International Journal Of Health, Engineering And Technology (IJHET) *E-ISSN 2829 - 8683*
Volume 4, Number 6, March 2026, *Page. 2673 - 2679*
Email : editorijhess@gmail.com

D-Dimer in Pregnancy

Danny Ernest Jonas Luhulima[1)*], Batara Imanuel Sirait[2)]
[1)] Department of Clinical Pathology, Medical Faculty, Universitas Kristen Indonesia, Indonesia
[2)] Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Kristen Indonesia, Indonesia

*Corresponding Author
Email : danny.luhulima@uki.ac.id

Abstract

D-dimer is a fibrin degradation product that serves as a vital biomarker in the fibrinolytic system. This review aims to examine the role and mechanism of D-dimer during pregnancy and its measurement methods. The method used is a literature review of clinical studies and references related to hemostasis in pregnancy. Results show that pregnancy physiologically increases coagulation activity as a natural mechanism to prevent hemorrhage during delivery. Increased D-dimer levels are found in 27% of first-trimester pregnancies, 87% in the second trimester, and 100% in the third trimester. Pathological conditions such as preeclampsia, eclampsia, and venous thromboembolism (VTE) risks are closely linked to significant surges in D-dimer levels. While ELISA remains the gold standard for D-dimer testing, immunoturbidimetric and immunofiltration methods are more commonly used due to their speed and efficiency. In conclusion, although D-dimer levels naturally rise during pregnancy, monitoring this parameter is crucial for predicting medical emergencies like disseminated intravascular coagulation (DIC) to reduce maternal mortality rates

Keywords: D-Dimer, Pregnancy, Preeclampsia, Coagulation, VTE

INTRODUCTION

Coagulation Process and D-Dimer Structure

The blood clotting mechanism is a natural bodily process aimed at stopping bleeding or maintaining blood in a liquid state. This process is a complex mechanism involving four main factors: platelet factors, coagulation factors, vascular factors, and the fibrinolysis process. If vascular endothelial damage occurs, these four factors are automatically activated to repair the condition.

Coagulation factors specifically begin through two pathways: the intrinsic pathway, triggered by contact activation and involving Factors XII, XI, IX, VIII, HMWK, PF3, and calcium ions; and the extrinsic pathway, triggered by tissue thromboplastin and involving Factor VII and calcium ions. This process occurs sequentially. Ultimately, both pathways merge into a common pathway involving Factors X and V, PF3, prothrombin, and fibrinogen. Fibrinogen consists of three pairs of polypeptide chains: 2 alpha, 2 beta, and 2 gamma. At the end of the common pathway, thrombin converts fibrinogen into fibrin monomers. Thrombin cleaves the alpha and beta chains at the N-terminal into fibrinopeptides A and B and fibrin monomers. These fibrin monomers then undergo polymerization to form fibrin polymers.

Fibrinolysis is the process of destroying fibrin deposits by the fibrinolytic system to reopen blood flow. This process aims to maintain the balance of the hemostasis mechanism. The enzyme responsible for this process is plasmin. Plasminogen (inactive plasmin) is activated to break down fibrin formations, creating Fibrin Degradation Products (FDP). The process continues by forming fragment X, which is then broken down into fragments Y, D, and E. Two D fragments and one E fragment bind strongly to form D-dimer; thus, D-dimer is the smallest fragment resulting from fibrin breakdown in the blood.

D-dimer has a relatively long half-life of approximately 8 hours. This D-dimer fragment is not formed during the degradation of fibrinogen or non-cross-linked fibrin; therefore, it is specific to the lysis of fibrin clots. D-dimer was first introduced in the 1970s and was used at that time to prove the presence of Disseminated Intravascular Coagulation (DIC). Several conditions can cause blood hypercoagulability for instance, in Deep Vein Thrombosis (DVT), where blood tends to clot

excessively, leading to increased D-dimer levels. Other conditions that can increase D-dimer production include pregnancy, inflammation, cancer, and surgery. Consequently, an increase in D-dimer is not a specific test for Venous Thromboembolism (VTE).

Blood clots generally occur in the veins but can also occur in the arteries. The combination of these two types of thrombosis is termed VTE. If a blood clot obstructs blood flow to vital organs such as the kidneys, brain, or heart, it can cause irreversible damage and organ failure. In such conditions, D-dimer levels will also increase. To date, there is no standardization for normal D-dimer values. Different laboratories apply different normal ranges based on the methods or instruments used. Generally, normal D-dimer values range from 0 to 300 ng/mL.

Hemostasis Changes in Pregnancy

In contrast to non-pregnant states, pregnancy activates the coagulation process, leading to a 20% to 200% increase in fibrinogen and factors II, VII, VIII, X, and XII. Fibrinogen levels typically measure around 300 mg/dL in non-pregnant women but can surge to 600 mg/dL during pregnancy. Other components also increase during this period, including von Willebrand factor, fibrinolytic inhibitors such as PAI-1 and PAI-2, thrombin degradation products, and inhibitors of protein C and thrombin. Conversely, factors V and IX, antithrombin, and Protein C remain relatively stable. Clinical parameters, specifically clotting time and bleeding time, also show no significant changes during pregnancy.

Other components also rise during this period, including von Willebrand factor, fibrinolytic inhibitors (PAI-1 and PAI-2), thrombin degradation products, and inhibitors of protein C and thrombin. Conversely, certain elements remain stable. Factors V and IX, antithrombin, and Protein C, along with clinical parameters such as clotting time and bleeding time, show relatively no change during pregnancy.During pregnancy, prothrombin and plasma thromboplastin time may decrease by approximately 20%; similarly, FXI, FXIII, Protein S, and fibrinolysis also undergo a decrease. However, in general, the hemostasis system increases during pregnancy. Several studies state that normal D-dimer values cannot be applied to pregnancy because D-dimer levels typically increase. Dyhan et al. noted that the average D-dimer level becomes higher in proportion to the progression of the pregnancy. Rahayuningsih et al. reported that increased D-dimer levels were found in 27% of pregnant women in the first trimester, 87% in the second trimester, and 100% in the third trimester.

There is an increased risk of VTE during pregnancy, which is associated with venous stasis due to the enlarging uterus and stimulation of a hypercoagulable state. Experts believe that the hypercoagulable state in pregnancy is a natural mechanism to anticipate bleeding during delivery. Preeclampsia and eclampsia are associated with complex coagulation abnormalities related to increased platelet function, activation of the fibrinolytic system, thrombin formation, and acceleration of the hypercoagulable state. Preeclampsia and eclampsia are frequent causes of death.

One of the most feared and threatening complications in severe preeclampsia and eclampsia is the occurrence of coagulopathy or Disseminated Intravascular Coagulation (DIC). In this condition, hematological abnormalities occur in the form of a simultaneous clotting process and bleeding due to fibrinolysis. This is because DIC involves coagulopathy and conditions that threaten the lives of both the mother and the fetus. In such cases, D-dimer plays a vital role in predicting medical emergencies and the healing process.

When the vasculature undergoes trauma resulting in bleeding, it triggers the activation of clotting factors. This activation occurs sequentially, leading to blood clotting through the coagulation cascade process. This process is necessary to stop bleeding and form a plaque or clot that plugs the wound.

The pregnancy process also affects platelets, characterized by an increase in platelet activity and consumption. Hemodilution also occurs during pregnancy; thus, both of these conditions lead to a lower platelet count compared to non-pregnant women. Furthermore, there is an increase in platelet production and volume, marked by an increase in platelet width. Thromboxane A2 levels also increase, and platelet aggregation is reported to rise as well.

Laboratory Test Methods for D-Dimer

The principle of D-dimer testing involves using monoclonal antibodies that recognize epitopes on D-dimer fragments. To date, several examination methods are available, including Enzyme-Linked Immunosorbent Assay (ELISA), Latex Agglutination, Whole Blood Agglutination, immunoturbidimetry, and immunofiltration. The ELISA method is the gold standard for D-dimer testing.

D-dimer testing using the latex slide agglutination method involves identifying visible (macroscopic) clumps of antigen-antibody particles. This method is most commonly performed because the procedure is easy and fast, requires no special equipment or skills, and is relatively inexpensive. With technological advancements, this method can now be performed using automated instruments, thereby improving precision. This method has been FDA-approved for evaluating D-dimer levels, particularly for assessing VTE disorders.

D-dimer examination by immunoturbidimetry is a method based on finding and quantitatively assessing antigen-antibody reactions, which cause turbidity. This is performed using automated tools and can detect D-dimer levels of less than 0.5 µg/mL. This method correlates well with the ELISA method.

The immunofiltration method for D-dimer testing detects antigen-antibody reactions by measuring immunity through flow (immunometric flowthrough). In this process, D-dimer molecules attach to a membrane coated with D-dimer-specific monoclonal antibodies, followed by the addition of a conjugate to bind the D-dimer. If D-dimer is present, a color change occurs, which is then read by a reader device. The use of immunofiltration is easy, fast, does not require highly trained personnel, and is cost-effective. David Rustandi et al. state that this method is also reliable for D-dimer examination. There is no difference in the D-dimer method test in pregnant and non-pregnant women.

RESEARCH METHODS

The principle of D-dimer testing involves using monoclonal antibodies that recognize epitopes on D-dimer fragments. To date, several examination methods are available, including Enzyme-Linked Immunosorbent Assay (ELISA), Latex Agglutination, Whole Blood Agglutination, immunoturbidimetry, and immunofiltration. The ELISA method is the gold standard for D-dimer testing.

D-dimer testing using the latex slide agglutination method involves identifying visible (macroscopic) clumps of antigen-antibody particles. This method is most commonly performed because the procedure is easy and fast, requires no special equipment or skills, and is relatively inexpensive. With technological advancements, this method can now be performed using automated instruments, thereby improving precision. This method has been FDA-approved for evaluating D-dimer levels, particularly for assessing VTE disorders.

D-dimer examination by immunoturbidimetry is a method based on finding and quantitatively assessing antigen-antibody reactions, which cause turbidity. This is performed using automated tools and can detect D-dimer levels of less than 0.5 µg/mL. This method correlates well with the ELISA method.

The immunofiltration method for D-dimer testing detects antigen-antibody reactions by measuring immunity through flow (immunometric flowthrough). In this process, D-dimer molecules attach to a membrane coated with D-dimer-specific monoclonal antibodies, followed by the addition of a conjugate to bind the D-dimer. If D-dimer is present, a color change occurs, which is then read by a reader device. The use of immunofiltration is easy, fast, does not require highly trained personnel, and is cost-effective. David Rustandi et al. state that this method is also reliable for D-dimer examination.

RESULTS AND DISCUSSION

The activity of the hemostasis system undergoes significant changes as gestational age increases. Based on the literature review, coagulation parameters such as fibrinogen levels increase drastically compared to non-pregnant conditions. This represents a physiological adaptation to prevent massive hemorrhage during the delivery process. This increase is also accompanied by a surge in D-dimer levels, which serves as an indicator of fibrin formation and breakdown within the blood circulation.

D-dimer levels show a linear increasing trend with gestational age. This is confirmed by clinical findings summarizing the percentage of increased D-dimer levels in each pregnancy trimester, as presented in the following table :

Tabel 1 Percentage of D-dimer increase based on pregnancy trimester

No	Trimester Kehamilan	Persentase Kenaikan Kadar (%)
1	Trimester I	27
2	Trimester II	87
3	Trimester III	100

Source: Rahayuningsih et al. (2019)

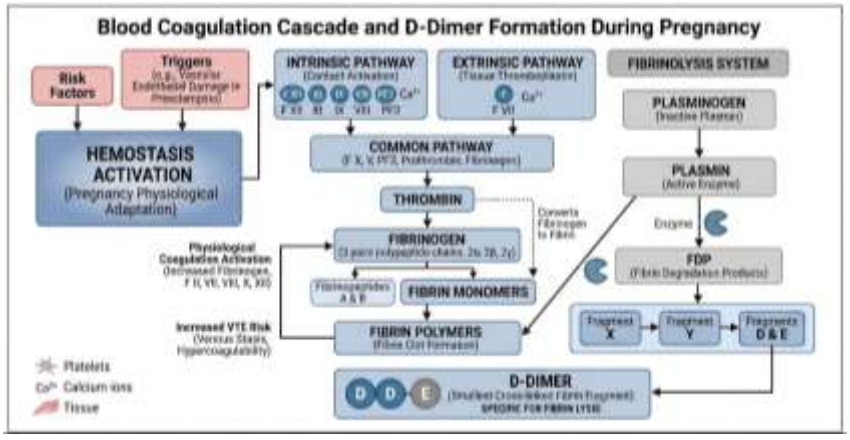
Data in Table 1 indicate that all pregnant women in the third trimester will have D-dimer levels above the normal reference value for healthy adults. The difference in the proportion of the increase between the first and third trimesters reaches nearly fourfold, signifying that hypercoagulability reaches its peak at the end of pregnancy. Therefore, the use of a single threshold (cut-off) of 300 ng/mL or 500 ng/mL is ineffective for excluding thromboembolism risk in the pregnant population.

Pathological conditions such as preeclampsia and eclampsia exacerbate this coagulation activation. In these cases, vascular endothelial dysfunction occurs, triggering massive platelet activation and thrombin formation. If this process is uncontrolled, patients are at risk of developing disseminated intravascular coagulation (DIC). In this context, D-dimer serves as a crucial predictor. Extremely elevated levels in preeclampsia patients reflect the severity of intravascular fibrin deposition, which can lead to organ failure or maternal death.

The examination method also determines diagnostic accuracy. Although ELISA is the gold standard due to its high sensitivity, the immunoturbidimetric method is preferred in clinical practice because of its processing speed via automated instruments. The immunofiltration method also serves as a reliable alternative due to its operational ease and more affordable cost without compromising the validity of examination results in detecting D-dimer fragments.

Overall, the increase in D-dimer during pregnancy is a natural defense mechanism (hypercoagulable) to anticipate postpartum hemorrhage. However, clinicians must be able to distinguish between this physiological rise and pathological increases leading to VTE or DIC. Monitoring D-dimer level trends is more meaningful than observing a single value to determine appropriate medical interventions in efforts to reduce maternal mortality rates.

Figure 1 Coagulation and Fibrinolysis Pathways in Pregnancy



In addition to monitoring level trends, the choice of testing method is crucial for diagnostic accuracy in clinical settings. The characteristics of the most commonly used methods are presented in the following table :

Tabel 2 Characteristics of D-dimer Testing Methods

Testing Method	Main Characteristics	Advantages	Disadvantages
ELISA	Uses specific monoclonal antibody standards.	Recognized as the gold standard with very high sensitivity.	Requires long processing time and complex procedures.
Latex Agglutination	Identifies macroscopic clumps of antigen-antibody particles.	Fast procedure, easy, inexpensive, and requires no special equipment.	Lower precision if performed manually compared to automated methods.
Immunoturbidimetry	Assesses antigen-antibody reactions based on turbidity.	Highly precise, automated, and correlates well with the ELISA method.	Requires investment in automated laboratory instruments.
Immunofiltration	Measures immunity through flow (immunometric flowthrough).	Reliable, fast, cost-effective, and does not require highly trained personnel.	Depends on the availability of specific reader devices.

CONCLUSION

The increase in D-dimer levels during pregnancy is a physiological phenomenon reflecting the body's hemostatic adaptation to prevent postpartum hemorrhage through hypercoagulation mechanisms. These levels rise progressively and peak in the third trimester, rendering normal reference values for healthy adults ineffective as a sole evaluation standard for pregnant women. Although this increase is natural, monitoring D-dimer levels remains crucial for detecting pathological complications such as preeclampsia, eclampsia, and the risk of venous thromboembolism. The use of rapid and accurate examination methods, such as immunoturbidimetry or immunofiltration, is essential in assisting clinicians to predict medical emergencies like disseminated intravascular coagulation. Consequently, a thorough understanding of D-dimer dynamics during pregnancy serves as a strategic instrument in efforts to reduce maternal morbidity and mortality rates.

REFERENCES

Bellesini, M., Robert-Ebadi, H., Combescure, C., Dedionigi, C., Le Gal, G., & Righini, M. (2021). D-dimer to rule out venous thromboembolism during pregnancy: a systematic review and meta-analysis. Journal of Thrombosis and Haemostasis, 19(10), 2454-2467.

Birawa, A. D. (2009). Kadar D-dimer pada ibu hamil dengan preeklampsia berat dan normotensi di RSUP Dr. Kariadi. Indonesian Journal of Obstetrics and Gynecology.

Endo-Kawamura, N., Obata-Yasuoka, M., Yagi, H., Ohara, R., Nagai, Y., Mayumi, M., ... & Hamada, H. (2016). Higher D-dimer level in the early third trimester predicts the occurrence of postpartum hemorrhage. *Journal of perinatal medicine*, *44*(5), 551-556.

Gungor, B., Atici, A., Baycan, O. F., Alici, G., Ozturk, F., Tugrul, S., ... & Barman, H. A. (2021). Elevated D-dimer levels on admission are associated with severity and increased risk of mortality in COVID-19: A systematic review and meta-analysis. The American journal of emergency medicine, 39, 173-179.

Hu, W., Wang, Y., Li, J., Huang, J., Pu, Y., Jiang, Y., ... & Luo, Q. (2020). The predictive value of D-dimer test for venous thromboembolism during puerperium: a prospective cohort study. Clinical and Applied Thrombosis/Hemostasis, 26, 1076029620901786.

Imelda, A. D., & Putriana, Y. (2018). Penanganan Awal Kejadian Preeklamsia Berat dan Eklampsia Salah Satu Rumah Sakit di Provinsi Lampung. Jurnal Ilmiah Keperawatan Sai Betik, 13(2), 203-208.

Komurcuoglu, B., Ulusoy, S., Gayaf, M., Guler, A., & Ozden, E. (2011). Prognostic value of plasma D-dimer levels in lung carcinoma. Tumori Journal, 97(6), 743-748.

Linkins, L. A., & Takach Lapner, S. (2017). Review of D-dimer testing: Good, Bad, and Ugly. International Journal of Laboratory Hematology, 39, 98-103.

Luhulima, D. E. J. (2021). D–DIMER PADA KEHAMILAN.

Means Jr, R. J., Rodgers, G., Glader, B., Arber, D. A., Appelbaum, F. R., Dispenzieri, A., ... & Leonard, J. P. (2023). Wintrobe's clinical hematology. Lippincott Williams & Wilkins.

Moiz, B. (2017). A review of hemostasis in normal pregnancy and puerperium. Nat J Health Sci, 2(3), 123-127.

Muhani, N., & Besral, B. (2015). Pre-eklampsia berat dan kematian Ibu. Kesmas, 10(2), 80-86.

Naymagon, L., Zubizarreta, N., Feld, J., van Gerwen, M., Alsen, M., Thibaud, S., ... & Tremblay, D. (2020). Admission D-dimer levels, D-dimer trends, and outcomes in COVID-19. Thrombosis research, 196, 99-105.

Rahmawati, F. (2021). Mata Kuliah: Komunikasi Kesehatan dalam Pembelajaran.

Schafer, K., Goldschmidt, E., Oostra, D., Fish, J., Russell, T., & Lurie, F. (2022). The clinical significance of ultra-high D-dimer levels. Journal of Vascular Surgery: Venous and Lymphatic Disorders, 10(1), 8-13.

Shah, S., Shah, K., Patel, S. B., Patel, F. S., Osman, M., Velagapudi, P., ... & Garg, J. (2020). Elevated D-dimer levels are associated with increased risk of mortality in coronavirus disease 2019: a systematic review and meta-analysis. Cardiology in review, 28(6), 295-302.

Shao, H., Gao, S., Dai, D., Zhao, X., Hua, Y., & Yu, H. (2021). The association of antenatal D-dimer and fibrinogen with postpartum hemorrhage and intrauterine growth restriction in preeclampsia. BMC Pregnancy and Childbirth, 21(1), 605.

Xu, Q., Dai, L., Chen, H. Q., Xia, W., Wang, Q. L., Zhu, C. R., & Zhou, R. (2023). Specific changes and clinical significance of plasma D-dimer during pregnancy and puerperium: a prospective study. BMC Pregnancy and Childbirth, 23(1), 248.

Yao, J., Bai, T., Yang, B., & Sun, L. (2021). The diagnostic value of D-dimer in acute aortic dissection: a meta-analysis. Journal of cardiothoracic surgery, 16(1), 343.

Yu, B., Li, X., Chen, J., Ouyang, M., Zhang, H., Zhao, X., ... & Tang, J. (2020). Evaluation of variation in D-dimer levels among COVID-19 and bacterial pneumonia: a retrospective analysis. Journal of thrombosis and thrombolysis, 50(3), 548-557.

Yu, H. H., Qin, C., Chen, M., Wang, W., & Tian, D. S. (2020). D-dimer level is associated with the severity of COVID-19. Thrombosis research, 195, 219-225.

Zhan, H., Chen, H., Liu, C., Cheng, L., Yan, S., Li, H., & Li, Y. (2021). Diagnostic value of D-dimer in COVID-19: a meta-analysis and meta-regression. Clinical and Applied Thrombosis/Hemostasis, 27, 10760296211010976.