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Uterine artery doppler indices as early predictors of pregnancy in the second half of stimulated cycles

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Abstract
Background: Uterine artery (UtA) Doppler examination has the ability to anticipate pregnancy difficulties linked with uteroplacental insufficiency prior to the appearance of clinical symptoms. Colour flow Doppler is used, and the UtA is recognised at the cervicocorporeal junction level. The purpose of this work was to assess the role of UtA Doppler indices in the second half of stimulated cycle as predicator of early pregnancy occurrence.
Methods: This cross-sectional work was performed on 80 infertile women aged from 20 to 35 years old, non-smokers, body mass index 29.9KG/m^2 or less, who are treated by stimulant drugs for ovulation induction, history of primary infertility and normal semen analysis based on WHO. All patients were subjected to transvaginal sonography (TVU) in mid luteal phase (day 21:22) for detection of right and left UtA resistance Index (RI) and pulsatility Index (PI).
Results: There was an insignificantly different among pregnant and non-pregnant women regarding menstrual regulation and infertility period. PI and RI were insignificantly different among pregnant and non-pregnant women.
Conclusion: Doppler parameters have no significant prediction of pregnancy, in the second half of stimulated cycles.

Keywords: Uterine artery, doppler indices, predictors, pulsatility index, resistance index

Introduction
Goswamy and Steptoe (1988), they were the pioneers in proposing a potential link between aberrant blood flow in the uterine artery (UtA) and infertility. Additionally, they were the first to create a system for categorising the waveforms of UtA blood flow. The researchers established a connection between certain irregular wave patterns and the recurring inability of embryos to implant in individuals undergoing *in vitro* fertilisation (IVF). They effectively enhanced blood flow in the uterus and improved the process of embryo implantation by administering therapeutic levels of estrogen [1, 2].

Ovarian stimulation with gonadotropins leads to a rise in the velocity of blood flow in the stromal tissue, as seen in 2-dimensional colour Doppler investigations [3]. The rise in the velocity of blood flow in the stromal tissue is linked to a simultaneous rise in the levels of vascular endothelial growth factor (VEGF) in the serum. VEGF, as well as hypoxia-induced factor (HIF), is a substance that stimulates the growth of endothelial cells and has strong capabilities for promoting the formation of new blood vessels. It causes the splitting, budding, branching, and enlargement of the walls of vessels, particularly in areas where the endothelium tips are most sensitive. Perifollicular blood flow is positively correlated with serum VEGF levels. This may be readily evaluated using 2-dimensional Colour and Pulsed Doppler ultrasound [4].

UtA Doppler analysis has the capacity to anticipate pregnancy difficulties linked to uteroplacental insufficiency prior to the manifestation of clinical symptoms. Colour flow Doppler is utilised to detect the UtA at the cervicocorporeal junction [5]. Measures are obtained at this location prior to the UtA dividing into the arcuate arteries [6].

The reduced UtA pulsatility index (UtAPI), especially throughout the luteal phase, together with the elevated blood velocity in the UtA and its vascular network, suggests a rise in uterine perfusion in anticipation of implantation. Low PI of the UtA and endometrial flow have been demonstrated to be linked with higher frequencies of successful implantation.

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This finding provides more evidence that enhanced local blood flow promotes the successful establishment of apregnancy [7, 8].

The purpose of this work was to assess the role of UtA Doppler indices in the second half of stimulated cycle as predicator of early pregnancy occurrence.

Patients and Methods

This cross-sectional work was performed on 80 infertile women aged from 20 to 35 years old, non-smokers, body mass index (BMI): 29.9KG/m^2 or less, who are treated by stimulant drugs for ovulation induction, history of primary infertility and normal semen analysis based on World Health Organization (WHO). The work was conducted following permission from the Ethics Committee Tanta University Hospitals, Tanta, Egypt. Each subject provided a well-informed written consent.

Criteria for exclusion were the patient refused the consent, history of systemic disease and history of gynacological disease.

Each participant had been submitted to taking of history, clinical examinations, laboratory tests [Full blood picture (CBC) and serum beta-human chorionic gonadotropin (B_HCG)] and radiological investigations [Transvaginal ultrasonographic examination to detect right and left UtA flow, index, and resistance in the second half of stimulated cycles]

All patients in the study with stimulated cycles, was subjected to transvaginal sonography (TVU) in mid luteal phase (day 21:22) for detection of right and left UtA PI and RI, and average values was recorded. While the patient was in the lithotomy position utilised colour Doppler ultrasound with 7.5MHZ pulse endovaginal. Doppler system for blood flow analysis, the women's bladder was emptied before examinations UtA is positioned laterally to isthmic region of uterus. All patients was followed for occurrence of pregnancy using serum BHCG level.

Sample Size Calculation

The sample size and power analysis were computed utilising the Epi-Info programme statistical tool created by WHO and the Centre for Disease Control and Prevention, located in Atlanta, Georgia, USA. The version used was 2002. The criteria employed when calculating the sample size had been as follows: [Study design is a cross sectional for evaluation of diagnostic techniques, 95% confidence limit, expected sensitivity of UtA indices as early predictor of pregnancy in the second half of the stimulated cycles at 85% with a margin of error of 10% (75%-95%), the sample size depending on the prior mentioned criteria was found at N=49. We were increased the sample size to 80 to compensate for missed information and improving quality of data of the study.

Statistical analysis

The statistical analysis had been performed utilising SPSS v26 software (IBM Inc., Chicago, IL, USA). The quantitative parameters were expressed as the mean and standard deviation (SD) and contrasted among both groups utilising an unpaired Student's t-test. The qualitative parameters were shown as frequency and percentage (%) and were analysed employing either the Chi-square test or Fisher's exact test, when appropriate. A two-tailed P value < 0.05 was considered statistically significant.

Results

There was insignificantly different among pregnant and non-pregnant women in terms of age and BMI. Table 1.

Table 1: Comparison between pregnant and non-pregnant women in terms of age and BMI

	Pregnant	Not pregnant	P
Age (Years)	27.97±3.18	28.40±3.518	
<26 Years	9(27.3%)	10(21.3%)	0.287
26-30 Years	16(48.5%)	25(53.2%)	
>30 Years	8(24.2%)	12(25.5%)	
BMI (kg/m^2)	26.36±2.36	25.14±2.173	
<24.9	11(33.33%)	25(53.19%)	0.068
24.9-28	12(36.36%)	18(38.30%)	
>28	10(30.30%)	4(8.51%)	

Data are presented as mean ± SD or frequency (%). BMI: Body mass index.

There was insignificantly different among pregnant and non-pregnant women in terms of menstrual regulation and infertility period. Table 2.

Table 2: Comparison between pregnant and non-pregnant women in terms of menstrual regulation and infertility period

		Pregnant	Not pregnant	P
Menstrual regulation	Regular	30(90.91%)	44(93.6%)	0.328
	Irregular	3(9.09%)	3(6.4%)	
Infertility period (years)		4.03±1.31	4.13±1.262	
<3 years		5(15.2%)	6(12.8%)	0.370
3 - 5 years		23(69.7%)	34(72.3%)	
> 5 years		5(15.2%)	7(14.9%)	

Data are presented as mean ± SD or frequency (%).

PI and RI were insignificantly variation among pregnant and non-pregnant women. Table 3.

Table 3: Comparison between pregnant and non-pregnant women regarding PI and RI

		Pregnant	Not pregnant	P
PI	Right	2.33±0.28	2.25±0.211	0.092
	Left	2.32±0.29	2.28±0.228	0.264
RI	Right	0.84±0.09	0.83±0.085	0.253
	Left	0.93±0.33	0.95±0.268	0.352

Data are presented as frequency (%). PI: pulsatility index, RI: Resistance index.

Discussion

Transvaginal Doppler ultrasonography has enhanced the comprehension of the pathophysiological processes involved in blood circulation inside the female pelvis. This approach is valuable for analysing the blood circulation in the ovaries, uterus, and even the follicles [9].

Regarding UtA measurements, it was found that the left and right PI and RI showed insignificant difference in the two studied groups (Pregnant and non-pregnant). In line with our findings, Guzel et al. [10] conducted a study on 80 women who had infertility without explanation for a minimum of one year. The objective was to assess the ovarian and uterine artery Doppler velocimetries as indicators of the likelihood of achieving a successful pregnancy. The participants were administered oral CC at a dosage of 100 mg per day, starting on day 3 and continuing until day 7 of their menstrual cycles. At the conclusion of the trial, a total of 6 participants, accounting for 7.5% of those who participated, successfully obtained pregnancy. The instances were categorised into two groups depending on the patients' pregnancy outcomes. The analysis revealed that no statistically significant variations were existed in the demographic and clinical factors among both groups. The Doppler velocimetry readings did not exhibit any statistically

significant variations among the groups in terms of RI and PI. Consistent with our research findings, Hoozemans *et al*. [11] reported that no significant variation was existed in the average PI of UtA between women who had a successful pregnancy and those who had unsuccessful surgical procedures. Contrary to our findings, Ivanovski *et al*. [12] discovered a substantial reduction in the mean UtA PI and RI in the pregnant group when contrasted to the non-pregnant group. In a 2015 study conducted by Adibi A *et al*. [13], the researchers examined the role of arcuate and uterine artery Doppler readings recorded on the trigger day on anticipating pregnancy in women undergoing IVF therapy. The research revealed a statistically significant decrease in the average PI and RI values of both arcuate and uterine arteries in pregnant women compared to non-pregnant women.

Limitations of this work including the relatively small sample size. So, we recommended that more studies are needed with a large sample size to evaluate if any impact of doppler indices in predicting the pregnancy in combination with other biological marker to increase the prediction value. UtA doppler values only are not efficient in anticipating pregnancy success.

Conclusion
Doppler parameters have no significant prediction of pregnancy, in the second half of stimulated cycles.

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