

GEBELİKTE GASTROİNTESTİNAL DEĞİŞİKLİKLER

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GİRİŞ

Gebeliğe bağlı olarak, birçok sistem ve organlarda olduğu gibi, gastrointestinal sistemde (GİS) de önemli anatomik ve fizyolojik değişiklikler meydana gelmektedir. Büyümekte olan uterus nedeni ile komşuluğundaki mide, bağırsak ansları yukarı ve yanlara doğru yer değiştirmektedir. Apendix vermiformis konumunun değişmesi ilgili patolojinin (özellikle akut apandisit) klinik tablo ve prezentasyondaki farklılıkları beraberinde getirmektedir. Midenin yerleşimi sefalik yöne doğru değiştiğinden gebelikteki yanma ve diğer yakınmalar (pyrozis) daha sıktır. Safra kesesinin hacmi yaklaşık olarak %50 oranında artar. Karaciğer büyüklüğü ise, normal gebelikte değişmez (1).

Gebelikte ortaya çıkan progesteron artışına bağlı olarak, özofageal alt sfinkter tonusu azalır, intraözofageal basınç düşer, peristaltik hareketler hızı ve amplitüdü azalır. Midenin boşalma süresi ve hacmi gebelik boyunca değişmemektedir, ancak doğum eylemi başladığında veya analjezik ilaçlar uygulandığında mide boşalma süresi uzamakta ve genel anestezi açısından ciddi bir risk kaynağı olmaktadır (1).

Gebelikte, serum aspartat transaminaz (AST), alanin transaminaz (ALT), gama glutamil trans-

peptidaz (GGT) ve bilirubin düzeyleri hafif azalırken, alkalen fosfataz (ALP) yaklaşık 2 katına kadar yükselmektedir. Bunun esas nedeni plasenta kaynaklı, ısıya dayanıklı ALP miktarındaki artış kaynaklıdır. Serum albumin konsantrasyonu azalırken, serum globulin konsantrasyonu, ilk trimesterden itibaren artmaktadır. Albumin/globulin oranında düşüş gözlemlenmektedir. Buna benzer şekilde, serumdaki total ve direkt bilirubin düzeylerinde de düşüş saptanmıştır (2).

Progesteron etkisine bağlı olarak, safra kesesinin kontraktilitesi azalır, rezidüel volüm artar. Gelişen stazın ve safranin kolesterol saturasyonundaki artışın neticesinde, multipar kadınlarda, kolesterol taşlarının prevalansı artmaktadır (1).

Gebeliğin serum safra asitleri konsantrasyonları üzerindeki etkisi tam olarak ortaya konamamıştır. Gebeliğin intrahepatik kolestaz olgularında yapılan çalışmalar, belirli safra asitlerinin serumdaki konsantrasyonlarının artışına paralel olarak, obstetrik komplikasyonların (özellikle preterm doğum, ölü doğum) da arttığı vurgulanmaktadır (1,3).

Gebelikte ortaya çıkan anatomik ve fizyolojik değişiklikler, birçok organ ve sistemlerde olduğu gibi, gastrointestinal yakınma ve sorunların da te-

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SONUÇ

Gebelikte gastrointestinal sistemde meydana gelen değişiklikler, hem fizyolojik hem de anatomic bakımdan önemli etkiler oluşturmaktadır. Bu değişiklikler, anne adaylarının yaşam kalitesini etkileyebilecek ve bazı durumlarda tıbbi müdahale gerektirecek semptom ve hastalıklara yol açabilmektedir. Gastrointestinal sistem ile ilişkili bulantı, kusma, kabızlık, hemoroid gibi durumlar gebelikte sık görülmekte ve genellikle hormonal değişiklikler, büyüyen uterusun mekanik etkileri ve metabolik süreçlerdeki adaptasyonlarla ilişkilendirilmektedir. İnflamatuvar bağırsak hastalıkları, gastroözofageal reflü ve hiperemesis gravidarum gibi durumlar ise detaylı bir değerlendirme ve nitelikli bir yönetim gerektirir. Bu süreçte, anne sağlığına zarar vermeden ve fetal gelişimi olumsuz etkilemeden etkili tedavi yaklaşımlarının benimsenmesi kritik öneme sahiptir. Gebelik dönemine özgü fizyolojik değişikliklerin anlaşılması, olası patolojilerin yönetilmesinde ve anne ile fetus sağlığının korunmasında yol gösterici olmaktadır.

KAYNAKLAR

- Cunningham FG, Leveno KJ, Dashe JS. et al. (2022). Chapter 4: Maternal Physiology. In *Williams Obstetrics* (26th ed., p. 70). McGraw Hill.
- Das A, Teli AB, Borkotoki S. Study of liver function tests in normal pregnancy: a hospital based study. *Int J Health Sci Res.* 2016; 6(8):156-160.
- Ma Z, Liu Y, Chai L, et al. (2023). Metabolic changes in bile acids with pregnancy progression and their correlation with perinatal complications in intrahepatic cholestasis of pregnant patients. *Scientific Reports*, 13(1). <https://doi.org/10.1038/s41598-022-22974-8>
- Cunningham FG, Leveno KJ, Dashe JS, et al. Chapter 4: Maternal Physiology. In *Williams Obstetrics* (26th ed., p. 1012-1029). McGraw Hill.
- Verberg MF, Gillot DJ, Al-Fardan N, et al. Hyperemesis gravidarum, a literature review. *Hum Reprod Update.* 2005;11(5):527-539. DOI: 10.1093/humupd/dmi021
- Clark SM, Costantine MM, Hankins GF. Review of NVP and HG and early pharmacotherapeutic intervention. *Obstet Gynecol Int.* 2012; 2012:252676. DOI: 10.1155/2012/252676
- Niebyl JR, Goodwin JM. Overview of nausea and vomiting of pregnancy with an emphasis on vitamins and ginger. *Am J Obstet Gynecol.* 2002;186(5 Suppl Understanding):S253-255. DOI: 10.1067/mob.2002.122595
- Koch KL. Gastrointestinal factors in nausea and vomiting of pregnancy. *Am J Obstet Gynecol.* 2002;186(5 Suppl Understanding):S198-203. DOI: 10.1067/mob.2002.122598
- Einarson TR, Piwko C, Koren G. Quantifying the global rates of nausea and vomiting of pregnancy: a meta-analysis. *J Popul Ther Clin Pharmacol* 2013;20:e171-83. PMID:23863575
- Fell DB, Dodds L, Joseph KS, et al. Risk factors for hyperemesis gravidarum requiring hospital admission during pregnancy. *Obstet Gynecol* 2006;107:277-84. DOI: 10.1097/01.AOG.0000195059.82029.74
- Fiaschi L, Nelson-Piercy C, Tata L. J. Hospital admission for hyperemesis gravidarum: a nationwide study of occurrence, reoccurrence and risk factors among 8.2 million pregnancies. *Hum Reprod* 2016; 31:1675-84. DOI: 10.1093/humrep/dew128
- Nijsten K, Dean C, van der Minnen LM, et al. Recurrence, postponing pregnancy, and termination rates after hyperemesis gravidarum: follow-up of the MOTHER study. *Acta Obstet Gynecol Scand* 2021; 100:1636-43. DOI: 10.1111/aogs.14197
- Gabra A. Risk factors of hyperemesis gravidarum: review article. *Health Sci J* 2018;12. doi: 10.21767/1791-809X.1000603. DOI: 10.21767/1791-809X.1000603
- Nijsten K, Koot MH, van der Post JAM, et al. Thyroid-stimulating hormone and free thyroxine fail to predict the severity and clinical course of hyperemesis gravidarum: a prospective cohort study. *Acta Obstet Gynecol Scand* 2021; 100:1419-29. DOI: 10.1111/aogs.14131
- Niemeijer MN, Grooten IJ, Vos N, et al. Diagnostic markers for hyperemesis gravidarum: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2014;211: 150.e1-15. DOI: 10.1016/j.ajog.2014.02.012
- Fejzo M, Rocha N, Cimino I, et al. GDF15 linked to maternal risk of nausea and vomiting during pregnancy. *Nature* 2024; 625:760-7. DOI: 10.1038/s41586-023-06921-9
- Fejzo MS, Arzy D, Tian R, et al. Evidence GDF15 plays a role in familial and recurrent hyperemesis gravidarum. *Geburtshilfe Frauenheilkd* 2018; 78:866-70. DOI: 10.1055/a-0661-0287
- Li L, Li L, Zhou X, et al. Helicobacter pylori infection is associated with an increased risk of hyperemesis gravidarum: a meta-analysis. *Gastroenterol Res Pract* 2015; 2015:278905. DOI: 10.1155/2015/278905
- Tan PC, King AS, Omar SZ. Screening for urinary tract infection in women with hyperemesis gravidarum. *J Obstet Gynaecol Res* 2012; 38:145-53. DOI: 10.1111/j.1447-0756.2011.01652.x
- Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 189: Nausea And Vomiting Of Pregnancy. *Obstet Gynecol.* 2018 Jan;131(1): e15-e30. DOI: 10.1097/AOG.0000000000002456
- Koot MH, Boelig RC, Van't Hooft J, et al. Variation in hyperemesis gravidarum definition and outcome reporting in randomised clinical trials: a systematic review. *BJOG* 2018; 125:1514-21. DOI: 10.1111/1471-0528.15272
- Fairweather DV. Nausea and vomiting in pregnancy. *Am J Obstet Gynecol* 1968; 102:135-75. DOI: 10.1016/0002-9378(68)90445-6
- Koot MH, Grooten IJ, Post J, et al. Ketonuria is not associated with hyperemesis gravidarum disease severity.

- Eur J Obstet Gynecol Reprod Biol* 2020; 254:315-20. DOI: 10.1016/j.ejogrb.2020.08.014
23. Jansen LAW, Koot MH, Van't Hooft J, et al. The Windsor definition for hyperemesis gravidarum: a multistakeholder international consensus definition. *Eur J Obstet Gynecol Reprod Biol* 2021; 266:15-22. DOI: 10.1016/j.ejogrb.2021.09.004
 24. Birkeland E, Stokke G, Tangvik RJ, et al. Norwegian PUQE (Pregnancy-Unique Quantification of Emesis and nausea) identifies patients with hyperemesis gravidarum and poor nutritional intake: a prospective cohort validation study. *PLoS One* 2015;10: e0119962. DOI: 10.1371/journal.pone.0119962
 25. Grooten IJ, Roseboom TJ, Painter RC. Barriers and challenges in hyperemesis gravidarum research. *Nutr Metab Insights* 2016;8(Suppl 1):33-9. DOI: 10.4137/NMI.S29523
 26. Nijsten K, van der Minnen LM, Wiegers HMG, et al. Hyperemesis gravidarum and vitamin K deficiency: a systematic review. *Br J Nutr* 2022; 128:30-42. DOI: 10.1017/S0007114521002865
 27. Oudman E, Wijnia JW, Oey M, et al. Wernicke's encephalopathy in hyperemesis gravidarum: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2019; 236:84-93. DOI: 10.1016/j.ejogrb.2019.03.006
 28. Fiaschi L, Nelson-Piercy C, Gibson J, et al. Adverse maternal and birth outcomes in women admitted to hospital for hyperemesis gravidarum: a population-based cohort study. *Paediatr Perinat Epidemiol* 2018; 32:40-51. DOI: 10.1111/ppe.12416
 29. Nijsten K, van der Minnen LM, Dean C, et al. Depression, anxiety, and post-traumatic stress disorder symptoms after hyperemesis gravidarum: a prospective cohort study. *J Matern Fetal Neonatal Med* 2022; 35:10055-10063. DOI: 10.1080/14767058.2022.2089550
 30. Nana M, Tydeman F, Bevan G, et al. Hyperemesis gravidarum is associated with increased rates of termination of pregnancy and suicidal ideation: results from a survey completed by >5000 participants. *Am J Obstet Gynecol* 2021; 224:629-31. DOI: 10.1016/j.ajog.2021.03.006
 31. Poursharif B, Korst LM, Macgibbon KW, et al. Elective pregnancy termination in a large cohort of women with hyperemesis gravidarum. *Contraception* 2007; 76:451-5.
 32. Boelig RC, Barton SJ, Saccone G, et al. Interventions for treating hyperemesis gravidarum: a Cochrane systematic review and meta-analysis. *J Matern Fetal Neonatal Med* 2018;31:2492-505. DOI: 10.1080/14767058.2017.1342805
 33. Smith JA, Fox KA, Clark SM. Nausea and vomiting of pregnancy: treatment and outcome. UptoDate 2023. (31.05.2024 tarihinde https://www.uptodate.com/contents/nausea-and-vomiting-of-pregnancy-treatment-and-outcome?search=Nausea%20and%20vomiting%20of%20pregnancy%3A%20treatment%20and%20outcome&source=search_result&selectedTitle=1%7E93&usage_type=default&display_rank=1 adresinden ulaşılmıştır)
 34. Viljoen E, Visser J, Koen N, et al. A systematic review and meta-analysis of the effect and safety of ginger in the treatment of pregnancy-associated nausea and vomiting. *Nutr J*. 2014 Mar 19;13:20. DOI: 10.1186/1475-2891-13-20
 35. Werntoft E, Dykes AK. Effect of acupressure on nausea and vomiting during pregnancy. A randomized, placebo-controlled, pilot study. *J Reprod Med*. 2001 Sep;46(9):835-9. PMID: 11584487
 36. McParlin C, O'Donnell A, Robson SC, et al. Treatments for Hyperemesis Gravidarum and Nausea and Vomiting in Pregnancy: A Systematic Review. *JAMA*. 2016 Oct 04;316(13):1392-1401. DOI: 10.1001/jama.2016.14337
 37. Dean CR, Shemar M, Ostrowski GAU, et al. Management of severe pregnancy sickness and hyperemesis gravidarum. *BMJ* 2018;363: k5000. DOI: 10.1136/bmj. k5000
 38. Koren G, Pairaudeau N. Compliance with prenatal vitamins. Patients with morning sickness sometimes find it difficult. *Can Fam Physician* 2006; 52:1392-3. PMCID: PMC1783699
 39. Maltepe C, Koren G. Preemptive treatment of nausea and vomiting of pregnancy: results of a randomized controlled trial. *Obstet Gynecol Int* 2013; 2013:809787. DOI: 10.1155/2013/809787
 40. Vakil N, van Zanten SV, Kahrilas P, et al; Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol*. 2006; 101:1900-20; quiz 1943. DOI: 10.1111/j.1572-0241.2006.00630.x
 41. Becher A, El-Serag H. Systematic review: the association between symptomatic response to proton pump inhibitors and health-related quality of life in patients with gastro-oesophageal reflux disease. *Aliment Pharmacol Ther*. 2011; 34:618-27. DOI: 10.1111/j.1365-2036.2011.04774.x
 42. Richter JE, Rubenstein JH. Presentation and epidemiology of gastroesophageal reflux disease. *Gastroenterology*. 2018; 154:267-76. DOI: 10.1053/j.gastro.2017.07.045
 43. Vazquez JC. Heartburn in pregnancy. *BMJ Clin Evid*. 2015; 2015:1411. PMCID: PMC4562453
 44. Kellerman R, Kintanar T. Gastroesophageal reflux disease. *Prim Care*. 2017; 44:561-73. DOI: 10.1016/j.pop.2017.07.001
 45. Armstrong D, Marshall JK, Chiba N, et al. Canadian Consensus Conference on the management of gastroesophageal reflux disease in adults- update 2004. *Can J Gastroenterol*. 2005; 19:15-35. DOI: 10.1155/2005/836030
 46. Rey E, Rodriguez-Artalejo F, Herraiz MA, et al. Gastroesophageal reflux symptoms during and after pregnancy: a longitudinal study. *Am J Gastroenterol*. 2007; 102:2395-400. DOI: 10.1111/j.1572-0241.2007.01452.x
 47. Marrero JM, Goggin PM, de Caestecker JS, et al. Determinants of pregnancy heartburn. *Br J Obstet Gynaecol*. 1992; 99:731-4. DOI: 10.1111/j.1471-0528.1992.tb13873.x
 48. Richter JE. Gastroesophageal reflux disease during pregnancy. *Gastroenterol Clin North Am*. 2003; 32:235-61. DOI: 10.1016/s0889-8553(02)00065-1
 49. Van TDH, Gavalier JS, Joshi SN, et al. Heartburn of pregnancy. *Gastroenterology*. 1977; 72:666-8. PMID: 14050
 50. Ho SC, Chang CS, Wu CY, et al. Ineffective esophageal motility is a primary motility disorder in gastroesophageal reflux disease. *Dig Dis Sci*. 2002; 47:652-6. DOI: 10.1023/a:1017992808762
 51. Vakil N, van Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol*. 2006; 101:1900-20; quiz 1943. DOI: 10.1111/j.1572-0241.2006.00630.x

52. National Guideline Alliance (UK). Management of Heartburn in Pregnancy: Antenatal Care: Evidence Review S. London: NICE Evidence Reviews Collection. 2021.
53. Richter JE. Review article: the management of heartburn in pregnancy. *Aliment Pharmacol Ther.* 2005; 22:749–57. PMID: 34524761
54. Law R, Maltepe C, Bozzo P, et al. Treatment of heartburn and acid reflux associated with nausea and vomiting during pregnancy. *Can Fam Physician.* 2010; 56:143–4.
55. Patti MG. An evidence-based approach to the treatment of gastroesophageal reflux disease. *JAMA Surg.* 2016; 151:73–8. PMID: PMC2821234
56. FDA. Product information. Sucralfate. Aptalis Pharma; 2013. (03.12.2021 tarihinde https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/018333s034,019183s-016lbl.pdf adresinden ulaşılmıştır)
57. Food, Drug Administration HHS. Content and format of labeling for human prescription drug and biological products; requirements for pregnancy and lactation labeling. Final rule. *Fed Regist.* 2014; 79:72063–103. PMID: 25509060
58. Matok I, Gorodischer R, Koren G, et al. The safety of H(2)-blockers use during pregnancy. *J Clin Pharmacol.* 2010; 50:81–7. DOI: 10.1177/0091270009350483
59. Gill SK, O'Brien L, Einarson TR, et al. The safety of proton pump inhibitors (PPIs) in pregnancy: a meta-analysis. *Am J Gastroenterol.* 2009; 104:1541–5. DOI: 10.1038/ajg.2009.122
60. Nikfar S, Abdollahi M, Moretti ME, et al. Use of proton pump inhibitors during pregnancy and rates of major malformations: a meta-analysis. *Dig Dis Sci.* 2002; 47:1526–9. DOI: 10.1023/a:1015863018105
61. Majithia R, Johnson DA. Are proton pump inhibitors safe during pregnancy and lactation? Evidence to date. *Drugs.* 2012; 72:171–9. DOI: 10.2165/11597290-000000000-00000
62. Brown SR, Horton JD, Trivette E, et al. Bochdalek hernia in the adult: Demographics, presentation, and surgical management. *Hernia* 2011, 15, 23–30. DOI: 10.1007/s10029-010-0699-3
63. Eglinton TW, Coulter GN, Bagshaw PF, et al. Diaphragmatic hernias complicating pregnancy. *ANZ J Surg* 2006; 76:553–7. DOI: 10.1111/j.1445-2197.2006.03776.x
64. Thomas S, Kapur B. Adult Bochdalek hernia—clinical features, management and results of treatment. *Jpn J Surg* 1991; 21:114–9. DOI: 10.1007/BF02470876
65. Gedik E, Tuncer MC, Onat S, et al. A review of Morgagni and Bochdalek hernias in adults. *Folia Morphol (Warsz)* 2011; 70:5–12. PMID: 21604246
66. Kaloo PD, Studd R, Child A. Postpartum diagnosis of a maternal diaphragmatic hernia. *Aust NZ J Obstet Gynaecol* 2001; 41:461–3. DOI: 10.1111/j.1479-828x.2001.tb01333.x
67. Kurzel RB, Naunhein KS, Schwartz RA. Repair of symptomatic diaphragmatic hernia during pregnancy. *Obstet Gynecol* 1988; 71:869–71. PMID: 3285266
68. Choi JY, Yang SS, Lee JH, et al. Maternal Bochdalek Hernia during Pregnancy: A Systematic Review of Case Reports. *Diagnostics* 2021, 11, 1261. DOI: 10.3390/diagnostics11071261
69. Vaezi MF, Pandolfino JE, Yadlapati RH, et al. ACG clinical guidelines: diagnosis and management of achalasia. *Am J Gastroenterol* 2020; 115:1393-1411. DOI: 10.14309/ajg.0000000000000731
70. Furuzawa-Carballeda J, Torres-Landa S, Valdovinos MA, et al. New insights into the pathophysiology of achalasia and implications for future treatment. *World J Gastroenterol* 2016; 22:7892-907. DOI: 10.3748/wjg.v22.i35.7892
71. Becker J, Niebisch S, Ricchiuto A, et al. Comprehensive epidemiological and genotype-phenotype analyses in a large European sample with idiopathic achalasia. *Eur J Gastroenterol Hepatol* 2016; 28:689-695. DOI: 10.1097/MEG.0000000000000602
72. American College of Obstetricians and Gynecologists'Committee on Obstetric Practice. Committee opinion No. 656 summary: guidelines for diagnostic imaging during pregnancy and lactation. *Obstet Gynecol* 2016; 127:418. DOI: 10.1097/AOG.0000000000001309
73. Friedel D, Stavropoulos S, Iqbal S, et al. Gastrointestinal endoscopy in the pregnant woman. *World J Gastrointest Endosc* 2014; 6:156-167. DOI: 10.4253/wjge.v6.i5.156
74. Cappell MS. Risks versus benefits of gastrointestinal endoscopy during pregnancy. *Nat Rev Gastroenterol Hepatol* 2011; 8:610-634. DOI: 10.1038/nrgastro.2011.162
75. Peled Y, Melamed N, Hirsch L, et al. The impact of total parenteral nutrition support on pregnancy outcome in women with hyperemesis gravidarum. *J Matern Fetal Neonatal Med* 2014; 27:1146-1150. DOI: 10.3109/14767058.2013.851187
76. Caruso A, De Carolis S, Ferrazzani S, et al. Pregnancy outcome and total parenteral nutrition in malnourished pregnant women. *Fetal Diagn Ther* 1998; 13:136-140.
77. Tan M, Kim E, Koren G, et al. Botulinum toxin type A in pregnancy. *Can Fam Physician* 2013; 59:1183-1184. DOI: 10.1159/000020824
78. Li W, Tang M. Application of botulinum toxin in pregnancy and its impact on female reproductive health. *Expert Opin Drug Saf* 2020;19:83-91. DOI: 10.1080/14740338.2020.1707803
79. Kumar AR, Schnoll-Sussman FH, Katz PO. Botulinum toxin and pneumatic dilation in the treatment of achalasia. *Tec Gastrointest Endosc* 2014; 16:10-19. DOI: 10.1016/j.tgie.2013.10.002
80. Vela MF, Richter JE, Khandwala F, et al. The long-term efficacy of pneumatic dilatation and Heller myotomy for the treatment of achalasia. *Clin Gastroenterol Hepatol* 2006; 4:580-587. DOI: 10.1016/s1542-3565(05)00986-9
81. Eckardt VF, Kanzler G, Westemeier T. Complications and their impact after pneumatic dilation for achalasia: prospective long-term follow-up study. *Gastrointest Endosc* 1997; 45:349-353. DOI: 10.1016/s0016-5107(97)70142-1
82. Feng J, Ali RW, Hao JY, et al. Peroral endoscopic myotomy formotility disorders. *Esophagus* 2020; 17:11-18. DOI: 10.1007/s10388-019-00693-w
83. Van De Velde, M De Buck F. Anesthesia for non-obstetric surgery in the pregnant patient. *Minerva Anesthesiol* 2007; 73:235-240. PMID: 17473818
84. Vosko S, Cohen DL, Neeman O, et al. Achalasia During Pregnancy: Proposed Management Algorithm Based on a Thorough Literature Review. *J Neurogastroenterol Mo-*

- til, Vol. 27 No. 1 January, 2021 pISSN: 2093-0879 eISSN: 2093-0887
85. Capell MS. Gastric and duodenal ulcers during pregnancy. *Gastroenterol Clin North Am.* 2003; 32:263–308. DOI: 10.1016/s0889-8553(02)00063-8
 86. Kuronen M, Hantunen S, Alanne L, et al. (2020). Pregnancy, puerperium and perinatal constipation – an observational hybrid survey on pregnant and postpartum women and their age-matched non-pregnant controls. *BJOG*, 128(6), 1057–1064. <https://doi.org/10.1111/1471-0528.16559>
 87. Rao SS, Qureshi WA, Yan Y, et al. (2022). Constipation, hemorrhoids, and anorectal disorders in pregnancy. *the American Journal of Gastroenterology*, 117(10S), 16–25. <https://doi.org/10.14309/ajg.0000000000001962>
 88. Ferdinande K, Dorreman Y, Roelens K, et al. (2018). Anorectal symptoms during pregnancy and postpartum: a prospective cohort study. *Colorectal Disease*, 20(12), 1109–1116. <https://doi.org/10.1111/codi.14324>
 89. Story L, Rafique S, Samadi N, et al. (2020). Lower gastrointestinal bleeding in pregnancy: Differential diagnosis, assessment and management. *Obstetric Medicine*, 14(3), 129–134. <https://doi.org/10.1177/1753495x20948300>
 90. Poskus T, Buzinskienė D, Drasutienė G, et al. (2014). Haemorrhoids and anal fissures during pregnancy and after childbirth: a prospective cohort study. *BJOG an International Journal of Obstetrics & Gynaecology*, 121(13), 1666–1671. <https://doi.org/10.1111/1471-0528.12838>
 91. Wong H, Khalil M, Ahmed F. (2020). OnabotulinumtoxinA for chronic migraine during pregnancy: a real world experience on 45 patients. *The Journal of Headache and Pain*, 21(1). <https://doi.org/10.1186/s10194-020-01196-1>
 92. National Institute of Child Health and Human Development. (2024, February 15). OnabotulinumtoxinA. Drugs and Lactation Database (LactMed®)- NCBI Bookshelf. <https://www.ncbi.nlm.nih.gov/books/NBK562677/>. Son olarak 28.07.2024 tarihinde ziyaret edilmiştir.
 93. DuPont HL. (2014). Acute infectious diarrhea in immunocompetent adults. *New England Journal of Medicine*, 370(16), 1532–1540. <https://doi.org/10.1056/nejm-ra1301069>
 94. Riddle MS, DuPont HL, Connor BA. (2016). ACG Clinical Guideline: Diagnosis, treatment, and Prevention of Acute diarrheal infections in Adults. *The American Journal of Gastroenterology*, 111(5), 602–622. <https://doi.org/10.1038/ajg.2016.126>
 95. Ye G, Li N, Chen Y, et al. (2016). Clostridium difficile carriage in healthy pregnant women in China. *Anaerobe*, 37, 54–57. <https://doi.org/10.1016/j.anaerobe.2015.11.010>
 96. Al-Jashaami LS, DuPont HL. Management of Clostridium difficile Infection. *Gastroenterol Hepatol (N Y)*. 2016 Oct;12(10):609-616. PMID: 27917075; PMCID: PMC5114503.
 97. Ruiter-Ligeti J, Vincent S, Czuzoj-Shulman N, et al. (2018). Risk Factors, Incidence, and Morbidity Associated With Obstetric Clostridium difficile Infection. *Obstetrics and Gynecology*, 131(2), 387–391. <https://doi.org/10.1097/aog.0000000000002422>
 98. Bruner LP, White AM, Proksell S. (2023). Inflammatory bowel disease. *Primary Care*, 50(3), 411–427. <https://doi.org/10.1016/j.pop.2023.03.009>
 99. Friedman S, Blumberg RS. (2018). Inflammatory bowel disease. Jameson J, & Fauci A.S., & Kasper D.L., & Hauser S.L., & Longo D.L., & Loscalzo J(Eds.), *Harrison's Principles of Internal Medicine*, (20e, p. 2258). McGraw-Hill Education.
 100. Schmidt E, Dubinsky MC. (2022). Inflammatory bowel disease and pregnancy. *The American Journal of Gastroenterology*, 117(10S), 60–68. <https://doi.org/10.14309/ajg.0000000000001963>
 101. Şenates E, Çolak Y, Erdem ED, et al. (2013). Serum anti-Müllerian hormone levels are lower in reproductive-age women with Crohn's disease compared to healthy control women. *Journal of Crohn's and Colitis*, 7(2), e29–e34. <https://doi.org/10.1016/j.crohns.2012.03.003>
 102. Lee S, Crowe M, Seow CH, et al. (2019). The impact of surgical therapies for inflammatory bowel disease on female fertility. *Cochrane Library*. <https://doi.org/10.1002/14651858.cd012711.pub2>
 103. Nørgård BM, Larsen PV, Fedder J, et al. (2016). Live birth and adverse birth outcomes in women with ulcerative colitis and Crohn's disease receiving assisted reproduction: a 20-year nationwide cohort study. *Gut*, 65(5), 767–776. <https://doi.org/10.1136/gutjnl-2015-311246>
 104. Hernandez-Nieto C, Sekhon L, Lee J, et al. (2019). Infertile patients with inflammatory bowel disease have comparable in vitro fertilization clinical outcomes to the general infertile population. *Gynecological Endocrinology*, 36(6), 554–557. <https://doi.org/10.1080/09513590.2019.1684465>
 105. Kammerlander H, Nielsen J, Kjeldsen J, et al. (2018). Fecal calprotectin during pregnancy in women with Moderate-Severe Inflammatory Bowel Disease. *Inflammatory Bowel Diseases*, 24(4), 839–848. <https://doi.org/10.1093/ibd/izx055>
 106. Odufalu F, Long M, Lin K, et al. (2021). Exposure to corticosteroids in pregnancy is associated with adverse perinatal outcomes among infants of mothers with inflammatory bowel disease: results from the PIANO registry. *Gut*, 71(9), 1766–1772. <https://doi.org/10.1136/gutjnl-2021-325317>
 107. Nielsen OH, Gubatan JM, Juhl CB, et al. (2022). Biologics for Inflammatory Bowel Disease and their Safety in Pregnancy: A Systematic review and Meta-analysis. *Clinical Gastroenterology and Hepatology*, 20(1), 74–87.e3. <https://doi.org/10.1016/j.cgh.2020.09.021>
 108. Szymańska, E., Kisieliwski, R., & Kierkuś, J. (2021). Reproduction and pregnancy in Inflammatory Bowel Disease - Management and treatment based on current guidelines. *Journal of Gynecology Obstetrics and Human Reproduction*, 50(3), 101777. <https://doi.org/10.1016/j.jogoh.2020.101777>
 109. Brondfield MN, Mahadevan U. (2023). Inflammatory bowel disease in pregnancy and breastfeeding. *Nature Reviews Gastroenterology & Hepatology*, 20(8), 504–523. <https://doi.org/10.1038/s41575-023-00758-3>
 110. Friedman S, Zegers FD, Jølvig LR, et al. (2021). Postpartum Surgical Complications in Women with Inflammatory Bowel Disease After Caesarian Section: A Danish

- Nationwide Cohort Study. *Journal of Crohn's and Colitis*, 16(4), 625–632. <https://doi.org/10.1093/ecco-jcc/jjab187>
111. Aboubakr A, Gottlieb ZS, Riggs AR, et al. (2021). Peripartum exposure to biologic therapy does not impact postpartum wound healing in women with IBD. *Inflammatory Bowel Diseases*, 28(6), 843–849. <https://doi.org/10.1093/ibd/izab165>
 112. Torres J, Chaparro M, Julsgaard M, et al. (2022). European Crohn's and Colitis Guidelines on Sexuality, Fertility, Pregnancy, and Lactation. *Journal of Crohn's and Colitis*, 17(1), 1–27. <https://doi.org/10.1093/ecco-jcc/jjac115>
 113. Nguyen GC, Seow CH, Maxwell C, et al. (2016). The Toronto Consensus Statements for the Management of Inflammatory Bowel Disease in Pregnancy. *Gastroenterology*, 150(3), 734–757.e1. <https://doi.org/10.1053/j.gastro.2015.12.003>
 114. Frountzas M, Nikolaou C, Stergios K, et al. (2019). Is the laparoscopic approach a safe choice for the management of acute appendicitis in pregnant women? A meta-analysis of observational studies. *Annals of the Royal College of Surgeons of England*, 101(4), 235–248. <https://doi.org/10.1308/rcsann.2019.0011>
 115. Won RP, Friedlander S, Lee SL. Management and Outcomes of Appendectomy during Pregnancy. *Am Surg*. 2017 Oct 1;83(10):1103-1107. PMID: 29391104
 116. Jayaram P, Mohan M, Lindow S, et al. (2017). Postpartum Acute Colonic Pseudo-Obstruction (Ogilvie's Syndrome): A systematic review of case reports and case series. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 214, 145–149. <https://doi.org/10.1016/j.ejogrb.2017.04.028>