**Original Article (Galley Proof)**

©2019 NRITLD, *National Research Institute of Tuberculosis and Lung Disease, Iran*

TANAFFOS



ISSN: 1735-0344 *Tanaffos 2019; 18(2): ?????*

**Comparison of Fractional Estrogen and Progesterone Levels with D-dimer in Pregnant Women with and without Venous Thromboembolism in Third Trimester of Pregnancy**

|  |  |
| --- | --- |
| **Sahar Amel Shahbaz 1, Hamid Rouhi Broujeni 1, Sheyda Shabanian 2, Fatemeh Deris 4** | **Background:** During pregnancy Venous Thromboembolism Event (VTE) is one of the complications that may be severe and cause of morbidity and mortality in the mother and fetus. Because of D-dimer elevation during pregnancy especially in the third trimester, and because of complications of diagnostic procedures, diagnosis of VTE is more difficult in pregnant than other population. For this reason we decided to find early VTE detecting methods that were non-invasive and safe with respect to the fetus. Here, we investigated fractional estrogen and progesterone levels with D-dimer in pregnant women with and without VTE in third trimester of pregnancy.  **Materials and Methods:** 23 pregnant subjects with VTE and 46 age-matched healthy pregnant controls participated in this study. The D-dimer and estrogen and progesterone levels were measured in serum of both groups through immunofluorescence method  **Results:** Results showed that D-dimer/estrogen ratio (0.1±0.04 vs. 0.03±0.01, P<0.001) and D- dimer/progesterone ratio (10.64±3.2 vs. 3.43±0.87, P<0.001) in the VTE group was significantly higher as compared to control group. The overall accuracy for D-dimer/progesterone ratio and D-dimer/estrogen ratio at optimal cutoff points (5.7208 and 0.0583, respectively) were high (97.1 %) for diagnosing VTE.  **Conclusion:** Our results showed that diagnosing VTE during pregnancy by D-dimer/progesterone ratio and D-dimer/estrogen ratio are accurate with high sensitivity and specificity values. It allows predicting VTE in pregnant women immediately in Emergency and Obstetrics and Gynecology Departments.  **Key words:** D-dimer/estrogen ratio, D-dimer/progesterone, Venous thromboembolism events, Third trimester of pregnancy |
| 1 Department of Internal Medicine, Shahrekord University of Medical Sciences, Iran, 2 Department of Obstetrics and Gynecology, Shahrekord University of Medical Sciences, Iran, 3 Shahrekord University of Medical Sciences, Iran |
| *Received:*  *Accepted:*  *Correspondence to: Rouhi Broujeni H*  *Address: Department of Internal Medicine, Shahrekord University of Medical Sciences, Iran,*  *Email address: hammfer@yahoo.com* |

**introduction**

During pregnancy Venus Thromboembolism Events (VTE) is one of the complications that may be severe and cause of morbidity and mortality in mother and fetus (1-4) including Deep Venous Thrombosis (DVT) and Pulmonary Thromboembolism (PTE), which occurs one in every 1000 pregnancies (1, 2). VTE causes maternal mortality (3, 4) and non-fatal complications such as pulmonary hypertension, and post-thrombotic syndrome (5). Previous studies have shown that hypertension drug and hormonal drugs such as estrogen and progesterone, cigarette smoking, obesity, multiple gestations, increased parity and PLA2 polymorphism of glycoprotein IIb /IIIa are risk factors for VTE (4-6), which indicates that majority of pregnant women are at the risk of VTE (6, 7). On the other hand, venous stasis, hypercoagulability, and vascular damage are considered as Virchow triad which are observed during pregnancy (8-9-10), therefore, the incidence of VTE increases more than four to five times during pregnancy and about 20 times in postpartum period (11, 12). Unfortunately, despite the strong correlation between VTE and pregnancy, there is inadequate study about preventive or curative methods for VTE during pregnancy (1).

Because of complication of diagnostic procedures such as lung CT scan perfusion, lung scan and poor patient acceptance for these procedure and fear of fetus complication, diagnosis of VTE is more difficult in pregnant women than other population, thus, for this causes we decided to find methods that were non-invasive and safe with respect to the fetus for detecting VTE in early stages.

Checking D-dimer is important in detecting VTE in non-pregnant cases, but D-dimer testing in VTE diagnosis in pregnancy has not been adequately studied (13). On the other hand, it has been established that D-dimer increases throughout gestational age and cannot be specific (14). Therefore, another non-invasive and safe method is needed. Moreover, studies demonstrated that hormones such as estrogen and progesterone are significantly associated with VTE events; however, according to pulmonary textbooks and various experiences there wasn`t enough prospective study on the role of D-dimer and estrogen and progesterone in diagnosis of VTE especially during pregnancy, therefore, this is the one of the first studies designed to evaluate and compare fractional estrogen and progesterone levels with D-dimer in pregnant women with and without VTE in third trimester of pregnancy..

**materials and Methods**

This prospective case-control study was performed in Internal medicine and Obstetrics Departments of Shahrekord Hajar Hospital, center of Iran from November 2017 to May

2018. The serum levels of D-dimer and estrogen and progesterone in pregnant women with

VTE (case group) were compared to healthy pregnant individuals (control group). Inclusion criteria for case group consisted of third trimester pregnant women that had referred to Internal medicine and Obstetrics and Gynecology Departments with a diagnosis of VTE in the form of DVT or PTE based on ultrasound or lung CT scan with PTE protocol. Inclusion criteria for control group consisted of healthy third trimester pregnant subjects that had referred to Obstetrics and Gynecology clinic without significant systemic diseases. None of the participants of the two groups had any systemic disease. They had age range between 18-40 years (age-matched) and signed a consent form to participate in the study. Exclusion criteria consisted of subjects (in both groups) with any local or systemic inflammation or other underlying disease that would change serum levels of D-dimer and estrogen and progesterone such as high rheumatoid factor, liver disease, malignancy, inflammation, trauma, recent surgery, consuming anticoagulant drugs, age below 18 years or more than 40 years, and dissatisfaction to participate and/or to continue the study. We also excluded patients with uncompleted data.

**Study design**

In this study we performed algorithm-based diagnostic and evaluation that is shown in figure 1. According to this algorithm 25 subjects with diagnosis of VTE were selected. This study received ethics approval from the Ethics Committee of Shahrekord University of Medical Sciences. After obtaining informed consent, eligible subjects and healthy control were enrolled. Then 5 ml blood sample was obtained from both groups and stored at −20°C until analysis. After completing sampling, the serum levels of D-dimer and estrogen and progesterone were measured in both groups. D-dimer was measured through immunofluorescence method by VIDAS device and estrogen and progesterone level through immunofluorescence method by ELEXIS device in laboratory of Shahrekord Hajar Hospital according to the manufacturer's protocols, which was 300 μg/ml for D-dimer. The ratio of the numerical fraction between D-dimer to the estrogen level and the numerical fraction ratio between D-dimer to the progesterone level was obtained.

**Data analysis**

Data were analyzed and reported only for patients with completed information. Statistical analysis of data was performed using SPSS version 22 software (SPSS Inc., Chicago, IL, USA). Chi-square test was used to compare qualitative variables between groups. Kolmogorov-Smirnov test was used in order to evaluate the normal distribution of all quantitative studied parameters. Independent t-test was used for variables with normal distribution; on the other handMann- Whitney test was used for variables without normal distribution. In order to evaluate the differences between the more than two groups, Kruskal Wallis test was used. Two tailed p-value less than 0.05 was considered significant.

**Results**

Demographic features in terms of age (P=0.942), gestational age (P=0.588), gravid(number of pregnancy) (P=0.907), education (P=0.154), and job (P=0.201) in both groups were similar ، Moreover the number of fetus did not have significant differences between groups (P=0.659). Results showed that the serum levels of estrogen and progesterone in both groups was similar (P>0.05), while serum levels of D- dimer in the VTE group was significantly higher as compared to control group (1387.83±303.93 ng/ml vs. 457.39±126.31 ng/ml, P<0.001). Moreover, D-dimer/estrogen ratio (0.1 ± 0.04 vs. 0.03±0.01, P<0.001) and D-dimer/progesterone ratio (10.64±3.2 vs. 3.43±0.87, P<0.001) in the VTE group was significantly higher as compared to control group (Table 1). In the control group, the ratio of D-dimer increased by about 52% and in VTE group by 362% according to reference.

In the control group, Pearson correlation coefficient showed a direct and significant correlation between D-dimer and estrogen (r=0.453, P=0.002) and progesterone (r=0.485, P=0.001) levels, but there was no such correlation in VTE group. However, there was a direct and significant correlation between gravidity and D-dimer level in VTE group (r=0.443, P=0.034) (Table 2).

The sensitivity, specificity, positive and negative predictive values, overall accuracy for D- dimer/progesterone ratio in optimal cutoff points 5.7208 for diagnosing VTE were 95.7, 97.8, 95.7, 97.8 and 97.1%, respectively. Moreover, the sensitivity, specificity, positive and negative predictive values, overall accuracy for D-dimer/estrogen ratio in best optimal cutoff points 0.0583 for diagnosing VTE were 95.7, 97.8, 95.7, 97.8 and 97.1 %, respectively (Table 3).

**Table 1.** Studied variables in both control and VTR groups

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Groups Variables** | | **VTE (n=23)** | **Control (n=46)** | **P-value** |
| Age (year) | | 30.91 ± 4.73 | 30.83 ± 4.57 | 0.942 |
| Gestational age (week) | | 33.13 ± 3.75 | 33.61 ± 3.28 | 0.588 |
| Gravidity | | 2.91 ± 1.47 | 2.96 ± 1.44 | 0.907 |
| Education | Under the diploma | 7 (30.4 %) | 10 (21.7 %) | 0.154 |
| Diploma and Advanced Diploma | 11 (47.8 %) | 15 (32.6 %) |
| Bachelor's degree and higher | 5 (21.7 %) | 21 (45.7 %) |
| Job | Housekeeper | 15 (65.2 %) | 24 (52.2 %) | 0.201 |
| Employee | 8 (34.8 %) | 16 (34.8 %) |
| Student | 0 | 6 (13 %) |
| No. fetus | One | 21 (91.3 %) | 42 (91.3 %) | 0.659 |
| Two | 2 (8.7 %) | 4 (8.7 %) |
| Estrogen (pg/mL) | | 14466.17 ± 2861.45 | 14461.52 ± 2822.93 | 0.995 |
| Progesterone (ng/ml) | | 133.91 ± 18.6 | 133.7 ± 18.57 | 0.964 |
| D-dimer (ng/ml) | | 1387.83 ± 303.93 | 457.39 ± 126.31 | <0.001 |
| D-dimer/estrogen ratio | | 0.1 ± 0.04 | 0.03 ± 0.01 | <0.001 |
| D-dimer/progesterone ratio | | 10.64 ± 3.2 | 3.43 ± 0.87 | <0.001 |

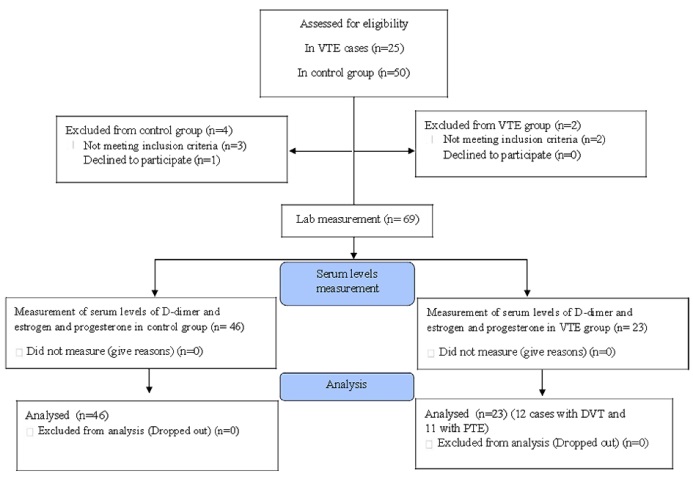
**Table 2.** Correlation between variables in VTE and control groups

|  |  |  |
| --- | --- | --- |
|  | D-dimer | |
| VTE | Control |
| Age | 0.38 (0.863) | 0.05 (0.743) |
| Gravidity | 0.443 (0.034) | - 0.047 (0.757) |
| No. fetus | 0.189 (0.387) | 0.253 (0.089) |
| Estrogen | - 0.075 (0.733) | 0.453 (0.002) |
| Progesterone | - 0.104 (0.637) | 0.485 (0.001) |

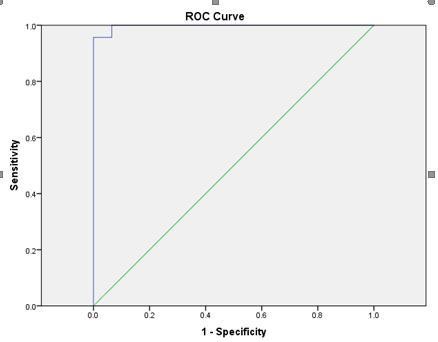
**Table 3**. Sensitivity, specificity, PPV and NPV of D-dimer to estrogen and progesterone ratio in diagnosing VTE

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Method | Cut of point | Sensitivity | Specificity | PPV | NPV | Overall accuracy | P-value |
| D-dimer/  progesterone ratio | 5.6036 | 95.7% | 95.7% | 91.7  % | 97.8% | %95.7 | <0.001 |
| 5.7208 | 95.7% | 97.8% | 95.7% | 97.8% | 97.1% | <0.001 |
| D-dimer/ estrogen ratio | 0.0523 | 95.7% | 93.5% | 88 | 97.7% | 94.2% | <0.001 |
| 0.0547 | 95.7% | 95.7% | 91.7% | 97.8% | 95.7% | <0.001 |
| 0.0583 | 95.7% | 97.8% | 95.7% | 97.8% | 97.1% | <0.001 |

PPV: Positive predictive value, NPV: Negative predictive value



**Figure 1.** Study flowchart.



**Figure**  ROC curve of D-dimer/estrogen ratio in diagnosing VTE

**Discussion**

VTE is one of treatable diseases in hospital and if diagnosed and treated early, morbidity and mortality decreases. Thus, this disease must always be taken care of cautiously. In some people it is an inherited disorder and according to previous researches in Iran especially in

Shahrekord city that is in high altitude and has a population with frequent genetic disorder (4-6) the frequency of VTE is higher than normal. Thus, other studies were needed to evaluate this disorder.

According to the results of this study, D-dimer serum levels were significantly higher in VTE pregnant women than control. Moreover, D-dimer/progesterone ratio in optimal cutoff points 5.7208 and D-dimer/estrogen ratio in optimal cutoff points 0.0583 had high diagnostic value for diagnosing VTE.

In a study done by Damodaram M and koladini M ,lukit I, yoone W , the specificity and sensitivity of the

D-dimer test in pulmonary embolism events were

measured and in order to calculation sensitivity for d-

dimer test was 73%and spesifity was 15%. In order to

eliminate the diagnosis of pulmonary embolism (PE) in

pregnancy, the negative result of D-dimer is better than a

positive testTherefore, given the diagnostic need for

pulmonary embolism during pregnancy, a D- dimer test in

these patients does not aid in the diagnosis and severity of

embolism in these patients and is therefore not

recommended. (14).

In a study of Kovac M, [Mikovic Z](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mikovic%20Z%5BAuthor%5D&cauthor=true&cauthor_uid=19804940) [Rakicevic L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rakicevic%20L%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), and et al

In evaluation of pregnant women in the control group who had no evidence of thromboembolism, D-dimer in the first 3 months of pregnancy was normal in 84% of pregnant women and 33% in pregnant women in the second trimester. And in the third trimester of pregnancy, this value was only 1%, indicating that if the diagnostic threshold of the D-Dimer test was 230ng/ml, the D-dimer is not of much diagnostic value in thromboembolism. All pregnant women who had positive ultrasound findings in the diagnosis of thromboembolism also had statistically significant results. They did not attend the damping test(15)

In the study performed by Kara H et al. k they determine the diagnostic threshold of D- dimer equal to 350 ng/ml in pregnancy, so measuring dimer does not help in diagnosis of thromboembolism. If gets more screening value such as D-dimer greater than 500 ng/ml, and fractional D-dimer level with fibrinogen in diagnosis validity increase , although measurement of this fraction suitable for screening than diagnosis of thromboemboli.

In this study they showed that if selected D-dimer above 350 ng /ml ,diagnosis sensitivity was 100% and specifity only 27%.anf if perfomed cut off ratio for D-dimer /fibrinogen greater than 0.13 sensitivity was 100% and spesifity was 37%. (17). While, Tamar Sokal-Arnon et al. demonstrated that D-dimer serum levels increased during ovarian stimulation; however, levels rarely exceeded the normal range. Therefore, short-term exposure to supraphysiological E2 levels in IVF does not seem to affect thromboembolic status as expressed by D-dimer levels. D-dimer increase was associated with a shorter Prothrombin time (PT) on down regulation (DR) (E2 ≤200 pmol/L) day and tended to be comprehensive and higher among overweight women. Therefore, obesity may pose a risk factor for thromboembolism (18 -19).

In a study conducted by Hendragon, ... it was found that diimeres increase during pregnancy, but given the large fluctuations between different individuals and biological differences during normal pregnancy, therefore, the repeated measurement of dimer clinical value during pregnancy for No diagnosis in the studies (1), whereas studies by ... showed that the diagnosis threshold of a DiMerke test was measured in a prospective study in pregnant women at the first 2 months of pregnancy; and at the second 6 months; In the last 6 months of pregnancy, which indicates that the test is negative in the last 6 months Has a more diagnostic diagnosis of embolism

In a study performed by Hedengran et al. results showed that D-dimer increased during pregnancy; the maximal fluctuation was approximately 20 percentile points in approximately half of the women. In one out of ten women, the D-dimer values fluctuated by more than 50 percentile points. Due to the biological variation in D-dimer within each individual woman during normal pregnancy, repeated D-dimer measurements are of no clinical use in the evaluation of thromboembolic events during pregnancy (19). While, Swaroopa Pulivarthi et al. showed that new cutoff values of D-dimer testing were analyzed in a recent prospective study of pregnant women; they are 286 ng DDU/ml, 457 ng DDU/ml, and 644 ng DDU/ml for the first, second, and third trimesters, respectively (20).

**Conclusion**

Our results showed that diagnosing VTE during pregnancy by D-dimer/progesterone ratio and D- dimer/estrogen ratio are accurate and with high sensitivity and specificity values. It allows predicting VTE in pregnant women immediately in Emergency and Obstetrics and Gynecology Departments and more critically ill patients with low clinical and para-clinical evidence such as imaging may benefit from these advantages of this scoring system, therefore, training this method to emergency physicians and obstetricians and gynecologists should be considered in our country or other countries. Further studies are required to confirm our findings.

# Conflict of interest

The authors have indicated that they have no conflict of interests regarding the content of this article.

# Acknowledgments

This study was funded and supported by Deputy of Research, Shahrekord University of Medical Sciences. We gratefully acknowledge the dedicated efforts of the investigators, the coordinators, and the volunteer cases who participated in this study.

**References**

1. Heit JA. Venous thromboembolism: disease burden, outcomes and risk factors. ***J Thromb Haemost*** 2005;3(8):1611-7.
2. Muellner SK, Haut ER, Streiff MB, Holcomb JB, Cotton BA. ABO blood group as a potential risk factor for venous thromboembolism in acutely injured patients. ***Thromb Haemost*** 2011;105(1):5-13.
3. James AH, Jamison MG, Brancazio LR, Myers ER. Venous thromboembolism during pregnancy and the postpartum period: incidence, risk factors, and mortality. ***Am J Obstet Gynecol*** 2006;194(5):1311-5.
4. Boroujeni HR, Pourgheysari B, Hasheminia A, Boroujeni PR, Drees F. Effect of Platelet Glycoprotein IIb/IIIa PLA2 Polymorphism on Severity of Pulmonary Thromboembolism. ***Tanaffos*** 2014;13(3):14-22.
5. Pourgheysari B, Boroujeni HR, Hasheminia AM, Drees F. PLA2 polymorphism of platelet glycoprotein IIb/IIIa but not Factor V Leiden and prothrombin G20210A polymorphisms is associated with venous thromboembolism and more recurrent events in central Iran. ***Blood Coagul Fibrinolysis*** 2013;24(5):471-6.
6. Rouhi-Broujeni H, Pourgheysari B, Hasheminia AM. Association of Homozygous Thrombophilia Polymorphisms and Venous Thromboembolism in Shahrekord, Iran. ***Tanaffos*** 2016;15(4):218-224.
7. Anderson Jr FA, Spencer FA. Risk factors for venous thromboembolism. ***Circulation*** 2003;107(23\_suppl\_1):I-9.
8. Kovac M, Mikovic Z, Rakicevic L, Srzentic S, Mandic V, Djordjevic V, Radojkovic D, et al. The use of D-dimer with new cutoff can be useful in diagnosis of venous thromboembolism in pregnancy. ***Eur J Obstet Gynecol Reprod Biol*** 2010;148(1):27-30.
9. Kline JA, Williams GW, Hernandez-Nino J. D-dimer concentrations in normal pregnancy: new diagnostic thresholds are needed. ***Clin Chem*** 2005;51(5):825-9.
10. Nolan TE, Smith RP, Devoe LD. Maternal plasma D-dimer levels in normal and complicated pregnancies. ***Obstet Gynecol*** 1993;81(2):235-8.
11. Morse M. Establishing a normal range for D-dimer levels through pregnancy to aid in the diagnosis of pulmonary embolism and deep vein thrombosis. ***J Thromb Haemost*** 2004;2(7):1202-4.
12. Brenner B. Haemostatic changes in pregnancy. ***Thromb Res*** 2004;114(5-6):409-14.
13. Mallick S, Petkova D. Investigating suspected pulmonary embolism during pregnancy. ***Respir Med*** 2006;100(10):1682-7.

# 14- [Damodaram M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Damodaram%20M%5BAuthor%5D&cauthor=true&cauthor_uid=19274539)1, [Kaladindi M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kaladindi%20M%5BAuthor%5D&cauthor=true&cauthor_uid=19274539), [Luckit J](https://www.ncbi.nlm.nih.gov/pubmed/?term=Luckit%20J%5BAuthor%5D&cauthor=true&cauthor_uid=19274539), [Yoong W](https://www.ncbi.nlm.nih.gov/pubmed/?term=Yoong%20W%5BAuthor%5D&cauthor=true&cauthor_uid=19274539) D-dimers as a screening test for venous thromboembolism in pregnancy: is it of any use? Obstet Gynaecol.2009 Feb;29(2):101-3.

15-[Kovac M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kovac%20M%5BAuthor%5D&cauthor=true&cauthor_uid=19804940)1, [Mikovic Z](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mikovic%20Z%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Rakicevic L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rakicevic%20L%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Srzentic S](https://www.ncbi.nlm.nih.gov/pubmed/?term=Srzentic%20S%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Mandic V](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mandic%20V%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Djordjevic V](https://www.ncbi.nlm.nih.gov/pubmed/?term=Djordjevic%20V%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Radojkovic D](https://www.ncbi.nlm.nih.gov/pubmed/?term=Radojkovic%20D%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Elezovic I](https://www.ncbi.nlm.nih.gov/pubmed/?term=Elezovic%20I%5BAuthor%5D&cauthor=true&cauthor_uid=19804940) **The use of D-dimer with new cutoff can be useful in diagnosis of venous thromboembolism in pregnancy.** [Eur J Obstet Gynecol Reprod Biol.](https://www.ncbi.nlm.nih.gov/pubmed/19804940) 2010 Jan;148(1):27-30. doi: 10.1016/j.ejogrb.2009.09.00

15- H. Kara

1

, A. Bayir

1

, S. Degirmenci

1

, S. A. Kayis

2

, M. Akinci

1

,A.Ak

1

, B. Celik

3

,

A. Dogru

1

, B. Ozturk

415- H. Kara

16- H. Kara1, A. Bayir1, S. Degirmenci1, S. A. Kayis2, M. Akinci1,A.Ak1, B. Celik3,A. Dogru1, B. Ozturk4, A. Bayir H. Kara

D-dimer and D-dimer/fibrinogen ratio in

predicting pulmonary embolism in patients

evaluated in a hospital emergency department [Acta Clin Belg.](https://www.ncbi.nlm.nih.gov/pubmed/25012747) 2014 Aug;69(4):240-5.

15-[Kovac M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kovac%20M%5BAuthor%5D&cauthor=true&cauthor_uid=19804940)1, [Mikovic Z](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mikovic%20Z%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Rakicevic L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Rakicevic%20L%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Srzentic S](https://www.ncbi.nlm.nih.gov/pubmed/?term=Srzentic%20S%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Mandic V](https://www.ncbi.nlm.nih.gov/pubmed/?term=Mandic%20V%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Djordjevic V](https://www.ncbi.nlm.nih.gov/pubmed/?term=Djordjevic%20V%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Radojkovic D](https://www.ncbi.nlm.nih.gov/pubmed/?term=Radojkovic%20D%5BAuthor%5D&cauthor=true&cauthor_uid=19804940), [Elezovic I](https://www.ncbi.nlm.nih.gov/pubmed/?term=Elezovic%20I%5BAuthor%5D&cauthor=true&cauthor_uid=19804940) **The use of D-dimer with new cutoff can be useful in diagnosis of venous thromboem**I[Eur J Obstet Gynecol Reprod Biol.](https://www.ncbi.nlm.nih.gov/pubmed/19804940) 2010 Jan; D-dimer and D-dimer/fibrinogen ratio in

predicting pulmonary embolism in patients

evaluated in a hospital emergency department

H. Kara

1

, A. Bayir

1

, S. Degirmenci

1

, S. A. Kayis

2

, M. Akinci

1

,A.Ak

1

, B. Celik

3

,

A. Dogru

1

, B.

Original Article

D-dimer and D-dimer/fibrinogen ratio in

predicting pulmonary embolism in patients

evaluated in a hospital emergency department

H. Kara

1

, A. Bayir

1

, S. Degirmenci

1

, S. A. Kayis

2

, M. Akinci

1

,A.Ak

1

, B. Celik

3

,

A. Dogru

1

, B. Ozturk

**16-** Original Article

D-dimer and D-dimer/fibrinogen ratio in

predicting pulmonary embolism in patients

evaluated in a hospital emergency department

H. Kara

1

, A. Bayir

1

, S. Degirmenci

1

, S. A. Kayis

2

, M. Akinci

1

,A.Ak

1

, B. Celik

3

,

A. Dogru

1

, B. Ozturk

**1** D-dimer and D-dimer/fibrinogen ratio in

predicting pulmonary embolism in patients

evaluated in a hospital emergency department

H. Kara

1

, A. Bayir

1

, S. Degirmenci

1

, S. A. Kayis

2

, M. Akinci

1

,A.Ak

1

, B. Celik

3

,

A. Dogru

1

, B. Ozturk

4

D-dimer and D-dimer/fibrinogen ratio in

predicting pulmonary embolism in patients

evaluated in a hospital emergency departme

18-Sokal-Arnon, Tamar, et al. "The effect of short-term elevation of 17B estradiol (E2) levels on the coagulation system as measured by D-Dimer in women undergoing in vitro fertilization." *IVF Lite*, vol. 1, no. 2, 2014, p. 94. *Gale Academic Onefile*, Accessed 24 Nov. 2019

19-[Tamar Sokal-Arnon](http://www.ivflite.org/searchresult.asp?search=&author=Tamar+Sokal%2DArnon&journal=Y&but_search=Search&entries=10&pg=1&s=0)**1,**[Zofnat Wiener-Megnazi](http://www.ivflite.org/searchresult.asp?search=&author=Zofnat+Wiener%2DMegnazi&journal=Y&but_search=Search&entries=10&pg=1&s=0)**1,**[Ron Auslender](http://www.ivflite.org/searchresult.asp?search=&author=Ron+Auslender&journal=Y&but_search=Search&entries=10&pg=1&s=0)**1,**[Aliza Kassel](http://www.ivflite.org/searchresult.asp?search=&author=Aliza+Kassel&journal=Y&but_search=Search&entries=10&pg=1&s=0)**2,**[Miriam Quitt](http://www.ivflite.org/searchresult.asp?search=&author=Miriam+Quitt&journal=Y&but_search=Search&entries=10&pg=1&s=0)**2,**[Martha Dirnfeld](http://www.ivflite.org/searchresult.asp?search=&author=Martha+Dirnfeld&journal=Y&but_search=Search&entries=10&pg=1&s=0) -[Eur J Obstet Gynecol Reprod Biol.](https://www.ncbi.nlm.nih.gov/pubmed/19804940) 2010 Jan;148(1):27-30. doi: 10.1016/j.ejogrb.2009.09.005 IVF Lite | March-April 2014 | Vol 1

20-[Katrine K. Hedengran](https://www.ncbi.nlm.nih.gov/pubmed/?term=Hedengran%20KK%5BAuthor%5D&cauthor=true&cauthor_uid=27190521),\*[Malene R. Andersen](https://www.ncbi.nlm.nih.gov/pubmed/?term=Andersen%20MR%5BAuthor%5D&cauthor=true&cauthor_uid=27190521), [Steen Stender](https://www.ncbi.nlm.nih.gov/pubmed/?term=Stender%20S%5BAuthor%5D&cauthor=true&cauthor_uid=27190521), and [Pal B. Szecsi](https://www.ncbi.nlm.nih.gov/pubmed/?term=Szecsi%20PB%5BAuthor%5D&cauthor=true&cauthor_uid=27190521) Large D-Dimer Fluctuation in Normal Pregnancy: A Longitudinal Cohort Study of 4,117 Samples from 714 Healthy Danish Women [Obstet Gynecol Int](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4852125/). 2016; 2016: 3561675.

Published online 2016 Apr 17. doi: [10.1155/2016/3561675](https://dx.doi.org/10.1155%2F2016%2F3561675)

[Go to:](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4852125/" \o "Go to other sections in this page)

Venous thromboembolism (VTE) is the leading cause of morbidity and mortality among hospitalized patients. We searched the PubMed database and reviewed the articles published until June 2011. Articles related to the D-dimer and VTE were considered to write this paper. Many factors play a key role in changing the sensitivity and specificity of D-dimer testing, including the extent of thrombosis and fibrinolytic activity, duration of symptoms, anticoagulant therapy, comorbidity due to surgical or medical illnesses, inflammatory diseases, cancer, elderly age, pregnancy and the postpartum period, and previous VTE. Many previous studies have shown that the D-dimer test is highly sensitive (>95%) in acute deep venous thrombosis or pulmonary embolism, usually with a cut-off value of 500 μg FEU/l, which reasonably rules out acute VTE, particularly in patients with low clinical probability (LCP) or intermediate clinical probability. Patients with high D-dimer levels upon presentation may prompt a more intense diagnostic approach, irrespective of pretest probability. Studies performed after a negative D-dimer for 3 months proved the high negative predictive value (NPV) of D-dimer testing together with LCP in patients with suspected VTE. Among oncology patients, D-dimer testing has the highest sensitivity and NPV in excluding VTE. The new cutoff values of D-dimer testing were analyzed in a recent prospective study of pregnant women; they are 286 ng DDU/ml, 457 ng DDU/ml, and 644 ng DDU/ml for the first, second, and third trimesters, respectively.