RESEARCH ARTICLE

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Assessing the role of doppler ultrasound and D-dimer level in predicting asymptomatic DVT during pregnancy

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ABSTRACT **Background:** The d-dimer test is positive even in cases of natural pregnancies. Due to the pregnancy-related hypercoagulable condition, this shows elevated activity of thrombin and enhanced fibrinolysis after formation of fibrin throughout gestation. As a result, this test is unreliable and non-specific for diagnosing venous thrombosis in pregnancy. **Objective of the research:** the current research was aiming at exploring the role of ultrasound examination in addition to d-dimer investigation in detecting "thrombosis of deep veins" in suspected pregnant women. **Patients and methods:** A cross observational sectional study was carried out by the researcher in the department of medicine in Adiwaniyah Teaching Hospital, Diwaniyah Province, Iraq between February 2022 and March 2023. Inclusion criteria were as following: pregnant women with clinical suspicion of deep venous thrombosis based on clinical features identified by 2 specialists in internal medicine and who were referred by the Department of Gynecology and Obstetrics. A vacuum tube was used to collect a sample of venous blood from a peripheral vein and was send to central laboratory in the teaching hospital in order to measure d-dimer level. **Results:** The current study included 90 women of whom 31 (34.4 %) had positive Doppler findings consistent with deep venous thrombosis. There was statistical disparity in the level of d dimer between those with positive DVT Doppler findings and women with negative DVT Doppler findings, 3523.30 ±1773.65ng/ml versus 2553.50 ±1737.96 ng/ml, respectively ($p = 0.014$). Performance of receiver operating characteristic (ROC) test, showed a cutoff value of > 2200 ng/ml which is a reliable predictor of deep venous thrombosis in pregnant woman with 69 % sensitivity level and 71.8 % specificity level. **Conclusion:** assessment of serum level of d-dimer is an essential adjunct in the work up for assessment of pregnant women with suspicion of deep venous thrombosis despite the fact that pregnancy is a hypercoagulable state.

KEYWORDS pregnancy, d-dimer, deep venous thrombosis

1. INTRODUCTION

Puerperium and pregnancy are well-documented risk determinants for thromboembolism phenomenon of veins, a disorder that includes deep venous thrombosis and embolic events in the lung. The incidence of embolic events in lung that is silent in those with symptomatic "deep venous thrombosis" is in the range of 40 to 50%. Asymptomatic "deep venous thrombosis", in addition, is associated with 30% of isolated attacks of pulmonary embolism [1].

Those disorders are more frequent in pregnant females than in non-pregnant females; moreover, the pathophysiology in pregnancy setting is more complex. The risk of acquiring deep venous thrombosis in pregnant women is five times that seen in non-pregnant ladies [2]–[4]. The mean count of thrombotic attacks in all three trimesters is approximately similar, and there is an increase in the mean count of these attacks during the initial six weeks after delivery [3], [5], [6].

The leading cause of death in women during their reproductive age is pulmonary embolism in countries that are developed [7], [8]. Significant proportions of these mortalities are caused by delayed diagnosis or delayed appropriate medical intervention [1]. The situation of pregnancy is naturally associated with increased blood coagulability, and this is suggested to be a natural protective mechanism against excessive blood loss during delivery [9], [10]. The activity of fibrinolysis is decreased, fibrin production gets higher, and there is an increment in the amount of coagulation factors II, VII, VIII, and X. Furthermore, there is a gradual reduction in protein S concentrations and increased resistance to active protein C [1]. Indeed, excessive blood loss is the principal obstetrical cause of death in developing countries [11]. Added to the immediate morbidity, the majority of women who experience deep venous thrombosis at the time of pregnancy develop long-term complications that range from skin changes and edema to recurrent ulceration [12].

The most typical signs of deep vein thrombosis are erythema, swelling, discomfort in the extremities, and difficulty walking. However, normal pregnancy-related swelling and discomfort can mask these symptoms, making it more difficult to diagnose deep vein thrombosis during pregnancy [1].

TABLE 1. Comparison of pregnant women characteristics between those with positive DVT Doppler findings and women with negative DVT Doppler findings

Characteristic	Total n = 90	Positive n = 31	Negative n = 59	p
Age (years)				
Mean ±SD	30.33 ±5.88	32.84 ±5.32	29.02 ±5.76	0.003 I **
Range	20 -49	23 -41	20 -49	
Gestational age (weeks)				
Mean ±SD	30.09 ±8.33	30.87 ±7.14	29.68 ±8.93	0.522 I
Range	9 -39	17 -39	9 -39	NS
BMI (kg/m2)				
Mean ±SD	29.41 ±4.26	29.71 ±4.48	29.25 ±4.17	0.632 I
Range	18 -41	23 -39	18 -41	NS
Gravidity				
Median (IQR)	3 (3)	5 (3)	2 (2)	0.003 M **
Range	1 -9	1 -9	1 -8	
Parity				
Median (IQR)	1 (2)	3 (3)	1 (2)	0.005 M **
Range	0 -7	0 -7	0 -6	
Abortion				
Median (IQR)	0 (1)	0 (1)	0 (1)	0.254 M
Range	0 -3	0 -3	0 -3	NS
Hypertension				
Positive, n (%)	10 (11.1 %)	5 (16.1 %)	5 (8.5 %)	0.456 Y
Negative, n (%)	80 (88.9 %)	26 (83.9 %)	54 (91.5 %)	NS
Diabetes mellitus				
Positive, n (%)	4 (4.4 %)	2 (6.5 %)	2 (3.4 %)	0.606 F
Negative, n (%)	86 (95.6 %)	29 (93.5 %)	57 (96.6 %)	NS
Family history				
Positive, n (%)	12 (13.3 %)	7 (22.6 %)	5 (8.5 %)	0.122 Y
Negative, n (%)	78 (86.7 %)	24 (77.4 %)	54 (91.5 %)	NS
Antiphospholipid antibodies				
Positive, n (%)	3 (3.3 %)	1 (3.2 %)	2 (3.4 %)	1.000 F
Negative, n (%)	87 (96.7 %)	30 (96.8 %)	57 (96.6 %)	NS

BMI: body mass index; SD: standard deviation; IQR: inter-quartile range; I: independence samples t-test; M: Mann Whitney U test; Y: Yates correction test; F: Fischer exact test; NS: not significant; **: significant at $p \leq 0.01$

The d-dimer test is positive even in cases of natural pregnancies. Due to the pregnancy-related hypercoagulable condition, this shows elevated thrombin activity and enhanced fibrinolysis after formation of fibrin throughout gestation. As a result, this test is unreliable and non-specific for diagnosing venous thrombosis in pregnancy [13]. Therefore, the use of imaging investigations is mandatory in pregnant women with a suspicion of "deep venous thrombosis" to make the diagnosis certain and avoid unwanted morbidity or mortality as a result of missed cases [14]. Unfortunately, much debate and controversy exist concerning the sensitivity and specificity of ultrasound in detecting deep venous thrombosis in pregnant women; therefore, the current study was aiming at exploring the role of ultrasound examination in addition to d-dimer investigation in detecting "deep venous thrombosis" in suspected pregnant women.

2. PATIENTS AND METHODS

2.1. Study design and enrolled patients

A cross observational sectional study was carried out by the researcher in the department of medicine in Adiwaniyah Teaching Hospital, Diwaniyah Province, Iraq between February 2022 and March 2023. Inclusion criteria were as following: pregnant women with clinical suspicion of deep venous thrombosis based on clinical features identified by 2 specialists in internal medicine and who were referred by the "Department of Gynecology and Obstetrics". At the end of the study 90 women were enrolled. Exclusion criteria were as following: pregnant women with multiple gestation or any of obstetric complications; women with past history of "deep venous thrombosis"; females having chronic medical illness such as hypertension, diabetes mellitus, kidney disease and thyroid problem.

2.2. Collection of samples

Throughout pregnancy, a blood sample was obtained from each participant in order to assess the d-dimer levels. The collection of peripheral venous blood was conducted using a vacuum tube and was send to central laboratory in the teaching hospital in order to measure d-dimer level.

2.3. Diagnosis

The diagnosis of deep venous thrombosis was based on the results of Doppler ultrasound examination of popliteal veins.

2.4. Ethical considerations

All participating women provided their informed consent. The research was approved by the committee of ethical consideration in the college of medicine /University of Al-Qadisiyha.

2.5. Statistical analysis

The statistical package for social sciences (SPSS) (IBM, Chicago, USA, version 16) was utilized for purpose of statistical analysis and description. Qualitative data were expressed as percentage and number. Data that are quantitative were shown as standard deviation, range, mean, inter-quartile range and median. Comparison of means was done using Mann Whitney U test or student t-test based on proper statistical assumptions. Comparison of proportions was done using chi-square test, Fischer exact or Yates correction test based on proper statistical assumptions. The significance level was considered when $p \leq 0.05$.

3. RESULTS

The current study included 90 women of whom 31 (34.4 %) had positive Doppler findings consistent with deep venous thrombosis. Comparison of pregnant women characteristics between those with positive DVT Doppler findings and women with negative DVT Doppler findings is shown in Table 1. Women with positive Doppler findings were significantly older than women with negative Doppler findings, 32.84 ±5.32 years versus 29.02 ±5.76 years, respectively ($p = 0.003$). There was no statistical disparity in mean age of gestational between the study groups ($p = 0.522$). There was also no statistical disparity in mean body mass index (BMI) between both groups ($p = 0.632$). Gravity expressed in median was significantly greater in women with positive DVT Doppler findings in comparison with women with negative DVT Doppler findings, 5 versus 2, respectively ($p = 0.003$). The same was applied to parity ($p = 0.005$); whereas, there was no statistical disparity in rate of abortion ($p = 0.254$).

Hypertension, diabetes mellitus, positive family history and positive antiphospholipid antibodies were all not associated significantly with positive Doppler findings ($p > 0.05$).

Comparison of D dimer level between those with positive DVT Doppler findings and women with negative DVT Doppler findings is shown in Table 2. There existed a statistical disparity in the d-dimer level among those with positive DVT Doppler findings and women with negative DVT Doppler findings, 3523.30 ±1773.65 ng/ml versus 2553.50 ±1737.96 ng/ml, respectively ($p = 0.014$). Performance of "receiver operating characteristic (ROC) test showed a cutoff value of > 2200 ng/ml which is a reliable predictor of deep venous thrombosis in pregnant woman with 69 % sensitivity level and 71.8 % specificity level, Table 3 and Figure 2.

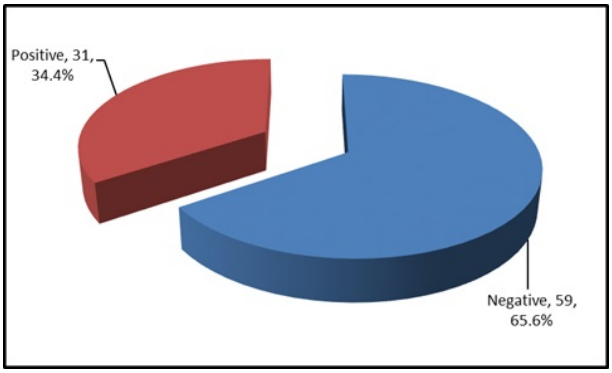

FIGURE 1. **Pie chart showing the proportion of pregnant women with positive Doppler findings**

TABLE 2. **Comparison of D dimer level between those with positive DVT Doppler findings and women with negative DVT Doppler findings**

Characteristic	Total n = 90	Positive n = 31	Negative n = 59	p
D dimer (ng/ml)				
Mean ±SD	2887.50 ±1800.99	3523.30 ±1773.65	2553.50 ±1737.96	0.014 I *
Range	801 -10000	1606 -8010	801 -10000	

SD: standard deviation; I: independence samples t-test; *: significant at $p \leq 0.05$

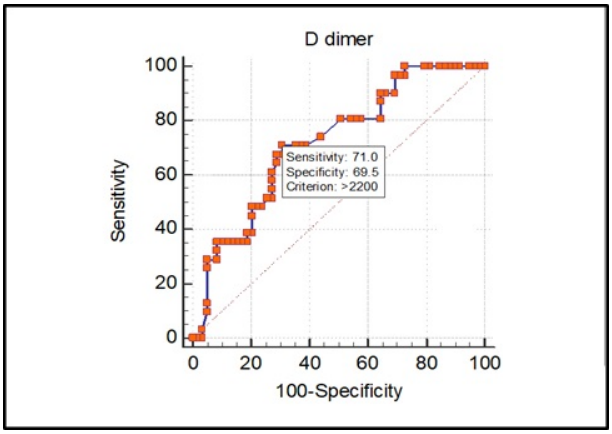

FIGURE 2. **Receiver operating characteristic (ROC) characteristic to find the D-dimer cutoff value that can predict a diagnosis of leg DVT in pregnant women**

TABLE 3. **The characteristic of ROC curve**

Characteristic	Result
Cutoff value	>2200
AUC	0.718
95 % CI	0.613 to 0.808
p-value	<0.001 ***
Sensitivity %	71.0
Specificity %	69.0
Accuracy %	71.8

AUC: area under curve; CI: confidence interval; ***: significant at $p \leq 0.001$

4. DISCUSSION

A combination of clinical evaluation, a d-dimer assessment, and an imaging technique "ultrasonography" is the most common—is used to diagnose deep venous thrombosis in a nonpregnant population [15], [16]. Though the consequences of a misdiagnosis can be severe, only minute fraction of pregnant females with a suspicion of deep vein thrombosis really have the condition [17], [18]. When the value of d-dimer falls below a specific threshold, deep vein thrombosis can be ruled out with high certainty, according to guidelines for women who are not pregnant [19].

According to certain research, the threshold during pregnancy ought to be as high as 1 or 2 mg/L [20], [21]. D-dimer use at time of pregnancy is not advised, according to a number of recently published guidelines for diagnosing deep vein thrombosis in expectant mothers [17], [18], [22], [23]. Deep vein thrombosis risk may be reduced in pregnancy if the D-dimer is less than 0.5 mg/L, although false positives are common. If the d-dimer value is determined, the outcome needs to be interpreted with caution. After compiling data on the D-dimer concentration's sensitivity in ruling out deep vein thrombosis in pregnancy, some writers came to the conclusion that more study is required [24].

The main obstacle to determining D-dimer's contribution to the diagnosis of deep vein thrombosis in pregnant females is the fact that, even in healthy women with an uncomplicated pregnancy, D-dimer levels significantly increase with gestational age [25]–[28]. To rule out the illness, a healthy woman with an otherwise low clinical probability of deep vein thrombosis may have a normal D-dimer, especially in the early stages of pregnancy. In contrast to the nonpregnant state, D-dimer levels may be elevated as early as the first few weeks of pregnancy [25] and a comparatively high number of women will require testing. In order to determine the appropriate reference value, it is necessary to first define the clinical application of various thresholds based on gestational age in a sufficient number of pregnant healthy women across a range of weeks of gestation [13]. At labor, all females had D-dimer concentrations higher than 0.5 mg/ml [13]. Thus, this investigation is not reliable and not specific for the detection of DVT at time of gestation [1]. Based on the observations of Hedengran et al. [19] there is significant fluctuations in levels of d -dimer during normal uneventful pregnancy and they concluded repeated measurements of d-dimer at time

of pregnancy are clinically of no value in assessing thromboembolic events, owing to the inherent biological variability within each pregnant woman.

However, in the present study, we found statistically significant variation in mean serum amount of d-dimer between women with positive Doppler findings (consistent with "deep venous thrombosis") and women with negative Doppler findings (ruling out the possibility of deep venous thrombosis). Therefore, we suggest, that in our health institute, assessment of d-dimer levels in conjunction with clinical findings and Doppler ultrasound are still needed to rule out the possibility of "deep venous thrombosis" in pregnant females.

5. CONCLUSION

Assessment of serum level of d-dimer is an essential adjunct in the work up for assessment of females with gestation with suspicion of deep venous thrombosis despite the fact that pregnancy is a hypercoagulable state.

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