

# BÖLÜM 17

## Gebelikte Karaciğer, Safra ve Pankreas Hastalıkları



Ömer Gökhan EYİSOY<sup>1</sup>

### Giriş

Gebelik sırasındaki karaciğer hastalıkları hem anne hem de fetüsün yaşamını etkileyebilecek benzersiz klinik sorunlar oluşturabilir. Şiddetli karaciğer hastalıkları nadir olmasına rağmen, gebelikte ilişkili karaciğer hastalıkları gebeliklerin yaklaşık %3'ünü etkiler ve ölümcül olabilir. Uygun yönetim stratejileri oluşturmak için zamanında tanı çok önemlidir. Bu zorlu vakaların yönetiminde en iyi yaklaşım şekli konsültan hepatologlar ile birlikte obstetrisyenlerin ve çoğu zaman da yüksek riskli gebelik uzmanlarının birlikte oluşturdukları multidisipliner yaklaşımdır.

Gebelikte karaciğer hastalıkları sıklıkla 2 temel alt başlıkta incelenir: (1) gebelikte ilişkili karaciğer hastalıkları, (2) gebelikte eş zamanlı olarak saptanan karaciğer hastalıkları. Gebeliğe özgü karaciğer hastalıkları gebelik zamanına ilişkin özellikler sergilerken, gebelikte ilişkisiz karaciğer hastalıkları her an ortaya çıkabilir. Klinik bulguların ve anormal karaciğer testlerinin ortaya çıkış zamanı tanının belirlenmesinde ve tedavi stratejilerinde önemlidir. Örneğin hiperemesis gravidarum (HG) erken gebeliğe özgü iken gebeliğin intrahepatik kolestazi (GIK), karaciğeri etkileyen preeklampsi ve gebeliğin akut yağlı karaciğeri (AYK) geç gebelikte ortaya çıkan hastalıklardır (1-3).

Gebelikte ilişkili karaciğer hastalıklarına bağlı maternal mortalite oranı literatürde %0-25 arasında raporlanmıştır. Maternal prognozun belirlenmesinde ana

<sup>1</sup> Uzm. Dr., Zeynep Kamil Eğitim ve Araştırma Hastanesi Perinatoloji Kliniği, dr.gokhaneyisoy@gmail.com



Komplike olmayan pankreatitte maternal mortalite düşüktür, ancak komplike pankreatitte %10'u geçer (58). Fetal sonuçlar genellikle hafif ila orta dereceli pankreatit için iyidir ancak şiddetli pankreatitte kötü olabilir. Bununla birlikte orta derecede şiddetli pankreatit bazen ilk trimesterde fetal ölüm ile ilişkilidir ve üçüncü trimesterde erken doğum ile ilişkilidir (66). Şiddetli pankreatitte TPN içeriği gebe hastanın ekstra beslenme gereksinimlerini karşılayacak şekilde olmalıdır (67).

## Kaynaklar

1. Henry F, Quatresooz P, Valverde-Lopez JC, Pierard GE. Blood vessel changes during pregnancy: a review. *Am J Clin Dermatol.* 2006;7(1):65-9.
2. Kamimura K, Abe H, Kawai H, Kamimura H, Kobayashi Y, Nomoto M, et al. Advances in understanding and treating liver diseases during pregnancy: A review. *World Journal of Gastroenterology: WJG.* 2015;21(17):5183.
3. Westbrook RH, Dusheiko G, Williamson C. Pregnancy and liver disease. *J Hepatol.* 2016;64(4):933-45.
4. Murali AR, Devarbhavi H, Venkatachala PR, Singh R, Sheth KA. Factors that predict 1-month mortality in patients with pregnancy-specific liver disease. *Clinical Gastroenterology and Hepatology.* 2014;12(1):109-13.
5. Robson S, Mutch E, Boys R, Woodhouse K. Apparent liver blood flow during pregnancy: a serial study using indocyanine green clearance. *BJOG: An International Journal of Obstetrics & Gynaecology.* 1990;97(8):720-4.
6. Joshi D, James A, Quaglia A, Westbrook RH, Heneghan MA. Liver disease in pregnancy. *The Lancet.* 2010;375(9714):594-605.
7. Liver IAftSot. Italian Association for the Study of the Liver AISF. AISF position paper on liver disease and pregnancy *Dig Liver Dis.* 2016;48:120-37.
8. Tamay A, Kuşçu N. Hyperemesis gravidarum: current aspect. *Journal of Obstetrics and Gynaecology.* 2011;31(8):708-12.
9. Conchillo J, Pijnenborg J, Peeters P, Stockbrugger R, Fevery J, Koek G. Liver enzyme elevation induced by hyperemesis gravidarum: aetiology, diagnosis and treatment. *Neth J Med.* 2002;60(9):374-8.
10. Geenes V, Williamson C. Intrahepatic cholestasis of pregnancy. *World journal of gastroenterology: WJG.* 2009;15(17):2049.
11. Glantz A, Marschall HU, Mattsson LÅ. Intrahepatic cholestasis of pregnancy: relationships between bile acid levels and fetal complication rates. *Hepatology.* 2004;40(2):467-74.
12. Marschall HU, Wikström Shemer E, Ludvigsson JF, Stephansson O. Intrahepatic cholestasis of pregnancy and associated hepatobiliary disease: a population-based cohort study. *Hepatology.* 2013;58(4):1385-91.
13. Lee NM, Brady CW. Liver disease in pregnancy. *World journal of gastroenterology: WJG.* 2009;15(8):897.
14. Gabzdyl EM, Schlaeger JM. Intrahepatic cholestasis of pregnancy. *The Journal of perinatal & neonatal nursing.* 2015;29(1):41-50.
15. Ozkan S, Ceylan Y, Ozkan OV, Yildirim S. Review of a challenging clinical issue: Intrahepatic cholestasis of pregnancy. *World Journal of Gastroenterology: WJG.* 2015;21(23):7134.
16. Shekhar S, Diddi G. Liver disease in pregnancy. *Taiwanese Journal of Obstetrics and Gynecology.* 2015;54(5):475-82.



17. Bacq Y, Sapey T, Brechot M, Pierre F, Fignon A, Dubois F. Intrahepatic cholestasis of pregnancy: a French prospective study. *Hepatology*. 1997;26(2):358-64.
18. Ahmed KT, Almashhrawi AA, Rahman RN, Hammoud GM, Ibdah JA. Liver diseases in pregnancy: diseases unique to pregnancy. *World Journal of Gastroenterology: WJG*. 2013;19(43):7639.
19. Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: a prospective population-based case-control study. *Hepatology*. 2014;59(4):1482-91.
20. Boregowda G, Shehata HA. Gastrointestinal and liver disease in pregnancy. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2013;27(6):835-53.
21. Bacq Y, Sentilhes L, Reyes HB, Glantz A, Kondrackiene J, Binder T, et al. Efficacy of ursodeoxycholic acid in treating intrahepatic cholestasis of pregnancy: a meta-analysis. *Gastroenterology*. 2012;143(6):1492-501.
22. Frezza M, Centini G, Cammareri G, Le Grazie C, Di Padova C. S-adenosylmethionine for the treatment of intrahepatic cholestasis of pregnancy. Results of a controlled clinical trial. *Hepato-gastroenterology*. 1990;37:122-5.
23. Geenes V, Chambers J, Khurana R, Shemer EW, Sia W, Mandair D, et al. Rifampicin in the treatment of severe intrahepatic cholestasis of pregnancy. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2015;189:59-63.
24. Wood AM, Livingston EG, Hughes BL, Kuller JA. Intrahepatic cholestasis of pregnancy: a review of diagnosis and management. *Obstetrical & gynecological survey*. 2018;73(2):103-9.
25. Tran TT, Ahn J, Reau NS. ACG clinical guideline: liver disease and pregnancy. *Official journal of the American College of Gastroenterology* | ACG. 2016;111(2):176-94.
26. Liu J, Ghaziani TT, Wolf JL. Acute fatty liver disease of pregnancy: updates in pathogenesis, diagnosis, and management. *Official journal of the American College of Gastroenterology* | ACG. 2017;112(6):838-46.
27. Santos L, Patterson A, Moreea S, Lippiatt C, Walter J, Henderson M. Acute liver failure in pregnancy associated with maternal MCAD deficiency. *Journal of inherited metabolic disease*. 2007;30(1):103-.
28. Knight M, Nelson-Piercy C, Kurinczuk JJ, Spark P, Brocklehurst P. A prospective national study of acute fatty liver of pregnancy in the UK. *Gut*. 2008;57(7):951-6.
29. Vigil-de Gracia P, Montufar-Rueda C. Acute fatty liver of pregnancy: diagnosis, treatment, and outcome based on 35 consecutive cases. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2011;24(9):1143-6.
30. Ch'Ng C, Morgan M, Hainsworth I, Kingham J. Prospective study of liver dysfunction in pregnancy in Southwest Wales. *Gut*. 2002;51(6):876-80.
31. Goel A, Ramakrishna B, Zachariah U, Ramachandran J, Eapen C, Kurian G, et al. How accurate are the Swansea criteria to diagnose acute fatty liver of pregnancy in predicting hepatic microvesicular steatosis? *Gut*. 2011;60(1):138-9.
32. Hartwell L, Ma T. Acute fatty liver of pregnancy treated with plasma exchange. *Digestive diseases and sciences*. 2014;59(9):2076-80.
33. Yu C-B, Chen J-J, Du W-B, Chen P, Huang J-R, Chen Y-M, et al. Effects of plasma exchange combined with continuous renal replacement therapy on acute fatty liver of pregnancy. *Hepato-biliary & Pancreatic Diseases International*. 2014;13(2):179-83.
34. Westbrook RH, Yeoman A, Joshi D, Heaton N, Quaglia A, O'Grady J, et al. Outcomes of severe pregnancy-related liver disease: refining the role of transplantation. *American Journal of Transplantation*. 2010;10(11):2520-6.
35. Tan J, Surti B, Saab S. Pregnancy and cirrhosis. *Liver Transplantation*. 2008;14(8):1081-91.
36. Hagström H, Höijer J, Marschall HU, Williamson C, Heneghan MA, Westbrook RH, et al. Outcomes of pregnancy in mothers with cirrhosis: a national population-based cohort study



- of 1.3 million pregnancies. *Hepatology communications*. 2018;2(11):1299-305.
37. Cheng Y-S. Pregnancy in liver cirrhosis and/or portal hypertension. *American journal of obstetrics and gynecology*. 1977;128(7):812-22.
  38. Kapp N. WHO provider brief on hormonal contraception and liver disease. *Contraception*. 2009;80(4):325-6.
  39. Elinav E, Ben-Dov IZ, Shapira Y, Daudi N, Adler R, Shouval D, et al. Acute hepatitis A infection in pregnancy is associated with high rates of gestational complications and preterm labor. *Gastroenterology*. 2006;130(4):1129-34.
  40. Rac MW, Sheffield JS. Prevention and management of viral hepatitis in pregnancy. *Obstetrics and Gynecology Clinics*. 2014;41(4):573-92.
  41. Patra S, Kumar A, Trivedi SS, Puri M, Sarin SK. Maternal and fetal outcomes in pregnant women with acute hepatitis E virus infection. *Annals of internal medicine*. 2007;147(1):28-33.
  42. Zhang J, Zhang XF, Zhou C, Wang ZZ, Huang SJ, Yao X, et al. Protection against hepatitis E virus infection by naturally acquired and vaccine-induced immunity. *Clinical microbiology and infection*. 2014;20(6):O397-O405.
  43. Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. *New England Journal of Medicine*. 2014;370(23):2211-8.
  44. Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology*. 2016;63(1):261-83.
  45. Weinbaum CM, Williams I, Mast EE, Wang SA, Finelli L, Wasley A, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. 2008.
  46. van Zonneveld M, Van Nunen A, Niesters H, De Man R, Schalm S, Janssen H. Lamivudine treatment during pregnancy to prevent perinatal transmission of hepatitis B virus infection. *Journal of viral hepatitis*. 2003;10(4):294-7.
  47. Nguyen V, Tan P, Greenup AJ, Glass A, Davison S, Samarasinghe D, et al. Anti-viral therapy for prevention of perinatal HBV transmission: extending therapy beyond birth does not protect against post-partum flare. *Alimentary pharmacology & therapeutics*. 2014;39(10):1225-34.
  48. Diseases AAFtSoL, America IDSo. Recommendations for Testing, Managing, and Treating Hepatitis C [<http://www.hcvguidelines.org>] Accessed. 2018;1.
  49. Marrero JA, Ahn J, Reddy RK, Gastroenterology PPCotACo. ACG clinical guideline: the diagnosis and management of focal liver lesions. *Official journal of the American College of Gastroenterology* | ACG. 2014;109(9):1328-47.
  50. Checa Cabot CA, Stoszek SK, Quarleri J, Losso MH, Ivalo S, Peixoto MF, et al. Mother-to-child transmission of hepatitis C virus (HCV) among HIV/HCV-coinfected women. *Journal of the pediatric infectious diseases society*. 2013;2(2):126-35.
  51. Westbrook RH, Yeoman AD, Kriese S, Heneghan MA. Outcomes of pregnancy in women with autoimmune hepatitis. *Journal of autoimmunity*. 2012;38(2-3):J239-J44.
  52. Schramm C, Herkel J, Beuers U, Kanzler S, Galle PR, Lohse AW. Pregnancy in autoimmune hepatitis: outcome and risk factors. *Official journal of the American College of Gastroenterology* | ACG. 2006;101(3):556-60.
  53. Walcott WO, WO W, DE D, JJ J. Successful pregnancy in a liver transplant patient. 1978.
  54. Westbrook RH, Yeoman AD, Agarwal K, Aluvihare V, O'Grady J, Heaton N, et al. Outcomes of pregnancy following liver transplantation: The King's College Hospital experience. *Liver Transplantation*. 2015;21(9):1153-9.
  55. Lucey MR, Terrault N, Ojo L, Hay JE, Neuberger J, Blumberg E, et al. Long-term management of the successful adult liver transplant: 2012 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Liver transplantation*. 2013;19(1):3-26.



56. Ko CW, Beresford SA, Schulte SJ, Matsumoto AM, Lee SP. Incidence, natural history, and risk factors for biliary sludge and stones during pregnancy. *Hepatology*. 2005;41(2):359-65.
57. Davis A, Katz V, Cox R. Gallbladder disease in pregnancy. *The Journal of reproductive medicine*. 1995;40(11):759-62.
58. Ramin KD, Ramsey PS. Disease of the gallbladder and pancreas in pregnancy. *Obstetrics and gynecology clinics of North America*. 2001;28(3):571-80.
59. Ghumman E, Barry M, Grace P. Management of gallstones in pregnancy. *Journal of British Surgery*. 1997;84(12):1646-50.
60. Glasgow R, Visser B, Harris H, Patti M, Kilpatrick S, Mulvihill S. Changing management of gallstone disease during pregnancy. *Surgical endoscopy*. 1998;12(3):241-6.
61. Pitchumoni CS, Yegneswaran B. Acute pancreatitis in pregnancy. *World journal of gastroenterology: WJG*. 2009;15(45):5641.
62. Laraki M, Harti A, Boudarka M, Barrou H, Matar N, Benaguida M. Acute pancreatitis and pregnancy. *Revue française de gynécologie et d'obstétrique*. 1993;88(10):514-6.
63. Karsenti D, Bacq Y, Bréchet J-F, Mariotte N, Tichet J. Serum amylase and lipase activities in normal pregnancy: a prospective case-control study. *The American journal of gastroenterology*. 2001;96(3):697-9.
64. Cappell MS, Friedel D. Abdominal pain during pregnancy. *Gastroenterology Clinics*. 2003;32(1):1-58.
65. Briggs GG, Freeman RK, Yaffe SJ. *Drugs in pregnancy and lactation: a reference guide to fetal and neonatal risk*: Lippincott Williams & Wilkins; 2012.
66. Legro R, Laifer S. First-trimester pancreatitis. Maternal and neonatal outcome. *The Journal of reproductive medicine*. 1995;40(10):689-95.
67. Badgett T, Feingold M. Total parenteral nutrition in pregnancy: case review and guidelines for calculating requirements. *Journal of Maternal-Fetal Medicine*. 1997;6(4):215-7.