Role of first trimester uterine artery Doppler indices in Prediction of pre-eclampsia

Mostafa Mohamed Khodary[a], Ahmed Hashim Abdel Ellah[a], Suma Abdelraheem Abouelwafa[a*], Mahmoud Soliman Iews[a]

[a]Obstetrics and Gynecology Department, Faculty of Medicine, South Valley University, Qena, Egypt

Abstract

Background: Pre-eclampsia (PE) is associated with a high rate of maternal and perinatal morbidity and mortality, so its prediction has a tremendous impact on its management.

Objectives: To evaluate the role of uterine artery Doppler indices in the prediction of pre-eclampsia during the first trimester of pregnancy**.**

Patients and methods: During the early stages of their pregnancies, 60 expectant mothers received early pregnancy care at South Valley University Hospital between weeks 9 and 11. Assessments included clinical exams, medical history, lab tests, abdominal ultrasound, and uterine artery Doppler scans at 9, 11, and 18 weeks.

Results: The mean age of patients was 24.8 ± 3.4 years, with a mean body mass index (BMI) of 24 ± 2.3 kg/m2. There were 13 patients (23.6%) with PE; out of them, 9 patients had a severe form of PE, and 42 patients (76.4%) had no PE. Doppler flow study of the uterine artery at 9–11 and 18 weeks showed statistically significant (p-value<0.05) increased left and right uterine artery pulsatility index (PI) and residence index (RI) in patients with PE (1.17±0.33) when compared with patients without PE (0.95±0.28), and there was a highly statistically significant (p-value<0.05) increased percentage of presence of notch in patients with PE (7 patients, 53.8%) when compared with patients without PE.

Conclusion: We found statistically significant increases in uterine artery PI and RI in patients with PE when compared with patients without PE. The presence of notch in the uterine artery wave is highly predictive for development of preeclampsia.

Keywords: Uterine Artery Doppler; Pre-eclampsia; Pregnancy

***Correspondence**: sm493190@gmail.com

DOI: 10.21608/svuijm.2023.236407.1698

Received: 1 September, 2023.

Revised: 30 September, 2023.

Accepted: 1 October, 2023.

Published: 10 February, 2024

Cite this article as: Mostafa Mohamed Khodary, Ahmed Hashim Abdel Ellah, Suma Abdelraheem Abouelwafa, Mahmoud Soliman Iews (2024). Role of first trimester uterine artery Doppler indices in Prediction of pre-eclampsia. *SVU-International Journal of Medical Sciences*. Vol.7, Issue 1, pp: 304-316.

Introduction

Preeclampsia (PE) is a gestational disorder affecting approximately 2-3% of pregnancies on a global scale. It serves as a significant contributor to maternal and fetal health complications as well as mortality rates **(Dymara-Konopka et al., 2018).** Preeclampsia is intricately linked with an increased risk of iatrogenic preterm births, infants born with small for gestational age (SGA), placental abruption, perinatal mortality, and substantial maternal morbidity and mortality **(Hu et al., 2021).** Astonishingly, PE is accountable for approximately 30,000 maternal deaths annually, constituting roughly 14% of maternal fatalities, with a pronounced prevalence in low- and middle-income countries **(Kassebaum et al., 2014).** The definitive therapeutic intervention for preeclampsia continues to be the delivery of the fetus, underscoring the critical importance of early screening and preventive measures **(Abalos et al., 2014).**

The early identification of high-risk expectant mothers represents one of the foremost challenges in contemporary obstetrics. To address this, efficacious screening methodologies must be made accessible to facilitate the implementation of preventative strategies aimed at mitigating the risk of PE and its associated ramifications **(Gabbay-Benziv et al., 2016).** The concept of forecasting pregnancy complications during the first trimester has garnered increasing attention in medical literature over the past three decades, often referred to as the "inversion of the pyramid of prenatal care" **(Pedroso et al., 2018).**

The pathogenesis of preeclampsia is frequently associated with inadequate placental development. As elucidated by previous investigations **(Maged et al., 2015),** it involves endothelial junctional protein abnormalities, structural alterations in resistance arteries beneath the endothelial layer, and anomalous trophoblastic invasion.

The utilization of uterine artery Doppler velocimetry during the initial trimester, either as an independent approach or in conjunction with maternal medical history, emerges as a more efficacious method for preeclampsia screening. According to **Yu et al. (2005),** these techniques yield detection rates of 52% and 57%, respectively. Giles et al. initially established a correlation between aberrant uterine artery Doppler velocimetry and abnormal findings in umbilical artery Doppler assessments in 1985, which subsequently exerted an impact on neonatal outcomes. Harrington et al. conducted the first prospective study in 1997, with the objective of identifying first-trimester individuals at risk of developing preeclampsia **(Todd et al., 2010).** Since then, first-trimester screening has gained prominence, with numerous studies exploiting this opportunity to assess various pregnancy-related issues. Nevertheless, there remains professional discord regarding the utility of first-trimester screening in predicting preeclampsia.

The aim of our study was to evaluate the role of uterine artery Doppler indices in the prediction of pre-eclampsia in the first trimester.

Patients and methods

This research constitutes a prospective cohort study carried out within the Outpatient Clinic of the Obstetrics and Gynecology Department at South Valley University Hospital, spanning from June 2022 to the conclusion of June 2023. Sixty pregnant women who presented at South Valley University Hospital during this period for standard antenatal care assessments at 9 to 11 weeks of gestation were included in the investigation. Among these participants, five were lost to follow-up and subsequently excluded from the data analysis. Ultimately, a cohort of 55 women remained for the analytical phase of the study.

Inclusion criteria encompassed pregnant women seeking antenatal care at

the outpatient clinic of South Valley University Hospital. Exclusion criteria comprised pregnancies characterized by iatrogenic or spontaneous abortions occurring prior to the 24th week of gestation (unless attributed to preeclampsia), pregnancies associated with significant fetal chromosomal or structural abnormalities, and women with underlying medical conditions such as diabetes, pre-existing hypertension, renal disease, or autoimmune disorders. It is important to note that all participants provided written informed consent, and the study received approval from the institutional ethics committee of the Faculty of Medicine, Qena, under reference number IRB NO: **SVU-MED-NAP020-1-20-8-64.**

Each participant underwent a comprehensive evaluation, encompassing the following domains:

I. History and Clinical Examination: This involved the collection of data on maternal age, parity, occupation, method of conception (spontaneous, ovulation induction, intracytoplasmic sperm injection (ICSI), or in-vitro fertilization (IVF)), prior history of preeclampsia (PE), medication history (including anticoagulants or antihypertensive drugs), family history of PE, previous instances of intrauterine growth restriction (IUGR) in past pregnancies, gestational age, pregnancy intervals, and a history of comorbid conditions such as diabetes (DM), cardiac disease, and renal failure. A comprehensive clinical examination was conducted, including an assessment of the patient's overall condition and vital signs (pulse, blood pressure, respiratory rate, and temperature), as well as examinations of the abdominal, chest, and cardiac regions.

II. Laboratory Investigations: Various laboratory tests were conducted at the time of delivery, including a complete blood count, measuring hemoglobin concentration (Hb%), red blood cell (RBC) count, white blood cell (WBC) count, and platelet count using an Erma Automated Blood Count Machine. Liver function tests, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels. Estimation of serum creatinine levels using a COBAS 501 chemistry autoanalyzer Collection of urine samples in sterile containers to measure urine creatinine and albumin levels, with subsequent analysis using the Beckman Coulter (Synchron CX 9 ALX) Clinical Auto analyzer. The albumin-to-creatinine ratio (ACR) was calculated based on the method described by **Miller et al. in 2018.**

III. Imaging using Voluson s8 (General Electric HealthCare, USA): Study participants underwent the following imaging procedures:

1. Abdominal Ultrasonography: This examination involved assessing multiple parameters, including fetal quantification, evaluation of fetal cardiac activity, determination of fetal biometry, identification of congenital defects, measurement of amniotic fluid volume, and determination of placental placement **(Strauss et al., 2002).**
2. Uterine Artery Doppler: Doppler examinations of the uterine artery were conducted at 9-11 weeks of gestation, with a subsequent assessment at the 18-week mark. Identification of the uterine artery was based on its distinctive flow velocity waveform. Patients were positioned semi-recumbent, inclined at approximately 45° from the supine position, to locate the internal cervical os. Color flow mapping was utilized to identify the uterine artery's position, and pulsed wave Doppler with a 2 mm sampling gate was employed to encompass the entire vessel. Peak systolic velocity (S) and end diastolic velocity (D) measurements were taken, and the pulsatility index (PI) was calculated using the formula (S - D) / Vm, where Vm represents the mean velocity. The average pulsatility index (PI) for both left and right arteries was computed based on three

consecutive waveforms displaying similar characteristics. The Voluson S8 Ultrasound machine was used for these examinations, which included standard ultrasound assessments and Doppler tests (**Papageorghiou et al., 2004; Sciscione and Hayes, 2009). Figs. (1, 2).**

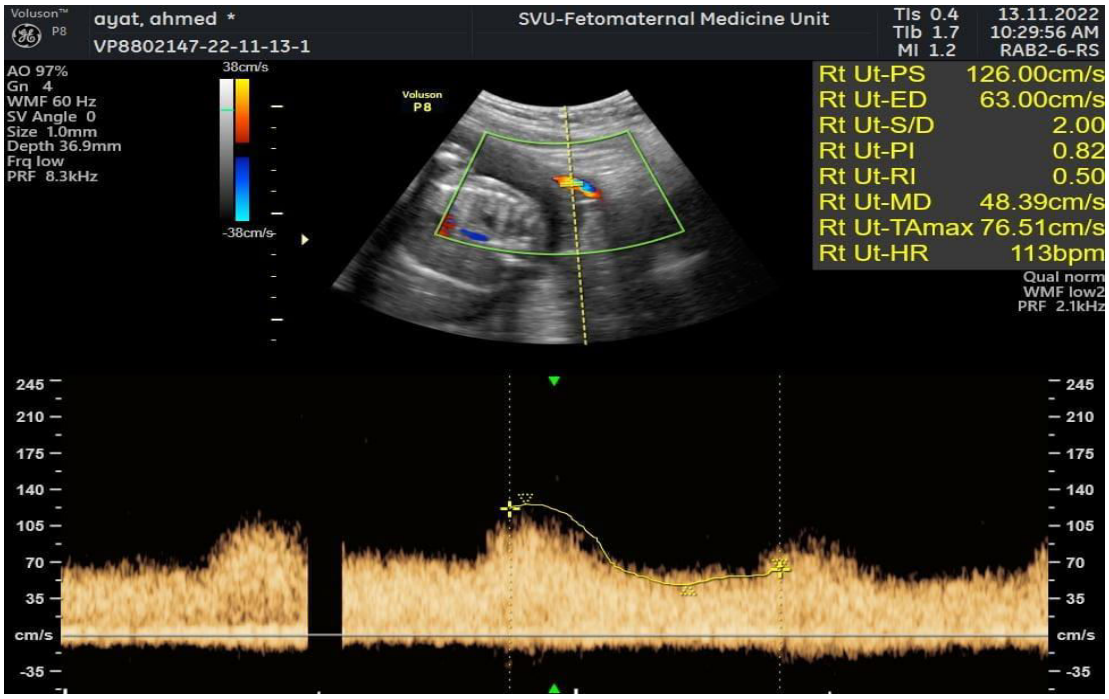

Fig.1. A case at 18-week pregnancy showing normal right uterine artery Doppler without notch

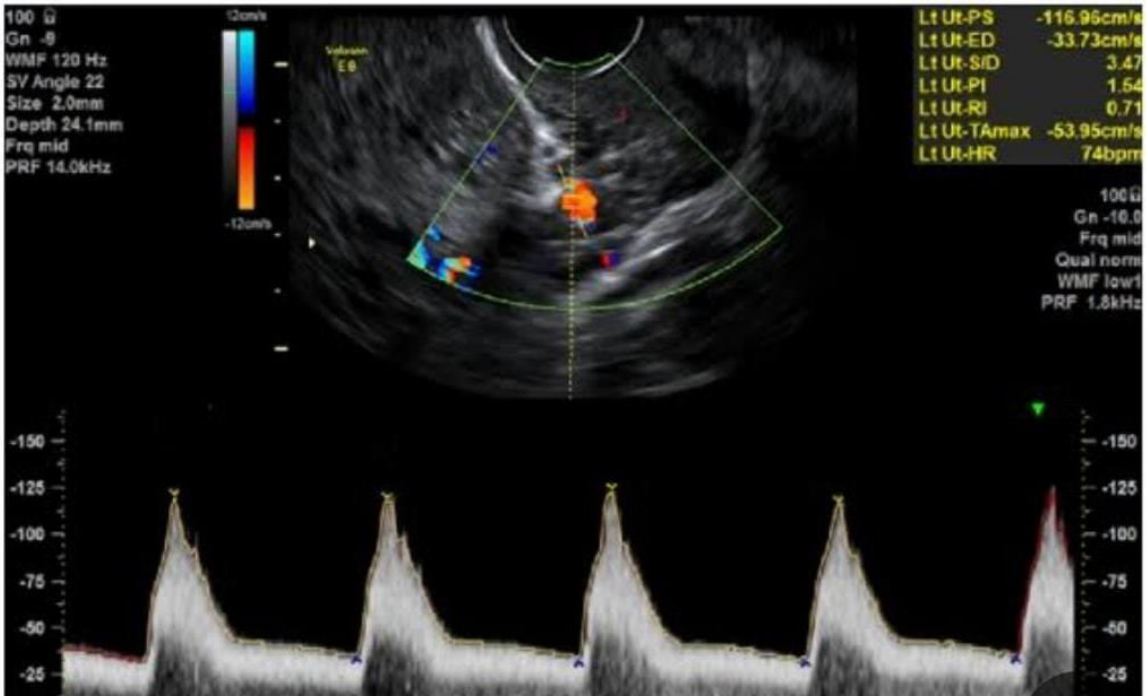

Fig.2. A case at 18-week pregnancy showing left uterine artery Doppler high.

IV. Preeclampsia Assessment: The diagnosis of preeclampsia was predicated on the presence of elevated blood pressure after the 20th week of gestation (≥140/90 mm Hg on two separate occasions at least 4 hours apart) and proteinuria (urinary

protein ≥300 mg/24 hours or persistent 30 mg/dL protein in random urine samples).
Follow-up: All the consented patients were followed until delivery during routine antenatal care, with particular concern for maternal outcomes, especially developing PE, and fetal outcomes, particularly the need for neonatal intensive care unit (NICU) admission and intrauterine fetal death (IUFD).

V. Ethical code: SVU-MED-OBG024-1-22-3-367

Statistical analysis

The data analysis was conducted using version 18.0 of the Statistical Software for Social Sciences (SPSS). The presentation of qualitative data included the use of frequency and percentage values (%), which were then compared using Student's t-test. On the other hand, quantitative data were provided in the form of mean and standard deviation (M SD). The chi-square test was used to do a non-parametric comparison of the data. The observed result was considered statistically significant at a significance level of 0.05.

Results

The mean age of all studied patients was 24.8 ± 3.4 years with mean BMI of 24 ± 2.3 kg/m^2. (**Table .1).**

Table 1. Age distribution in studied groups

Variables		Studied patients (N = 55)
Age (years)	**Mean ±SD**	24.8 ± 3.4
	Range	18 – 33
Body Mass Index (BMI :kg/m²)	**Mean ±SD**	24 ± 2.3
	Range	19.5 – 31
Gestational age (weeks)	**Mean ±SD**	37.7 ± 2.5
	Range	23 – 40

The mean values of ALT, AST and serum creatinine were 22.5 ± 19.7 U/L, 18.3 ± 15.3 U/L and 0.69 ± 0.16 mg/dl respectively. The mean values for various CBC parameters in the patient group were as follows, the mean hemoglobin (Hb) level was 13.91 ± 1.58 g/dL (with a median of 13.7 g/dL within a range of 11.5-18.1 g/dL), the mean hematocrit (Hct) level was 41.09 ± 5.2% (with a median of 40% within a range of 34-57%), the mean red blood cell count (RBCs) was 4.67 ± 0.48 *10^6 cells/mcL (with a median of 4.7 *10^6 cells/mcL within a range of 3.9-5.5 *10^6 cells/mcL), the mean white blood cell count (WBCs) was 7655.98 ± 1926.42 cells/mcL (with a median of 8211 cells/mcL within a range of 4297-10753 cells/mcL), the mean platelet count (Plt) was 342.02 ± 52.33 *10^3 cells/mcL (with a median of 346 *10^3 cells/mcL within a range of 253-467 *10^3 cells/mcL), the mean corpuscular volume (MCV) was 87.87 ± 5.73 fL (with a median of 88 fL within a range of 80-100 fL), the mean corpuscular hemoglobin (MCH) was 30.15 ± 1.99 pg (with a median of 30 pg within a range of 27-33 pg), and the mean corpuscular hemoglobin concentration (MCHC) was 33.8 ± 1.35% (with a median of 34% within a range of 32-36%). As regard protein in urine, there were 2 patients (3.6%) with (+) protein in urine, 6 patients (10.9%) with (++) protein in urine, 2 patients (3.6%) with (+++) protein in urine and 2 patients (3.6%) with (++++) protein in urine while there were 43 patients (78.2%) with no protein in urine. The systolic blood pressure exhibited a substantial increase in individuals with preeclampsia, with a mean value of 153.08 mmHg compared to 113.57 mmHg in those without preeclampsia. Likewise, the diastolic blood pressure showed a significant increase in the PE group, with a mean value of 97.69 mmHg, as opposed to 72.38 mmHg in the No PE group. These differences were highly statistically significant, with p-values less than 0.0001, underscoring the marked increase in both systolic and diastolic blood

pressure in patients affected by preeclampsia (**Table .2).**

Table 2. Description of clinical data in all studied patients

Variables		**Studied patients (N = 55)**	
ALT (U/L)	**Mean ±SD**	22.5 ± 19.7	
	Range	10 – 154	
AST (U/L)	**Mean ±SD**	18.3 ± 15.3	
	Range	10 – 120	
Creatinine (mg/dl)	**Mean ±SD**	0.69 ± 0.16	
	Range	0.4 – 1.4	
CBC Data			
Hb (g/dl)	Mean ± SD	13.91 ± 1.58	
	Median (Range)	13.7 (11.5-18.1)	
Hct (%)	Mean ± SD	41.09 ± 5.2	
	Median (Range)	40 (34-57)	
RBCs (*10^6 cells/mcL)	Mean ± SD	4.67 ± 0.48	
	Median (Range)	4.7 (3.9-5.5)	
WBCs (cells/mcL)	Mean ± SD	7655.98 ± 1926.42	
	Median (Range)	8211 (4297-10753)	
Plt (*10^3cells/mcL)	Mean ± SD	342.02 ± 52.33	
	Median (Range)	346 (253-467)	
MCV (fL)	Mean ± SD	87.87 ± 5.73	
	Median (Range)	88 (80-100)	
MCH (pg)	Mean ± SD	30.15 ± 1.99	
	Median (Range)	30 (27-33)	
MCHC (%)	Mean ± SD	33.8 ± 1.35	
	Median (Range)	34 (32-36)	
Protein in urine	**Nil**	43	78.2%
	(+)	2	3.6%
	(++)	6	10.9%
	(+++)	2	3.6%
	(++++)	2	3.6%
Systolic blood pressure	**Mean ±SD**	122.91 ± 19.78	
Diastolic blood pressure	**Mean ±SD**	78.36 ± 13.3	
	No PE N = 42	**PE N = 13**	**P. Value**
Systolic blood pressure	113.57 ± 10.32	153.08 ± 10.32	<0.0001*
Diastolic blood pressure	72.38 ± 8.5	97.69 ± 4.39	<0.0001*

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, Hb: Hemoglobin concentration, Hct: Hematocrit, RBCs: Red Blood Cell count, WBCs: White Blood Cell count, Plt: Platelet count, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, PE: Preeclampsia.

As regard maternal outcome, there were 13 patients (23.6%) with PE (out of them, 9 patients had severe form of PE) and 42 patients (76.4%) with no PE. As regard fetal outcome, among those without preeclampsia, all 42 infants, constituting 100% of the cases, did not require admission to the Neonatal Intensive Care Unit (NICU). In stark contrast, within the group of infants born to mothers with preeclampsia, 7 out of 13 infants, equivalent to 53.85%, necessitated NICU admission. This discrepancy demonstrated a highly significant difference with a p-value of less than 0.0001, indicating a substantial

increase in NICU admissions in cases of preeclampsia. Furthermore, when considering the need for NICU care specifically, there were no cases in the No PE group, whereas 5 out of 13 infants (38.46%) born to mothers with preeclampsia required NICU care, highlighting a significant increase with a p-value of 0.0004. Additionally, the incidence of Intrauterine Fetal Demise (IUFD) was evaluated, showing no significant difference between the two groups, with a p-value of 0.2453 (**Table .3).**

Table 3. Description of outcome (maternal & fetal) in all studied patients

Variables		**Studied patients (N = 55)**	
Maternal outcome (PE)	**No**	42	76.4%
	Yes	13	23.6%
Fetal outcome	**No PE N = 42**	**PE N = 13**	P. Value
• **No need for NICU**	42 (100%)	7 (53.85%)	<0.0001*
• **Need for NICU**	0 (0%)	5 (38.46%)	0.0004*
• **IUFD**	0 (0%)	1 (7.69%)	0.2453

PE: Preeclampsia, NICU: Neonatal Intensive Care Unit, IUFD: Intrauterine Fetal Distress.

When examining maternal outcomes in relation to the severity of preeclampsia (PE), it was observed that among the 13 cases of PE, 4 (30.77%) were categorized as mild, while the remaining 9 (69.23%) were classified as severe, with no cases falling into the moderate category. In terms of fetal outcomes among these cases, infants born to mothers with mild PE exhibited certain differences compared to those born to mothers with severe PE. Notably, among infants born to mothers with mild PE, 75% did not require admission to the Neonatal Intensive Care Unit (NICU), while 25% needed NICU care. In contrast, among infants born to mothers with severe PE, 44.44% did not require NICU admission, and an equal percentage, 44.44%, necessitated NICU care. These variations did not show significant differences, with p-values of 0.308 for both cases. Furthermore, the incidence of Intrauterine Fetal Demise (IUFD) was evaluated, indicating no significant difference between infants born to mothers with mild or severe PE, with a p-value of 0.98 (**Table .4).**

Table 4. Description of outcome (maternal & fetal) among patients with PE.

Maternal outcome (PE) N = 13	Mild	Moderate	Severe	P. Value
	4 (30.77%)	0 (0%)	9 (69.23%)	
Fetal outcome	**Mild N = 4**		**Severe N = 9**	
• **No need for NICU**	3 (75%)		4 (44.44%)	0.308
• **Need for NICU**	1 (25%)		4 (44.44%)	0.308

• **IUFD**	0 (0%)	1 (11.12%)	0.98

PE: Preeclampsia, NICU: Neonatal Intensive Care Unit, IUFD: Intrauterine Fetal Distress

In the current study, Doppler flow study of the uterine artery at 9–11 and 18 weeks showed statistically significant (p-value < 0.05) increased left and right uterine artery PI, and RI in patients with PE (1.17 ± 0.33) when compared with patients without PE (0.95 ± 0.28), and there was highly statistical significant (p-value < 0.05) increased percentage of presence of notch in patients with PE (7 patients, 53.8%) when compared with patients without PE (0 patients, 0%). (**Tables 5,6).**

Table 5. Relation between maternal outcome (PE) and uterine artery Doppler at 9 - 11 weeks of pregnancy

9 - 11 weeks Doppler		PE				Test	P-value
		No (N = 42)		Yes (N = 13)			
Lt. uterine artery PI	Mean	0.95		1.17		MW = 169.5	**0.039 S**
	±SD	0.28		0.33			
Rt. uterine artery PI	Mean	0.95		1.28		MW = 142	**0.009 S**
	±SD	0.40		0.37			
Rt. uterine artery RI	Mean	0.59		0.80		MW = 90	**< 0.001 HS**
	±SD	0.11		0.17			
Lt. uterine artery RI	Mean	0.66		0.79		MW = 114.5	**0.002 S**
	±SD	0.16		0.16			
Notch	No	42	100%	6	46.2%	X^2 = 25.9	**< 0.001 HS**
	Yes	0	0%	7	53.8%		

Lt.: Left, Rt.: Right, pulsatility index (PI), residence index (RI)

Table 6. Relation between maternal outcome (PE) and uterine artery Doppler at 18 weeks of pregnancy

18 weeks Doppler		PE		Test	P-value
		No (N = 42)	Yes (N = 13)		
Lt. uterine artery PI	Mean	0.85	1.26	MW = 82.5	**< 0.001 HS**
	±SD	0.24	0.31		
Rt. uterine artery PI	Mean	0.87	1.13	MW = 158.5	**0.023 S**
	±SD	0.31	0.36		
Rt. uterine artery RI	Mean	0.59	0.77	MW = 126	**0.004 S**
	±SD	0.17	0.20		

Lt. uterine artery RI	Mean	0.59		0.84		MW = 66.5	**< 0.001 HS**
	±SD	0.15		0.16			
Notch	No	42	100%	7	53.8%	$X^2 = 21.7$	**< 0.001 HS**
	Yes	0	0%	6	46.2%		

Lt.: Left, Rt.: Right, pulsatility index (PI), residence index (RI)

Notably, severe pre-eclampsia patients exhibited a significant decrease in age (23.22 ± 3.67 years) compared to mild cases (29 ± 4.55 years). Furthermore, severe cases showed a significant increase in diastolic blood pressure (DBP) (100 ± 0 mmHg) compared to mild cases (92.5 ± 5 mmHg). Several CBC parameters demonstrated significant differences, with severe pre-eclampsia cases having higher hemoglobin (Hb) levels (16.38 ± 1.1 g/dL), hematocrit (Hct) levels (50 ± 3.16%), and platelet counts (400.78 ± 42.41 *10^3 cells/mcL) compared to mild cases. Additionally, mean corpuscular hemoglobin (MCH) was significantly increased in severe cases (31.78 ± 1.3 pg), while mild cases showed lower MCH levels (29 ± 1.41 pg). Doppler measurements also revealed significant differences, particularly in the presence of a Notch and various pulsatility indices (**Table.7).**

Table 7. Comparison between mild and severe pre-eclampsia cases regarding all parameters

Variables	**Mild PET (N = 4)**	**Severe PET (N = 9)**	**P. Value**
Age (Years)	29 ± 4.55	23.22 ± 3.67	0.0323*
BMI (Kg/m2)	24.63 ± 2.56	24.67 ± 3.67	0.9841
Normal Conception	4 (100%)	9 (100%)	
Gestational Age (weeks)	34.07 ± 7.01	36.22 ± 2.56	0.4192
Smoking	0	0	-
Blood pressure (mmHg)			
• SBP	147.5 ± 5	155.56 ± 11.3	0.2066
• DBP	92.5 ± 5	100 ± 0	0.0006*
Lab Data			
• ALT (U/L)	19.25 ± 10.87	38.78 ± 43.82	0.4083
• AST (U/L)	18.75 ± 4.57	33.56 ± 34.55	0.4223
• Protein in urine	1.5 ± 0.58	2.44 ± 1.24	0.1795
• Serum creatinine (mg/dL)	0.7 ± 0.16	0.76 ± 0.27	0.7093
• CBC			
➢ Hb (g/dl)	14.85 ± 1.23	16.38 ± 1.1	0.04641*
➢ Hct (%)	43.25 ± 4.19	50 ± 3.16	0.00797*
➢ RBCs (*10^6 cells/mcL)	4.43 ± 0.22	4.99 ± 0.57	0.08663
➢ WBCs (cells/mcL)	8661.75 ± 1259.48	6509.33 ± 1802.22	0.05536
➢ Plt (*10^3cells/mcL)	347.25 ± 17.65	400.78 ± 42.41	0.03607*
➢ MCV (fL)	93.75 ± 5.44	88.33 ± 6.1	0.15668
➢ MCH (pg)	29 ± 1.41	31.78 ± 1.3	0.00527*
➢ MCHC (%)	34.75 ± 1.89	34.22 ± 1.64	0.61844
9-11 Week Doppler			
• LT PI	0.76 ± 0.19	1.36 ± 0.17	0.0001*
• RT PI	0.85 ± 0.3	1.47 ± 0.19	0.0007*

• RT RI	0.59 ± 0.06	0.9 ± 0.1	0.0001*
• LT RI	0.66 ± 0.23	0.85 ± 0.09	0.0527
• Notch	0 (0%)	7 (77.78%)	0.021*
18 Week Doppler			
• LT PI	0.87 ± 0.05	1.44 ± 0.17	<0.0001*
• RT PI	0.69 ± 0.25	1.33 ± 0.16	0.0001*
• RT RI	0.51 ± 0.09	0.88 ± 0.09	<0.0001*
• LT RI	0.64 ± 0.13	0.94 ± 0.05	0.0001*
• Notch	0 (0%)	6 (66.67%)	0.0699

BMI: Body Mass Index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, Hb: Hemoglobin concentration, Hct: Hematocrit, RBCs: Red Blood Cell count, WBCs: White Blood Cell count, Plt: Platelet count, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, MCHC: Mean Corpuscular Hemoglobin Concentration, PE: Preeclampsia, Lt.: Left, Rt.: Right, pulsatility index (PI), residence index (RI)

Discussion

The anticipation of preeclampsia (PE) holds paramount significance in contemporary antenatal care programs worldwide. Nevertheless, currently, there exists no flawless predictive test **(LI et al., 2022).** The assessment of uterine artery Doppler flow in the first trimester stands as a promising tool for predicting PE. In our present investigation, the Doppler flow study of the uterine artery at 9–11 and 18 weeks unveiled statistically significant findings (p-value < 0.05). Notably, it showed elevated pulsatility index (PI) and resistance index (RI) in both the left and right uterine arteries among patients with PE (1.17 ± 0.33), in contrast to those without PE (0.95 ± 0.28). Furthermore, a notably higher percentage of patients with PE (53.8%) exhibited the presence of a notch, compared to patients without PE (0%) (p-value < 0.05).

In alignment with our study, **Sileem et al. (2020)** conducted an investigation involving 170 pregnant women who had initiated antenatal care before the 18th week of gestation and were at an elevated risk of developing preeclampsia. Among these women, 12% developed preeclampsia during the follow-up period (the preeclampsia group), while the remaining 88% maintained normotensive status (the control group). **Sileem et al. (2020)** demonstrated that Doppler flow velocimetry of the uterine artery at 18–20 and 22–24 weeks of gestation proved to be a valuable predictive tool in high-risk pregnancies and for predicting preeclampsia when utilized as a standalone assessment.

Phupong et al. explored the effectiveness of Doppler uterine artery assessment in predicting the risk of preeclampsia. Their findings unveiled sensitivity, specificity, positive predictive value, and negative predictive value of 36.8%, 83.2%, 12.1%, and 95.5%, respectively, for the detection of preeclampsia **(Phupong et al., 2003).**

In harmony with our research, **Chyad et al. (2018)** conducted a prospective study involving 33 pregnant women between the 14th and 20th weeks of pregnancy to assess the utility of uterine artery Doppler in predicting preeclampsia. They concluded that uterine artery Doppler conducted between the 14th and 20th weeks of gestation represents a straightforward, rapid, and non-invasive procedure, offering a reliable indicator for predicting preeclampsia and serving as a valuable screening test **(Chyad et al., 2018).**

In cross-sectional research done by **Maged et al. (2015),** a cohort of 100 participants diagnosed with severe preeclampsia was examined, revealing that 76% of these individuals encountered maternal difficulties. The research findings indicated notable variations in the resistance index (RI) and pulsatility index (PI) among women who encountered difficulties such as unintentional bleeding, HELLP syndrome, acute pulmonary edema, and postpartum hemorrhage, in

comparison to those who did not experience these complications (P < 0.001 for all). Significantly, a notable difference was seen in relation to the Retinopathy Index (RI) (P < 0.001) and the Pulsatility Index (PI) (P = 0.005) between those presenting with problems and those without.

The results presented align with the outcomes of a research carried out by **de Melo et al. (2010),** which included a sample of 154 female participants at a teaching hospital located in Recife, Brazil. According to **de Melo et al. (2010),** the researchers identified increased mean uterine artery Doppler measures of PI (1.37) and RI (0.60) as indicators that were predictive of extended hospital stays and the need for continued use of antihypertensive drugs after discharge.

The findings of this investigation were consistent with those of a prospective observational study including 266 pregnant women who were at low risk and carrying a single fetus at a gestational age of 12-14 weeks. Within this cohort, a total of 14 individuals (constituting 5.26% of the sample) experienced the onset of preeclampsia. This finding serves to underscore the considerable promise of using PI measurements of uterine arteries during the first trimester as meaningful indicators for the prediction of preeclampsia **(Elkholi et al., 2016).**

In a similar manner, a sample of 388 pregnant women was selected for the purpose of assessing the resistive index (RI) and pulsatility index (PI) of the uterine artery. This evaluation was conducted throughout the gestational period ranging from 11 to 13 weeks. According to **Mohammed et al. (2022),** a notable rise in uterine resistance index (RI) and pulsatility index (PI) was seen among the 58 individuals diagnosed with preeclampsia in comparison to the normotensive patients (n = 330).

In addition, a prospective longitudinal study was conducted involving 120 pregnant women of Caucasian descent who had risk factors for preeclampsia (PE). The study found that performing Doppler examination of the uterine artery at an early stage, specifically between 11 and 14 weeks of gestation, enabled the identification of pregnancies that were likely to develop PE. The sensitivity of this detection method, based on PI analysis, was determined to be 61.5%, while the specificity was found to be 63.8%. According to **Oancea et al. (2020),** the findings of the research indicate that uterine artery Doppler examination is a valuable non-invasive screening tool for identifying the onset of preeclampsia in high-risk pregnancies, especially in healthcare settings where other biomarkers may be restricted in availability for evaluation.

The aforementioned results are consistent with a recent randomized controlled experiment carried out by **Elshabacy et al. (2021),** in which the objective was to evaluate the use of uterine artery Doppler in identifying preeclampsia at an early stage in pregnant women at 11-14 weeks of gestation. It is worth mentioning that the average pulsatility index (PI) of the uterine arteries exhibited a statistically significant increase in instances that ultimately developed preeclampsia compared to those that did not (2.97 ± 0.2 and 1.7 ± 0.5, respectively). The research conducted by **Elshabacy et al. (2021)** provided evidence supporting the effectiveness of using the uterine artery pulsatility index (PI) during the 11-14 week period of gestation as a reliable screening tool for preeclampsia.

Conclusion:

Doppler flow study of the uterine artery showed statistically significant increased left and right uterine artery PI, and RI in patients with PE when compared with patients without PE. The presence of notch in the uterine artery wave is highly predictive for development of preeclampsia

Limitations

The main limitation of this study was the small sample size and follow-up of the patients; further studies with a larger sample size will be needed.

List of abbreviations

PE Pre-eclampsia

BMI Body mass index

PI	Pulsatility index
RI	Resentence index
SGA	small for gestational age
ICSI	Intracytoplasmic sperm injection
IVF	In-vitro fertilization
IUGR	intrauterine growth restriction
Hb %	hemoglobin concentration
RBC	red blood cell
WBC	white blood cell
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ACR	albumin-to-creatinine ratio
S	Peak systolic velocity
D	end diastolic velocity
NICU	neonatal intensive care unit
IUFD	intra uterine fetal death
SPSS	Statistical Software for Social Sciences

References

- **Abalos E, Cuesta C, Carroli G, Qureshi Z, Widmer M, Vogel JP, et al**. **(2014)**. Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health. British Journal of Obstetrics and Gynaecology. 121(1):14–24.
- **Chyad MA, Azab EA, Shalaby MH, Aly AA. (2018).** The Role of Uterine Artery Doppler Sonography in Predicting Pre-eclampsia at 14-20 Weeks of Gestation. The Egyptian Journal of Hospital Medicine. 73 (11): 7850-7859.
- **De-Melo BC, de-Amorim MM, Katz L, Coutinho I, Veríssimo G**. **(2010).** Uterine artery Doppler in the third trimester of pregnancy and postnatal outcome of patients with severe preeclampsia. Hypertens Pregnancy. 29(2):135–47.
- **Dymara-Konopka W, Laskowska M, Oleszczuk J**. **(2018).** Preeclampsia-current management and future approach. Current pharmaceutical biotechnology. 19 (10):786-96.
- **Elkholi DG, Hefeda MAE, Nagy HM. (2016).** First Trimester Screening for Preeclampsia and Intrauterine Growth Restriction Using Uterine Artery Doppler and Maternal Serum Placental Growth Factor and Pregnancy Associated Plasma Protein- A. Reproductive Immunology Open. 1 (3): 1-6.
- **Elshabacy A, Tabl HA, Quashwa SH. (2021).** Is it Possible to Predict Preeclampsia Early by Maternal Pregnancy Associated Plasma Protein-A and Uterine Artery Doppler? A Randomized-Controlled Trial. The Egyptian Journal of Hospital Medicine. 83 (1): 1189-1194.
- **Gabbay-Benziv R, Oliveira N, Baschat AA**. **(2016).** Optimal first trimester preeclampsia prediction: a comparison of multimarker algorithm, risk profiles and their sequential application. Prenatal diagnosis. 36(01):34–39.
- **Hu J, Gao J, Liu J, Meng H, Hao N, Song Y, et al. (2021).** Prospective evaluation of first-trimester screening strategy for preterm pre-eclampsia and its clinical applicability in China. Ultrasound in Obstetrics & Gynecology. 58 (4): 529-39.
- **Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS**. **(2014).** Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease

Study 2013. Lancet. 38 (4): 980-1004.

- **Li S, Wang Z, Vieira LA, Zheutlin AB, Ru B, Schadt E, et al. (2022).** Improving preeclampsia risk prediction by modeling pregnancy trajectories from routinely collected electronic medical record data. Digital Medicine, 5(1): 56-68.
- **Maged AM, El-Nassery N, Fouad M, Abdelhafiz A, Al Mostafa W (2015).** Third-trimester uterine artery Doppler measurement and maternal postpartum outcome among patients with severe pre-eclampsia. International Journal of Gynecology and Obstetrics. 131 (1): 49–53.
- **Oancea, M., Grigore, M., Ciortea, R., Diculescu, D., Bodean, D., Bucuri, C., et al. (2020).** Uterine artery doppler ultrasonography for first trimester prediction of preeclampsia in individuals at risk from low-resource settings. Medicina, 56 (9): 419-428.
- **Papageorghiou AT, Christina KH, Nicolaides KH (2004).** The role of uterine artery Doppler in predicting adverse pregnancy outcome. Best practice and research Clinical obstetrics and gynaecology. 18(3): 383-396.
- **Pedroso MA, Palmer KR, Hodges RJ, Costa FD, Rolnik DL. (2018).** Uterine artery Doppler in screening for preeclampsia and fetal growth restriction. Revista brasileira de ginecologia e obstetricia. 40 (1): 287-93.
- **Phupong V, Dejthevaporn T, Tanawattanacharoen S, Manotaya S, Tannirandorn Y, Charoenvidhya D. (2003).** Predicting the risk of preeclampsia and small for gestational age infants by uterine artery Doppler in low-risk women. Archives of Obstetrics and Gynecology. 26 (8): 158–161.
- **Sciscione AC, Hayes EJ (2009).** Uterine artery Doppler flow studies in obstetric practice. American journal of Obstetrics and Gynecology. 201(2): 121-126.
- **Sileem SA, El-Barody MM, Okasha A, Abdelazem O. (2020).** The role of clinical and laboratory tests along with uterine artery Doppler indices in the prediction of pre-eclampsia and pregnancy outcome in Egypt. Al-Azhar Assiut Medical Journal. 18 (1): 348–358
- **Strauss A, Müller S, Heer IM. (2002).** Obstetrical ultrasonography. Gynakologisch-geburtshilfliche Rundschau. 42(2): 75-83.
- **Todd R, Lorraine D, and Henry L. (2010).** Uterine Artery Doppler and Prediction of Preeclampsia. Clinical obstetrics and gynaecology. 53 (4): 888–898.
- **Yu CK, Smith GC, Papageorghiou AT, Cacho AM, Nico laides KH. (2005).** An integrated model for the prediction of pre-eclampsia using maternal factors and uterine artery Doppler velocimetry in unselected low-risk women. American Journal of Obstetrics and Gynecology. 19 (3): 429–436.