30. BÖLÜM

ANEMİ

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Anemi günümüzde en önemli sağlık problemlerinden biridir. Anemi tanısı, hemoglobin seviyesinin normal sağlıklı populasyon ortalamasının 2 standart sapma altında olması ile konulur. Dünya Sağlık Örgütüne (DSÖ) göre dünya nüfusunun %24,8'i (1,62 milyar insan) anemiktir (McLean, Cogswell, Egli, Wojdyla, & De Benoist, 2009). DSÖ'nün yaptığı araştırmada ise tüm dünyada gebelerin %41,8'inin anemik olduğu saptanmıştır (C. WHO, 2008). Bu hastaların yaklaşık yarısında sebep demir eksikliği iken, kalan %50'de ise sebep vitamin B_{12}, A ve folat eksikliği ya da kronik hastalıklar, parazitik enfeksiyonlar ve kalıtsal patolojilerdir(U. WHO, 2001).

Anemi etyolojik mekanizmaya göre, kırmızı kan hücrelerinin morfolojisine göre ya da kalıtsal & akkiz olmasına göre sınıflandırılabilir(Obstetricians & Gynecologists, 2008).

Ortalama Korpuskular Hacim (MCV) 'ye Göre Sınıflandırma

1. Mikrositer Anemi (MCV < 80 femtolitre (fL))
   - Demir eksikliği anemisi
   - Talasemiler
   - Kronik hastalık anemisi
   - Sideroblastik anemi
   - Kurşun zehirlenmesine bağlı
   - Bakır eksikliğine bağlı
2. Normositer Anemi (MCV 80-100 fL)
   - Demir eksikliğinin erken dönemi
   - Akut kanamaya bağlı anemi
   - Kronik hastalık anemisi
   - Herediter sferositoz
   - Otoimmün hemolitik anemi
   - Böbrek yetmezliği
   - Hemolitik anemiler
   - Hipotiroidiye bağlı anemi
   - Hipopituitarizme bağlı anemi
3. Makrositer Anemi (MCV >100 fL)
   - Folik asit eksikliğine bağlı anemi
   - B_{12} eksikliği anemisi
   - Kronik alkol kullanımı
   - Kronik karaciğer hastalığı
   - Retikülositozis
   - Akut miyelodisplastik sendrom

Mekanizmaya Göre Sınıflama

4. Kırmızı kan hücresi üretiminde azalmaya bağlı anemi
   - Demir eksikliği
   - B_{12} eksikliği
   - Folik asit eksikliği
   - Kemik iliği depresyonu
   - Hipotiroidi
   - EPO seviyesinde azalma

ilaçlar hidroksiüre, ACE inhibitörleri ve demir şelasyon ajanları kesilmeli, bazal biyokimyasal değerlendirmeleri yapılmalı, hemoglobin/hemotokrit, ferritin, idrar tetkiki, idrar kültürü, 24 saatlik idrarda protein bakılmalı ve uygun durumda gebe kalmasına izin verilmelidir.Hastalara genetik danışmanlık verilmelidir. Preimplantasyon genetik tanı isteyen hastalar yardımcı üreme teknikleri ile gebe kalmaya yönlendirilebilirler. Gebe kaldıktan sonra tanı için koryon villus örnekleme ve amniyosentez önerilebilir.

Orak hücreli anemisi olan gebelere demir içermeyen vitaminler verilebilir, pnömokok aşısı uygulanmalıdır. Alloimmunizasyon riski bu hasta grubunda artığı için non- RH D alloimmunizasyon açısından yapın takip edilmesi önerilmektedir(Chou et al., 2013).

Doğum sırasında ise hastanın oksijenizasyonu ve hidrasyonu oldukça önemlidir. Doğum şekli kararı obstetrik endikasyona göre konulmalıdır. Fakat hem sezeryen hem de vajinal doğum sonrası venöz tromboemboli açısından profilaktik antikoagülan tedavi verilmesi önerilmektedir(Vichinsky, Simpson, & Barss, 2014).

KAYNAKLAR

Achebe, M. M., & Gafter-Gvili, A. (2017). How I treat anemia in pregnancy: iron, cobalamin, and folate. *Blood, 129*(8), 940-949.

Adams, P. C., Reboussin, D. M., Press, R. D., Barton, J. C., Acton, R. T., Moses, G. C., ... Gordeuk, V. R. (2007). Biological variability of transferrin saturation and unsaturated iron-binding capacity. *The American journal of medicine, 120*(11), 999. e991-999. e997.

Adebisi, O. Y., & Strayhorn, G. (2005). Anemia in pregnancy and race in the United States: blacks at risk. *FAMILY MEDICINE-KANSAS CITY-, 37*(9), 655.

Alger, L. S., Golbus, M. S., & Laros Jr, R. K. (1979). Thalassemia and pregnancy: results of an antenatal screening program. *American journal of obstetrics and gynecology, 134*(6), 662-673.

Angastiniotis, M., & Modell, B. (1998). Global epidemiology of hemoglobin disorders. *Annals of the New York academy of sciences, 850*(1), 251-269.

Auerbach, M., Abernathy, J., Juul, S., Short, V., & Derman, R. (2019). Prevalence of iron deficiency in first trimester, nonanemic pregnant women. *The Journal of Maternal-Fetal & Neonatal Medicine*, 1-4.

Beard, J. L. (2008). Why iron deficiency is important in infant development. *The Journal of nutrition, 138*(12), 2534-2536.

Beard, J. L., Dawson, H., & Piñero, D. J. (1996). Iron metabolism: a comprehensive review. *Nutrition reviews, 54*(10), 295-317.

Berkowitz, R. L., Bussel, J. B., & McFarland, J. G. (2006). Alloimmune thrombocytopenia: state of the art 2006. *American journal of obstetrics and gynecology, 195*(4), 907-913.

Bessos, H., Turner, M., & Urbaniak, S. (2005). Is there a relationship between anti-HPA-1a concentration and severity of neonatal alloimmune thrombocytopenia? *Immunohematology, 21*(3), 102-109.

Bhandal, N., & Russell, R. (2006). Intravenous versus oral iron therapy for postpartum anaemia. *BJOG: An International Journal of Obstetrics & Gynaecology, 113*(11), 1248-1252.

Bothwell, T. H. (2000). Iron requirements in pregnancy and strategies to meet them. *The American journal of clinical nutrition, 72*(1), 257S-264S.

Burrows, R. F., & Kelton, J. G. (1990). Low fetal risks in pregnancies associated with idiopathic thrombocytopenic purpura. *American journal of obstetrics and gynecology, 163*(4), 1147-1150.

Bussel, J. B., Berkowitz, R. L., Lynch, L., Lesser, M. L., Paidas, M. J., Huang, C. L., & McFarland, J. G. (1996). Antenatal management of alloimmune thrombocytopenia with intravenous γ-globulin: a randomized trial of the addition of low-dose steroid to intravenous γ-globulin. *American journal of obstetrics and gynecology, 174*(5), 1414-1423.

Bussel, J. B., Zabusky, M. R., Berkowitz, R. L., & McFarland, J. G. (1997). Fetal alloimmune thrombocytopenia. *New England Journal of Medicine, 337*(1), 22-26.

CALIŞ, P., Gizem, I., & KARCAALTINCABA, D. TÜRK GEBE POPÜLASYONUNDA 1.2. 3. TRİMESTER'DEKİ VIT B12, FOLAT VE HOMOSİSTEİN DÜZEYLERİNİN DEĞERLENDİRİLMESİ Vitamin B12, Folate and Homocystein Status in Turkish Pregnant Women for each Trimester. *Bozok Tıp Dergisi, 9*(2), 42-47.

Cao, A., Saba, L., Galanello, R., & Rosatelli, M. C. (1997). Molecular diagnosis and carrier screening for β thalassemia. *Jama, 278*(15), 1273-1277.

Care, A., Pavord, S., Knight, M., & Alfirevic, Z. (2018). Severe primary autoimmune thrombocytopenia in pregnancy: a national cohort study. *BJOG: An International Journal of Obstetrics & Gynaecology, 125*(5), 604-612.

Carles, G., Tobal, N., Raynal, P., Herault, S., Beucher, G., Marret, H., & Arbeille, P. (2003). Doppler assessment of the fetal cerebral hemodynamic response to moderate or severe maternal anemia. *American journal of obstetrics and gynecology, 188*(3), 794-799.

Castaman, G., Tosetto, A., & Rodeghiero, F. (2010). Pregnancy and delivery in women with von Willebrand's disease and different von Willebrand factor mutations. *Haematologica, 95*(6), 963-969.

Chou, S. T., Jackson, T., Vege, S., Smith-Whitley, K., Friedman, D. F., & Westhoff, C. M. (2013). High prevalence of red blood cell alloimmunization in sickle cell disease despite transfusion from Rh-matched minority donors. *Blood, 122*(6), 1062-1071.

Chui, D. H., Fucharoen, S., & Chan, V. (2003). Hemoglo-

bin H disease: not necessarily a benign disorder. *Blood, 101*(3), 791-800.

Colomer, J., Colomer, C., Gutierrez, D., Jubert, A., Nolasco, A., Donat, J., ... Alvarez-Dardet, C. (1990). Anaemia during pregnancy as a risk factor for infant iron deficiency: report from the Valencia Infant Anaemia Cohort (VIAC) study. *Paediatric and perinatal epidemiology, 4*(2), 196-204.

Conti, M., Mari, D., Conti, E., Muggiasca, M. L., & Mannucci, P. M. (1986). Pregnancy in women with different types of von Willebrand disease.

Control, C. f. D., & Prevention. (1998). Recommendations to prevent and control iron deficiency in the United States. *MMWR RR, 47*(3), 1-29.

Corwin, E. J., Murray-Kolb, L. E., & Beard, J. L. (2003). Low hemoglobin level is a risk factor for postpartum depression. *The Journal of nutrition, 133*(12), 4139-4142.

Daru, J., Allotey, J., Peña-Rosas, J., & Khan, K. (2017). Serum ferritin thresholds for the diagnosis of iron deficiency in pregnancy: a systematic review. *Transfusion Medicine, 27*(3), 167-174.

Daru, J., Zamora, J., Fernández-Félix, B. M., Vogel, J., Oladapo, O. T., Morisaki, N., ... Jayaratne, K. (2018). Risk of maternal mortality in women with severe anaemia during pregnancy and post partum: a multilevel analysis. *The Lancet Global Health, 6*(5), e548-e554.

Dashe, J. S., Ramin, S. M., & Cunningham, F. G. (1998). The long-term consequences of thrombotic microangiopathy (thrombotic thrombocytopenic purpura and hemolytic uremic syndrome) in pregnancy. *Obstetrics & Gynecology, 91*(5), 662-668.

Eisenstein, R. (1997). The IRE, the IRP and cytosolic aconitase: posttranslational regulation of mammalian iron metabolism. *Metal Ions and Gene Regulation*, 157-216.

Favaloro, E., Thom, J., & Baker, R. (2000). Assessment of current diagnostic practice and efficacy in testing for von Willebrand's disorder: results from the second Australasian multi-laboratory survey. *Blood coagulation & fibrinolysis, 11*(8), 729-737.

Finch, C. (1994). Regulators of iron balance in humans. *Blood, 84*(6), 1697-1702.

Fleming, A. (1972). Urinary excretion of folate in pregnancy. *BJOG: An International Journal of Obstetrics & Gynaecology, 79*(10), 916-920.

Gambling, L., DANZEISEN, R., Susan, G., CHARANIA, Z., SOLANKY, N., JOORY, K. D., . . . McARDLE, H. J. (2001). Effect of iron deficiency on placental transfer of iron and expression of iron transport proteins in vivo and in vitro. *Biochemical Journal, 356*(3), 883-889.

George, J. N. (2003). The association of pregnancy with thrombotic thrombocytopenic purpura–hemolytic uremic syndrome. *Current opinion in hematology, 10*(5), 339-344.

George, J. N., & Knudtson, E. (2008). Thrombocytopenia in pregnancy. *UpToDate. Avaible at: http://www. uptodate. com/contents/thrombocytopenia-inpregnancy*, 1-150.

Higgs, D., Vickers, M., Wilkie, A., Pretorius, I., Jarman, A., & Weatherall, D. (1989). A review of the molecular genetics of the human alpha-globin gene cluster. *Blood, 73*(5), 1081-1104.

James, A., & Jamison, M. (2007). Bleeding events and other complications during pregnancy and childbirth in women with von Willebrand disease. *Journal of Thrombosis and Haemostasis, 5*(6), 1165-1169.

Janbek, J., Sarki, M., Specht, I. O., & Heitmann, B. L. (2019). A systematic literature review of the relation between iron status/anemia in pregnancy and offspring neurodevelopment. *European journal of clinical nutrition*, 1.

Jaschevatzky, O., David, H., Bivas, M., Rosenberg, R., Ellenbogen, A., & Ballas, S. (1994). Outcome of pregnancies associated with marked gestational thrombocytopenia. *Journal of perinatal medicine, 22*(4), 351-355.

Kaplan, C. (2006). Foetal and neonatal alloimmune thrombocytopaenia. *Orphanet journal of rare diseases, 1*(1), 39.

Khalafallah, A. A., Hyppa, A., Chuang, A., Hanna, F., Wilson, E., Kwok, C., . . . Falloon, P. (2018). *A Prospective Randomised Controlled Trial of a single intravenous infusion of ferric carboxymaltose vs single intravenous iron polymaltose or daily oral ferrous sulphate in the treatment of iron deficiency anaemia in pregnancy.* Paper presented at the Seminars in hematology.

Lao, T. T. (2017). Obstetric care for women with thalassemia. *Best Practice & Research Clinical Obstetrics & Gynaecology, 39*, 89-100.

Lee, C., Chi, C., Pavord, S., Bolton-Maggs, P., Pollard, D., Hinchcliffe-Wood, A., & Kadir, R. (2006). The obstetric and gynaecological management of women with inherited bleeding disorders–review with guidelines produced by a taskforce of UK Haemophilia Centre Doctors' Organization. *Haemophilia, 12*(4), 301-336.

Lipe, B. C., Dumas, M. A., & Ornstein, D. L. (2011). Von Willebrand disease in pregnancy. *Hematology/Oncology Clinics, 25*(2), 335-358.

Mannucci, P. M. (2001). How I treat patients with von Willebrand disease. *Blood, 97*(7), 1915-1919.

McLean, E., Cogswell, M., Egli, I., Wojdyla, D., & De Benoist, B. (2009). Worldwide prevalence of anaemia, WHO vitamin and mineral nutrition information system, 1993–2005. *Public health nutrition, 12*(4), 444-454.

Mueller-Eckhardt, C., Grubert, A., Weisheit, M., Mueller-Eckhardt, G., Kiefel, V., Kroll, H., . . . Santoso, S. (1989). 348 cases of suspected neonatal alloimmune thrombocytopenia. *The Lancet, 333*(8634), 363-366.

Nichols, W., Hultin, M., James, A., Manco-Johnson, M., Montgomery, R., Ortel, T., . . . Yawn, B. (2008). von Willebrand disease (VWD): evidence-based diagnosis and management guidelines, the National Heart, Lung, and Blood Institute (NHLBI) Expert Panel report (USA) 1. *Haemophilia, 14*(2), 171-232.

Obstetricians, A. C. o., & Gynecologists. (2008). ACOG Practice Bulletin No. 95: anemia in pregnancy. *Obstetrics and gynecology, 112*(1), 201.

Obstetrics, A. C. o. (2007). ACOG Practice Bulletin No. 78: hemoglobinopathies in pregnancy. *Obstet Gynecol, 109*(1), 229-237.

Olsson, B., Andersson, P.-O., Jernås, M., Jacobsson, S., Carlsson, B., Carlsson, L. M., & Wadenvik, H. (2003). T-cell-mediated cytotoxicity toward platelets in chronic idiopathic thrombocytopenic purpura. *Nature medicine, 9*(9), 1123.

Organization, W. H. (1989). Preventing and controlling anaemia through primary health care: a guide for health ad-

ministrators and programme managers. Geneva.
Organization, W. H. (2012). *Guideline: daily iron and folic acid supplementation in pregnant women*: World Health Organization.
Parker, J. A., Barroso, F., Stanworth, S. J., Spiby, H., Hopewell, S., Doree, C. J., ... Allard, S. (2012). Gaps in the evidence for prevention and treatment of maternal anaemia: a review of systematic reviews. *BMC pregnancy and childbirth, 12*(1), 56.
Pavord, S., Daru, J., Prasannan, N., Robinson, S., Stanworth, S., Girling, J., & Committee, B. (2019). UK guidelines on the management of iron deficiency in pregnancy. *British journal of haematology*.
Pavord, S., Myers, B., Robinson, S., Allard, S., Strong, J., Oppenheimer, C., & Haematology, B. C. f. S. i. (2012). UK guidelines on the management of iron deficiency in pregnancy. *British journal of haematology, 156*(5), 588-600.
Perewusnyk, G., Huch, R., Huch, A., & Breymann, C. (2002). Parenteral iron therapy in obstetrics: 8 years experience with iron–sucrose complex. *British journal of nutrition, 88*(1), 3-10.
Pitkin, R. M. (1977). Nutritional influences during pregnancy. *The Medical Clinics of North America, 61*(1), 3-15.
Practice, C. o. G. (2013). Committee Opinion No. 580: von Willebrand disease in women. *Obstetrics and gynecology, 122*(6), 1368.
Provan, D., Stasi, R., Newland, A. C., Blanchette, V. S., Bolton-Maggs, P., Bussel, J. B., ... Godeau, B. (2010). International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood, 115*(2), 168-186.
Puolakka, J., Jänne, O., & Vihko, R. (1980). Evaluation by serum ferritin assay of the influence of maternal iron stores on the iron status of newborns and infants. *Acta Obstetricia et Gynecologica Scandinavica, 59*(S95), 53-56.
Radder, C., Brand, A., & Kanhai, H. (2003). Will it ever be possible to balance the risk of intracranial haemorrhage in fetal or neonatal alloimmune thrombocytopenia against the risk of treatment strategies to prevent it? *Vox sanguinis, 84*(4), 318-325.
Radlowski, E. C., & Johnson, R. W. (2013). Perinatal iron deficiency and neurocognitive development. *Frontiers in human neuroscience, 7*, 585.
Rasmussen, K. M. (2001). Is there a causal relationship between iron deficiency or iron-deficiency anemia and weight at birth, length of gestation and perinatal mortality? *The Journal of nutrition, 131*(2), 590S-603S.
Rayment, R., Brunskill, S. J., Soothill, P. W., Roberts, D. J., Bussel, J. B., & Murphy, M. F. (2011). Antenatal interventions for fetomaternal alloimmune thrombocytopenia. *Cochrane Database of Systematic Reviews*(5).
Reese, J. A., Peck, J. D., Deschamps, D. R., McIntosh, J. J., Knudtson, E. J., Terrell, D. R., ... George, J. N. (2018). Platelet counts during pregnancy. *New England Journal of Medicine, 379*(1), 32-43.
Remuzzi, G., & Garella, S. (1987). HUS and TTP: variable expression of a single entity. *Kidney international, 32*(2), 292-308.
Rouault, T. A., & Klausner, R. D. (1996). Post-transcriptional regulation of genes of iron metabolism in mammalian cells. *JBIC Journal of Biological Inorganic Chemistry, 1*(6), 494-499.
Rust, O. A., & Perry, J. K. (1995). Pregnancy complicated by sickle hemoglobinopathy. *Clinical obstetrics and gynecology, 38*(3), 472-484.
Sánchez-Luceros, A., Meschengieser, S. S., Turdó, K., Arizó, A., Woods, A. I., Casais, P., ... Lazzari, M. A. (2007). Evaluation of the clinical safety of desmopressin during pregnancy in women with a low plasmatic von Willebrand factor level and bleeding history. *Thrombosis research, 120*(3), 387-390.
Sandstead, H. H. (2000). Causes of iron and zinc deficiencies and their effects on brain. *The Journal of nutrition, 130*(2), 347S-349S.
Scholl, T. O. (2005). Iron status during pregnancy: setting the stage for mother and infant. *The American journal of clinical nutrition, 81*(5), 1218S-1222S.
Serjeant, G. R., Loy, L. L., Crowther, M., Hambleton, I. R., & Thame, M. (2004). Outcome of pregnancy in homozygous sickle cell disease. *Obstetrics & Gynecology, 103*(6), 1278-1285.
Spencer, J. A., & Burrows, R. F. (2001). Fetomaternal alloimmune thrombocytopenia: a literature review and statistical analysis. *Australian and New Zealand Journal of Obstetrics and Gynaecology, 41*(1), 45-55.
Stanworth, S. J., Hackett, G. A., & Williamson, L. M. (2001). Fetomaternal alloimmune thrombocytopenia presenting antenatally as hydrops fetalis. *Prenatal diagnosis, 21*(5), 423-424.
Sukumar, N., Rafnsson, S. B., Kandala, N.-B., Bhopal, R., Yajnik, C. S., & Saravanan, P. (2016). Prevalence of vitamin B-12 insufficiency during pregnancy and its effect on offspring birth weight: a systematic review and meta-analysis. *The American journal of clinical nutrition, 103*(5), 1232-1251.
Sukumar, N., Venkataraman, H., Wilson, S., Goljan, I., Selvamoni, S., Patel, V., & Saravanan, P. (2016). Vitamin B12 status among pregnant women in the UK and its association with obesity and gestational diabetes. *Nutrients, 8*(12), 768.
Sun, P. M., Wilburn, W., Raynor, B. D., & Jamieson, D. (2001). Sickle cell disease in pregnancy: twenty years of experience at Grady Memorial Hospital, Atlanta, Georgia. *American journal of obstetrics and gynecology, 184*(6), 1127-1130.
Taal, M. W., Chertow, G. M., Marsden, P. A., Skorecki, K., Alan, S., & Brenner, B. M. (2011). *Brenner and Rector's The Kidney E-Book*: Elsevier Health Sciences.
Tapiero, H., Gate, L., & Tew, K. (2001). Iron: deficiencies and requirements. *Biomedicine & pharmacotherapy, 55*(6), 324-332.
Terrell, D. R., Beebe, L. A., Vesely, S. K., Neas, B. R., Segal, J. B., & George, J. N. (2010). The incidence of immune thrombocytopenic purpura in children and adults: a critical review of published reports. *American journal of hematology, 85*(3), 174-180.
Vichinsky, E. P., Simpson, L. L., & Barss, V. A. (2014). Pregnancy in women with sickle cell disease: Uptodate.
Villers, M. S., Jamison, M. G., De Castro, L. M., & James, A. H. (2008). Morbidity associated with sickle cell disease in pregnancy. *American journal of obstetrics and gyneco-*

logy, 199(2), 125. e121-125. e125.
WHO, C. (2008). Worldwide prevalence of anaemia 1993–2005. *WHO global database on anaemia*.
WHO, U. (2001). UNU. Iron deficiency anaemia: assessment, prevention, and control. *Geneva, WHO*.
Youdim, M., & Ben-Shachar, D. (1987). Minimal brain damage induced by early iron deficiency: modified dopaminergic neurotransmission. *Israel journal of medical sciences, 23*(1-2), 19-25.