

Early doppler ultrasound screening in prediction of hypertensive disorders of pregnancy

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Abstract

Background: Preeclampsia is a pregnancy-specific hypertensive illness that continues to impact the practice of obstetrics globally despite several advances in antenatal care.

Aim: To detect the uterine artery Doppler value in two intervals, 11-13 weeks and 22-24 weeks, in the early prediction of hypertensive illnesses of pregnancy.

Patients and methods: This prospective research has been carried out on 100 pregnant females attending routine antenatal care visits at the outpatient clinics of Obstetrics and Gynecology in Luxor International Medical Complex and Al-Azhar University Hospitals, aiming to evaluate and analyze their health outcomes and experiences.

Results: At 11-13 weeks (UAD1), the cutoff value for Right Uterine Artery PI was 1.43, with an AUC of 0.9973, showing 100% sensitivity and 88% specificity ($P < 0.0001^*$). For Left Uterine Artery PI, the cutoff was 1.45, with an area under the curve of 0.9973, 100% sensitivity, and 90.2% specificity ($P < 0.0001^*$). At 22-24 weeks (UAD2), the cutoff for Right Uterine Artery PI was 0.735, with an area under the curve of 0.998, 100% sensitivity, and 85.9% specificity ($P < 0.0001^*$). For Left Uterine Artery PI, the cutoff was 0.81, with a perfect area under the curve of 1, 100% sensitivity, and 96.7% specificity ($P < 0.0001^*$). These results highlight the strong predictive accuracy of uterine artery PI in identifying hypertensive disorders during pregnancy.

Conclusion: The uterine artery Doppler is a valuable tool for predicting Preeclampsia and other pregnancy-related hypertension disorders, but further research is needed with a larger sample size.

Keywords: Pre-eclampsia; Uterine artery Doppler; Hypertensive

1. Introduction

Preeclampsia is a pregnancy-specific hypertensive illness that continues to impact the practice of obstetrics globally despite several advances in antenatal, intrapartum, and postpartum care. This illness is a significant contributor to perinatal and maternal mortality and morbidity, complicating approximately between two and ten percent of births globally, impacting around ten million women, and resulting in approximately 76,000 maternal fatalities each year due to related complications. Preeclampsia is a hypertensive disease associated with pregnancy that manifests following twenty gestation weeks.^{1,2}

The fundamental process behind the onset of Preeclampsia is believed to be the compromised trophoblastic invasion of maternal spiral

arteries, resulting in their transformation from restricted muscular vessels to large non-muscular channels, independent of maternal vasomotor regulation.³

Doppler measures of uterine blood flow may serve as a screening test based on this knowledge.⁴

This research aimed to assess the efficacy of uterine artery Doppler assessment at two intervals (11-13 weeks and 22-24 weeks) for the early prediction of hypertensive disorders throughout pregnancy. The research has been performed on pregnant women with singleton pregnancies who attended routine antenatal care visits at Luxor International Medical Complex and Al-Azhar University Hospitals, including those with a gestational age of 11-13 weeks, while excluding cases with pre-existing hypertension or vascular diseases.

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2. Patients and methods

This prospective research has been conducted on 100 pregnant females attending routine antenatal care visits at the outpatient clinics of Obstetrics and Gynecology in Luxor International Medical Complex and Al-Azhar University Hospitals, aiming to evaluate and analyze their health outcomes and experiences.

Inclusion criteria: Pregnant women, GA at 11-13 weeks, and singleton pregnancy.

Exclusion criteria: Essential hypertension (renal disease, pregravid blood pressure >140/90, vascular illness, or DM and women who did not wish to participate in the study.

Sample Size: - This study would be done on 100 pregnant women who will attend their routine antenatal care visits at the outpatient clinic of Obstetrics and Gynecology in Luxor International Medical Complex and Al-Azhar University hospitals

Methods

All pregnant women have been exposed to the following: Complete history taking, complete physical assessment. Participants were monitored for vital signs, clinical signs, gestational age, maternal weight, height, and BMI during pregnancy, with the last menstrual period and ultrasound scans confirming gestational age.

All participants underwent an US scan to verify age of pregnancy through measurement fetal crown-rump length (CRL), screen for major fetal anomalies, and assess nuchal translucency thickness as part of chromosomal abnormality screening.⁵ Additionally, laboratory investigations included a complete blood count (CBC), fasting and 2-hour postprandial blood sugar levels, urine analysis, and liver and kidney function tests.

Ultrasound examination

Prospective sequential Doppler recordings of the uterine artery (UtA) have been acquired in singleton pregnancies throughout two gestational age intervals: 11-13 weeks and 22-24 weeks. Participants have been positioned in the lithotomy posture, and a transvaginal transducer has been applied to acquire a sagittal slice of the cervix. The probe was laterally repositioned to see the paracervical vascular plexus, and color Doppler was utilized to locate the uterine artery at the cervicocorporeal junction, ensuring that measures have been recorded prior to the branching of the uterine artery into the arcuate arteries. The insonation angle has been kept below thirty degrees, and the pulsed Doppler gate has been positioned across the full width of the vessel. Angle correction has been implemented, and spectral Doppler signals from three successive waveforms have

been acquired. The pulsatility index (PI) of the left and right arteries has been assessed, and the average PI has been computed. The existence or nonexistence of a bilateral early diastolic notch was also recorded. The left and right uterine arteries have been assessed by color and pulsed Doppler, with the mean pulsatility index and the occurrence of a bilateral protodiastolic notch documented throughout both periods. Pregnancies were subsequently observed for the emergence of hypertensive diseases.



Figure 1. Typical uterine artery color Doppler signals and Doppler velocity waveform with an early diastolic notch at 11-14 weeks .⁶



Figure 2. Ultrasound machine displaying a fetal scan, illustrating the technology used for uterine artery Doppler assessments in the study.

Ethical consideration

Informed consent has been acquired from all participants after they were thoroughly informed about the study's aims, processes, and applicable objectives. The research procedures were designed to ensure no harmful impacts on the participants, and the standard of care was maintained throughout. The principal researchers safeguarded individual data as private and confidential information. Participants were not required to pay any

additional fees, as all associated costs were covered by the investigators.

Statistical analysis

Data entry and analysis have been carried out with SPSS software (Version 20.0). The mean, proportion, and percentage had been computed. The chi-square test has been utilized to determine the correlation.

3. Results

Table 1 showed that, the subjects' mean age was 27.37 years (± 2.43). Parity averaged 1.57 (± 0.87), with distributions as follows: 2% nulliparous, 62% with 1 parity, 19% with 2, 13% with 3, and 4% with 4. For Cesarean Section (CS), the mean was 0.77 (± 0.97), with 50% having no CS, 33% with one, 8% with two, 8% with three, and 1% with four. For Normal Vaginal Delivery (NVD), the mean was 0.8 (± 0.78), with 36% having no NVD, 53% with one, 7% with two, 3% with three, and 1% with four. Maternal weight gain averaged 1.34 kg/month (± 0.31), and gestational age at data collection was 12.13 weeks (± 0.62).

Table 1. Demographic data and general characteristics of included subjects

	VALUE (N = 100)
AGE (YEARS)	27.37 $\pm$ 2.43
PARITY	1.57 $\pm$ 0.87
0	2 (2%)
1	62 (62%)
2	19 (19%)
3	13 (13%)
4	4 (4%)
PREVIOUS DELIVERY	
CS	0.77 $\pm$ 0.97
0	50 (50%)
1	33 (33%)
2	8 (8%)
3	8 (8%)
4	1 (1%)
NVD	0.8 $\pm$ 0.78
0	36 (36%)
1	53 (53%)
2	7 (7%)
3	3 (3%)
4	1 (1%)
MATERNAL WEIGHT GAIN DURING PREGNANCY (KG) (PER MONTH)	1.34 $\pm$ 0.31
GA (WEEKS)	12.13 $\pm$ 0.62

Table 2 showed that, at 11–13 weeks gestation (UAD1), the mean Right Uterine Artery Pulsatility Index (UTA PI) was 1.35 (± 0.26), and the Left Uterine Artery PI was 1.39 (± 0.28). Bilateral protodiastolic notch was observed in

6% of cases. At 22–24 weeks gestation (UAD2), the mean Right Uterine Artery PI decreased to 0.72 (± 0.16), and the Left Uterine Artery PI was 0.71 (± 0.14). The occurrence of bilateral protodiastolic notch increased to 12% at this stage.

Table 2. Uterine Artery Doppler of included subjects

	VALUE (N = 100)
UAD1 (11–13 W)	
RIGHT UTA PI	1.35 $\pm$ 0.26
LEFT UTA PI	1.39 $\pm$ 0.28
BILATERAL PROTODIASTOLIC NOTCH	6 (6%)
UAD2 (22–24 W)	
RIGHT UTA PI	0.72 $\pm$ 0.16
LEFT UTA PI	0.71 $\pm$ 0.14
BILATERAL PROTODIASTOLIC NOTCH	12 (12%)

Table 3 showed that, gestational Hypertension (G. HTN) is reported in 7% of cases, while Pre-Eclampsia is observed in 8%. Among cases of Pre-Eclampsia, 3% manifest early (before 34 weeks gestation), and 5% develop late (after thirty-four weeks gestation). The majority of subjects, constituting 85%, remain normal by hypertensive disorders. The gestational age (GA) at which hypertensive disorders are detected is presented as a mean of 31.2 weeks with a standard deviation of 3.93.

Table 3. Development of hypertensive disorders among included subjects

	VALUE (N = 100)
G. HTN	7 (7%)
PRE-ECLAMPSIA	8 (8%)
EARLY (BEFORE 34WK)	3 (3%)
LATE (AFTER 34WK)	5 (5%)
NORMAL	85 (85%)
GA OF HYPERTENSIVE DISORDER DETECTION	31.2 $\pm$ 3.93

Table 4 showed that, at 11–13 weeks (UAD1), the Pre-Eclampsia group had higher Right Uterine Artery PI (2.18 $\pm$ 0.22) compared to G. HTN (1.6 $\pm$ 0.24) and normal groups (1.29 $\pm$ 0.11), with significant differences ($P < 0.0001^*$). Left Uterine Artery PI and Bilateral Notch were also significantly higher in Pre-Eclampsia ($P < 0.0001^*$). At 22–24 weeks (UAD2), Pre-Eclampsia showed higher Right Uterine Artery PI (1.18 $\pm$ 0.15) vs. G. HTN (0.77 $\pm$ 0.18) and normal (0.67 $\pm$ 0.05) groups ($P < 0.0001^*$). Left Uterine Artery PI and Bilateral Notch were also significantly elevated in Pre-Eclampsia ($P < 0.0001^*$).

Table 4. Comparison between different sub groups regarding Uterine Artery Doppler data

	G. HTN (N = 7)	PRE-ECLAMPSIA (N = 8)	NORMAL (N = 85)	P. VALUE (1/2)	P. VALUE (1/3)	P. VALUE (2/3)	F/X
UAD1 (11–13 W)							
RIGHT UTA PI	1.6 $\pm$ 0.24	2.18 $\pm$ 0.22	1.29 $\pm$ 0.11	0.0004*	<0.0001*	<0.0001*	<0.0001*
LEFT UTA PI	1.6 $\pm$ 0.28	2.16 $\pm$ 0.23	1.3 $\pm$ 0.1	0.0009*	<0.0001*	<0.0001*	<0.0001*
BILATERAL PROTODIASTOLIC NOTCH	2 (28.57%)	4 (50%)	0 (0%)	0.4346	<0.0001*	<0.0001*	<0.0001*
UAD2 (22–24 W)							
RIGHT UTA PI	0.77 $\pm$ 0.18	1.18 $\pm$ 0.15	0.67 $\pm$ 0.05	0.0004*	0.0001*	<0.0001*	<0.0001*
LEFT UTA PI	0.78 $\pm$ 0.13	1.17 $\pm$ 0.15	0.66 $\pm$ 0.05	0.0001*	<0.0001*	<0.0001*	<0.0001*
BILATERAL PROTODIASTOLIC NOTCH	5 (71.43%)	7 (87.5%)	0 (0%)	0.4738	<0.0001*	<0.0001*	<0.0001*

P (1/2): G. HTN group vs. Pre-Eclampsia group, P (1/3): G. HTN group vs. Normal group, P (2/3): Pre-Eclampsia group vs. Normal group

Table 5 showed that, at 11–13 weeks (UAD1), the Right Uterine Artery PI was 2.31 ± 0.2 in Early PE and 2.1 ± 0.21 in Late PE, with no significant difference ($P = 0.1993$). Similarly, the Left Uterine Artery PI was 2.32 ± 0.25 in Early PE and 2.06 ± 0.17 in Late PE, also not significant ($P = 0.1313$). Bilateral Notch occurrence was 33.33% in Early PE and 60% in Late PE, with no significant difference ($P = 0.537$). At 22–24 weeks (UAD2), the Right Uterine Artery PI significantly decreased in Late PE (1.09 ± 0.07) compared to Early PE (1.32 ± 0.13) ($P = 0.0196^*$). Similarly, the Left Uterine Artery PI decreased in Late PE (1.09 ± 0.06) vs. Early PE (1.3 ± 0.17) ($P = 0.0351^*$). Bilateral Notch prevalence was 66.67% in Early PE and 100% in Late PE, with no significant difference ($P = 0.2199$).

Table 5. Comparison between early and late PE cases regarding Uterine Artery Doppler data

	EARLY (BEFORE 34WK)	LATE (AFTER 34WK)	P. VALUE
UAD1 (11-13 W)			
RIGHT UTA PI	2.31 ± 0.2	2.1 ± 0.21	0.1993
LEFT UTA PI	2.32 ± 0.25	2.06 ± 0.17	0.1313

Table 6. Roc curve analysis of UAD for detection of (Pre-Eclampsia) PE.

	CUTOFF VALUE	AUC	STD. ERROR	ASYMPTOTIC 95% CONFIDENCE INTERVAL		SENSITIVITY	SPECIFICITY	P. VALUE
				Lower Bound	Upper Bound			
UAD1 (11-13 W)								
RIGHT UTA PI	1.43	0.9973	0.0036	0.9903	1	100%	88%	<0.0001*
LEFT UTA PI	1.45	0.9973	0.0036	0.9902	1	100%	90.20%	<0.0001*
UAD2 (22-24 W)								
RIGHT UTA PI	0.735	0.998	0.0029	0.9923	1	100%	85.90%	<0.0001*
LEFT UTA PI	0.81	1	0	1	1	100%	96.70%	<0.0001*

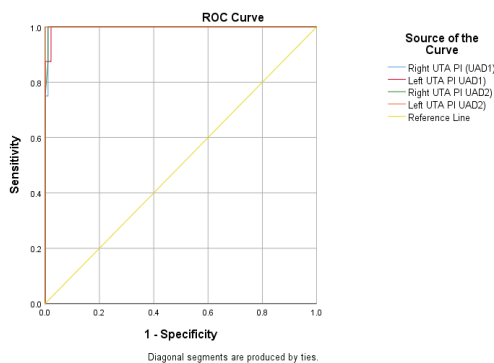


Figure 3. Roc curve analysis of UAD for detection of (Pre-Eclampsia) PE.

CASE PRESENTATION

A case of female patient 26 years old, multigravida 22 weeks, prev 1 cs with Rt Ut PI 1.39 and Lt Ut PI 1.08 with no presence of protodiastol notch in both sides.

BILATERAL PROTODIASTOLIC NOTCH	1 (33.33%)	3 (60%)	0.537
UAD2 (22-24 W)			
RIGHT UTA PI	1.32 ± 0.13	1.09 ± 0.07	0.0196*
LEFT UTA PI	1.3 ± 0.17	1.09 ± 0.06	0.0351*
BILATERAL PROTODIASTOLIC NOTCH	2 (66.67%)	5 (100%)	0.2199

Table 6 showed that, at 11–13 weeks (UAD1), the cutoff value for Right Uterine Artery PI was 1.43, with an area under the curve of 0.9973, showing 100% sensitivity and 88% specificity ($P < 0.0001^*$). For Left Uterine Artery PI, the cutoff was 1.45, with an area under the curve of 0.9973, 100% sensitivity, and 90.2% specificity ($P < 0.0001^*$). At 22–24 weeks (UAD2), the cutoff for Right Uterine Artery PI was 0.735, with an area under the curve of 0.998, 100% sensitivity, and 85.9% specificity ($P < 0.0001^*$). For Left Uterine Artery PI, the cutoff was 0.81, with a perfect area under the curve of 1, 100% sensitivity, and 96.7% specificity ($P < 0.0001^*$). These results highlight the strong predictive accuracy of uterine artery PI in identifying hypertensive disorders during pregnancy.

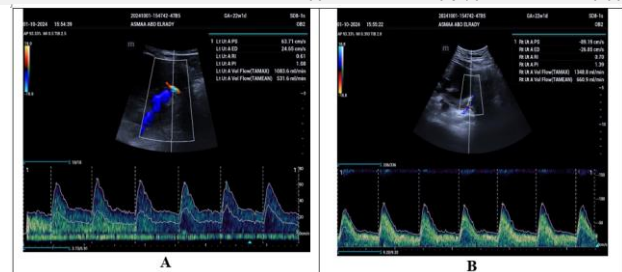


Figure 4. (A): Doppler ultrasound of the left uterine artery at 22 weeks' gestation showing a pulsatility index (PI) of 1.08 and a volume flow of 531.6 ml/min, without evidence of a protodiastolic notch. (B): Doppler ultrasound of the right uterine artery at 22 weeks' gestation with a pulsatility index (PI) of 1.39, end-diastolic velocity of -26.85 cm/s, resistance index (RI) of 0.70, and a volume flow of 660.9 ml/min, also without a protodiastolic notch

4. Discussion

In our research, the mean age of participants was 27.37 ± 2.43 years, and the mean parity was 1.57 ± 0.87 , distributed as follows: 2% nulliparous, 62% with one parity, 19% with 2, 13% with 3, and 4% with four parities. The incidence of previous normal vaginal delivery (NVD) was 0.8 ± 0.78 , with 36% having no previous NVD, 53% with one, 7% with two, 3%

with three, and 1% with four previous NVDs. For cesarean section (CS), the incidence was 0.77 ± 0.97 , with 50% having no previous CS, 33% with one, 8% with two, 8% with three, and 1% with four previous CS deliveries. Maternal weight gain throughout pregnancy averaged 1.34 ± 0.31 kg per month, and the mean gestational age (GA) at data collection was 12.13 ± 0.62 weeks.

The previous research by Poon et al.⁷ performed a prospective screening investigation for hypertensive diseases, examining over eight thousand pregnancies, involving more than three hundred cases that developed Preeclampsia or gestational hypertension. Additionally, the efficacy of screening for hypertensive illnesses in pregnancy at eleven to thirteen weeks will be assessed with a mix of uterine artery Doppler imaging, maternal history, and blood pressure measurements.

Our study showed that UAD1 measurements at 11-13 weeks of gestation reveal a mean Right UTA PI of 1.35 ± 0.26 . The Left UTA PI was 1.39 ± 0.28 . Additionally, the occurrence of Bilateral Protodiastolic Notch was observed in 6% of cases at this gestational stage. UAD2 measurements at 22-24 weeks of gestation with a mean Right UTA PI of 0.72 ± 0.16 . The Left Uterine Artery Pulsatility Index was 0.71 ± 0.14 . Bilateral Protodiastolic Notch was observed in 12% of cases at this later gestational stage.

In a recent study Akinboboye et al.,⁸ found that, abnormal uterine artery S/D ratio has been found in 17.5% and 15.5% of both the left and right uterine arteries respectively while uterine artery RI had abnormal findings in 14.4% and 17.5% in both the left and right uterine arteries of the study population. Presence of a diastolic notch was found in 15.5% of the study population.

In our study, Gestational Hypertension (G. HTN) was reported in 7% of cases. While, Preeclampsia has been observed in 8%. Among cases of Preeclampsia, 3% manifest early (before 34 weeks of gestation), and 5% develop late (after thirty-four weeks of gestation). The majority of subjects, constituting 85%, remain normal for hypertensive disorders. The gestational age (GA) at which hypertensive disorders were detected was presented as a mean of 31.2 ± 3.93 weeks.

The prevalence of Preeclampsia in this study was similar to 8.8%, Musa et al.,⁹, which is comparable to the prevalence of 9.3% (9 out of 97 patients), as reported by Akinboboye et al.⁸. However, it is higher than the prevalence of 7.6% reported by Okwudire et al.,¹⁰

Among 598 women enrolled in the study of An et al.,¹¹ there were 20 patients who developed Preeclampsia (3.3 percent), seven developed

early-onset Preeclampsia (1.2%), fifty-two developed gestational hypertension (8.7percent), 10 developed gestational hypertension with delivery prior to thirty-seven weeks (1.7%).

Our study showed that, for UAD measurements at 11-13- and 22-24-weeks' gestation, a significant increase was observed in Right and left UTA PI in the Preeclampsia group compared to both G. HTN and Normal groups ($p < 0.0001$). Also, the occurrence of Bilateral Protodiastolic Notch at 11-13- and 22-24-weeks' gestation was notably elevated in the Preeclampsia group compared to the G. HTN and Normal groups, with a statistically significant variance (p -value less than 0.0001).

Poon et al.⁷ demonstrated that the uterine artery pulsatility index (PI) was significantly elevated in both late and early Preeclampsia compared to the unaffected group (P -value less than 0.0001). And in GH compared to the unaffected group (P -value equal 0.014).

Our study showed that, for UAD1 measurements at 11-13 weeks of gestation, an insignificant variation has been observed among early and late PE cases in the Right and left UTA PI. Moving to UAD2 measurements at 22-24 weeks of gestation, a significant decrease is noted in the Right and left UTA PI in Late PE cases compared to Early PE cases. ($P = 0.0196$, = 0.0351). The prevalence of Bilateral Protodiastolic Notch at 22-24 weeks of gestation is 66.67% in Early PE cases and 100% in Late PE cases, with no significant difference observed ($P = 0.2199$).

In agreement with our findings were the results of Poon et al.,⁷ who found that the uterine artery L-PI was significantly greater in early PE than late Preeclampsia or GH ($P < 0.0001$).

In our study, we showed that, as regards Roc curve analysis of UAD for detection of PE, for UAD1 measurements at 11-13 weeks of gestation, the Cutoff Value for Right UTA PI is determined to be 1.43, exhibiting an Area Under the Curve (AUC) of 0.9973. The analysis reveals a high Sensitivity of 100%, Specificity of 88%, and a statistically significant p -value of < 0.0001 . Similarly, for Left UTA PI at 11-13 weeks, the Cutoff Value is 1.45, with an AUC of 0.9973. The analysis demonstrates a Sensitivity and Specificity of 100% and 90.20%, respectively, with a highly significant P -value of < 0.0001 . For UAD2 measurements at 22-24 weeks of gestation, the Cutoff Value for Right UTA PI is 0.735, with an AUC of 0.998. The analysis exhibits a remarkable Sensitivity and Specificity of 100% and 85.9% respectively, along with a statistically significant p -value of < 0.0001 . Similarly, for Left UTA PI at 22-24 weeks, the Cutoff Value is 0.81, with a perfect AUC of 1. The analysis reveals a Sensitivity and Specificity of 100% and 96.70%,

respectively, with a highly significant P-value of <0.0001.

Antsaklis et al.¹² found that the expectation of Preeclampsia by Doppler is contingent upon gestational age; specifically, at twenty-four weeks of gestation, the Doppler values exhibit high sensitivity (76.1%), Specificity (95.1%), and positive predictive value (34%).

An et al.¹¹ revealed that the second-trimester uterine artery pulsatility index was the most statistically significant predictor of Preeclampsia. The mean PI during the second trimester, as a single marker, had the highest sensitivity (83.3%) and Specificity (88.5%) in the preeclampsia screening test, with a false positive rate of 11.5% and a likelihood ratio of 7.2 (p=0.003).

Shinde et al.¹³ showed that the sensitivity of mean uterine artery Doppler in detecting PE at eleven to fourteen weeks of gestation was 89.3 percent, Specificity was 95.8 percent, positive predictive value was 90.5 percent, negative predictive value was 95.1 percent, and p-value was less than 0.001.

4. Conclusion

In conclusion, our results suggest that, uterine artery Doppler is the best indicator for the prediction of Preeclampsia. It has a great usefulness in develop Preeclampsia and early prediction of all hypertensive illnesses of pregnancy. However, these findings require confirmation by larger, more-powered study with larger sample size.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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