

# 10. BÖLÜM

## PRETERM EYLEM

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### TANIM

Doğum ağırlığından bağımsız olarak 20 .gebelik haftası ile 37. gebelik haftaları arasında gerçekleşen doğumlar preterm doğum olarak tanımlanır. Preterm eylem neonatal mortalite ve morbiditenin en önde gelen sebeplerinden biridir. Mortalite ve morbidite gestasyonel yaşın azalması ile ters orantılı olarak artar.

Preterm doğum insidansı coğrafi farklılıklara göre değişiklik göstermektedir. Avrupa ülkelerinde %5-10 Amerika Birleşik Devletlerinde (ABD) %11-12 arasındadır. Dünya Sağlık Örgütü (WHO) 2005 yılındaki tüm doğumların %9,6'sının preterm olduğunu tahmin etmektedir. Dünya genelinde her yıl 15 milyon erken doğum gerçekleşmektedir (Blencowe, 2013). 20. yüzyılın ikinci yarısında, ABD'de ve dünyadaki diğer ülkelerde PTB hızında endişe verici bir artış meydana gelmiştir (Martin, 2015; Lawn, 2010). Erken doğum oranındaki bu artışa; ortalama anne yaşının artış, yardımcı üreme tekniklerinin kullanım sıklığındaki artış, infertiliteden bağımsız çoğul gebeliklerdeki artış, endikasyon üzerine erken doğum ve sezaryen oranlarındaki artış gibi birçok faktörün katkıda bulunduğu düşünülmektedir (Chang, 2013)

### PRETERM DOĞUM PATOFİZYOLOJİSİ

Ortalama gestasyonel periyod  $280 \pm 14$  gündür. Preterm eylem; seyrinde giden gebeliğin patolojik aktivasyonla zamanında önce doğumla sonuçlanmasıdır. Term ve preterm eylemin her ikisinde de bilinmeyen bir uyarı ile gebeliğin devamını sağlayan mekanizmaların devre dışı kalması sonucu myometrium eksojen uyarılara cevap verebilir hale gelir ve bu uyarılar sonucu oluşan uterusun kontraksiyonlarında ilerleyici servikal dilatasyon ve silinmeye neden olur. Bir seri alevlendirici olay prematür doğumlara neden olur. (Romero, 1988, 1994, 1997). Bu olaylar; desidual hemoraji (abrupsiyon), hormonal değişimler (fetal ve maternal stres) ve subklinik-klinik enfeksiyonu içerir. Özellikle enfeksiyon; erken gestasyonel haftalarda meydana gelen preterm eylemin üçte birinden sorumludur (Goldenberg 2000).

Endike preterm doğumlar; bu patofizyolojik mekanizmalardan bağımsız olarak erken doğumların yaklaşık üçte birini oluşturur. Endike erken doğumlar anne ve/veya fetus için gebelik devam ettiği takdirde hayati risk oluşturacak durumlarda gerçekleştirilir. Endike erken doğumlara en sık preeklampsi, fetal distress, intrauterin gelişme geriliği, ablasyo plasenta, plasenta previa tanıları neden olmaktadır.

indüksiyon kararı verilir. Takip kararı verilen hastalar oligohidroamnios ve pulmoner hipoplazi açısında seri ultrasonografi ile takip edilmelidir.  $\geq 23$  hafta fetuslarda grup  $\beta$  streptokok(GBS)proflaksisi, kortikosteroid uygulaması ve nöroprotektif amaçlı magnezyum sülfat önerilir.

### **Preterm Olgular (24-33 6/7 hafta);**

ACOG, 24<sup>o</sup> ile 33<sup>+6</sup> haftalar arasındaki membran rüptürü olan gebeler için; güven vermeyen fetal durum, klinik koryoamniyonit veya ablasyo plasenta olmadığı taktirde izlem yöntemini önermektedir. Bu hastalara GBS proflaksisi, tek kür kortikosteroid ve 32 hafta altı olgularda nöroprotektif amaçlı MGSO<sub>4</sub> yapılması önerilmektedir.

### **Geç Preterm Olgular(34- 36 0/7 hafta);**

34-36 hafta arası P-EMR olgularında yapılan çalışmalarda; konservatif yaklaşımın yenidoğan sonuçlarında belirgin iyileşme yapmadan koryoamniyonit riskini arttırdığından GBS proflaksisi ve doğum önerilmektedir.

## **KAYNAKLAR**

- Blencowe H. et al: Born too soon: the global epidemiology of 15 million preterm births: *Reprod Health*. 10: S2,2013
- Martin J.A, Hamilton B.E, Osterman M.J, Curtin S.C, Matthews T.J: Births: final data for 2013. *National vital statistics reports*. 64. *National Center for Health Statistics, Hyattsville, MD*1-65,2015
- Lawn J.E, Gravett M.G, Nunes T.M, Rubens C.E, Stanton C, Group G.R: Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data: *BMC Pregn Child-birth*. 10: S1,2010
- Chang H.H et al: Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *Lancet*. 381: 223-234,2013
- Romero R, Mazor M. Infection and preterm labor. *Clin Obstet Gynecol* 31: 553- 84;1988
- Romero R, Gomez R, Mazor M, Ghezzi F, Yoon B.H. The preterm labor syndrome. In: MG Elder, R Romero, RF Lamont, editors. *Preterm Labor*. New York: Churchill Livingstone; 1997. p. 29- 49.
- Romero R, Mazor M, Munoz H, Gomez R, Galasso M, Sherer DM. The preterm labor syndrome. *Ann N Y Acad Sci* 734: 414- 29;1994
- Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *N Engl J Med*. 342: 1500-1507;2000
- Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *N Engl J Med* 342:1500-1507;2000
- Czikk MJ, McCarthy FP, Murphy KE. Chorioamnionitis: from pathogenesis to treatment. *Clin Microbiol Infect* 17:1304-1311;2011
- Krauss-Silva et al: A randomised controlled trial of probiotics for the prevention of spontaneous preterm delivery associated with bacterial vaginosis: preliminary results. *Trials*. 12: 239;2011
- Leitich H, Bodner-Adler B, Brunbauer M, Kaider A, Egarter C, Husslein P. Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. *Am J Obstet Gynecol*. 189: 139-147;2003
- Jessamyn RM, Ranjitha K, Valerie R. Oral health during pregnancy. *J Women Health* 10: 880-882; 2005.
- Lopez NJ, Smith PC, Gutierrez J. Higher risk of preterm birth and low birth weight in women with periodontal disease. *J Dent Res* 81: 58-63;2002.
- Brocklehurst P, Gordon A, Heatley E, Milan S.J. Antibiotics for treating bacterial vaginosis in pregnancy. *Cochrane Database Syst Rev*. 2013; 1: CD000262
- Zhong Y, Cahill AG, Macones GA, Zhu F, Odibo AO. The association between prepregnancy maternal body mass index and preterm delivery. *Am J Perinatol*. 27(4):293-8;2010
- Bhattacharya S, et al. Inherited predisposition to spontaneous preterm delivery. *Obstet Gynecol* 115(6):1125-33; 2010
- Kyrklund-Blomberg NB, Cnattingius S. Preterm birth and maternal smoking: risks related to gestational age and onset of delivery. *Am J Obstet Gynecol* . 179(4):1051-5;1998
- Egawa M, et al. Smoking enhances oxytocin-induced rhythmic myometrial contraction. *Biol Reprod*.68(6):2274-80;2003
- Borges G, Lopez-Cervantes M, Medina-Mora ME, Tapia-Conyer R, Garrido F. Alcohol consumption, low birth weight, and preterm delivery in the National Addiction Survey (Mexico). *Int J Addict* .28(4): 355-68;1993
- Chan YY, Jayaprakasan K, Tan A, Thornton JG, Coomarasamy A, Raine-Fenning NJ. Reproductive outcomes in women with congenital uterine anomalies: a systematic review. *Ultrasound Obstet Gynecol*. 38(4):371-82;2011
- Hobel CJ, Goldstein A, Barrett ES. Psychosocial stress and pregnancy outcome. *Clin Obstet Gynecol*. 51(2):333-48;2008
- Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Arch Gen Psychiatry*. 67(10):1012-24;2010
- Schaaf J.M, Liem S.M, Mol B.W, Abu-Hanna A, Ravelli A.C. Ethnic and racial disparities in the risk of preterm birth: a systematic review and meta-analysis. *Am J Perinatol*. 30: 433-450;2013
- Goldenberg RL, et al. Medical, psychosocial, and behavioral risk factors do not explain the increased risk for low birth weight among black women. *Am J Obstet Gy-*

- necol.* 175: 1317-1324;1996
30. Mercer BM, et al. The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. *Am J Obstet Gynecol* 181(5 Pt 1):1216-21,1999
  31. McManemy J, Cooke E, Amon E, Leet T. Recurrence risk for preterm delivery. *Am J Obstet Gynecol* 196(6):571-6,2007
  32. Bhattacharya S, et al. Inherited predisposition to spontaneous preterm delivery. *Obstet Gynecol* 115(6):1125-33,2010
  33. Makhlof MA, et al. Adverse pregnancy outcomes among women with prior spontaneous or induced abortions. *Am J Perinatol.* 31(9):765-72,2014
  34. Reddy UM, Wapner RJ, Rebar RW, Tasca RJ. Infertility, assisted reproductive technology, and adverse pregnancy outcomes: executive summary of a National Institute of Child Health and Human Development workshop. *Obstet Gynecol.* 109(4):967-77,2007
  35. Romero R, et al. The preterm parturition syndrome. *BJOG.* 113: 17-42,2006
  36. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet.* 5;371(9606):75-84,2008
  37. Fuchs IB, Henrich W, Osthues K, Dudenhausen JW. Sonographic cervical length in singleton pregnancies with intact membranes presenting with threatened preterm labor. *Ultrasound Obstet Gynecol* 24:554-7,2004
  38. McPheeters ML, et al. The epidemiology of threatened preterm labor: a prospective cohort study. *Am J Obstet Gynecol.* 192:1325-9,2005
  39. Berghella V, Saccone G. Fetal fibronectin testing for reducing the risk of preterm birth.
  40. *Cochrane Database Syst Rev.* 29;7:CD006843,2019
  41. Gyamfi-Bannerman C, al. Antenatal betamethasone for women at risk for late preterm delivery. NICHD Maternal-Fetal Medicine Units Network. *N Engl J Med.* 374:1311-20,2016
  42. Steven Gabbe Jennifer Niebyl Joe Simpson Mark Landon Henry Galan Eric Jauniaux Deborah Driscoll Vincenzo Berghella William Grobman. *Obstetrics: Normal and Problem Pregnancies.* 7th Edition,2016
  43. Berghella V, Saccone G. Cervical assessment by ultrasound for preventing preterm delivery.
  44. *Cochrane Database Syst Rev.* 2019 Sep 25;9:CD007235.
  45. Kovacevich GJ, et al. The prevalence of thromboembolic events among women with extended bed rest prescribed as part of the treatment for premature labor or preterm premature rupture of membranes. *Am J Obstet Gynecol.* 182:1089-92,2000
  46. Sosa CG, Althabe F, Belizán JM, Bergel E. Bed rest in singleton pregnancies for preventing preterm birth. *Cochrane Database Syst Rev.* 2015;(3):CD003581.
  47. Kaji T, et al. Effect of bed rest during pregnancy on bone turnover markers in pregnant and postpartum women. *Bone.* 40:1088-94,2007
  48. Flenady V, Wojcieszek AM, Papatsonis DN, Stock OM, Murray L, Jardine LA, Carbonne B. Calcium channel blockers for inhibiting preterm labour and birth. *Cochrane Database Syst Rev.* 2014 Jun 5;(6):CD002255
  49. Flenady V, Hawley G, Stock OM, Kenyon S, Badawi N. Prophylactic antibiotics for inhibiting preterm labour with intact membranes. *Cochrane Database Syst Rev.* 2013 Dec 5;(12):CD000246
  50. Premature rupture of membranes. ACOG Practice Bulletin No. 80. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2007;109:1007-19.
  51. Prevention of perinatal group B streptococcal disease — revised guidelines from CDC, 2010. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases. *MMWR Recomm Rep* 2010;59 (RR-10):1-36.
  52. Prevention of early-onset group B streptococcal disease in newborns. Committee Opinion No. 485. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2011;117:1019-27
  53. Ramin SM, Vidaeff AC, Gilstrap LC 3rd, Bishop KD, Jenkins GN, Alcorn JL. The effects of dexamethasone and betamethasone on surfactant protein-B messenger RNA expression in human type II pneumocytes and human lung adenocarcinoma cells. *Am J Obstet Gynecol.* 190(4):952-9,2004
  54. Antenatal Corticosteroid Therapy for Fetal Maturation. Committee Opinion No. 677. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2016; 128:e187-94.
  55. Garite TJ, Kurtzman J, Maurel K, Clark R. Impact of a 'rescue course' of antenatal corticosteroids: a multi-center randomized placebo-controlled trial. *Obstetrix Collaborative Research Network* [published erratum appears in *Am J Obstet Gynecol* 2009;201:428]. *Am J Obstet Gynecol* 2009;200:248
  56. Crowther CA, McKinlay CJ, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. *Cochrane Database of Systematic Reviews* 2015, Issue 7. Art. No.: CD003935.
  57. Marret S, et al. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial. *PREMAG trial group.* *BJOG* 2007;114:310-8.
  58. Crowther CA, Hiller JE, Doyle LW, Haslam RR. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. *Australasian Collaborative Trial of Magnesium Sulphate (ACTOMg SO4) Collaborative Group.* *JAMA* 2003;290:2669-76.
  59. Rouse DJ, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. *Eunice Kennedy Shriver NICHD Maternal-Fetal Medicine Units Network.* *N Engl J Med* 2008;359:895-905.
  60. Rouse DJ, et al: A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. *N Engl J Med.* 359(9):895-905,2008
  61. Costantine MM, Weiner SJ. Effects of antenatal exposure to magnesium sulfate on neuroprotection and mortality in preterm infants: a meta-analysis. *Obstet Gynecol.* 114(2 Pt 1):354-64,2009
  62. Crowther CA, Brown J, McKinlay CJ, Middleton P. Magnesium sulphate for preventing preterm birth in

- threatened preterm labour. *Cochrane Database Syst Rev*. 2014 Aug 15;(8):CD001060
64. Neilson JP, West HM, Dowswell T. Betamimetics for inhibiting preterm labour. *Cochrane Database Syst Rev*. 2014 Feb 5;(2):CD004352.
  65. King JF, Flenady V, Papatsonis D, Dekker G, Carbonne B. Calcium channel blockers for inhibiting preterm labour. *Cochrane Database of Systematic Reviews* 2003: CD002255
  66. King JF, Flenady V, Cole S, Thornton S. Cyclo-oxygenase (COX) inhibitors for treating preterm labour. *Cochrane Database of Systematic Reviews* 2005: CD001992.
  67. Flenady V, Wojcieszek AM, Papatsonis DN, Stock OM, Murray L, Jardine LA, Carbonne B. Calcium channel blockers for inhibiting preterm labour and birth. *Cochrane Database Syst Rev*. 2014: CD002255
  68. U.S.Food and Drug Administration. FDA drug safety communication: new warnings against use of terbutaline to treat preterm labor. Silver Spring (MD): FDA; 2011.
  69. Reinebrant HE, et al. Cyclo-oxygenase (COX) inhibitors for treating preterm labour. *Cochrane Database Syst Rev*. 2015 Jun 5;(6):CD001992
  70. Vermillion ST, Scardo JA, Lashus AG, Wiles HB. The effect of indomethacin tocolysis on fetal ductusarteriosus constriction with advancing gestational age. *Am J Obstet Gynecol*. 1997 Aug;177(2):256-9; discussion 259-61.
  71. Savage AH, Anderson BL, Simhan HN. The safety of prolonged indomethacin therapy. *Am J Perinatol*. 2007 Apr;24(4):207-13.
  72. Crowther CA, Brown J, McKinlay CJ, Middleton P. Magnesium sulphate for preventing preterm birth in threatened preterm labour. *Cochrane Database Syst Rev*. 2014 Aug 15;(8):CD001060.
  73. Flenady V, Reinebrant HE, Liley HG, Tambimuttu EG, Papatsonis DN. Oxytocin receptor antagonists for inhibiting preterm labour. *Cochrane Database Syst Rev*. 2014 Jun 6;(6):CD004452
  74. Han S, Crowther CA, Moore V. Magnesium maintenance therapy for preventing preterm birth after threatened preterm labour. *Cochrane Database of Systematic Reviews* 2010: CD000940.
  75. Dodd JM, Crowther CA, Dare MR, Middleton P. Oral betamimetics for maintenance therapy after threatened preterm labour. *Cochrane Database of Systematic Reviews* 2006: CD003927. CD003927
  76. Briery CM, Klauser CK, Martin RW, Magann EF, Chauhan SP, Morrison JC. The use of 17-hydroxy progesterone in women with arrested preterm labor: a randomized clinical trial. *J Matern Fetal Neonatal Med*. 2014 Dec;27(18):1892-6.
  77. Kamat S, Veena P, Rani R. Comparison of nifedipine and progesterone for maintenance tocolysis after arrested preterm labour. *J Obstet Gynecol*. 2014 May;34(4):322-5.
  78. Zhu JJ, Bao YY, Zhang GL, Ma LX, Wu MY. No relationship between mode of delivery and neonatal mortality and neurodevelopment in very low birth weight infants aged two years. *World J Pediatr*. 2014 Aug;10(3):227-31.
  79. ni M, Makino Y, Matsui H. Survival rate of extremely low birth weight infants and its risk factors: case-control study in Japan. *Obstet Gynecol*. 2013 Nov 25;2013:873563.
  80. Bergenhengouwen LA, Meertens LJ, Schaaf J, Nijhuis JG, Mol BW, Kok M, Scheepers HC. Vaginal delivery versus caesarean section in preterm breech delivery: a systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2014 Jan;172:1-6.
  81. Dyson DC, et al. Monitoring women at risk for preterm labor. *N Engl J Med* 1998;338:15-9.
  82. Andrews WW, et al. Randomized clinical trial of metronidazole plus erythromycin to prevent spontaneous preterm delivery in fetal fibronectin-positive women. *Obstet Gynecol* 2003;101:847-55.
  83. Carey JC, et al. Metronidazole to prevent preterm delivery in pregnant women with asymptomatic bacterial vaginosis. *N Engl J Med* 2000;342:534-40.
  84. Edlow AG, Srinivas SK, Elovitz MA. Second-trimester loss and subsequent pregnancy outcomes: What is the real risk? *Am J Obstet Gynecol* 2007;197:581.
  85. Meis PJ, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. *N Engl J Med* 2003;348:2379-85.
  86. Use of progesterone to reduce preterm birth. ACOG Committee Opinion No. 419. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2008;112: 963-5.
  87. Tita AT, Rouse DJ. Progesterone for preterm birth prevention: an evolving intervention. *Am J Obstet Gynecol* 2009;200:219-24.
  88. Durnwald CP, et al. Second trimester cervical length and risk of preterm birth in women with twin gestations treated with 17-alpha hydroxyprogesterone caproate. *J Matern Fetal Neonatal Med* 2010;23:1360-4.
  89. Rouse DJ, et al. A trial of 17 alpha-hydroxyprogesterone caproate to prevent prematurity in twins. *N Engl J Med* 2007;357:454-61.
  90. Norman JE, et al. Progesterone for the prevention of preterm birth in twin pregnancy (STOPPIT): a randomised, double-blind, placebo-controlled study and meta-analysis. *Lancet* 2009;373:2034-40.
  91. Combs CA, Garite T, Maurel K, Das A, Porto M. 17-hydroxyprogesterone caproate for twin pregnancy: a double-blind, randomized clinical trial. *Am J Obstet Gynecol* 2011;204:221.
  92. Caritis SN, et al. Prevention of preterm birth in triplets using 17 alpha-hydroxyprogesterone caproate: a randomized controlled trial. *Obstet Gynecol* 2009;113:285-92.
  93. Combs CA, Garite T, Maurel K, Das A, Porto M. Failure of 17-hydroxyprogesterone to reduce neonatal morbidity or prolong triplet pregnancy: a double-blind, randomized clinical trial. *Am J Obstet Gynecol* 2010;203:248
  94. Garite TJ, Freeman RK. Chorioamnionitis in the preterm gestation. *Obstet Gynecol* 1982;59:539-45.
  95. Mercer BM, et al. The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. *Am J Obstet Gynecol* 1999;181:1216-21.

98. Asrat T, et al. Rate of recurrence of preterm premature rupture of membranes in consecutive pregnancies. *Am J Obstet Gynecol* 1991;165:1111–5.
99. Goldenberg RL, et al. The Preterm Prediction Study: prediction of preterm premature rupture of membranes through clinical findings and ancillary testing. The National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. *Am J Obstet Gynecol* 2000;183:738–45
100. Lee SE, Park JS, Norwitz ER, Kim KW, Park HS, Jun JK. Measurement of placental alpha-microglobulin-1 in cervicovaginal discharge to diagnose rupture of membranes. *Obstet Gynecol* 2007;109:634–40.
101. Cousins LM, Smok DP, Lovett SM, Poeltler DM. Amni-Sure placental alpha microglobulin-1 rapid immunoassay versus standard diagnostic methods for detection of rupture of membranes. *Am J Perinatol* 2005;22: 317–20.