

Bölüm 19

HEPATİTLER VE SİROZ



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|HEPATİT A

Hepatit A virüsü (HAV), pikornavirüs ailesinin 27 nm doğrusal, tek sarmallı ribonükleik asit (RNA) virüsüdür ve akut viral hepatitin en yaygın nedenidir⁽¹⁾. HAV enfeksiyonunun prevalansı, ülkeden ülkeye ve sınıflandırma farklılıklarına bağlı olarak değişiklik göstermektedir. Gebelikte HAV insidansı genel popülasyona göre düşüktür; yaklaşık olarak %0.016'dır². Fekal-oral yolla bulaşır^{3,4}.

Akut HAV enfeksiyonu genellikle kendi kendini sınırlamaktadır. Kronik enfeksiyona yol açmamaktadır. HAV, viral hepatitlere bağlı ölümlerin %0.5'ini oluşturmaktadır⁵. Hepatit B ya da E ile koenfeksiyon olmadıkça fulminan hepatite dönüşme ihtimali oldukça düşüktür⁶. İnkübasyon süresi 2-6 hafta arasında değişmekle birlikte ortalama 4 haftadır⁷. İlk enfekte olunan zamandan 12 gün sonrakanda ve feçeste saptanmaktadır⁷. Bulantı, kusma, halsizlik, karın ağrısı gibi spesifik olmayan bulgularla kendini gösterebilir. Bulgular 2 aydan daha uzun sürmektedir. Atipik olarak yaklaşık 2 ay kadar süren bifazik patern gösteren serum aminotransferaz enzim yüksekliği, daha da uzun süreler devam eden kolestaz bulguları ve hatta akut böbrek hasarı nadir de olsa karşımıza çıkmaktadır⁸. Serum HAV IgM pozitifliği ile birlikte; serum total bilirubin, alkalın fosfataz (ALP), alanin aminotransferaz (ALT) ve aspartat aminotransferaz (AST) yükseklikleri akut HAV enfeksiyonunu doğrulamaktadır⁹. Erken serolojik tanı, IgM Anti-HAV

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preeklampsi, preterm doğum, postpartum hemoraji gibi komplikasyonların riskleri artmıştır¹⁰⁸. Maternal karaciğer ve böbrek yetmezliği gibi komplikasyonlar açısından dikkatli olunmalıdır¹⁰⁸. Eşlik eden özefagial varisler ve splenik arter anevrizmasının rüptür riski nedeniyle doğum esnasında valsalva manevrasından kaçınılmalıdır⁽¹⁰⁹⁻¹¹¹⁾.

SONUÇ

- HBV enfeksiyonu olan gebeler hızlıca belirlenmeli ve güvenli bir şekilde tedavi edilmelidir. Vertikal bulaşın önlenmesi çok önemlidir. Vertikal geçişin önlenmesi, gebelik sırasında antiviral ilaç tedavisini ve ardından neonatal pasif ya da aktif immünoprofilaksiyi içermektedir.
- Hepatit A, C, D ve E'nin vertikal geçişi mümkündür.
- Hamile kadınların, hamile olmayan kadınlara göre fulminan hepatit E'ye yakalanma şansı daha yüksektir.
- Ribavirin ile PEG-INFa kombinasyonu kontrendike olduğundan hamilelik sırasında akut hepatit E tedavisi destekleyici olmaya devam etmektedir.
- Hepatit A, C ve D ile enfekte kadınlarda emzirme teşvik edilmeli, ancak akut hepatit E ile enfekte kadınlar için teşvik edilmemelidir.
- Otoimmün hepatit ve siroz ile birlikte seyreden gebeliklerde obstetrik komplikasyonlar açısından takipler özenli yapılmalıdır.

KAYNAKLAR

1. Koff RS. Hepatitis A. *Lancet (London, England)*. 1998;351(9116):1643-1649. doi:10.1016/S0140-6736(98)01304-X
2. Elinav E, Ben-Dov IZ, Shapira Y, et al. Acute hepatitis A infection in pregnancy is associated with high rates of gestational complications and preterm labor. *Gastroenterology*. 2006;130(4):1129-1134. doi:10.1053/j.gastro.2006.01.007
3. Rivas V, Barrera A, Pino K, et al. Hepatitis A outbreak since November 2016 affecting men who have sex with men (MSM) in Chile connected to the current outbreak in MSM in Europe, situation up to October 2017. *Euro Surveill Bull Eur sur les Mal Transm = Eur Commun Dis Bull*. 2018;23(9). doi:10.2807/1560-7917.ES.2018.23.9.18-00060
4. Nelson R. Hepatitis A outbreak in the USA. *Lancet Infect Dis*. 2018;18(1):33-34. doi:10.1016/S1473-3099(17)30718-1
5. Seto MT, Wang K, Hung IFN. Best Practice & Research Clinical Obstetrics and Gynaecology Management of viral hepatitis A , C , D and E in pregnancy. *Best Pract Res Clin Obstet Gynaecol*. 2020;(xxxx). doi:10.1016/j.bpobgyn.2020.03.009
6. Kumar A, Beniwal M, Kar P, et al. Hepatitis E in pregnancy. *Int J Gynaecol Obstet Off organ Int Fed Gynaecol Obstet*. 2004;85(3):240-244. doi:10.1016/j.ijgo.2003.11.018
7. Chai SJ, Gu W, O'Connor KA, et al. Incubation periods of enteric illnesses in foodborne outbreaks, United States, 1998-2013. *Epidemiol Infect*. 2019;147:e285. doi:10.1017/S0950268819001651

8. Jeong S-H, Lee H-S. Hepatitis A: clinical manifestations and management. *Intervirology*. 2010;53(1):15-19. doi:10.1159/000252779
9. Tong MJ, el-Farra NS, Grew MI. Clinical manifestations of hepatitis A: recent experience in a community teaching hospital. *J Infect Dis*. 1995;171 Suppl:S15-8. doi:10.1093/infdis/171.supplement_1.s15
10. Koff RS, Pannuti CS, Pereira ML, et al. Hepatitis A and non-A, non-B viral hepatitis in São Paulo, Brazil: epidemiological, clinical and laboratory comparisons in hospitalized patients. *Hepatology*. 1982;2(4):445-448. doi:10.1002/hep.1840020409
11. Gottesman LE, Del Vecchio MT, Aronoff SC. Etiologies of conjugated hyperbilirubinemia in infancy: a systematic review of 1692 subjects. *BMC Pediatr*. 2015;15:192. doi:10.1186/s12887-015-0506-5
12. Renge RL, Dani VS, Chitambar SD, et al. Vertical transmission of hepatitis A. *Indian J Pediatr*. 2002;69(6):535-536. doi:10.1007/BF02722662
13. McDuffie RSJ, Bader T. Fetal meconium peritonitis after maternal hepatitis A. *Am J Obstet Gynecol*. 1999;180(4):1031-1032. doi:10.1016/s0002-9378(99)70678-2
14. Chaudhry SA, Koren G. Hepatitis A infection during pregnancy. *Can Fam Physician*. 2015;61(11):963-964.
15. Simsek Y, Isik B, Karaer A, et al. Fulminant hepatitis A infection in second trimester of pregnancy requiring living-donor liver transplantation. *J Obstet Gynaecol Res*. 2012;38(4):745-748. doi:10.1111/j.1447-0756.2011.01757.x
16. Daudi N, Shouval D, Stein-Zamir C, et al. Breastmilk hepatitis A virus RNA in nursing mothers with acute hepatitis A virus infection. *Breastfeed Med Off J Acad Breastfeed Med*. 2012;7:313-315. doi:10.1089/bfm.2011.0084
17. Zhao Y, Jin H, Zhang X, et al. Viral hepatitis vaccination during pregnancy. *Hum Vaccin Immunother*. 2016;12(4):894-902. doi:10.1080/21645515.2015.1132129
18. Nasser R, Rakedzon S, Dickstein Y, et al. Are all vaccines safe for the pregnant traveller? A systematic review and meta-analysis. *J Travel Med*. 2020;27(2). doi:10.1093/jtm/taz074
19. Kim DK, Hunter P. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older - United States, 2019. *MMWR Morb Mortal Wkly Rep*. 2019;68(5):115-118. doi:10.15585/mmwr.mm6805a5
20. Bhatt B, Jindal H, Malik JS, et al. Vaccination for pregnant women: need to address. *Hum Vaccin Immunother*. 2014;10(12):3627-3628. doi:10.4161/hv.32255
21. Cho GJ, Kim YB, Kim SM, et al. Hepatitis A virus infection during pregnancy in Korea: Hepatitis A infection on pregnant women. *Obstet Gynecol Sci*. 2013;56(6):368-374. doi:10.5468/ogs.2013.56.6.368
22. Victor JC, Monto AS, Surdina TY, et al. Hepatitis A vaccine versus immune globulin for post-exposure prophylaxis. *N Engl J Med*. 2007;357(17):1685-1694. doi:10.1056/NEJMoa070546
23. Tu T, Budzinska MA, Shackel NA, et al. HBV DNA Integration: Molecular Mechanisms and Clinical Implications. *Viruses*. 2017;9(4). doi:10.3390/v9040075
24. Euler GL, Wooten KG, Baughman AL, et al. Hepatitis B surface antigen prevalence among pregnant women in urban areas: implications for testing, reporting, and preventing perinatal transmission. *Pediatrics*. 2003;111(5 Pt 2):1192-1197.
25. Lok ASF. Chronic hepatitis B. *N Engl J Med*. 2002;346(22):1682-1683. doi:10.1056/NEJM200205303462202
26. Lee C, Gong Y, Brok J, et al. Hepatitis B immunisation for newborn infants of hepatitis B surface antigen-positive mothers. *Cochrane database Syst Rev*. 2006;(2):CD004790. doi:10.1002/14651858.CD004790.pub2
27. Nelson NP, Easterbrook PJ, McMahon BJ. Epidemiology of Hepatitis B Virus Infection and Impact of Vaccination on Disease. *Clin Liver Dis*. 2016;20(4):607-628. doi:10.1016/j.cld.2016.06.006

28. Sookoian S. Liver disease during pregnancy: acute viral hepatitis. *Ann Hepatol.* 2006;5(3):231-236.
29. Bartholomew ML. Management of Hepatitis B Infection in Pregnancy. 2017;00(00).
30. Maraolo AE, Gentile I, Buonomo AR, et al. Current evidence on the management of hepatitis B in pregnancy. *World J Hepatol.* 2018;10(9):585-594. doi:10.4254/wjh.v10.i9.585
31. Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. *MMWR Recomm reports Morb Mortal Wkly report Recomm reports.* 2005;54(RR-16):1-31.
32. Terrault NA, Levy MT, Cheung KW, et al. Viral hepatitis and pregnancy. *Nat Rev Gastroenterol Hepatol.* 2021;18(2):117-130. doi:10.1038/s41575-020-00361-w
33. Dionne-Odom J, Tita ATN, Silverman NS. #38: Hepatitis B in pregnancy screening, treatment, and prevention of vertical transmission. *Am J Obstet Gynecol.* 2016;214(1):6-14. doi:10.1016/j.ajog.2015.09.100
34. Ko TM, Tseng LH, Chang MH, et al. Amniocentesis in mothers who are hepatitis B virus carriers does not expose the infant to an increased risk of hepatitis B virus infection. *Arch Gynecol Obstet.* 1994;255(1):25-30. doi:10.1007/BF02390671
35. Yi W, Pan CQ, Hao J, et al. Risk of vertical transmission of hepatitis B after amniocentesis in HBs antigen-positive mothers. *J Hepatol.* 2014;60(3):523-529. doi:10.1016/j.jhep.2013.11.008
36. Han G-R, Cao M-K, Zhao W, et al. A prospective and open-label study for the efficacy and safety of telbivudine in pregnancy for the prevention of perinatal transmission of hepatitis B virus infection. *J Hepatol.* 2011;55(6):1215-1221. doi:10.1016/j.jhep.2011.02.032
37. Han L, Zhang H-W, Xie J-X, et al. A meta-analysis of lamivudine for interruption of mother-to-child transmission of hepatitis B virus. *World J Gastroenterol.* 2011;17(38):4321-4333. doi:10.3748/wjg.v17.i38.4321
38. Tsai P-JS, Chang A, Yamada S, et al. Use of tenofovir disoproxil fumarate in highly viremic, hepatitis B mono-infected pregnant women. *Dig Dis Sci.* 2014;59(11):2797-2803. doi:10.1007/s10620-014-3230-3
39. Levy M, Koren G. Hepatitis B vaccine in pregnancy: maternal and fetal safety. *Am J Perinatol.* 1991;8(3):227-232. doi:10.1055/s-2007-999384
40. Connell LE, Salihu HM, Salemi JL, et al. Maternal hepatitis B and hepatitis C carrier status and perinatal outcomes. *Liver Int Off J Int Assoc Study Liver.* 2011;31(8):1163-1170. doi:10.1111/j.1478-3231.2011.02556.x
41. Smith BD, Morgan RL, Beckett GA, et al. Recommendations for the identification of chronic hepatitis C virus infection among persons born during 1945-1965. *MMWR Recomm reports Morb Mortal Wkly report Recomm reports.* 2012;61(RR-4):1-32.
42. Hughes BL, Page CM, Kuller JA. Hepatitis C in pregnancy: screening, treatment, and management. *Am J Obstet Gynecol.* 2017;217(5):B2-B12. doi:10.1016/j.ajog.2017.07.039
43. Tran TT, Ahn J, Reau NS. ACG Clinical Guideline: Liver Disease and Pregnancy. *Am J Gastroenterol.* 2016;111(2):176-194; quiz 196. doi:10.1038/ajg.2015.430
44. Wilson E, Beckmann M. Antenatal screening for hepatitis C: Universal or risk factor based? *Aust N Z J Obstet Gynaecol.* 2015;55(4):318-322. doi:10.1111/ajo.12296
45. Floreani A. Hepatitis C and pregnancy. *World J Gastroenterol.* 2013;19(40):6714-6720. doi:10.3748/wjg.v19.i40.6714
46. Lingala S, Ghany MG. Natural History of Hepatitis C. *Gastroenterol Clin North Am.* 2015;44(4):717-734. doi:10.1016/j.gtc.2015.07.003
47. Alter MJ, Kuhnert WL, Finelli L. Guidelines for laboratory testing and result reporting of antibody to hepatitis C virus. Centers for Disease Control and Prevention. *MMWR Recomm reports Morb Mortal Wkly report Recomm reports.* 2003;52(RR-3):1-13, 15; quiz CE1-4.

48. Page CM, Hughes BL, Rhee EHJ, et al. Hepatitis C in Pregnancy: Review of Current Knowledge and Updated Recommendations for Management. *Obstet Gynecol Surv.* 2017;72(6):347-355. doi:10.1097/OGX.0000000000000442
49. Benova L, Mohamoud YA, Calvert C, et al. Vertical transmission of hepatitis C virus: systematic review and meta-analysis. *Clin Infect Dis an Off Publ Infect Dis Soc Am.* 2014;59(6):765-773. doi:10.1093/cid/ciu447
50. Gagnon A, Davies G, Wilson RD. Prenatal invasive procedures in women with hepatitis B, hepatitis C, and/or human immunodeficiency virus infections. *J Obstet Gynaecol Canada JOGC = J d'obstetrique Gynecol du Canada JOGC.* 2014;36(7):648-653. doi:10.1016/S1701-2163(15)30546-6
51. Kosikowska U, Biernasiuk A, Korona-Główniak I, et al. The Association of Chronic Hepatitis C with Respiratory Microbiota Disturbance on the Basis of Decreased Haemophilus Spp. Colonization. *Med Sci Monit Int Med J Exp Clin Res.* 2016;22:625-632. doi:10.12659/msm.895544
52. Sinclair SM, Jones JK, Miller RK, et al. The Ribavirin Pregnancy Registry: An Interim Analysis of Potential Teratogenicity at the Mid-Point of Enrollment. *Drug Saf.* 2017;40(12):1205-1218. doi:10.1007/s40264-017-0566-6
53. Garcia-Tejedor A, Maiques-Montesinos V, Diago-Almela VJ, et al. Risk factors for vertical transmission of hepatitis C virus: a single center experience with 710 HCV-infected mothers. *Eur J Obstet Gynecol Reprod Biol.* 2015;194:173-177. doi:10.1016/j.ejogrb.2015.09.009
54. Mast EE, Hwang L-Y, Seto DSY, et al. Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy. *J Infect Dis.* 2005;192(11):1880-1889. doi:10.1086/497701
55. Foster GR, Tudor-Williams G, White J, et al. Effects of mode of delivery and infant feeding on the risk of mother-to-child transmission of hepatitis C virus. *BJOG.* 2003;110(1):91; author reply 91. doi:10.1046/j.1471-0528.2003.01036_1.x
56. Kumar RM, Shahul S. Role of breast-feeding in transmission of hepatitis C virus to infants of HCV-infected mothers. *J Hepatol.* 1998;29(2):191-197. doi:10.1016/s0168-8278(98)80003-2
57. Gibb DM, Goodall RL, Dunn DT, et al. Mother-to-child transmission of hepatitis C virus: evidence for preventable peripartum transmission. *Lancet (London, England).* 2000;356(9233):904-907. doi:10.1016/s0140-6736(00)02681-7
58. Bhola K, McGuire W. Does avoidance of breast feeding reduce mother-to-infant transmission of hepatitis C virus infection? *Arch Dis Child.* 2007;92(4):365-366. doi:10.1136/adc.2006.112458
59. Freriksen JJM, van Seyen M, Judd A, et al. Review article: direct-acting antivirals for the treatment of HCV during pregnancy and lactation - implications for maternal dosing, foetal exposure, and safety for mother and child. *Aliment Pharmacol Ther.* 2019;50(7):738-750. doi:10.1111/apt.15476
60. Mansour W, Malick F-ZF, Sidiya A, et al. Prevalence, risk factors, and molecular epidemiology of hepatitis B and hepatitis delta virus in pregnant women and in patients in Mauritania. *J Med Virol.* 2012;84(8):1186-1198. doi:10.1002/jmv.23336
61. Jaiswal SP, Jain AK, Naik G, et al. Viral hepatitis during pregnancy. *Int J Gynaecol Obstet Off organ Int Fed Gynaecol Obstet.* 2001;72(2):103-108. doi:10.1016/s0020-7292(00)00264-2
62. Ricco G, Popa DC, Cavallone D, et al. Quantification of serum markers of hepatitis B (HBV) and Delta virus (HDV) infections in patients with chronic HDV infection. *J Viral Hepat.* 2018;25(8):911-919. doi:10.1111/jvh.12895
63. Cheung KW, Seto MTY, Kan ASY, et al. Immunoprophylaxis Failure of Infants Born to Hepatitis B Carrier Mothers Following Routine Vaccination. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc.* 2018;16(1):144-145. doi:10.1016/j.cgh.2017.07.013
64. Sellier PO, Maylin S, Brichler S, et al. Hepatitis B Virus-Hepatitis D Virus mother-to-child co-transmission: A retrospective study in a developed country. *Liver Int Off J Int Assoc Study*

- Liver*. 2018;38(4):611-618. doi:10.1111/liv.13556
65. Krause A, Haberkorn U, Mier W. Strategies for the treatment of HBV/HDV. *Eur J Pharmacol*. 2018;833:379-391. doi:10.1016/j.ejphar.2018.06.030
 66. Kimmich N, Dutkowski P, Krähenmann F, et al. Liver Transplantation during Pregnancy for Acute Liver Failure due to HBV Infection: A Case Report. *Case Rep Obstet Gynecol*. 2013;2013:356560. doi:10.1155/2013/356560
 67. Cheung KW, Seto MTY, Lao TT-H. Prevention of perinatal hepatitis B virus transmission. *Arch Gynecol Obstet*. 2019;300(2):251-259. doi:10.1007/s00404-019-05190-0
 68. Cheung KW, Seto MTY, So PL, et al. The effect of rupture of membranes and labour on the risk of hepatitis B vertical transmission: Prospective multicentre observational study. *Eur J Obstet Gynecol Reprod Biol*. 2019;232:97-100. doi:10.1016/j.ejogrb.2018.11.017
 69. Khuroo MS, Khuroo MS. Hepatitis E: an emerging global disease - from discovery towards control and cure. *J Viral Hepat*. 2016;23(2):68-79. doi:10.1111/jvh.12445
 70. Izopet J, Labrique AB, Basnyat B, et al. Hepatitis E virus seroprevalence in three hyperendemic areas: Nepal, Bangladesh and southwest France. *J Clin Virol Off Publ Pan Am Soc Clin Virol*. 2015;70:39-42. doi:10.1016/j.jcv.2015.06.103
 71. Kawada T. Prevalence of hepatitis E infection. *J Clin Virol Off Publ Pan Am Soc Clin Virol*. 2016;83:5. doi:10.1016/j.jcv.2016.08.288
 72. Ekanem E, Ikobah J, Okpara H, et al. Seroprevalence and predictors of hepatitis E infection in Nigerian children. *J Infect Dev Ctries*. 2015;9(11):1220-1225. doi:10.3855/jidc.6736
 73. El Sayed Zaki M, El Razek MMA, El Razek HMA. Maternal-Fetal Hepatitis E Transmission: Is It Underestimated? *J Clin Transl Hepatol*. 2014;2(2):117-123. doi:10.14218/JCTH.2014.00006
 74. Khuroo MS, Kamili S, Jameel S. Vertical transmission of hepatitis E virus. *Lancet (London, England)*. 1995;345(8956):1025-1026. doi:10.1016/s0140-6736(95)90761-0
 75. Jin H, Zhao Y, Zhang X, et al. Case-fatality risk of pregnant women with acute viral hepatitis type E: a systematic review and meta-analysis. *Epidemiol Infect*. 2016;144(10):2098-2106. doi:10.1017/S0950268816000418
 76. Sehgal R, Patra S, David P, et al. Impaired monocyte-macrophage functions and defective Toll-like receptor signaling in hepatitis E virus-infected pregnant women with acute liver failure. *Hepatology*. 2015;62(6):1683-1696. doi:10.1002/hep.28143
 77. Aggarwal R, Krawczynski K. Hepatitis E: an overview and recent advances in clinical and laboratory research. *J Gastroenterol Hepatol*. 2000;15(1):9-20. doi:10.1046/j.1440-1746.2000.02006.x
 78. Seifoleslami M. An update of the incidence of fulminant hepatitis due to viral agents during pregnancy. *Interv Med Appl Sci*. 2018;10(4):210-212. doi:10.1556/1646.10.2018.40
 79. Banait VS, Sandur V, Parikh F, et al. Outcome of acute liver failure due to acute hepatitis E in pregnant women. *Indian J Gastroenterol Off J Indian Soc Gastroenterol*. 2007;26(1):6-10.
 80. Berglöv A, Hallager S, Weis N. Hepatitis E during pregnancy: Maternal and foetal case-fatality rates and adverse outcomes-A systematic review. *J Viral Hepat*. 2019;26(11):1240-1248. doi:10.1111/jvh.13129
 81. Sharma S, Kumar A, Kar P, et al. Risk factors for vertical transmission of hepatitis E virus infection. *J Viral Hepat*. 2017;24(11):1067-1075. doi:10.1111/jvh.12730
 82. El Sayed Zaki M, El Aal AA El, Badawy A, et al. Clinicolaboratory study of mother-to-neonate transmission of hepatitis E virus in Egypt. *Am J Clin Pathol*. 2013;140(5):721-726. doi:10.1309/AJCPT55TDMJNPLLV
 83. Bose PD, Das BC, Kumar A, et al. High viral load and deregulation of the progesterone receptor signaling pathway: association with hepatitis E-related poor pregnancy outcome. *J Hepatol*. 2011;54(6):1107-1113. doi:10.1016/j.jhep.2010.08.037
 84. Pecoraro V, Banzi R, Cariani E, et al. New Direct-Acting Antivirals for the Treatment of Patients With Hepatitis C Virus Infection: A Systematic Review of Randomized Controlled Tri-

- als. *J Clin Exp Hepatol*. 2019;9(4):522-538. doi:10.1016/j.jceh.2018.07.004
85. Kinast V, Burkard TL, Todt D, et al. Hepatitis E Virus Drug Development. *Viruses*. 2019;11(6). doi:10.3390/v11060485
 86. Bertuzzo VR, Ravaioli M, Morelli MC, et al. Pregnant woman saved with liver transplantation from acute liver failure due to hepatitis E virus. *Transpl Int Off J Eur Soc Organ Transplant*. 2014;27(9):e87-9. doi:10.1111/tri.12305
 87. Zhang J, Zhang X-F, Huang S-J, et al. Long-term efficacy of a hepatitis E vaccine. *N Engl J Med*. 2015;372(10):914-922. doi:10.1056/NEJMoa1406011
 88. Hepatitis E vaccine: WHO position paper, May 2015--Recommendations. *Vaccine*. 2016;34(3):304-305. doi:10.1016/j.vaccine.2015.07.056
 89. Rivero-Juarez A, Frias M, Rodriguez-Cano D, et al. Isolation of Hepatitis E Virus From Breast Milk During Acute Infection. *Clin Infect Dis an Off Publ Infect Dis Soc Am*. 2016;62(11):1464. doi:10.1093/cid/ciw186
 90. Chibber RM, Usmani MA, Al-Sibai MH. Should HEV infected mothers breast feed? *Arch Gynecol Obstet*. 2004;270(1):15-20. doi:10.1007/s00404-002-0466-5
 91. Simons JN, Leary TP, Dawson GJ, et al. Isolation of novel virus-like sequences associated with human hepatitis. *Nat Med*. 1995;1(6):564-569. doi:10.1038/nm0695-564
 92. Linnen J, Wages JJ, Zhang-Keck ZY, et al. Molecular cloning and disease association of hepatitis G virus: a transfusion-transmissible agent. *Science*. 1996;271(5248):505-508. doi:10.1126/science.271.5248.505
 93. Ma A, Widell A. Perinatal Transmission of Hepatitis G Virus (GB Virus Type C) and Hepatitis C Virus Infections — A Comparison. 1999:816-821.
 94. Alter MJ, Gallagher M, Morris TT, et al. Acute non-A-E hepatitis in the United States and the role of hepatitis G virus infection. Sentinel Counties Viral Hepatitis Study Team. *N Engl J Med*. 1997;336(11):741-746. doi:10.1056/NEJM199703133361101
 95. Roth WK, Waschk D, Marx S, et al. Prevalence of hepatitis G virus and its strain variant, the GB agent, in blood donations and their transmission to recipients. *Transfusion*. 1997;37(6):651-656. doi:10.1046/j.1537-2995.1997.37697335162.x
 96. Alter HJ, Nakatsuji Y, Melpolder J, et al. The incidence of transfusion-associated hepatitis G virus infection and its relation to liver disease. *N Engl J Med*. 1997;336(11):747-754. doi:10.1056/NEJM199703133361102
 97. Yeo AE, Matsumoto A, Hisada M, Shih JW, et al. Effect of hepatitis G virus infection on progression of HIV infection in patients with hemophilia. Multicenter Hemophilia Cohort Study. *Ann Intern Med*. 2000;132(12):959-963. doi:10.7326/0003-4819-132-12-200006200-00006
 98. Dawson GJ, Schlauder GG, Pilot-Matias TJ, et al. Prevalence studies of GB virus-C infection using reverse transcriptase-polymerase chain reaction. *J Med Virol*. 1996;50(1):97-103. doi:10.1002/(SICI)1096-9071(199609)50:1<97::AID-JMV16>3.0.CO;2-V
 99. Shev S, Björkman P, Norkrans G, et al. GBV-C/HGV infection in hepatitis C virus-infected deferred Swedish blood donors. *J Med Virol*. 1998;54(2):75-79. doi:10.1002/(sici)1096-9071(199802)54:2<75::aid-jmv1>3.0.co;2-l
 100. Feucht HH, Zollner B, Polywka S, et al. Vertical transmission of hepatitis G. *Lancet (London, England)*. 1996;347(9001):615-616.
 101. Yoshida M, Okamoto H, Mishihiro S. Detection of the GBV-C hepatitis virus genome in serum from patients with fulminant hepatitis of unknown aetiology. *Lancet (London, England)*. 1995;346(8983):1131-1132. doi:10.1016/s0140-6736(95)91802-7
 102. Martinot M, Marcellin P, Boyer N, et al. Influence of hepatitis G virus infection on the severity of liver disease and response to interferon-alpha in patients with chronic hepatitis C. *Ann Intern Med*. 1997;126(11):874-881. doi:10.7326/0003-4819-126-11-19970610-00004
 103. Heneghan MA, Norris SM, O'Grady JG, et al. Management and outcome of pregnancy in autoimmune hepatitis. *Gut*. 2001;48(1):97-102. doi:10.1136/gut.48.1.97

104. Schramm C, Herkel J, Beuers U, et al. Pregnancy in autoimmune hepatitis: outcome and risk factors. *Am J Gastroenterol*. 2006;101(3):556-560. doi:10.1111/j.1572-0241.2006.00479.x
105. Steven MM, Buckley JD, Mackay IR. Pregnancy in chronic active hepatitis. *Q J Med*. 1979;48(192):519-531.
106. Whelton MJ, Sherlock S. Pregnancy in patients with hepatic cirrhosis. Management and outcome. *Lancet (London, England)*. 1968;2(7576):995-999. doi:10.1016/s0140-6736(68)91294-4
107. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. *Am Fam Physician*. 2006;74(5):756-762.
108. Flemming JA, Mullin M, Lu J, et al. Outcomes of Pregnant Women With Cirrhosis and Their Infants in a Population-Based Study. *Gastroenterology*. 2020;159(5):1752-1762.e10. doi:10.1053/j.gastro.2020.07.052
109. Schreyer P, Caspi E, El-Hindi JM, et al. Cirrhosis--pregnancy and delivery: a review. *Obstet Gynecol Surv*. 1982;37(5):304-312. doi:10.1097/00006254-198205000-00002
110. Westbrook RH, Yeoman AD, O'Grady JG, et al. Model for end-stage liver disease score predicts outcome in cirrhotic patients during pregnancy. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc*. 2011;9(8):694-699. doi:10.1016/j.cgh.2011.03.036
111. Cheng YS. Pregnancy in liver cirrhosis and/or portal hypertension. *Am J Obstet Gynecol*. 1977;128(7):812-822. doi:10.1016/0002-9378(77)90727-x