



## BÖLÜM 10

# KRONİK BÖBREK HASTALIĞI OLAN GEBELERDE HORMONAL DEĞİŞİKLİKLER

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Son dönem böbrek hastalığı (SDBH) olan kadınlardaki hormonal değişiklikler hem konsepsiyonu, hem de gebeliği etkilemektedir. Bu etki gonadotropin-releasing hormon (GnRH), luteinizan hormon (LH), folikül stimulan hormon (FSH) ve östrojen (E) gibi seks hormonlarının anormal salgılanmasından ortaya çıkmaktadır. Diyabet, tiroid hastalığı, paratiroid hastalığı ve feokromositoma gibi yandaş endokrin patolojilerin varlığı gebeliği daha da karmaşık hale getirmektedir. Bu bölümde ileri derecede böbrek hastalığı olan gebelerde gelişen anormal hormonal patofizyolojiyi ve bu değişikliklerin yönetimi tartışılacaktır. Yine postpartum bakım da ele alınacaktır.

### **SON DÖNEM BÖBREK HASTALIĞI OLAN KADINLARDA KONSEPSİYON**

Son dönem böbrek hastalığı olan kadınlarda hormonal dengesizliklerden ötürü konsepsiyon oldukça karmaşıktır. Tipik olarak GnRH hipotalamus tarafından pulsatil biçimde salgınır. GnRH hipofizden FSH ve LH salgısını uyarır. FSH overde folikül oluşumunu sağlarken; bu etki overden yapılan östrojen ve inhibin tarafından inhibe edilir. LH ise ovulasyonu sağlarken; düşük E seviyesi ovulasyonu baskılamakta, yüksek E ise ovulasyonu uyarmaktadır (Şekil10.1). Eğer fertilizasyon gerçekleşirse, progesteron düzeyi implantasyona yardımcı olmak için artmaktadır. Eğer ovulasyon olmaz ise menstrüel kanamanın gerçekleşmesi için progesteron seviyesi azalmaktadır. Bu hasta popülasyonunda bazı kadınlar normal menstrüel döngüye sahipken, hastaların büyük kısmında oligomenore izlenmektedir. Oligomenoresi olan kadınlar, endometriumda karşılanmamış östrojen uyarısının engellenmesi için progesteron tedavisinden fayda görebilirler. Karşılanmamış östrojen uyarısının polikistik over



ve kan basıncı kontrolü bakımından gebelik öncesinde, gebelikte ve gebelik sonrası dönemde değerlendirilmelidirler. Tiroid hastalığı, hiperparatiroidisi ya da feokromasitoma tanısı olan kadınlar multidisipliner olarak değerlendirilmelidirler.

## KAYNAKLAR

1. Palmer BF, Clegg DJ. Gonadal dysfunction in chronic kidney disease. *Rev Endocr Metab Disord* [Internet]. 2016 [cited 2017 Jan 23]. Available from: <https://doi.org/10.1007/s11154-016-9385-9>
2. Palmer B. Sexual dysfunction in men and women with chronic kidney disease and end-stage kidney disease. *Adv Ren Replace Ther*. 2003;10(1):48–60.
3. Adamczak M, Więcek A. Endocrine disorders in chronic kidney disease. Arici M. Management of chronic kidney disease [Internet]. Berlin: Springer Berlin Heidelberg; 2014 [cited 2016 Dec 30], p. 267–78. Available from: [https://doi.org/10.1007/978-3-642-54637-2\\_19](https://doi.org/10.1007/978-3-642-54637-2_19).
4. Holley JL. The hypothalamic-pituitary axis in men and women with chronic kidney disease. *Adv Chronic Kidney Dis*. 2004;11(4):337–41.
5. Sikora-Grabka E, Adamczak M, Kuczera P, Szotowska M, Madej P, Wiecek A. Serum anti-Müllerian hormone concentration in young women with chronic kidney disease on hemodialysis, and after successful kidney transplantation. *Kidney Blood Press Res*. 2016;41(5):552–60.
6. Palmer BF. Sexual dysfunction in uremia. *J Am Soc Nephrol*. 1999;10(6):1381–8.
7. Basok EK, Atsu N, Rifaioglu MM, Kantarci G, Yildirim A, Tokuc R. Assessment of female sexual function and quality of life in predialysis, peritoneal dialysis, hemodialysis, and renal transplant patients. *Int Urol Nephrol*. 2009;41(3):473–81.
8. Castillo AA, Lew SQ, Smith AM, Bosch JP. Women issues in female patients receiving peritoneal dialysis. *Adv Ren Replace Ther*. 1999;6(4):327–34.
9. Gardner D, Shoback D. Greenspan's basic & clinical endocrinology. 8th ed. New York: McGraw Hill; 2007. p. 662–743.
10. Young W. The Netter collection of medical illustrations. 2nd ed. Philadelphia: Elsevier Saunders; 2011. p. 131–51.
11. Molina P. Endocrine pancreas. In: *Endocrine physiology*. 3rd ed. New York: McGraw Hill; 2010.
12. Kumar V, Abbas AK, Astor JC. Endocrine system. In: *Robbin's basic pathology*. 9th ed. Philadelphia: Elsevier Health Sciences; 2013. p. 716–64.
13. Mingjun C, Huansheng D, Qingjie P, Hongjun W, Xiao D. Progress in early pancreas development and reprogramming of terminally differentiated cells into  $\beta$  cells. *Yi Chuan Hered*. 2014;36(6):511–8.
14. Shanmugasundar G, Bhansali A, Walia R, Dutta P, Upreti V. Comparison of thrice daily biphasic human insulin (30/70) versus basal detemir & bolus aspart in patients with poorly controlled type 2 diabetes mellitus – a pilot study. *Indian J Med Res*. 2012;135: 78–83.
15. Health Quality Ontario. Continuous glucose monitoring for patients with diabetes: an evidence-based analysis. *Ont Health Technol Assess Ser*. 2011;11(4):1–29.
16. Thabit H, Hovorka R. Continuous subcutaneous insulin infusion therapy and multiple daily insulin injections in type 1 diabetes mellitus: a comparative overview and future horizons. *Expert Opin Drug Deliv*. 2016;13(3):389–400.
17. Tomita T. Apoptosis in pancreatic  $\beta$ -islet cells in type 2 diabetes. *Bosn J Basic Med Sci*. 2016;16(3):162–79.
18. Presswala L, Shubrook J. Intensive insulin therapy as the primary treatment for type 2 diabetes. *Clin Diabetes*. 2011;29(4):151–3.



19. Zelmanovitz T, Gerchman F, Balthazar AP, Thomazelli FC, Matos JD, Canani LH. Diabetic nephropathy. *Diabetol Metab Syndr*. 2009;1(1):10.
20. Kumar Pasupulati A, Chitra PS, Reddy GB. Advanced glycation end products mediated cellular and molecular events in the pathology of diabetic nephropathy. *Biomol Concepts*. 2016;7(5-6):293-309.
21. Nasri H, Rafieian-Kopaei M. Diabetes mellitus and renal failure: prevention and management. *J Res Med Sci Off J Isfahan Univ Med Sci*. 2015;20(11):1112-20.
22. Kontomanolis EN, Panagoutsos S, Pasadakis P, Koukouli Z, Liberis A. Chronic renal failure, diabetes mellitus type-II, and gestation: an overwhelming combination. *Clin Exp Obstet Gynecol*. 2016;43(2):276-8.
23. Feldman AZ, Brown FM. Management of type 1 diabetes in pregnancy. *Curr Diab Rep*. 2016;16(8):76.
24. Practice Guidelines. ACOG releases guideline on gestational diabetes. *Am Fam Physician*. 2014;90(6):416-7.
25. Kimmerle R, Zass RP, Cupisti S, Somville T, Bender R, Pawlowski B, et al. Pregnancies in women with diabetic nephropathy: long-term outcome for mother and child. *Diabetologia*. 1995;38(2):227-35.
26. Jones DC, Hayslett JP. Outcome of pregnancy in women with moderate or severe renal insufficiency. *N Engl J Med*. 1996;335(4):226-32.
27. Purdy LP, Hantsch CE, Molitch ME, Metzger BE, Phelps RL, Dooley SL, et al. Effect of pregnancy on renal function in patients with moderate-to-severe diabetic renal insufficiency. *Diabetes Care*. 1996;19(10):1067-74.
28. Helen CCT, Tajunisah I, Reddy SC. Adverse outcomes in Type I diabetic pregnant women with proliferative diabetic retinopathy. *Int J Ophthalmol*. 2011;4(4):443-6.
29. American Diabetes Association. 13Management of diabetes in pregnancy. *Diabetes Care*. 2017;40(Suppl 1):S114-9.
30. Lipska KJ, Bailey CJ, Inzucchi SE. Use of metformin in the setting of mild-to-moderate renal insufficiency. *Diabetes Care*. 2011;34(6):1431-7.
31. Davies M, Chatterjee S, Khunti K. The treatment of type 2 diabetes in the presence of renal impairment: what we should know about newer therapies. *Clin Pharmacol Adv Appl*. 2016;8:61-81.
32. Hendrick van D, Soldin SJ. *Advances in clinical chemistry*. 1st ed. Vol. 61. San Diego: Academic; 2013. p. 241.
33. Stockigt JR. Free thyroid hormone measurement. *Endocrinol Metab Clin N Am*. 2001;30(2):265-89.
34. Cooper DS, Laurberg P. Hyperthyroidism in pregnancy. *Lancet Diabetes Endocrinol*. 2013;1(3):238-49.
35. Moleti M, Trimarchi F, Vermiglio F. Thyroid physiology in pregnancy. *Endocr Pract*. 2014;20(6):589-96.
36. Soldin OP, Soldin SJ. Thyroid hormone testing by tandem mass spectrometry. *Clin Biochem*. 2011;44(1):89-94.
37. De Groot L, Abalovich M, Alexander EK, Amino N, Barbour L, Cobin RH, et al. Management of thyroid dysfunction during pregnancy and postpartum: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2012;97(8):2543-65.
38. Smith TJ, Hegedüs L. Graves' disease. Longo DL, editor. *N Engl J Med*. 2016;375(16):1552-65.
39. Chang DLF, Pearce EN. Screening for maternal thyroid dysfunction in pregnancy: a review of the clinical evidence and current guidelines. *J Thyroid Res*. 2013;2013:1-8.
40. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, et al. 2016 Guidelines of the



- American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid* [Internet]. 2017 [cited 2017 Jan 19]. Available from: <https://doi.org/10.1089/thy.2016.0457>.
41. Manisco G, Poti' M, Maggiulli G, Di Tullio M, Losappio V, Vernaglione L. Pregnancy in end-stage renal disease patients on dialysis: how to achieve a successful delivery. *Clin Kidney J*. 2015;8(3):293–9.
  42. Screening for maternal thyroid dysfunction in pregnancy: a review of the clinical evidence and current guidelines. [Internet]. [Cited 2016 Dec 30]. Available from: <https://www.hindawi.com/journals/jtr/2013/851326/abs/>.
  43. Goodman WG, Quarles LD. Development and progression of secondary hyperparathyroidism in chronic kidney disease: lessons from molecular genetics. *Kidney Int*. 2008;74(3):276–88.
  44. Bakas P, Chados N, Hassiakos D, Creatsa M, Liapis A, Creasas G. Secondary hypoparathyroidism during pregnancy – a case report and review of the literature. *Clin Exp Obstet Gynecol*. 2014;42(6):825–6.
  45. Hussain S, Savin V, Piering W, Tomasi J, Blumenthal S. Phosphorus-enriched hemodialysis during pregnancy: two case reports. *Hemodial Int*. 2005;9(2):147–52.
  46. Kirby BJ, Ma Y, Martin HM, Buckle Favaro KL, Karaplis AC, Kovacs CS. Upregulation of calcitriol during pregnancy and skeletal recovery after lactation do not require parathyroid hormone: PTH DURING PREGNANCY AND LACTATION. *J Bone Miner Res*. 2013;28(9):1987–2000.
  47. Souberbielle J-C, Cavalier E, Delanaye P, Massart C, Brailly-Tabard S, Cormier C, et al. Serum calcitriol concentrations measured with a new direct automated assay in a large population of adult healthy subjects and in various clinical situations. *Clin Chim Acta*. 2015;451:149–53.
  48. Scholl TO, Chen X, Stein TP. Vitamin D, secondary hyperparathyroidism, and preeclampsia. *Am J Clin Nutr*. 2013;98(3):787–93.
  49. Podymow T, August P, Akbari A. Management of renal disease in pregnancy. *Obstet Gynecol Clin N Am*. 2010;37(2):195–210.
  50. Vera L, Oddo S, Di Iorgi N, Bentivoglio G, Giusti M. Primary hyperparathyroidism in pregnancy treated with cinacalcet: a case report and review of the literature. *J Med Case Rep* [Internet]. 2016 [cited 2017 Jan 5];10(1):361. Available from: <https://doi.org/10.1186/s13256-016-1093-2>.
  51. Nadarasa K, Bailey M, Chahal H, Raja O, Bhat R, Gayle C, et al. The use of cinacalcet in pregnancy to treat a complex case of parathyroid carcinoma. *Endocrinol Diabetes Metab Case Rep* [Internet]. 2014 [cited 2017 Jan 5]. Available from: <https://doi.org/10.1530/EDM-14-0056>
  52. Kovacs CS, Kronenberg HM. Maternal-fetal calcium and bone metabolism during pregnancy, puerperium, and lactation. *Endocr Rev*. 1997;18(6):832–72.
  53. Balzer MS, Gross MM, Lichtinghagen R, Haller H, Schmitt R. Got milk? Breastfeeding and milk analysis of a mother on chronic hemodialysis. Sands JM, editor. *PLoS One*. 2015;10(11):e0143340.
  54. Kiernan CM, Solórzano CC. Pheochromocytoma and paraganglioma: diagnosis, genetics, and treatment. *Surg Oncol Clin N Am*. 2016;25(1):119–38.
  55. Wyskida M, Wyskida K, Maruniak-Chudek I, Sikora J, Chudek J. Pheochromocytoma in pregnancy. *Postepy Hig Med Dosw Online*. 2014;68:749–53.
  56. Weingarten M, Rao S, Lincoln K. Successful management of phaeochromocytoma in the



- third trimester of pregnancy with the use of rapid sequential alpha-adrenergic blockage. *Eur J Obstet Gynecol Reprod Biol.* 2016;198:174–5.
57. Memon MA, Aziz W, Abbas F. Surgical management of pheochromocytoma in a 13-week pregnant woman. *BMJ Case Rep.* 2014;2014.
  58. Mohamed Ismail NA, Abd Rahman R, Abd Wahab N, Muhammad R, Nor Azmi K. Pheochromocytoma and pregnancy: a difficult and dangerous ordeal. *Malays J Med Sci.* 2012;19(1):65–8.
  59. Adenekan A, Faponle A, Badmus T, Sanusi A. Anaesthetic management of giant phaeochromocytoma in a patient with chronic renal disease. *J West Afr Coll Surg.* 2011;1(2):112–22.
  60. Centers for Disease Control Prevention (CDC). National diabetes statistics report 2014. [Internet]. Centers for Disease Control Prevention; 2014 [Cited 2016 Jun 9]. Available from: <http://www.cdc.gov/diabetes/data/statistics/2014statisticsreport.html>.