

# The Role of “Uterine Artery Doppler” at 11 to 13+6 Weeks for Prediction of Preeclampsia: A Systematic Review

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## Abstract

**Objective:** This systematic review is aimed to review the role of uterine artery Doppler in first trimester of pregnancy along with use of maternal characteristics as a predictor of early and late on set pre-eclampsia (PE). **Selection Criteria:** The search was limited by selecting; only original articles, prospective & retrospective study designs, role of uterine artery Doppler done at 11 to 14 weeks, done on singleton pregnancy and written in English language were included. **Data Collection and Analysis:** The data extracted for author name, year of publication, place of study, duration of study, study design, outcomes and study variables including maternal factors, uterine artery Doppler and serum markers. Then detailed analysis of uterine artery Doppler performance as predictor in the form of Area under curve, Sensitivity, Specificity, Positive predictive value, Negative Predictive Value and its relation to preeclampsia, Early PE and Late PE. **Results:** Following the search strategy of PRISMA, 148 full articles reviewed, and 21 articles were included from 2010 to 2021. Out of 21 articles, 19 articles had “prospective study design” whereas two had “retrospective. Out of 21 researches, 15 assessed early preeclampsia, 4 assessed late preeclampsia, 4 assessed both, however 7 articles studies only preeclampsia as an outcome. The extracted estimate show value of first trimester uterine Doppler as a predictor of early and late preeclampsia. **Conclusions:** The uterine artery Doppler with maternal characteristics is a valuable, noninvasive tool to be used at 11 to 14 weeks as predictor of preeclampsia in the low resource settings where serum markers cannot be available to general population.

**Keywords:** uterine artery Doppler, preeclampsia, first trimester, predictor.

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## INTRODUCTION

Hypertensive disorders affect 2 to 10% of the pregnancies, out of which preeclampsia contributes 7 to 10% and is associated with significant maternal & fetal morbidity & mortality all around the world (Amin *et al.*, 2020). Among many risk factors, primiparity itself is a risk factor for development of preeclampsia in 5 to 7 % cases (Amin *et al.*, 2020). There are different screening models being practiced by FMF (Fetal Medicine Foundation), Barcelona, USA etc. for the screening of high-risk pregnancy and then recommend starting low dose Aspirin in first trimester of pregnancy. Different parameters like maternal characteristics, blood pressure, uterine artery Dopplers and serum markers are used in screening for predicting preeclampsia in pregnancy (Renzo *et al.*, 2019; Sotiriadis *et al.*, 2019; & Poon *et al.*, 2018).

According to Lopez-Mendez *et al.*, (2013) and Neravi, and Udayashree, (2018) in low resource countries, like Pakistan the use of serum markers for screening of PE is challenging because of economic concerns. However, the uterine artery Doppler ultrasound is one of noninvasive, cheap method to predict preeclampsia. Literature has evidenced about the role of uterine artery notching examined in second trimester is effective tool to predict preeclampsia (Neravi & Udayashree, 2018). Similarly, the role of uterine artery Doppler in second trimester for the prediction of preeclampsia has been evidenced in Pakistan by number of researchers Awan *et al.*, (2016) and Tabassum *et al.*, (2016), however its role in first trimester yet needs to be recommended as part of routine first trimester ultrasound in our setup. So, this systematic review is aimed to review the role of uterine artery Doppler in first trimester along with use of

maternal characteristics and other serum markers to predict preeclampsia.

## 2. METHODS

### 2.1. Search Strategy

The “PRISMA” methodology was used in this systematic review. Different electronic databases including Google scholar, PubMed, Web of Science, Taylor & Frans, Willey online, ProQuest, Springers link, Elsevier, LWW were searched for relevant article with the help of library staff of Shalamar Medical & Dental College in multiple sittings, started from Nov.2020. Different search words used like “Prediction of preeclampsia”, “role of uterine artery Doppler in first trimester”, “Uterine artery Doppler and prediction of preeclampsia”, “uterine artery Doppler and pregnancy outcome” in different combination were used. The search was limited by defining the inclusion criteria, only original articles, prospective & retrospective study designs, role of uterine artery Doppler done at 11 to 14 weeks, done on singleton pregnancy and written in English language were included in study. This systematic review included the original articles only of last 10 years starting from 2010 to 2021, however the systematic reviews, thesis, preconference proceedings, case reports, books, other than English language paper, researches with study design other than prospective& retrospective, pregnancy with multiple gestations or with malformations were excluded from the review. The title and abstract were reviewed followed by the review of relevant articles. However, those full text articles were included which met the inclusion criteria. Following operational definition were used while reviewing full articles:

- **Pre-Eclampsia (PE):** The presence of hypertension (140/90mmHg, taken 4 hours apart) with proteinuria at or beyond 20 weeks’ gestation.
- **Early Onset Pre-Eclampsia (E-PE):** Early-onset preeclampsia is usually defined as preeclampsia (Pregnancy induced hypertension plus proteinuria) that develops before 34 weeks of gestation
- **Late Onset Pre-Eclampsia (L-PE):** Late-onset preeclampsia (Pregnancy induced hypertension plus proteinuria) develops at or after 34 weeks of gestation).

We used those studies in which uterine artery Doppler pulsatility index (PI) mean value was taken at 11 to 13+6 weeks by transabdominal or transvaginal Ultrasound. We included those studies in which uterine artery Doppler performance has been assessed as a predictor of either alone or combination with maternal history, mean arterial pressure and serum markers. We included the researches which evaluated the predictor value of uterine artery as prospectively as well as retrospectively. The performance of uterine artery

Doppler can be assessed by the calculations of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios. Area under curve (AUC) was also used to explain the performance as predictor. We included those studies in which statistical tests were used to calculate sensitivity and specificity, however, those studies with calculations of likelihood ratios without calculation of sensitivity and specificity were excluded from this systematic review.

### 2.2. Quality Assessment

Quality assessment was assured by analyzing the quality, if included articles were following the guidelines given by CASP (Critical Appraisal Skill Programme) Cohort study checklist for observational studies.

### 2.3 Data Extraction

The data extracted after reviewing the full articles fulfilling the inclusion criteria. From all included articles, the following information were extracted: author name, year of publication, country in which the study was done, duration of study, study design, outcomes and study variables including maternal factors, uterine artery Doppler and serum markers. Then detailed analysis of uterine artery Doppler performance as predictor was done by extracting data in the form of AUC (Area under curve), Sensitivity, Specificity, PPV (Positive predictive value), NPV (Negative Predictive Value) and its relation to preeclampsia, Early- PE(Early Preeclampsia), Late-PE(Late Preeclampsia).

## 3. RESULTS

Following the search strategy of PRISMA, 148 full articles reviewed and finally 21 articles included in this systematic review which were fulfilled inclusion criteria (Fig 1). This systematic review from 2010 to 2021 revealed that out of 21 articles, 19 articles had “prospective study design” whereas two had “retrospective study design”. Table 1 shows the characteristics of articles showing Author name, year of publication, country in which study was done, duration of study, study design and outcomes and study variables including maternal factors, uterine artery Doppler and serum markers. Then, detailed analysis of uterine artery Doppler performance as predictor done by extracting data in the form of AUC, Sensitivity, Specificity, PPV, NPV and its relation to preeclampsia, Early- PE, Late-PE is shown in table 2. From 2011 onwards till 2017, the area of interest was PE and late PE, however, from 2017 onwards the role of uterine artery Doppler as predictor is being assessed for early preeclampsia. Out of 21 researches, 15 assessed early Preeclampsia) 4 assessed late Preeclampsia), 4 assessed both, however 7 articles studies only PE as an outcome shown in table 2.

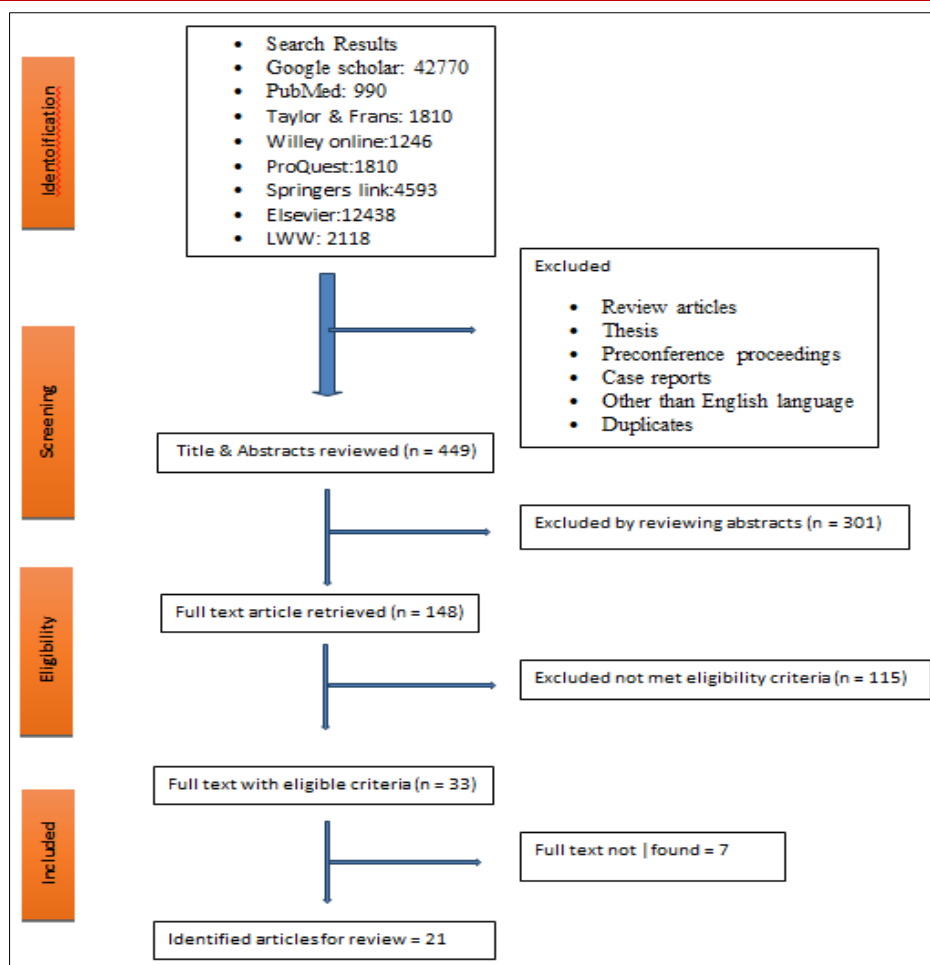


Figure 1: PRISMA Diagram for study selection

Table 1: Characteristics of articles showing Author name, year of publication, country name, duration of study, study design and followed by and outcomes and study variables including maternal factors, uterine artery doppler and serum markers. MC=Maternal Characteristics, HTN =hypertension, DM=Diabetes Mellitus, MAP = Mean Arterial Pressure

Author,	Year	Outcome
Elwakel AM, 2021	2021	PE
Oancea M	2021	PE
Monckerberg M	2020	E-PE
Shinde T	2020	1
Lakshmy	2020	E-PE
Parkansamut N	2019	PE
Song WL	2019	E-PE
Wright A	2019	E-PE
Mula R	2018	L-PE
Demes S	2017	E-PE
Agarwal R	2017	E-PE
Scazzocchio	2017	E-PE
Karampas GA	2016	PE
BindalJ	2016	PE
Gedikbasi,A	2016	PE
Gomaa MF	2015	PE
Baschat A	2014	E-PE
Parra-Cordero	2013	P-PE
Myatt	2012	
Anthony O	2011	PE

No of predictor	5	1	9	1	8	2	1	4	4	4	4	9	3	1	3	2	6	SGA	3
MC																Y			
Age	Y		Y		Y				Y	Y		Y					Y	Y	
Parity	Yes		Nulliparou		Yes			Yes		Yes (N)		Yes					Yes	Yes	
Race									Cac			Yes							
Family H/O																			
PastH/O PE	Yes		Yes		Yes							Yes					Yes		
HTN			Yes		Yes							Yes					Yes		
DM			Yes									Yes							
EXAM																			
BMI	Yes		Yes		Yes			Yes		Yes	Yes	Yes	Yes			Yes		Yes	
Sys/DiasBP			Yes																
MAP			Yes		Yes			Yes	Yes		Yes	Yes					Yes		
Uterine AD																			
Mean PI	Yes		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
B/L Notching														Yes					
Serum Markers																			
PAPP-A															Yes				Yes
Pl GF					Yes														
HCG										Yes									
Others						SHARP									NGAL	Placental vol	TNF Alpha	CRL	PP13

**Table 2: Detailed analysis of uterine artery doppler performance as predictor done by extracting data in the form of AUC, Sensitivity, Specificity, PPV, NPV and its relation to preeclampsia, (PE) Early PE(E-EP), Late PE(L-PE)**

Author,	Elwakel AM,2021	Oancea M	Monckerberg M	Shinde T	Lakshmy	Chemsaithe P	Parkansamut N	Song WL	Wright A	Mula R	Demes S	Agarwal R	Scazzocchio	Karampas GA	BindalJ	Gedikbasi,A	Gomaa MF	Baschat A	Parra-Cordero	Myatt	Anthony O
Year	2021	2020	2020	2020	2020	2019	2019	2019	2019	2018	2017	2017	2017	2016	2016	2016	2015	2014	2013	2012	2011
Design	Prospective	Prospectiv	Retrospecti	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Retrospecti	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective	Prospective
Sample	103	100	1051132	240	6289	10,935	405	247	61.174	1777	232/4,676	300	5170	541	100	602	500	108/244	82/2536		477
E-PE																					
Ut A PI cut off	1.95			2.3	>95th	1,18	>95th														
AUC(95% CI)	0.948	0.65				0.9		0.876		0.74	0.69	0.965						0.83			0.77
DR/Sensit	66.70%	61%	33%	89.30%	98%	64%		100%	85%		45%	86%	75%					55%	43%	54%	59%
Specificity	98.90%	63%		95.80%		90%		74.20%		90%	90%	90%	3%					90%	90%	96.15%	90%
PPV	80%		3.51%	90%									98.90%							85%	
NPV	2%		99.63%	95.10%																89%	
L-PE																					
AUC(95% CI)											0.52										
DR/Sensiti vty			18%		68%								52%								
Specificity																					
PPV			10.53%										7.8								

NPV			97.80%								98.9								
PE																			
AUC(95% CI)																	0.82		
DR/Sensitivity						6%		67%	40%			80%	75%	70.73%	100%		49%	28%	
Specificity						95.40%						91.90%	60.80%	95.32%	84.40%				
PPV						10.50%						73%	57.14%	58.00%	41.70%				
NPV						91.50%						94%	67.78%	97.27%	100%				

**4: DISCUSSION**

The value of uterine artery Doppler in first trimester for the prediction of pre-eclampsia has been extensively studied in last decade. It is non-invasive, effective tool which can be used either alone or in combination with maternal characteristics and serum markers. However, in low resource setting, the role of uterine artery Doppler for identification of high-risk pregnancy cannot be overemphasized when used in combination with maternal characteristics (Akolekar *et al.*, 2013; Wright *et al.*, 2015; Khong *et al.*, 2015; & Ridder *et al.*, 2019) [13-16].

**4.1: Role of Uterine a Doppler as a Sole Predictor**

In this systematic review, 5 articles authorized by Elwaikel AM, Oancea M, Shinde T, Song WL, Bindal J respectively, studied the role of uterine artery as a sole predictor for predictor for pre-eclampsia (Elwakel *et al.*, 2020 & Oancea *et al.*, 2020) [17-21]. This is based on the pathophysiological changes in the spiral arterioles in the form of inadequate trophoblastic invasion (Ridder *et al.*, 2019) [16]. The trophoblastic invasion of spiral arterioles takes place in two waves. In the trophoblastic invasion, the resistance of the arterioles decreases, arterioles changed to high blood flow channel and the Doppler artery of uterine artery. These changes lead to a gradual decline of PI (Pulsatility Index) from first trimester to second and finally third trimester. (Ridder *et al.*, 2019; Oancea *et al.*, 2020; & Bindal & Chugh 2016) [16-18]. However, even high values of PI uterine arteries along with presence of bilateral notching taken in first trimester in the patients has been related with higher rates of preeclampsia later (Ridder *et al.*, 2019 & Shinde & Bhalerao 2021) [16-20]. This association is the basis for using uterine artery Doppler as part of screening

programme along with maternal characteristics, maternal arterial pressure and serum markers by FMF, NICE guidelines, ACOG etc. (Oancea *et al.*, 2020; Song *et al.*, 2019; & Chaemsaihong *et al.*, 2019).

The sole use of Uterine Artery as predictor has a sensitivity and specificity around 66%.64%, 89% as shown by the researches included in this systematic review which is same as evidenced by FMF (Lakshmy *et al.*, 2018 & Chaemsaihong *et al.*, 2019) [22, 23]. However, Song WL reported sensitivity as 100% which is different from rest of the papers (Song *et al.*, 2019). This may be explained by the cut off value of mean PI taken as 1.63 whereas rest of researches showed that if the cut off value of PI taken as 1.91, then there was sensitivity of 57%and 86% specificity for the prediction of preeclampsia (Elwakel *et al.*, 2020 & Oancea *et al.*, 2020) [17-21]. Out of these 5 articles in which sole role of uterine artery Doppler was studied, three authors mentioned uterine a notching in addition to uterine artery PI for prediction of early Preeclampsia. Bindal J concluded the addition of uterine notching to uterine artery PI increased the sensitivity and specificity to 75% and 60% respectively to predict early preeclampsia which share same results as shown by Bachat A Gomaa MF and although Gomaa MF used combination of uterine A Doppler with other predictors like TNF Alpha (Bachat *et al.*, 2014 & Gomaa *et al.*, 2015) [24, 25].

**4.2: Role of Uterine a Doppler as Predictor when Combined with other Predictors**

**4.2. A: Prediction of Early Preeclampsia (E-PE)**

The pathogenesis of Preeclampsia includes the imbalance between angiogenic factors which lead to the persistence of resistance by vasculature and results in Preeclampsia. On this basis, there are certain markers

including the maternal age, parity, race, past history and certain biomarkers like Placental growth factor (PIGF), Pregnancy associated antigen (PAPP-A), Tumor necrotic factor Alpha (TNF-Alpha), SHARP 1, which are used in screening programs in addition to uterine artery Doppler for the prediction of preeclampsia (Al-Rubaie *et al.*, 2016 & Chaemsaitong *et al.*, 2019) [23, 26]. In this systematic review, out of 21 articles, 16 were those in which along with uterine artery doppler, other markers also were studied. Among these, 5 authors used maternal characteristics including age, parity, race, past history, medical history, BMI (Body Mass Index) , MAP (Mean arterial pressure) with uterine Artery PI revealing the sensitivity for prediction of E-PL values as 33%, 54%,69%,74%,83% with high negative predictive value 90% most of studies (Myatt *et al.*, 2012& Mönckeberg *et al.*, 2020) [27-30]. The same has also been evidenced by FMF 60% sensitivity for the prediction of E-PE (Al-Rubaie *et al.*, 2016; Lakshmy *et al.*, 2018; & Chaemsaitong *et al.*, 2019) [22, 23, 26]. Monckeberg M reported sensitivity of 33% for the prediction of E-PE which is lower as compare to rest of the authors, this can be explained as it was retrospective research, involving small sample size and thirdly the cut off value for uterine artery PI taken was 4.0 and lastly this sensitivity is calculated with fixed false positive of 5% whereas other researchers took fixed false positive as 10% [27, 31, 32]. The researches including this systematic revealed high negative predictive value of the combination of maternal factors and uterine A Doppler PI which is valuable for the low resource settings like Pakistan (Lakshmy *et al.*, 2018) [22].

The predictive performance of uterine A Doppler further increased when used with serum markers in addition to maternal factors as evidenced the values of AUC (Area under curve, plotted on ROC Curve at 95%CI) as 0.9 by most of researchers in this systematic review and same evidence is supported by (Al-Rubaie *et al.*, 2016) [26].

#### 4.2. B: Prediction of Late Preeclampsia (L-PE)

Late Pre-eclampsia (L-PE) prediction with use of uterine artery Doppler in combination with maternal factor and serum markers and use of predictor model resulted in the prediction of L-PE much lower as compared to early PE, this is same in agreement to Predictor model run by FMF UK, NICE guidelines etc (Al-Rubaie *et al.*, 2016; Lakshmy *et al.*, 2018; & Chaemsaitong *et al.*, 2019) [22, 23, 26].

#### 4.2. C: Prediction of Preeclampsia (PE)

Overall PE (pre-eclampsia) can be predicted by uterine artery Doppler in combination with other parameters is not as much as for early preeclampsia and late preeclampsia [24, 25, 31].

## 5. CLINICAL IMPLEMENTATION

The uterine artery Doppler with maternal characteristics is a valuable tool to be used as predictor

of preeclampsia in the low resource settings as it helps not only in detecting high risk pregnancy but also give reassurance by its high negative predicative value to follow the low risk patients with minimum antenatal visits which otherwise reduce the economic burden as well (Lakshmy *et al.*, 2018) [22].

## 6. CONCLUSION

The uterine artery Doppler with maternal characteristics is a valuable, non-invasive tool to be used at 11 to 14 weeks as predictor of preeclampsia in the low resource settings where serum markers cannot be available to general population. It is used to identify the high-risk patients to whom low dose aspirin can be started to prevent pre-eclampsia. It also has a role in identification of low risk patients who can be managed with minimum antenatal visits, so it is valuable in low resource settings.

## 7. LIMITATIONS

The limitation of this systematic review is that all articles has been reviewed are from different countries but none of article has been included from Pakistan because no study has already been conducted in our country keeping in view. Characteristic of our population in terms of risks for preeclampsia.

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## 9-CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

## REFERENCES

1. Agarwal, R., Chaudhary, S., Kar, R., Radhakrishnan, G., & Tandon, A. (2017). Prediction of preeclampsia in primigravida in late first trimester using serum placental growth factor alone and by combination model. *Journal of Obstetrics and Gynaecology*, 37(7), 877-882.
2. Akolekar, R., Syngelaki, A., Poon, L., Wright, D., & Nicolaides, K. H. (2013). Competing risks model in early screening for preeclampsia by biophysical and biochemical markers. *Fetal diagnosis and therapy*, 33(1), 8-15.
3. Al-Rubaie, Z. T. A., Askie, L. M., Ray, J. G., Hudson, H. M., & Lord, S. J. (2016). The performance of risk prediction models for pre-eclampsia using routinely collected maternal characteristics and comparison with models that include specialised tests and with clinical guideline

- decision rules: a systematic review. *BJOG: An International Journal of Obstetrics & Gynaecology*, 123(9), 1441-1452.
4. Amin, O., Tasnim, N., & Naeem, S. (2020). Prevention of pre-eclampsia with low dose aspirin in primigravida. *MOJ Women's Health*, 9(1), 28-32. DOI: 10.15406/mojwh.2020.09.00264
  5. Awan, F., Ullah, H., & Ahmad, M. (2016). Role of uterine artery doppler ultrasound in predicting preeclampsia in primigravida. *Pakistan Armed Forces Medical Journal (PAFMJ)*, 66(6), 886-90.
  6. Baschat, A. A., Magder, L. S., Doyle, L. E., Atlas, R. O., Jenkins, C. B., & Blitzler, M. G. (2014). Prediction of preeclampsia utilizing the first trimester screening examination. *American journal of obstetrics and gynecology*, 211(5), 514-e1.
  7. Bindal, J., & Chugh, N. (2016). Utility of uterine artery Doppler and pulsatility index at 11-14 weeks of normal pregnancy in prediction of preeclampsia in third trimester. *Int J Med Res Rev.*, 4(3), 432-6. <https://ijmrr.medresearch.in/index.php/ijmrr/article/view/495>
  8. Chaemsaitong, P., Pooh, R. K., Zheng, M., Ma, R., Chaiyasit, N., Tokunaka, M., ... & Poon, L. C. (2019). Prospective evaluation of screening performance of first-trimester prediction models for preterm preeclampsia in an Asian population. *American journal of obstetrics and gynecology*, 221(6), 650-e1.
  9. El-Hassab, M. S., Rashed, R. M., Elghannam, M. Z., & Megahed, A. E. M. (2020). Predictive Value of both Serum Placental Protein-13 Level and Uterine Artery Doppler for Prediction of Pre-Eclampsia. *International Journal of Medical Arts*, 2(3), 528-534.
  10. Elwakel, A. M., Azab, S. M., & Elbakry, A. M. (2020). First-trimester uterine artery Doppler in the prediction of later pregnancy complication. *Menoufia Medical Journal*, 33(3), 966.
  11. FIGO Working Group on Good Clinical Practice in Maternal-Fetal Medicine, Di Renzo, G. C., Fonseca, E., Gratacos, E., Hassan, S., Kurtser, M., ... & Tosto, V. (2019). Good clinical practice advice: First trimester screening and prevention of pre-eclampsia in singleton pregnancy. *International Journal of Gynecology & Obstetrics*, 144(3), 325-329.
  12. Gomaa, M. F., Naguib, A. H., Swedan, K. H., & Abdellatif, S. S. (2015). Serum tumor necrosis factor- $\alpha$  level and uterine artery Doppler indices at 11–13 weeks' gestation for preeclampsia screening in low-risk pregnancies: a prospective observational study. *Journal of Reproductive Immunology*, 109, 31-35.
  13. Gomez, O., Martinez, J. M., Figueras, F., Del Rio, M., Borobio, V., Puerto, B., ... & Vanrell, J. A. (2005). Uterine artery Doppler at 11–14 weeks of gestation to screen for hypertensive disorders and associated complications in an unselected population. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*, 26(5), 490-494.
  14. Guzmán, Y. N., Uriel, M., Ramírez, A. P., & Romero, X. C. (2022). Uterine Artery Pulsatility Index as a Pre-eclampsia Predictor in the 3 Trimesters in Women with Singleton Pregnancies. *Revista Brasileira de Ginecologia e Obstetrícia*, 43, 904-910.
  15. Khong, S. L., Kane, S. C., Brennecke, S. P., & da Silva Costa, F. (2015). First-trimester uterine artery Doppler analysis in the prediction of later pregnancy complications. *Disease markers*, 2015.
  16. Lakshmy, S. R., Praveenkumar, M., Shobana, U., & Thasleem, Z. (2018). Uterine artery Doppler: changing concepts in prediction and prevention of PE and FGR. *Journal of Fetal Medicine*, 5(2), 93-105.
  17. Lopez-Mendez, M. A., Martinez-Gaytan, V., Cortes-Flores, R., Ramos-Gonzalez, R. M., Ochoa-Torres, M. A., Garza-Veloz, I., ... & Martinez-Fierro, M. L. (2013). Doppler ultrasound evaluation in preeclampsia. *BMC research notes*, 6(1), 1-6.
  18. Maxim, L. D., Niebo, R., & Utell, M. J. (2014). Screening tests: a review with examples. *Inhalation toxicology*, 26(13), 811-828.
  19. Metz, T. D., Berry, R. S., Fretts, R. C., Reddy, U. M., Turrentine, M. A., & American College of Obstetricians and Gynecologists. (2020). Obstetric care consensus# 10: management of stillbirth:(replaces practice bulletin number 102, March 2009). *American Journal of Obstetrics and Gynecology*, 222(3), B2-B20.
  20. Mönckeberg, M., Arias, V., Fuenzalida, R., Álvarez, S., Toro, V., Calvo, A., ... & Illanes, S. E. (2020). Diagnostic performance of first trimester screening of preeclampsia based on uterine artery pulsatility index and maternal risk factors in routine clinical use. *Diagnostics*, 10(4), 182.
  21. Myatt, L., Clifton, R. G., Roberts, J. M., Spong, C. Y., Hauth, J. C., Varner, M. W., ... & Anderson, G. D. (2012). The utility of uterine artery Doppler velocimetry in prediction of preeclampsia in a low-risk population. *Obstetrics & Gynecology*, 120(4), 815-822.
  22. Neravi, A., & Udayashree, V. (2018). Role of uterine artery Doppler at 12 to 16 weeks of gestation in prediction of pre-eclampsia an observational study. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, 7(8), 3162-3168.
  23. Oancea, M., Grigore, M., Ciortea, R., Diculescu, D., Bodean, D., Bucuri, C., ... & Mihu, D. (2020). Uterine artery Doppler ultrasonography for first trimester prediction of preeclampsia in individuals at risk from low-resource settings. *Medicina*, 56(9), 428.



24. Poon, L. C., McIntyre, H. D., Hyett, J. A., da Fonseca, E. B., & Hod, M. (2018). The first-trimester of pregnancy—A window of opportunity for prediction and prevention of pregnancy complications and future life. *Diabetes research and clinical practice*, 145, 20-30.
25. Ridder, A., Giorgione, V., Khalil, A., & Thilaganathan, B. (2019). Preeclampsia: the relationship between uterine artery blood flow and trophoblast function. *International journal of molecular sciences*, 20(13), 3263.
26. Salem, M. A. A., & Ammar, I. M. M. (2018). First-trimester uterine artery pulsatility index and maternal serum PAPP-A and PIGF in prediction of preeclampsia in primigravida. *The Journal of Obstetrics and Gynecology of India*, 68(3), 192-196.
27. Shinde, T., & Bhalerao, A. (2021). Evaluation of Uterine Artery Doppler (Mean Pulsatility Index) at 11–14 Weeks of Gestation as Predictor of Hypertensive Disorders of Pregnancy: A Prospective Observational Study. *The Journal of Obstetrics and Gynecology of India*, 71(1), 27-32.
28. Song, W. L., Zhao, Y. H., Shi, S. J., Liu, X. Y., Zheng, G. Y., Morosky, C., ... & Wang, X. J. (2019). First trimester Doppler velocimetry of the uterine artery ipsilateral to the placenta improves ability to predict early-onset preeclampsia. *Medicine*, 98(16).
29. Sotiriadis, A., Hernandez-Andrade, E., da Silva Costa, F., Ghi, T., Glanc, P., Khalil, A., ... & ISUOG CSC Pre-eclampsia Task Force. (2019). ISUOG Practice Guidelines: role of ultrasound in screening for and follow-up of pre-eclampsia. *Ultrasound in Obstetrics & Gynecology*, 53(1), 7-22.
30. Tabassum, A., Aftab, S., & Khan, T. Utility of Uterine Doppler Ultrasonography in Prediction of Pre-Eclampsia in Primigravidae. *Annals of PIMS ISSN, 1815, 2287*.
31. Wright, D., Syngelaki, A., Akolekar, R., Poon, L. C., & Nicolaides, K. H. (2015). Competing risks model in screening for preeclampsia by maternal characteristics and medical history. *American journal of obstetrics and gynecology*, 213(1), 62-e1.
32. Wojtowicz, A., Zembala-Szczerba, M., Babczyk, D., Kołodziejczyk-Pietruszka, M., Lewaczyńska, O., & Huras, H. (2019). Early-and late-onset preeclampsia: a comprehensive cohort study of laboratory and clinical findings according to the new ISHHP criteria. *International journal of hypertension*, 2019.