

## Role of Mid-trimesteric Uterine Artery Doppler Velocimetry in Prediction of Placenta Previa Resolution at the End of Third Trimester of Pregnancy

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### Abstract

**Background** many placenta previa cases diagnosed at mid-trimester resolve later in pregnancy, hence comes the importance of searching for predictive factors for placenta previa resolution. Uterine artery velocimetry parameters were suggested to play this role. **Aim of work** is to evaluate the predictive role of uterine artery Doppler velocimetry at mid-trimester of gestation for placenta previa resolution at end of pregnancy third trimester. **Methods** prospective cohort study was carried upon 200 pregnant women. Placenta-cervix os distance was measured both at 22–24 weeks and after 36 weeks of gestation. Uterine artery Doppler velocimetry parameters were measured at 22–24 weeks of gestation. **Results** Subjects were assigned to control group (n=139), resolved group (n=36), and placenta previa group (n=25) according to their diagnosis of placenta previa at mid-term and third trimester end. Differences in uterine artery Doppler velocimetry parameters (S/D ratio, PI, and RI) between different studied groups were used for analysis. Mean S/D ratio, PI, and RI of uterine arteries in placenta previa group were significantly lower than in both control and resolved groups. No differences were observed between control group and resolved group. Areas under the ROC curve were 0.895, 0.898, and 0.908 for the means of S/D ratio, PI, and RI, respectively ( $P$  value < 0.001). **Conclusion** uterine artery Doppler velocimetry parameters at mid-trimester are much lower in patients with persistent placenta previa than in control and resolved groups and have potential to predict

placenta previa resolution.

### Keywords

Mid-trimester ultrasound, Placenta previa, Placenta previa resolution, Uterine artery Doppler velocimetry parameters.

## Introduction

Placenta previa causes serious complications of pregnancy. The term placenta previa refers to placenta that completely or partially covers internal os. (1) Placenta previa causes maternal and neonatal outcomes as it increases risk of vaginal bleeding and preterm labor. (2) Wide performance of routine second-trimester ultrasonography makes placenta previa diagnosis a more frequent finding. (3) Placental migration is the cause of resolution of many mid-trimester diagnosed placenta previa after 30 weeks gestation. (4) There is lack of effective predictive criteria for resolution of mid-trimester diagnosed placenta previa in late pregnancy, which leads to unnecessary ultrasound examinations, costs, and inconvenience to patients. (5) Uterine artery is essential for blood supply of uterus and is required for fetal growth and development.

(6)

During development of placenta, invasion of trophoblasts is critical for remodeling of uterine artery, which affects uterine artery blood flow. (7) Uterine vascular blood supply has been associated with migration of placenta as pregnancy progresses. (8) It has been shown that ratio of systolic peak to end-diastolic frequency obtained by ultrasonography is associated with location of placenta. (9)

However, relationship between uterine artery Doppler velocimetry at mid-trimester of pregnancy and incidence of placenta previa at third trimester end is still not known.

## Aim of the work

Evaluation of the role of mid-trimesteric uterine artery Doppler velocimetry in prediction of placenta previa resolution at the end of third trimester of pregnancy

## Patients and methods

A prospective cohort study was carried upon 200 pregnant women attending antenatal care at obstetrics and gynecology clinic at Benha University Hospital from April 2021 to December 2022.

This study was approved by Benha Faculty of Medicine research ethical committee with code number (MD 7-3-2021).

Informed consent was obtained from all participants included in the study.

## Sample size calculation:

The sample size was obtained through results from OpenEpi, Version 3, open-source calculator--SSMean (10). The least sample size is 108 cases.

It was calculated using Cochran's formula, 95% CI (confidence interval), and 80% power.

$$N = \frac{Z^2 * (P) * (1-P)}{E^2}$$

Where N= minimal sample size

Z= Z value (e.g., 1.96 for 95% confidence level)

P= percentage picking a choice expressed as a decimal (.5 used for sample size needed)

E= (sample error) the desired level of precision, expressed as decimal (e.g., .05=±5)

**Inclusion criteria:**

Patients less than 40 years old, with BMI ( $<30\text{kg/m}^2$ ), and with no medical (as DM& hypertension) or surgical diseases (as more than 2 cs, D&C, and myomectomy).

**Exclusion criteria:**

Patients with multiple gestations, and with placenta accreta.

**Subjects and methods:**

Participants were subjected to history taking, physical examination, and ultrasound examination.

(VOULSON 730 PRO V, GE Health care, USA) ultrasound diagnostic apparatus was used for abdominal ultrasound examination by single observer, at probe frequency of 2.0-5.0 MHz.

Participants had ultrasound examination at 22-24 weeks with localization of placenta and estimation of bilateral uterine artery Doppler velocimetry parameters (S/D ratio, PI, and RI). **figure (1,2)** At 36 weeks gestation, ultrasound examination was done to localize placenta. **figure (3)**

Patients were divided into two groups, control group, and study group according to site of the placenta at 22-24 weeks of gestation. Control group involved patients who had normal placental fundal positions. Study group involved patients who were diagnosed with placenta previa at 22-24 weeks of gestation.

Participants who were diagnosed as placenta previa both at 22– 24 weeks and after 36 weeks of gestation were assigned to placenta previa group.

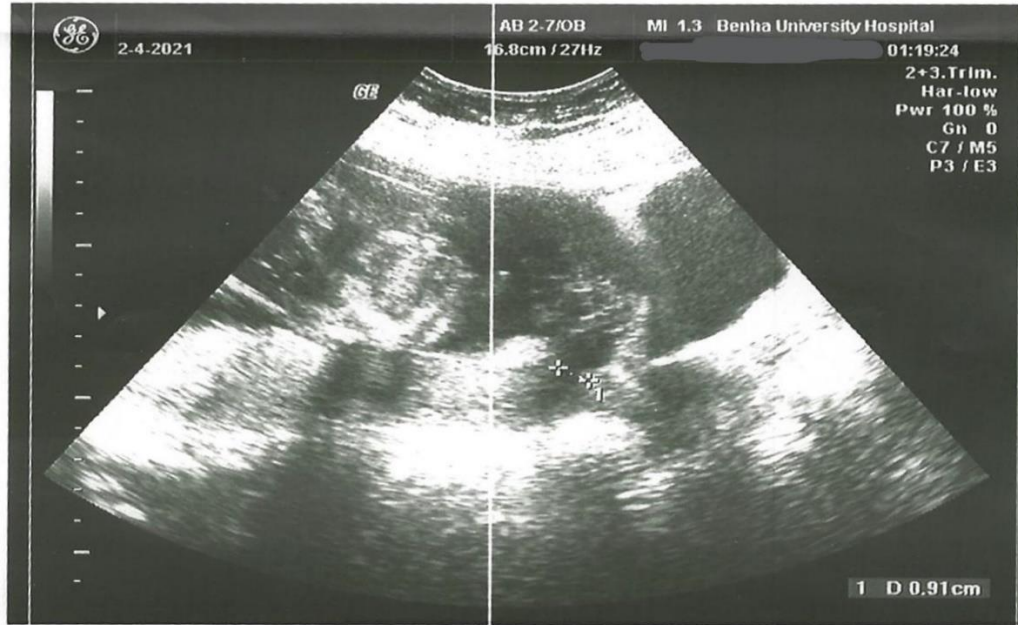
Participants who were diagnosed as placenta previa at 22–24 weeks of gestation but resolved after 36 weeks of gestation were assigned to resolved group.

Participants who were diagnosed as having normal placenta positions both at 22–24 weeks and after 36 weeks of gestation were assigned to control group.

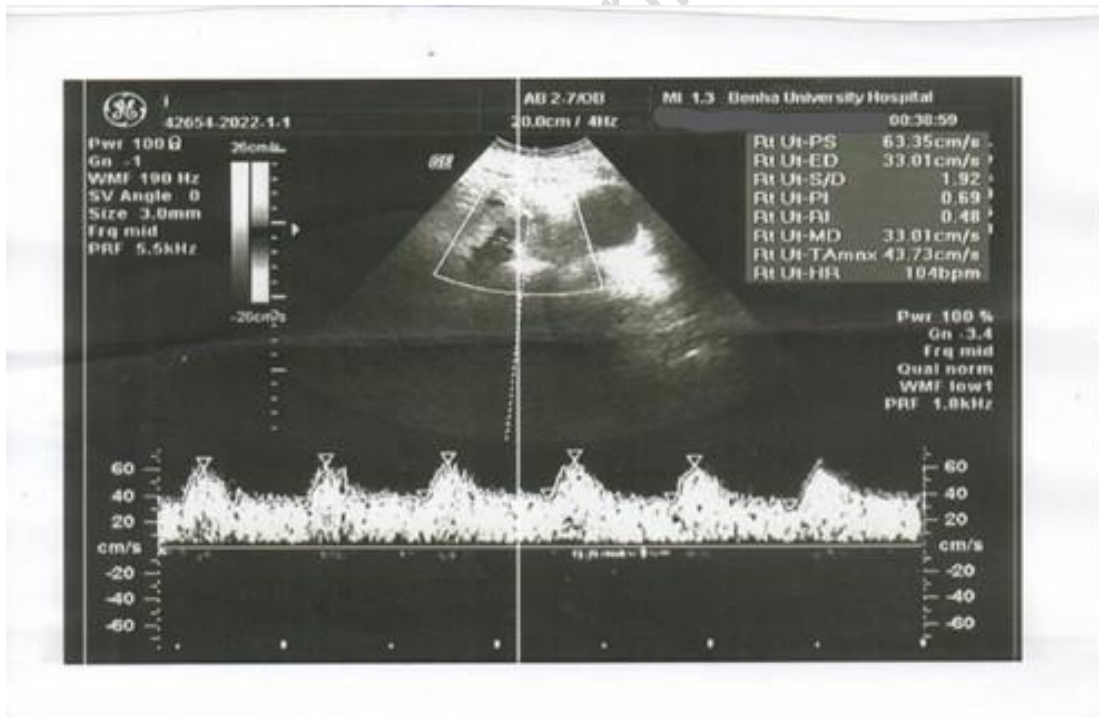
Placenta previa was diagnosed as having distance between placenta and internal cervical os less than 20 mm.

**Statistical methods: -**

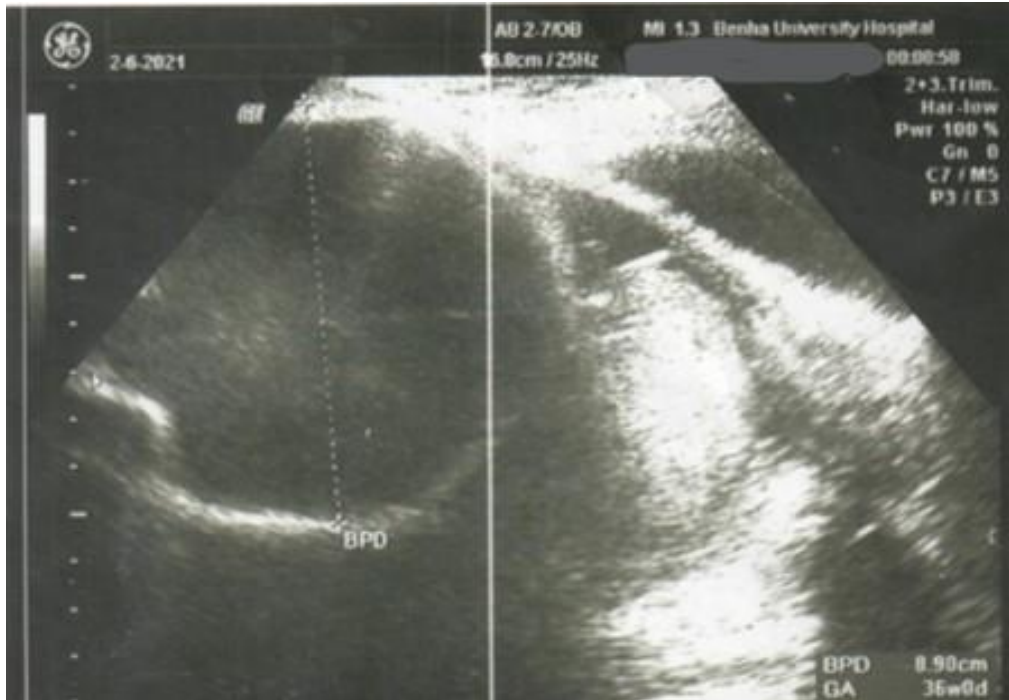
Collected data was recorded then presented, and statistically analyzed by computer using Statistical Package for Social Sciences (SPSS) 28.0 for windows (SPSS Inc., Chicago, IL, USA) as follows: data were presented in tables and graphs, normality of distribution for analyzed variables was tested using Kolmogorov-Smirnov test, Collected data were summarized in terms of mean and standard deviation and in median and Inter Quartile Range (IQR) for nonparametric data as appropriate and as number and percentage for qualitative data. Sensitivity, specificity values, and Area under the curve (AUC) of anterior and posterior approach predictability of resolving were calculated using ROC Curve (Receiver Operating Characteristic). All tests were two-sided, accepted level of significance in this work was ( $p < 0.05$ ), ( $p \leq 0.001$ ) was considered highly statistically Significant (HS), and ( $p > 0.05$ ) was considered Non statistically Significant (NS).



**Figure (1)** showed placenta previa posterior located at a distance of 0.91 cm from the internal os of the cervix at 23 weeks gestational age.



**Fig. (2)** showed right uterine artery Doppler velocimetry parameters measurement at 22 weeks gestational age.



**Fig. (3)** showed placenta previa major completely covering internal cervical os at 36 weeks gestation.

## Results

This prospective cohort study was carried upon 200 pregnant women attending for antenatal care at the Clinic of Obstetrics and Gynecology at Benha University Hospital from April 2021 to December 2022.

**Table (1)** showed that the median age of the included subjects in the study was 27 and the IQR was (25-31).

**Table (2)** showed that in the control group, the median age was 25 with IQR (24-30), while in the resolved group was 27 with IQR (26-29.8), and in the placenta previa group was 31, and IQR was (29-32.5) with a *p*-value less than 0.001 which is highly significant and indicate a possible relationship between age and placenta previa resolution.

Regarding parity shown in **table (1)**, primigravidae were 52 subjects (26%), P1

was 63 subjects (31.5%), P2 was 49 subjects (24.5%), P3 was 28 subjects (14%), P4 was six subjects (3%), and P5 was two subjects (1%).

**Table (1)** showed the BMI of the included subjects in the study. Subjects with BMI less than 20 kg/m<sup>2</sup> were 21 (10.5%), a BMI of 20-25 kg/m<sup>2</sup> was 62 (31%), and a BMI of 25-30 kg/m<sup>2</sup> was 117 (58.5%).

Among the 200 subjects involved in the study, 139 subjects (69.5%) had normally positioned placenta at 22–24 weeks and 36 weeks gestation and were assigned to the control group.

Sixty-one subjects (30.5%) were diagnosed as having placenta previa at mid-term gestation (22-24 weeks gestation) and were assigned to the study group, out of them 36 subjects (59.01%) had their placenta found

to be migrated to a normal position after 36 weeks gestation and were assigned to the resolved group. The remaining 25 subjects (40.99%) who had placenta previa after 36 weeks gestation were assigned to the placenta previa group. **Table (3,4)**

**Table (5)** showed the means and standard deviations for the mean uterine artery Doppler velocimetry parameters (S/D ratio, PI, and RI) for the different groups of the study. The mean $\pm$ SD of the mean S/D ratio, PI, and RI for the control group was 2.273 $\pm$ 0.434, 0.872 $\pm$ 0.168, and 0.559 $\pm$ 0.057 respectively. The mean $\pm$ SD of the mean S/D ratio, PI, and RI for the resolved group was 2.426 $\pm$ 0.431, 0.887 $\pm$ 0.200, and 0.555 $\pm$ 0.057 respectively. The mean $\pm$ SD of the mean S/D ratio, PI, and RI for the placenta previa group was 1.810 $\pm$ 0.280, 0.640 $\pm$ 0.199, and 0.474 $\pm$ 0.054 respectively.

Statistics were analyzed using the means of S/D ratio, PI, and RI on both sides of each subject. **Table (6)** and **figure (4)** show the predictive value of mean uterine artery

Doppler parameters for placenta previa resolution which was assessed using the Receiver Operating Characteristic (ROC) curve. Area Under the Curve for mean S/D, PI, and RI = 0.895, 0.898, and 0.908 respectively. Sensitivity of mean S/D, PI, and RI = 88.9%, 94.4%, and 83.3% respectively. Specificity of mean S/D, PI, and RI = 72%, 80%, and 88% respectively. The 95% confidence interval of mean S/D, PI, and RI = 0.817-0.973, 0.811-0.984, and 0.838-0.979 respectively. The cut-off points for mean S/D, PI, and RI = 1.84, 0.712, and 0.527 respectively.

Through comparison, we found that mean uterine artery parameters (S/D ratio, PI, and RI) were much lower in placenta previa group than those in control and resolved groups with ( $P$  value < 0.001) for all three parameters, while no differences were found between control and resolved groups which indicates a potential predictive role for the three parameters on the resolution of diagnosed placenta previa at mid-trimester.

**Table (1)** baseline characteristics of the included participants in the study.

| Variable (total=200) |                         | No.        | Percentage% |
|----------------------|-------------------------|------------|-------------|
| <b>Age</b>           | Median(IQR)             | 27 (25-31) |             |
| <b>Parity</b>        | PG                      | 52         | 26          |
|                      | P1                      | 63         | 31.5        |
|                      | P2                      | 49         | 24.5        |
|                      | P3                      | 28         | 14          |
|                      | P4                      | 6          | 3           |
|                      | P5                      | 2          | 1           |
| <b>BMI</b>           | < 20 kg/m <sup>2</sup>  | 21         | 10.5        |
|                      | 20-25 kg/m <sup>2</sup> | 62         | 31          |
|                      | 25-30 kg/m <sup>2</sup> | 117        | 58.5        |

**Table (2)** showed differences between the different groups regarding age.

| Variable | Study group     |         |          |         | Control group |       | Kruskal-Wallis Test | P value    |
|----------|-----------------|---------|----------|---------|---------------|-------|---------------------|------------|
|          | Placenta previa |         | Resolved |         | Median        | IQR   |                     |            |
|          | Median          | IQR     | Median   | IQR     |               |       |                     |            |
| Age      | 31              | 29-32.5 | 27       | 26-29.8 | 25            | 24-30 | 17.96               | <.001 (HS) |

**Table (3):** showed ultrasound findings at 22-24 weeks gestational age in both the control and study groups.

| Groups (no.=200)                        | Placenta type   | No. | Percentage % |
|---|-----------------|-----|--------------|
| <b>Control group</b><br>(no.=139) 69.5% | Anterior        | 36  | 25.9         |
|   | Posterior       | 103 | 74.1         |
| <b>Study group</b><br>(no.=61) 30.5%    | Major anterior  | 17  | 27.9         |
|   | Minor anterior  | 28  | 45.9         |
|   | Major posterior | 10  | 16.4         |
|   | Minor posterior | 6   | 9.8          |

**Table (4):** showed ultrasound findings of the study group at 36 weeks of gestational age.

| Groups (no.=200)                            | Placenta type                               | No.             | Percentage % |      |
|---|---|-----------------|--------------|------|
| <b>Study group</b><br>(no.=61) 30.5%        | Placenta previa group<br>(no.=25)<br>40.99% | Major anterior  | 14           | 56   |
|   |   | Minor anterior  | 3            | 12   |
|   |   | Major posterior | 6            | 24   |
|   |   | Minor posterior | 2            | 8    |
| <b>Resolved group</b><br>(no.=36)<br>59.01% | Anterior                                    | 28              | 77.8         |      |
|   |   | Posterior       | 8            | 22.2 |

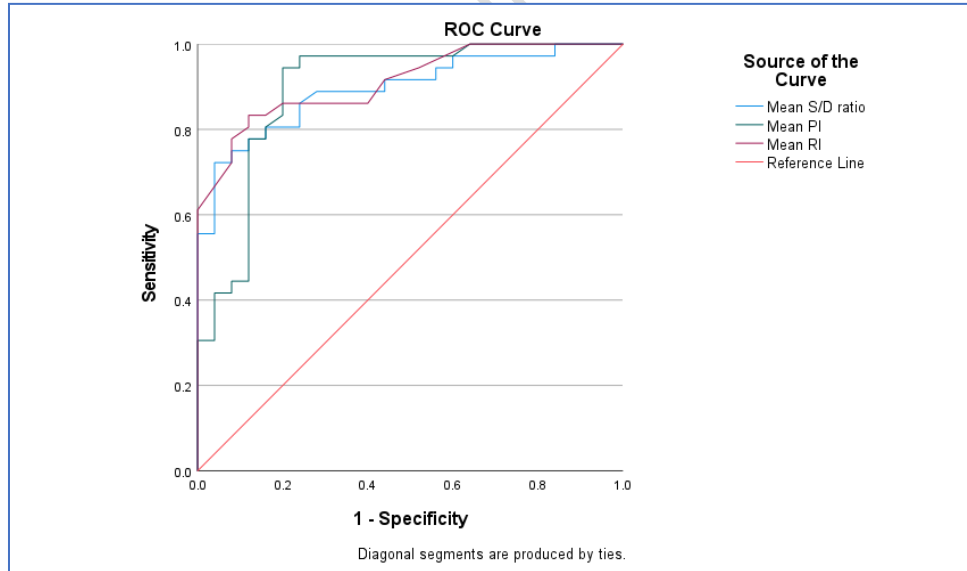
**Table (5)** : showed differences between study groups regarding mean uterine artery Doppler parameters with significant difference with the placenta previa group.

| Variable       | Placenta previa group | Resolved group | Control group | P value    |
|----------------|-----------------------|----------------|---------------|------------|
|                | Mean±SD               | Mean±SD        | Mean±SD       |            |
| Mean S/D ratio | 1.810±0.280           | 2.426±0.431    | 2.273±0.434   | <.001 (HS) |
| Mean PI        | 0.640±0.199           | 0.887±0.200    | 0.872±0.168   | <.001 (HS) |
| Mean RI        | 0.474±0.054           | 0.555±0.057    | 0.559±0.057   | <.001 (HS) |

**Table (6)** shows sensitivity, and specificity of mean uterine artery Doppler parameters in different groups in addition to AUC (Area under the curve), C.I (Confidence interval), and P value.

| Variable       | AUC   | 95 % C.I      | Sensitivity (%) | Specificity (%) | p-value    |
|----------------|-------|---------------|-----------------|-----------------|------------|
| Mean S/D ratio | 0.895 | 0.817 - 0.973 | 88.9%           | 72%             | <.001 (HS) |
| Mean PI        | 0.898 | 0.811 - 0.984 | 94.4%           | 80%             | <.001 (HS) |
| Mean RI        | 0.908 | 0.838 - 0.979 | 83.3%           | 88%             | <.001 (HS) |

The cut-off point for mean S/D= is 1.84, for left PI=0.712, and for left RI=0.527.



**Figure (4):** ROC curve (Receiver Operating Characteristic curve) of mean uterine artery Doppler parameters.



## Discussion

The great majority of placenta previa cases diagnosed early in pregnancy migrate to a fundal position in late pregnancy, hence evolving the importance of finding effective predictive factors for the resolution of early diagnosed placenta previa. Thus we performed this prospective cohort study on 200 pregnant women attending antenatal care at Obstetrics and Gynecology Clinic at Benha University Hospital to study predictive role of mid-trimester uterine artery Doppler velocimetry parameters on the resolution of placenta previa.

Placental migration is due to the elongation of the lower uterine segment in the third trimester leading to uterine enlargement in an opposite direction from the cervical os moving away low-lying placenta from the cervical os. **(11)**

In a previous study, in pregnancies with unilateral placental location, ipsilateral uterine artery S/D ratio was significantly lower than that of contralateral artery, which suggests that uterine vessels supplying placental site have lower vascular resistance. **(12)**

In a previous study, there was a difference in blood flow in uteroplacental compartment in relation to placental localization and proved that this change takes place in both uterine and arcuate arteries. **(13)**

A retrospective cohort study was carried out on 504 subjects to study relation between uterine artery Doppler velocimetry and placental previa resolution. They found that out of the 504 cases included in the study,

351 cases were assigned to the control group with fundal placental position diagnosed both at 22–24 weeks and after 36 weeks of pregnancy. One hundred and fifty-three cases were diagnosed as placenta previa at mid-term gestation, among which 89 cases (58.2% out of mid-term previa) resolved after 36 weeks of gestation and were assigned to resolving group, the rest 64 cases (41.8% out of mid-term previa), which had persistent placenta previa until delivery were assigned to placenta previa group. **(10)** This was consistent with a previous study, in which those with placenta previa at 15–19 weeks, 20–23 weeks, 24–27 weeks, 28–31 weeks, and 32–35 weeks, Previa persisted until delivery in 12%, 34%, 49%, 62%, and 73%, respectively. **(14)**.

In a previous study, the majority of both complete and marginal previas resolved in the interval between the first ultrasound and the third-trimester ultrasound. **(15)**

A previous study found that low-lying placenta or placenta previa was diagnosed in almost 1 of 10 women at mid-trimester transvaginal ultrasound survey. Most women who returned for additional assessments had resolutions, and 95% of resolutions occurred by 17 weeks from diagnosis. **(16)**

In a previous study, posterior placentae were found to have a higher tendency to migrate than anterior placentae by three times **(17)**, but in another study, there was no difference reported in the likelihood of resolution between anterior and posterior situated placentae. **(4)**

In a previous study, among pregnant women with placenta completely or partially covered internal os at the 28<sup>th</sup> week of pregnancy, 37.5% were resolved at the 36<sup>th</sup> week and 25.8% persisted as placenta previa marginalis. (18)

A study reported that in women admitted at 29 weeks gestation, the average migration rate was 0.3 mm/wk in women with previous cesarean delivery. The average migration rate was 5.4 mm/wk in women who had a previous vaginal delivery. (19)

A prior case-control study reported that previous cesarean delivery added risk for detection of placenta previa at second-trimester sonography. And also found that patients with prior cesarean delivery had lower likelihood of spontaneous placenta previa resolution, and these patients had an increased risk of placenta previa at term. (20)

Other retrospective study findings confirm that scarred lower uterine segment from prior surgery causes placental migration impedance, leading to less resolution frequency. (21)

Our results were consistent with previous reports in which by ultrasound examination at 18 weeks, 45.1% of placentas were posterior and 42.1% anterior. By 34 weeks, slight variations in placental location were seen with more apparent 'migration' for placentas attached to the posterior wall than anterior. All of the posterior low-lying placentae and all but 3.4% of anterior low-lying placentas 'migrated' away from the cervical os (22)

In our study, we found that the mean uterine artery parameters were much lower in placenta previa group than those in the

control and resolved groups with no differences were found between the control and resolved groups.

This was consistent with a previous study, in which they also found that the mean uterine artery parameters were much lower in the placenta previa group than in control and resolving groups with no differences between control and resolved groups (10)

A previous study found that right uterine artery blood flow indices in placenta previa cases significantly differed from those in women with placenta accreta. The pulsatility index in the right uterine artery was significantly lower in patients with placenta accreta as compared with patients with placenta previa and those with normally positioned placenta groups (23)

In a previous study, the mean left UtA-PI showed in both left- and right-sided placenta a decrease of 0.04/week, compared to a mean right UtA-PI decrease of 0.03/week in both left- and right-sided placenta. These findings indicate a raised resistance in contralateral uterine arteries when compared with their ipsilateral counterparts in the case of placenta laterality (24)

In a previous study, ipsilateral artery PI measurements were consistently lower than contralateral ones in both singleton and twin pregnancies indicating that placental location has an impact on uterine artery hemodynamics (25)

In a previous study, uterine artery PI measurements did not show any statistical difference according to placental locations (26)

In a previous study, Doppler ultrasound was used to examine blood flow in uterine arteries. Measurements were performed on

the 20-22<sup>nd</sup>, 30-32<sup>nd</sup>, and 35-36<sup>th</sup> weeks of gestation. Blood flow in uterine arteries of patients with placenta previa was much higher as compared with women with normal placental localization (23)

The conditions of placenta accreta and placenta previa are associated with a decrease in peripheral vascular resistance in both uterine arteries during all periods of gestation. This conclusion is supported by lower values of the pulsatility index in these blood vessels in comparison to values in patients with normal placental localization (23)

In a previous study, Doppler examinations of uterine arteries were performed in 247 singleton pregnancies. There was no correlation between maternal age and uterine artery velocimetry parameters (27)

This was contrary to our study in which, the median age of the included subjects in control group was 25 with IQR (24-30), while in resolved group was 27 with IQR (26-29.8), and in placenta previa group was 31, and IQR was (29-32.5) with a *p*-value less than 0.001, and this reflects the relation between uterine artery velocimetry Doppler parameters and age.

There are limitations to our study. Firstly, the number of study subjects in the placenta previa group and the resolved group was not too big, so more studies with huge patients' number are needed. Also, we only studied one factor (i.e. the uterine artery Doppler velocimetry parameters) as a predictive factor for the resolution of placenta previa, and more studies are needed to combine more than one factor. Considering possible bias between different operators, a multicenter study is needed.

Although more efforts are needed, our results suggest a predictive role for uterine artery velocimetry measurements on placenta previa resolution.

## Conclusion

Uterine artery Doppler velocimetry parameters at mid-trimester are much lower in patients with persistent placenta previa than in control and resolved groups and have potential to predict placenta previa resolution.

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