST

All authors declare that he does not have any competing interests.

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