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Uterine artery doppler ultrasound in prediction of preterm labor in pregnant women with threatened preterm labor

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Abstract
Objective: The aim of this study was to assess the value of uterine artery pulsatility index (UA-PI) measured in women with threatened preterm labor, in prediction of preterm delivery.
Methods: The current study was conducted at Obstetrics and Gynecology Department, Zagazig University Hospital, Zagazig, Egypt, during period between June 2018 and August 2019. The study included singleton pregnant women who present to the casualty at gestations between 28 and 34 weeks of gestation with symptoms and signs of threatened preterm labor. On admission, during obstetric ultrasound scanning, bilateral uterine artery Doppler ultrasound velocimetry was performed using the transabdominal technique. Uterine artery Doppler scans were both conducted at the peak of uterine contraction and in between contractions when the uterus is fully relaxed.
Results: A total 283 women presenting with threatened preterm labor were included in the study. The mean gestational age at presentation was 30.86 ± 1.71 weeks (range: 28 – 33.86 weeks). Of the included 283, 91 (32.2%) delivered within 7 days, while 192 (67.8%) delivered after 7 days of presentation. The mean uterine artery pulsatility index (UA-PI) measured both basally and at the peak contraction were significantly higher among women who delivered within 7 days. ROC curves showed that both basal and contraction UA-PI were significant predictors of delivery within 7 days. There was a significant negative correlation between contraction UA-PI and birth weight.
Conclusion: Uterine artery Doppler ultrasound velocimetry measured in women with threatened preterm labor, seems to be a significant predictor of actual preterm labor within 7 days of admission.

Keywords: preterm labor, uterine artery Doppler

Introduction
Preterm labor and its resulting prematurity remain the main cause of perinatal mortality and morbidity [1]. Most of these cases present with threatened preterm labor some time before they give birth. Nevertheless, no more than one-fifth of women who present with threatened preterm labor will eventually deliver prematurely [2, 4]. Management of such women who present with threatened preterm labor includes exclusion of serious obstetric and non-obstetric conditions that might have precipitated preterm labor, tocolysis, maternal steroid administration to enhance fetal lung maturation and transfer to a tertiary maternity unit with adequate neonatal facilities, should preterm delivery ensue [1]. Delivery at such a tertiary unit as well as, proper and timely handling of the preterm neonate are both essential for minimizing the risk of neonatal morbidity and mortality [5]. Therefore, prediction of preterm labor among women who present with symptoms of threatened preterm labor is vital. True uterine contractions that can eventually be effective to cause cervical dilatation is associated with compression of the intramyometrial arteries resulting in reduction or even disappearance of the diastolic component of the uterine artery blood flow [6, 11]. Furthermore, a correlation was found between intensity of uterine contractions and this reduction in diastolic blood flow [9-10]. A recent review [11] and two studies [12, 13] have found significant association between uterine artery Doppler velocimetry and preterm delivery in women with threatened preterm labor. The aim of the current study was to evaluate such an association in a group of pregnant women in our institute.

Methods
The current prospective diagnostic test accuracy study was conducted at Obstetrics and Gynecology Department, Zagazig University Hospital, Zagazig, Egypt, during period between June 2018 and August 2019. The study protocol agreed to Helsinki Declaration for Ethical Medical Research [last updated in Brazil, 2013]. All participating women signed informed written consent. The study included singleton pregnant women who present to the casualty at gestations between 28 and 34 weeks of gestation with symptoms and signs of threatened preterm labor (defined as presence of at least one uterine contraction per 10 minutes, lasting at least 30 seconds, with a cervical dilatation ≤ 3 cm, and a cervical effacement < 80%). Women with ruptured fetal membranes, signs of chorioamnionitis, fetal compromise, maternal obstetric or non-obstetric complication (e.g. severe pre-eclampsia/eclampsia, acute abdomen, liver impairment) were not

recruited in the study. After revising medical history and performing general, abdominal and local examination, obstetric ultrasound, non-stress test (NST) for fetal heart rate tracing and complete blood count (CBC), women were subjected to intramuscular steroid injection (dexamethasone 6 mg every 12 hours for 48 hours) and tocolysis (using oral nifedipine 10 mg capsule every 20 minutes until uterine contractions have faded away). On admission, during obstetric ultrasound scanning, bilateral uterine artery Doppler ultrasound velocimetry was performed using the transabdominal technique. The probe was placed longitudinally in the lower lateral quadrant of the abdomen, angled medially. Color flow mapping was used to identify the uterine artery while crossing the external iliac artery. The sample volume was placed 1 cm downstream from this crossover point. If the uterine artery was seen to branch before the intersection of the external iliac artery, the sample volume was placed on the artery just before the uterine artery bifurcation. The same process was repeated for the contralateral artery [14]. Uterine artery Doppler scans were both conducted at the peak of uterine contraction and in between contractions when the uterus is fully relaxed. The pulsatility indices (both basal and contraction scans) were calculated bilaterally, and the mean value of both right and left vessels was taken. All ultrasound scans and uterine artery Doppler ultrasound measurements were taken by a sonographer with at least 3-year experience with such scans. After receiving the standard management, women were observed for few days in the hospital. According to the practice guidelines adopted by our Department, no long-term maintenance tocolytic treatment was given to women who recovered from threatened preterm labor. Women who had not delivered imminently were contacted later by phone to note the gestational age at delivery and birth weight.

Statistical analysis was performed using MedCalc version 7.0, setting the significance level at 0.05. Normally distributed variables were described in terms of mean and standard deviation; the difference between two independent groups for such variables was analyzed using independent t-test and expressed in terms of mean difference and its 95% confidence interval. Non-normally distributed variables were described in terms of median and interquartile; the difference between two independent groups for such variables was analyzed using Mann-Whitney's U-test and expressed in terms of median difference and its 95% confidence interval. Receiver operator characteristics (ROC) curves were constructed for estimating the association between both basal and contraction pulsatility indices and delivery within 7 days of presentation. Association between uterine artery pulsatility index and birth weight was estimated using Spearman's correlation coefficient.

Results

A total 283 women presenting with threatened preterm labor were included in the study. The mean age of included women was 32.19 ± 5.14 years (range: 24 – 41 years). The median parity was 2 (range: 0 – 4; interquartile range: 1 – 3). The mean body mass index (BMI) was 27.37 ± 4.7 kg/m^2 (range: 17.58 – 39.19 kg/m^2). The mean gestational age at presentation was 30.86 ± 1.71 weeks (range: 28 – 33.86 weeks). Of the included 283, 91 (32.2%) delivered within 7 days, while 192 (67.8%) delivered after 7 days of presentation. There were no significant differences between women of both groups regarding the age, parity, BMI or gestational age (table-1). The mean uterine artery pulsatility index (UA-PI) measured both basally and at the peak contraction were significantly higher among women who delivered within 7 days (table-2). ROC curves showed that both basal and contraction UA-PI were significant predictors of delivery within 7 days (figure-1). There was a significant negative correlation between contraction UA-PI and birth weight (r=-0.478, 95% CI (-0.563 to -0.383), p<0.001) (figure-2).

Table 1: Difference between Groups regarding Initial Characteristics

	Women Delivered ≤ 7 Days (n=91)	**Women Delivered > 7 Days (n=192)**	**MD/MedD (95% CI)**	***P***
Age (years)	32.8 ± 5.3	31.9 ± 5.1	1.0 (-3.0 to 5.1)	0.614 [1]
Parity	2 (1 – 3)	2 (1 – 3)	-1.0 (-2.0 to 0.0)	0.243 [2]
BMI (kg/m^2)	27.7 ± 4.5	27.2 ± 4.8	-0.12 (-3.8 to 3.6)	0.947 [1]
Gestational Age (weeks)	30.6 ± 1.7	30.9 ± 1.7	-0.28 (-1.40 to 0.84)	0.618 [1]

Data presented as mean ± standard deviation; or median (interquartile range) BMI body mass index MD (95% CI) mean difference and its 95% confidence interval MedD (95% CI) median difference and its 95% confidence interval

1 Analysis using independent student's t-test

2 Analysis using Mann-Whitney's U-Test

Table 2: Difference between Groups regarding UA-PI

	Women Delivered ≤ 7 Days (n=91)	**Women Delivered > 7 Days (n=192)**	**MedD (95% CI)**	***P*** [1]
Basal UA-PI	0.83 (0.76 – 0.9)	0.78 (0.71 – 0.84)	0.05 (0.03 to 0.07)	<0.001
Contraction UA-PI	1.91 (1.58 – 2.17)	1.11 (0.91 – 1.35)	0.74 (0.64 to 0.85)	<0.001

Data presented as median (interquartile range) UA-PI uterine artery pulsatility index MedD (95% CI) median difference and its 95% confidence interval 1 Analysis using Mann-Whitney's U-Test

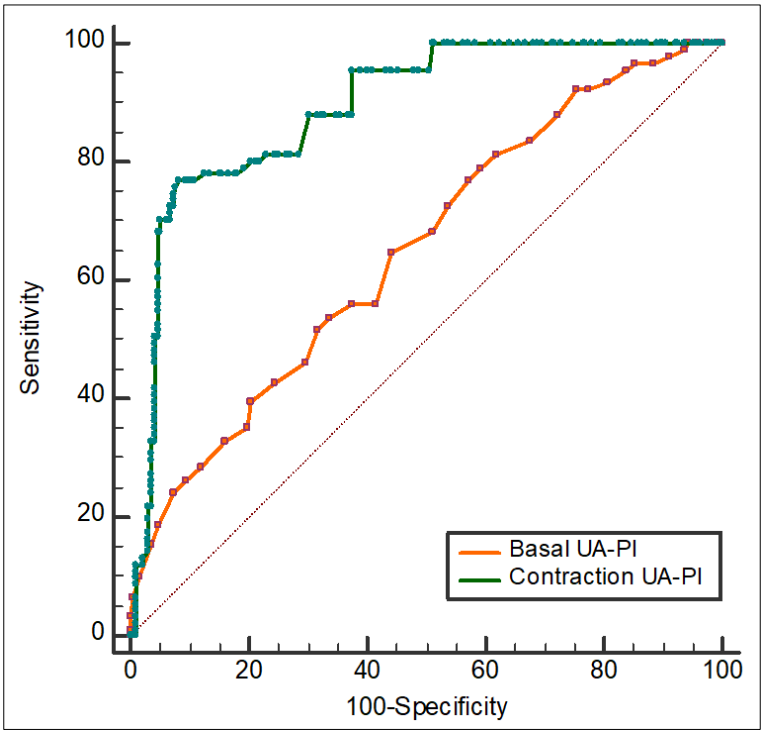
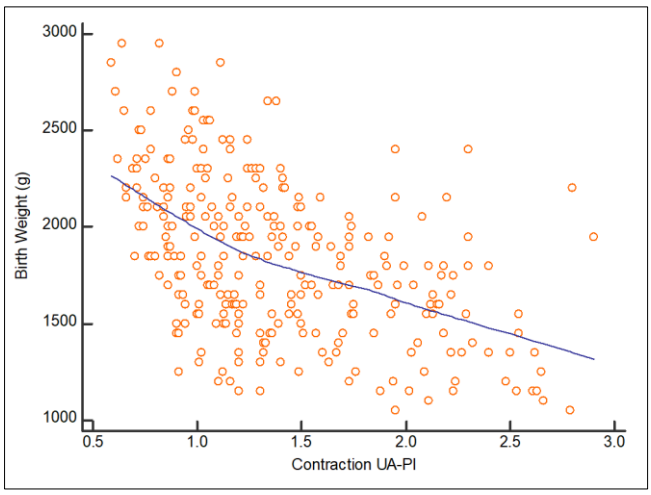


Fig 1: ROC Curves for Basal and Contraction UA-PI in Prediction of Preterm Labor within 7 Days

Table 3

	AUC	Cutoff Value	Sensitivity	Specificity	LR+	LR-
Basal UA-PI	0.651 (0.592 to 0.707)	≥ 0.78	64.84 (54.1 to 74.6)	55.73 (48.4 to 62.9)	1.46 (1.2 to 1.8)	0.63 (0.5 to 0.9)
Contraction UA-PI	0.892 (0.850 to 0.925)	≥ 1.55	76.92 (66.9 to 85.1)	91.67 (86.8 to 95.2)	9.23 (5.7 to 15.0)	0.25 (0.2 to 0.4)

Data presented as value (95% confidence interval) UA-PI uterine artery pulsatility index AUC area under the curve LR+ positive likelihood ratio LR- negative likelihood ratio



r = -0.478, 95% CI (-0.563 to -0.383), p<0.001

Fig 2: Scatterplot for the Association between Contraction UA-PI and Birth Weight

Discussion

Although the current evidence assigns the cervical length as an objective method for prediction of preterm labor [5, 15], transvaginal scan seems undesirable to some pregnant women. In addition, each of UA Doppler scan and cervical length measurement, assesses a different component of preterm labor; the former assesses the contraction component, while the latter assesses cervical ripening [12], and therefore, each of them can identify women at risk of preterm labor, yet not showing changes in the other component. Uterine artery Doppler scan is, however, disadvantaged by the fact that its indices should be affected in women with abnormal trophoblast invasion or placental insufficiency, and in women with multiple pregnancy or polyhydramnios due to rise in intrauterine pressure [12]. The current study showed a promising role of uterine artery Doppler measurement in prediction of actual preterm labor in women presenting with preterm labor.

Although an early retrospective analysis, conducted on 234 pregnancies who had spontaneous preterm delivery and 5472 pregnancies who delivered at term, found no significant difference between both groups regarding the screening uterine artery Doppler findings performed at 18 – 24 weeks of gestation [16], these findings does not contradict the results of the current study for two obvious reasons. First, that retrospective analysis targeted asymptomatic pregnant women who had no threatened preterm labor. Second, the timing and circumstances of uterine artery Doppler scanning are both quite different in what proposed in the current study. The main value of uterine artery Doppler is in women with threatened preterm labor. This is further confirmed by two studies conducted on the role of uterine artery Doppler velocimetry in prediction of spontaneous preterm labor in women with threatened preterm labor. In one of them that was

conducted by Olgan and Celiloglu in 2016, the authors studied the relationship between contraction-based uterine artery PI and preterm delivery in 172 women with threatened preterm labor at gestations between 24 and 32 weeks. The mean values of basal and contraction PI among women who delivered within 7 days were significantly higher than those in women who delivered after 7 days [0.76 ± 0.22 vs. 0.98 ± 0.37, p<0.001; and 2.66 ± 1.05 vs. 1.03 ± 0.64, p<0.001; respectively and respectively]. In this study, cervical length was also evaluated. The authors found that accuracy of uterine artery PI was comparable to that of cervical length measured by transvaginal scan in prediction of preterm labor within 7 days [AUC 0.88, 95% CI (0.82 to 0.94), p<0.05 and 0.85, 95% CI (0.77 to 0.93), p<0.05, respectively] **[12]**. In the second very recent study, just published in November 2019, conducted on 100 Iranian pregnant women admitted for having threatened preterm labor at a tertiary maternity hospital in Tehran, the uterine artery PI was significantly higher among women who delivered within 48 hours [than those who delivered after 48 hours: 1.4 ± 0.5 vs. 0.9 ± 0.3, respectively, p<0.001], women who delivered within 7 days [than those who delivered after 7 days: 1.1 ± 0.3 vs. 0.9 ± 0.3, respectively, p=0.01], and women who delivered within 14 days [than those who delivered after 14 days: 1.3 ± 0.3 vs. 0.9 ± 0.3, respectively, p=0.001]. In this study the best cutoff values for uterine artery PI for prediction of labor within 48 hours, 7 days and 14 days were 0.98 [sensitivity 75% and specificity 70%], 1.0 [sensitivity 84% and specificity 76%] and 0.95 [sensitivity 63% and specificity 69%], respectively [13]. The figures reported by this study are quite different from those of the current study and those reported by Olgan and Celiloglu [12]. This might be explained by relatively small sample size and the measurement of uterine artery Doppler in the relaxed state of the uterus.

In conclusion, uterine artery Doppler ultrasound velocimetry measured in women with threatened preterm labor, seems to be a significant predictor of actual preterm labor within 7 days of admission.

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