

## BÖLÜM 4

### GEBELİK VE TROMBOFİLİ

İlayda GERCİK ARZIK<sup>1</sup>

#### GİRİŞ

Gebelik fizyolojik olarak hiperkoagülan bir durumdur ve bu adaptasyon, doğum sırasında meydana gelebilecek kan kayıplarına karşı bir koruyucu mekanizma olarak kabul edilir. Bu değişim; pıhtılaşma faktörlerinde artış(fibrinojen, faktör VII, VIII, X), doğal antikoagülanlarda azalma(özellikle protein S) ve fibrinolitik aktivitede azalma ile karakterizedir [1]. Ancak bu hemostatik denge, bazı kadınlarda gebelik sürecinde venöz tromboembolizm (VTE), tekrarlayan gebelik kaybı, fetal büyüme geriliği, intrauterin fetal ölüm (IUFD) ve preeklampsi gibi ciddi komplikasyonlara neden olabilecek şekilde bozulabilir [2].

Bu sonuçlara neden olan durumlardan bir tanesi trombofililerdir. Trombofili, kişinin pıhtılaşmaya eğilimli bir yapıya sahip olmasıdır. Kalıtsal ve edinsel olarak iki ana grupta sınıflandırılır. Gebelikte trombofili varlığı, maternal veya fetal morbidite riskini artırabilmektedir. Gebelik öncesinde ve gebelik sırasında hangi hastaların araştırılması ve de kime tedavi başlanması gerektiği bu morbidite ve mortalite riskindeki artış nedeniyle çok önemlidir.

Klinikte sık karşılaşılan bir problem olmasına karşın, trombofili taraması ve tedavi protokolleri konusunda uluslararası kılavuzlar arasında bazı farklılıklar bulunmaktadır. Tüm gebelere rutin trombofili testi yapılması önerilmezken; öykü ve risk faktörlerine göre seçilmiş hasta gruplarında test yapılması önerilir [3]. Riskli gruplara bakıldığında tekrarlayan gebelik kaybı, açıklanamayan IUFD, şiddetli preeklampsi veya erken başlangıçlı fetal büyüme geriliği gibi durumlar taramayı gerektirebilir [4].

Bu bölümde; gebelikle ilişkili trombofili türleri, tarama endikasyonları, güncel kılavuzlara göre risk sınıflaması ve tedavi yaklaşımları sistematik olarak ele alınacaktır.

<sup>1</sup> Op. Dr., İzmir Şehir Hastanesi, Perinatoloji Kliniği, ilgercik@gmail.com,  
ORCID iD: 0000-0001-7308-352X

termektedir [45, 46]. Her hasta için doğum şekli, antikoagülan zamanlaması ve postpartum yönetim, multidisipliner yaklaşımı gerektirir.

## KAYNAKLAR

1. Bremme KA. Haemostatic changes in pregnancy. *Best Practice & Research Clinical Haematology* 2003; 16: 153–168.
2. ACOG Practice Bulletin No. 197: Inherited Thrombophilias in Pregnancy. *Obstetrics & Gynecology* 2018; 132: e18–e34.
3. Middeldorp S, Nieuwlaar R, Baumann Kreuziger L, et al. American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing. *Blood Advances* 2023; 7: 7101–7138.
4. Royal College of Obstetricians and Gynaecologists. Reducing the Risk of Venous Thromboembolism During Pregnancy and the Puerperium, <https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf> (2015).
5. Croles F, Borjas-Howard J, Nasserinejad K, et al. Risk of Venous Thrombosis in Antithrombin Deficiency: A Systematic Review and Bayesian Meta-analysis. *Semin Thromb Hemost* 2018; 44: 315–326.
6. Kobayashi T, Sugiura K, Ojima T, et al. Thrombosis-related characteristics of pregnant women with antithrombin deficiency, protein C deficiency and protein S deficiency in Japan. *Thrombosis J* 2024; 22: 18.
7. Croles FN, Nasserinejad K, Duvekot JJ, et al. Pregnancy, thrombophilia, and the risk of a first venous thrombosis: systematic review and bayesian meta-analysis. *BMJ* 2017; j4452.
8. Ryu J, Rämö JT, Jurgens SJ, et al. Thrombosis risk in single- and double-heterozygous carriers of factor V Leiden and prothrombin G20210A in FinnGen and the UK Biobank. *Blood* 2024; 143: 2425–2432.
9. Klein K, Wing S, Chen L, et al. The Net Benefit of Venous Thromboembolism Prophylaxis in Mild-Risk Thrombophilia and Pregnancy: A Systematic Review and Meta-Analysis. *Blood* 2023; 142: 1272–1272.
10. Beyler Ö, Baş H, Balık B, et al. Hereditary thrombophilia and recurrent pregnancy loss: is it time to reassess routine genetic testing? *JCHOR* 2025; 3: 22–26.
11. Kjellberg U, Van Rooijen M, Bremme K, et al. Factor V Leiden mutation and pregnancy-related complications. *American Journal of Obstetrics and Gynecology* 2010; 203: 469.e1–469.e8.
12. Silver RM, Zhao Y, Spong CY, et al. Prothrombin Gene G20210A Mutation and Obstetric Complications. *Obstetrics & Gynecology* 2010; 115: 14–20.
13. Liew S-C, Gupta ED. Methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism: Epidemiology, metabolism and the associated diseases. *European Journal of Medical Genetics* 2015; 58: 1–10.
14. Liu X, Chen Y, Ye C, et al. Hereditary thrombophilia and recurrent pregnancy loss: a systematic review and meta-analysis. *Human Reproduction* 2021; 36: 1213–1229.
15. Kovalevsky G, Gracia CR, Berlin JA, et al. Evaluation of the Association Between Hereditary Thrombophilias and Recurrent Pregnancy Loss: A Meta-analysis. *Arch Intern Med* 2004; 164: 558.
16. Alijotas-Reig J, Esteve-Valverde E, Anunciación-Llunell A, et al. Pathogenesis, Diagnosis and Management of Obstetric Antiphospholipid Syndrome: A Comprehensive Review. *JCM* 2022; 11: 675.
17. Schreiber K, Sciascia S, De Groot PG, et al. Antiphospholipid syndrome. *Nat Rev Dis Primers* 2018; 4: 17103.
18. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *Journal of Thrombosis and Haemostasis* 2006; 4: 295–306.

19. Liu X, Zhu L, Liu H, et al. Non-criteria antiphospholipid antibodies in antiphospholipid syndrome: Diagnostic value added. *Front Immunol* 2022; 13: 972012.
20. Sebire NJ. Defective endovascular trophoblast invasion in primary antiphospholipid antibody syndrome-associated early pregnancy failure. *Human Reproduction* 2002; 17: 1067–1071.
21. Mulla MJ, Myrtolli K, Brosens JJ, et al. Antiphospholipid Antibodies Limit Trophoblast Migration by Reducing IL-6 Production and STAT3 Activity. *American J Rep Immunol* 2010; 63: 339–348.
22. D'Ippolito S, Barbaro G, Paciullo C, et al. Antiphospholipid Syndrome in Pregnancy: New and Old Pathogenetic Mechanisms. *IJMS* 2023; 24: 3195.
23. Gharavi AE, Pierangeli SS, Levy RA, et al. Mechanisms of Pregnancy Loss in Antiphospholipid Syndrome: *Clinical Obstetrics and Gynecology* 2001; 44: 11–19.
24. Murvai VR, Galiş R, Panaiteşcu A, et al. Antiphospholipid syndrome in pregnancy: a comprehensive literature review. *BMC Pregnancy Childbirth* 2025; 25: 337.
25. Branch DW, Lim MY. How I diagnose and treat antiphospholipid syndrome in pregnancy. *Blood* 2024; 143: 757–768.
26. Beça S, Borrell M, Cervera R, et al. Non-Criteria Obstetric Antiphospholipid Syndrome: Myth or Reality? *JCM* 2025; 14: 1299.
27. Forastiero R, Martinuzzo M. The emerging role of multiple antiphospholipid antibodies positivity in patients with antiphospholipid syndrome. *Expert Review of Clinical Immunology* 2015; 11: 1255–1263.
28. Bradáčová P, Slavík L, Skoumalová A, et al. Determination of Thrombogenicity Levels of Various Antiphospholipid Antibodies by a Modified Thrombin Generation Assay in Patients with Suspected Antiphospholipid Syndrome. *IJMS* 2022; 23: 8973.
29. Patriarcheas V, Tsamos G, Vasdeki D, et al. Antiphospholipid Syndrome: A Comprehensive Clinical Review. *JCM* 2025; 14: 733.
30. Tektonidou MG, Andreoli L, Limper M, et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. *Annals of the Rheumatic Diseases* 2019; 78: 1296–1304.
31. Guerby P, Fillion A, O'Connor S, et al. Heparin for preventing adverse obstetrical outcomes in pregnant women with antiphospholipid syndrome, a systematic review and meta-analysis. *Journal of Gynecology Obstetrics and Human Reproduction* 2021; 50: 101974.
32. Ziakas PD, Pavlou M, Voulgarelis M. Heparin Treatment in Antiphospholipid Syndrome With Recurrent Pregnancy Loss: A Systematic Review and Meta-Analysis. *Obstetrics & Gynecology* 2010; 115: 1256–1262.
33. Barros VIPVLD, Igai AMK, Oliveira ALMLD, et al. Obstetric antiphospholipid syndrome: Number 6 - June 2021. *Rev Bras Ginecol Obstet* 2021; 43: 495–501.
34. Gerde M, Ibarra E, Mac Kenzie R, et al. The impact of hydroxychloroquine on obstetric outcomes in refractory obstetric antiphospholipid syndrome. *Thrombosis Research* 2021; 206: 104–110.
35. Mekinian A, Lazzaroni MG, Kuzenko A, et al. The efficacy of hydroxychloroquine for obstetrical outcome in anti-phospholipid syndrome: Data from a European multicenter retrospective study. *Autoimmunity Reviews* 2015; 14: 498–502.
36. Bertolaccini ML, Contento G, Lennen R, et al. Complement inhibition by hydroxychloroquine prevents placental and fetal brain abnormalities in antiphospholipid syndrome. *Journal of Autoimmunity* 2016; 75: 30–38.
37. Ruffatti A, Tonello M, Hoxha A, et al. Effect of Additional Treatments Combined with Conventional Therapies in Pregnant Patients with High-Risk Antiphospholipid Syndrome: A Multi-centre Study. *Thromb Haemost* 2018; 47: 639–646.
38. Sophia Lontou, Maria Dagla, Victoria Vivilaki, et al. Antiphospholipid syndrome and pregnancy: A review article. *World J Adv Res Rev* 2025; 25: 143–151.
39. Lee EE, Jun JK, Lee EB. Management of Women with Antiphospholipid Antibodies or Antiphospholipid Syndrome during Pregnancy. *J Korean Med Sci* 2021; 36: e24.
40. Erton ZB, Sevim E, De Jesús GR, et al. Pregnancy outcomes in antiphospholipid antibody po-

- sitive patients: prospective results from the AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository ('Registry'). *Lupus Sci Med* 2022; 9: e000633.
41. Leffert L, Butwick A, Carvalho B, et al. The Society for Obstetric Anesthesia and Perinatology Consensus Statement on the Anesthetic Management of Pregnant and Postpartum Women Receiving Thromboprophylaxis or Higher Dose Anticoagulants. *Anesthesia & Analgesia* 2018; 126: 928–944.
  42. Zita A, Malinowski A, Carvalho J, et al. Risk of Recurrent Venous Thromboembolism and Hemorrhage Following Interruption of Anticoagulation at Delivery. *Blood* 2021; 138: 3233–3233.
  43. Bates SM, Greer IA, Hirsh J, et al. Use of Antithrombotic Agents During Pregnancy. *Chest* 2004; 126: 627S–644S.
  44. Marshall AL. Diagnosis, Treatment, and Prevention of Venous Thromboembolism in Pregnancy. *Postgraduate Medicine* 2014; 126: 25–34.
  45. Bates SM, Greer IA, Pabinger I, et al. Venous Thromboembolism, Thrombophilia, Antithrombotic Therapy, and Pregnancy. *Chest* 2008; 133: 844S–886S.
  46. Pabinger I, Vormittag R. Thrombophilia and pregnancy outcomes. *Journal of Thrombosis and Haemostasis* 2005; 3: 1603–1610.