

Gebelik ve Laktasyonda Tiroid Kanseri

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Özet

Tüm dünyada sıklığı gittikçe artan tiroid kanseri üreme çağındaki kadınları da sıklıkla etkilemektedir. Gebelikte tiroid kanseri iki farklı klinik olarak karşımıza çıkabilir. Daha önce tiroid kanseri tanısı almış ve takip altındaki hastalarda gebelik söz konusu olabileceği gibi tiroid kanseri tanısı ilk defa gebelikte de konabilir. Bu hastalarda göz önünde bulundurması gereken konular gebeliğin hastalık seyri üzerine etkisi, optimal tedavi zamanlaması ve tedavilerin hem anne hem de bebekte oluşturabileceği risklerdir. Gebelikte tiroid nodüllerine ve tiroid kanserine yaklaşım, radyoaktif iyot görüntüleme ve tedavisinin kontrendike olması dışında genel popülasyonla benzerdir. Genel olarak gebeliğin tiroid kanserinin daha agresif seyretmesine neden olmadığı ve prognozu kötüleştirmediği kabul edilmektedir. Gebelikte ikinci üç aylık dönemde cerrahi güvenli bir şekilde yapılabilse de, klinik ve ultrasonografik olarak yüksek risk özellikleri taşımayan iyi diferansiye tiroid kanserlerinde çoğunlukla cerrahi gebelik sonrasına ertelenebilir. Tiroid kanserinin doğurganlık ve gebelik sonuçları üzerine etkileri ile ilgili çalışmalarda farklı sonuçlar elde edilmiş, fakat geniş çaplı çalışmalarda genel olarak olumsuz etkisi olmadığı gösterilmiştir. Düşük riskini önlemek ve rezidü hastalık varsa tespit edilmesini sağlamak için radyoaktif iyot tedavisinden sonra 6-12 ay gebe kalınmaması önerilmektedir.

gebeliğin tiroid kanseri gelişimi veya progresyonu üzerine olumsuz etkileri bildirilmişse de geniş çaplı çalışmalar ve metaanalizler gebeliğin yeni tanı almış, tedavi edilmiş veya aktif takip edilen DTK'nde klinik olarak ilerleme ile ilişkili olmadığını göstermiştir. Gebelikte tiroid kanseri saptandığında bir çok hastada olduğu gibi yüksek risk oluşturabilecek agresif özellikler yoksa cerrahinin doğum sonrasına ertelenmesi önerilmektedir. Yüksek risk nedeniyle cerrahiye karar verilirse

cerrahi, ikinci üç aylık dönemde güvenli bir şekilde yapılabilir. Tiroid kanseri tedavisi görmüş ve yapısal veya biyokimyasal rekürensi olmayan hastalarda gebeliğin hastalık üzerine etkisi yoktur. Rekürensi olan hastaların ise düşük de olsa progresyon riski nedeniyle gebelik süresince yakın takip edilmesi gereklidir. RAİ tedavisi gebelikte ve emzirme durumunda kontrendikedir ve RAİ tedavisi alan hastaların en az 6-12 ay gebe kalmaları önerilmektedir.

Kaynaklar

1. <https://seer.cancer.gov/statfacts/html/thyro.html> (Erişim tarihi: 8 Temmuz 2019)
2. Shim MH, Mok CW, Chang KH, et al. Clinical characteristics and outcome of cancer diagnosed during pregnancy. *Obstet Gynecol Sci* 2016;59(1):1-8.
3. de Haan J, Verheecke M, Van Calsteren K, et al. International Network on Cancer and Infertility Pregnancy (INCIP). Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. *Lancet Oncol* 2018;19(3):337-46.
4. Lee YY, Roberts CL, Dobbins T, et al. Incidence and outcomes of pregnancy-associated cancer in Australia, 1994–2008: A populationbased linkage study. *BJOG*. 2012;119:1572-82.
5. Smith LH, Danielsen B, Allen ME, et al. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. *Am J Obstet Gynecol* 2003;189:1128-35.
6. Gibelli B, Zamperini P, Proh M, et al. Management and follow-up of thyroid cancer in pregnant women. *Acta Otorhinolaryngol Ital*. 2011;31(6):358-65.
7. Negri E, Dal Maso L, Ron E, et al. A pooled analysis of case-control studies of thyroid cancer. II. Menstrual and reproductive factors. *Cancer Causes Control* 1999;10(2):143-55.
8. Horn-Ross PL, Canchola AJ, Ma H, et al. Hormonal factors and the risk of papillary thyroid cancer in the California teachers study cohort. *Cancer Epidemiol Biomarkers Prev* 2011;20(8):1751-9.
9. Zamora-Ros R, Rinaldi S, Biesy C, et al. Reproductive and menstrual factors and risk of differentiated thyroid carcinoma: the EPIC study. *Int J Cancer* 2015;136(5):1218-27.
10. Glinioer D, Soto MF, Bourdoux Pet al. Pregnancy in patients with mild thyroid abnormalities: maternal and neonatal repercussions. *J Clin Endocrinol Metab* 1991;73:421-7.
11. Kung AW, Chau MT, Lao TT, et al. The effect of pregnancy on thyroid nodule formation. *J Clin Endocrinol Metab* 2002;87:1010-4.
12. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines-Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016;26(1):1-133.
13. Tan GH, Gharib H, Goellner JR, et al. Management of thyroid nodules in pregnancy. *Arch Intern Med* 1996;156:2317-20.
14. Marley EF, Oertel YC. Fine-needle aspiration of thyroid lesions in 57 pregnant and postpartum women. *Diagn Cytopathol* 1997;16:122-5.
15. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. *Thyroid*. 2017;27(3):315-89
16. Zhou YQ, Zhou Z, Qian MF, et al. Association of thyroid carcinoma with pregnancy: A meta-analysis. *Mol Clin Oncol* 2015;3(2):341-6.
17. Lee M L, Chen GG, Vlantis AC, et al. Induction of thyroid papillary carcinoma cell proliferation by estrogen is associated with an altered expression of Bcl-xL. *Cancer Journal* 2004;11(2):113-121.
18. Yoshimura M, Hershman JM. Thyrotropic action of human chorionic gonadotropin. *Thyroid* 1995;5:425-34.
19. Dalla Valle L, Ramina A, Vianello S, et al. Potential for estrogen synthesis and action in human normal and neoplastic thyroid tissues. *J Clin Endocrinol Metab* 1998;83:3702-9.
20. Del Senno L, Degli Uberti E, Hanau S, et al. In vitro effects of estrogen on tgb and c-myc gene expression in normal and neoplastic human thyroids. *Molecular and Cellular Endocrinology* 1989;63(1-2):67-74.
21. McTiernan AM, Weiss NS, Daling JR. Incidence of thyroid cancer in women in relation to reproductive and hormonal factors. *American Journal of Epidemiology*, 1984;120(3):423-35.
22. Mack WJ, Preston-Martin S, Bernstein L, et al. Reproductive and hormonal risk factors for thyroid cancer in Los Angeles County females. *Cancer Epidemiology Biomarkers and Prevention* 1999;8(11):991-7.
23. Chen AJ, Livhits MJ, Du L, et al. Recent pregnancy is not associated with high risk pathological features of well differentiated thyr-

- id cancer. *Thyroid* 2018;28:68-71.
24. Yasmeen S, Cress R, Romano PS, et al. Thyroid cancer in pregnancy. *Int J Gynecol Obstet* 2005;91:15-20.
 25. Herzon FS, Morris DM, Segal MN, et al. Coexistent thyroid cancer and pregnancy. *Archives of Otolaryngology-Head and Neck Surgery* 1994;120:1191-3.
 26. Moosa M, Mazzaferri EL. Outcome of differentiated thyroid cancer diagnosed in pregnant women. *J Clin Endocrinol Metab* 1997;82:2862-6.
 27. Uruno T, Shibuya H, Kitagawa W, et al. Optimal timing of surgery for differentiated thyroid cancer in pregnant women. *World J Surg* 2014;38(3):704-8.
 28. Doherty CM, Shindo ML, Rice DH, et al. Management of thyroid nodules during pregnancy. *Laryngoscope* 1995;105:251-5.
 29. Ito Y, Miyauchi A, Kudo T, et al. Effects of Pregnancy on Papillary Microcarcinomas of the Thyroid Re-Evaluated in the Entire Patient Series at Kuma Hospital. *Thyroid* 2016;26:156-60.
 30. Vannucchi G, Perrino M, Rossi S, et al. Clinical and molecular features of differentiated thyroid cancer diagnosed during pregnancy. *Eur J Endocrinol* 2010;162:145-51.
 31. Messuti I, Corvisieri S, Bardesono F, et al. Impact of pregnancy on prognosis of differentiated thyroid cancer: clinical and molecular features. *Eur J Endocrinol* 2014;170:659-66.
 32. Khaled H, Al Lahloubi N, Rashad N. A review on thyroid cancer during pregnancy: Multitasking is required. *J Adv Res.* 2016;7(4):565-70.
 33. Papini E, Negro R, Pinchera A, et al. Thyroid nodule and differentiated thyroid cancer management in pregnancy. An Italian Association of Clinical Endocrinologists (AME) and Italian Thyroid Association (AIT) joint statement for clinical practice. *J Endocrinol Invest* 2010;33 (8):579-86.
 34. Soldin OP, Tractenberg RE, Hollowell JG, et al. Trimester-specific changes in maternal thyroid hormone, thyrotropin, and thyroglobulin concentrations during gestation: trends and associations across trimesters in iodine sufficiency. *Thyroid* 2004;14(12):1084-90.
 35. Rosvoll RV, Winship T. Thyroid carcinoma and pregnancy. *Surg Gynecol Obstet* 1965;121:1039-42.
 36. Hill CS, Clark RL, Wolf M. The effect of subsequent pregnancy on patients with thyroid carcinoma. *Surg Gynecol Obstet* 1966;122:1219-22.
 37. Rosário PW, Barroso AL, Purisch S. The effect of subsequent pregnancy on patients with thyroid carcinoma apparently free of the disease. *Thyroid* 2007;17(11):1175-6.
 38. Imran SA, Rajarama M. Management of Differentiated Thyroid Cancer in Pregnancy *J Thyroid Res* 2011;2011:549609.
 39. Shindo H, Amino N, Ito Y, et al. Papillary thyroid microcarcinoma might progress during pregnancy. *Thyroid* 2014;24(5):840-4.
 40. Leboeuf R, Emerick LE, Martorella AJ, et al. Impact of pregnancy on serum thyroglobulin and detection of recurrent disease shortly after delivery in thyroid cancer survivors. *Thyroid* 2007;17:543-7.
 41. Budak A, Gulhan I, Aldemir OS, Ileri A, Ozeren M. Lack of influence of pregnancy on the prognosis of survivors of thyroid cancer. *Asian Pacific J Cancer Prevent APJCP* 2013;14:641-3.
 42. Hirsch D, Levy S, Tsvetov G, et al. Impact of pregnancy on outcome and prognosis of survivors of papillary thyroid cancer. *Thyroid* 2010;20(10):1179-85.
 43. Rakhlin L, Fish S, Tuttle RM. Response to Therapy Status Is an Excellent Predictor of Pregnancy-Associated Structural Disease Progression in Patients Previously Treated for Differentiated Thyroid Cancer. *Thyroid* 2017;27(3):396-401.
 44. Cho GJ, Kim SY, Lee HC, et al. Risk of adverse obstetric outcomes and the abnormal growth of offspring in women with a history of thyroid cancer. *Thyroid* 2019;29(6):879-85.
 45. Haymart MR, Pearce EN. How much should thyroid cancer impact plans for pregnancy? *Thyroid* 2017;27(3):312-4.
 46. Patel J, Landers K, Li H, et al. Thyroid hormones and fetal neurological development. *J Endocrinol* 2011;209:1-8.
 47. Casey BM, Dashe JS, Wells CE, McIntire DD, et al. Subclinical hyperthyroidism and pregnancy outcomes. *Obstetrics and Gynecology* 2006;107(2):337-41.
 48. Sisson JC, Freitas J, McDougall IR, et al. Radiation safety in the treatment of patients with thyroid diseases by radioiodine 131I: practice recommendations of the American Thyroid Association. *Thyroid* 2011;21:335-46.
 49. Bernard N, Jantzen H, Becker M, et al. Severe adverse effects of bromocriptine in lactation inhibition: a pharmacovigilance survey. *BJOG* 2015;122:1244-51.
 50. Bal C, Kumar A, Tripathi M, et al. High-dose radioiodine treatment for differentiated thyroid carcinoma is not associated with change in female fertility or any genetic risk to the offspring. *Int J Radiat Oncol Biol Phys* 2005;63:449-55.
 51. Dottorini ME, Lomuscio G, Mazzucchelli L, et al. Assessment of female fertility and carcinogenesis after I-131 therapy for differentiated thyroid cancer. *J Nucl Med* 1995;36:21-7.
 52. Anderson C, Engel SM, Weaver MA, et al. Birth rates after radioactive iodine treatment for differentiated thyroid cancer. *Int J Cancer.* 2017;141(11):2291-5.
 53. Raymond JP, Izembart M, Marliac V, et al. Temporary ovarian failure in thyroid cancer patients after thyroid remnant ablation with radioactive iodine. *J Clin Endocrinol Metab.* 1989; 69:186-90.
 54. Sawka AM, Lakra DC, Lea J, et al. A systematic review examining the effects of therapeutic radioactive iodine on ovarian function and future pregnancy in female thyroid cancer survivors. *Clin Endocrinol (Oxf).* 2008;69(3):479-90.
 55. Souza Rosário PW, Alvarenga Fagundes T, Villas-Boas Fagundes AS, et al. Ovarian function after radioiodine therapy in patients with thyroid cancer. *Exp Clin Endocrinol Diabetes* 2005;113:331-3
 56. Ceccarelli C, Bencivelli W, Morciano D, et al. 131I therapy for differentiated thyroid cancer leads to an earlier onset of menopause: results of a retrospective study.

- J Clin Endocrinol Metab 2001; 86:3512-5.
57. Ko KY, Yen RF, Lin CL, et al. Pregnancy Outcome After I-131 Therapy for Patients With Thyroid Cancer: A Nationwide Population-Based Cohort Study. *Medicine (Baltimore)*. 2016;95(5):e2685.
 58. Wu JX, Young S, Ro K, et al. Reproductive outcomes and nononcologic complications after radioactive iodine ablation for well-differentiated thyroid cancer. *Thyroid* 2015;25:133-8.
 59. Yaish I, Azem F, Gutfeld O, et al. A Single Radioactive Iodine Treatment Has a Deleterious Effect on Ovarian Reserve in Women with Thyroid Cancer: Results of a Prospective Pilot Study. *Thyroid* 2018;28(4):522-7.
 60. Evranos B, Faki S, Polat SB, et al. Effects of Radioactive Iodine Therapy on Ovarian Reserve: A Prospective Pilot Study. *Thyroid* 2018; Sep 29. doi: 10.1089/thy.2018.0129. [Epub ahead of print]
 61. Garsi JP, Schlumberger M, Rubino C, et al. Therapeutic administration of 131I for differentiated thyroid cancer: radiation dose to ovaries and outcome of pregnancies. *J Nucl Med* 2008;49:845-52.
 62. Schlumberger M, De Vathaire F, Ceccarelli C, et al. Exposure to radioactive iodine-131 for scintigraphy or therapy does not preclude pregnancy in thyroid cancer patients. *J Nucl Med* 1996;37(4):606-12.