Chapter 8

PREECLAMPSIA: PREDICTION AND PATHOPHYSIOLOGY

Faika Ceylan ÇİFTÇİ¹

INTRODUCTION

Preeclampsia (PE) is pregnancy-specific and represents one of the most important causes of maternal morbidity and mortality, affecting between 3-5% of all the pregnancies in the world. If PE is untreated it can also develop eclampsia. PE is characterized by the impairment of general vascular dilatation (Ciftci & etal., 2014). World Health Organization estimates that, worldwide, over 100.000 women die from preeclampsia each year (Soydemir F& Kenny L., 2006). It is known that the insufficiency of trophoblast invasion in early pregnancy leads to the impairment of angiogenesis of the mother, as well as upsetting the balance between nitric oxide and reactive oxygen products which controls vascular tonus and the coagulation cascade. This situation leads to the emergence of the clinical manifestations of the disease. The primary cause of the impaired circulatory homeostasis in PE is endothelial dysfunction. As a result; a maternal reaction occurs which involves endothelial cell dysfunction caused by the stimulated inflammatory response and hypertension development. It has been shown that significant oxidative stress is produced even before the beginning of PE, and this may play an important role in vasoconstriction which results in endothelial dysfunction (Ciftci & etal., 2014). It has been shown recently that patients with PE face an increased risk of developing cardiovascular diseases in later years (Ciftci & etal., 2014). Pre-eclampsia condition is defined by the sudden onset of hypertension (systolic blood pressure (BP) of >140 mm Hg and diastolic BP of >90 mm Hg, taken on two separate occasions at least 4-6 hours apart) and significant proteinuria (excretion of 300 mg or more of protein every 24 hours) after the 20th week of gestation (Hoodbhoy & etal., 2018).

Hypertension and proteinuria are essential for the diagnosis. Hypertensive disorders during pregnancy are chronic hypertension (High BP predating the pregnancy), gestational hypertension (When de novo HTN is present after 20

¹ Op.Dr. ,Koru Hospital/Ankara, faikaceylanciftci@gmail.com

lo-Ortega & et al., 2011). Antioxidant vitamins alone do not protect against preeclampsia (Brantsæter & et al.,2011). Outcomes from the Norwegian Mother and Child Cohort Study shows that supplementation of milk-based probiotics may decrease the risk of preeclampsia in primiparous women (Friedma, Lubarsky & Lim,2011).

PROGNOSIS

Preeclampsia and eclampsia are approximated to be responsible for about 14% of maternal deaths per year (50,000-75,000) worldwide (Butalia & etal.,2018). Morbidity and mortality in preeclampsia and eclampsia are correlated to systemic endothelial dysfunction, vasospasm and small-vessel thrombosis leading to tissue and organ ischemia together with seizures, strokes, intracerebral hemorrhage, acute tubular necrosis, coagulopathies, and placental abruption. Fetal exposure to preeclampsia is combined with a greater than twofold increase in the risk of autism spectrum disorder and a greater than fivefold increase in the risk of developmental delay. (Walker & etal, 2015), (Sullivan & et al.,1994).

RECURRENCE

Overall, the recurrence risk of preeclampsia in a woman whose previous pregnancy was complicated by preeclampsia near term is around 10%. The recurrence risk of preeclampsia in a woman whose previous pregnancy was complicated by preeclampsia with severe features (Including HELLP, eclampsia) is approximately 20%. If a woman has had HELLP syndrome or eclampsia, the recurrence risk of HELLP syndrome is 5% and of eclampsia, it is 2% (Chames & et al., 2003). If preeclampsia appeared clinically before 30 weeks' gestation, the possibility of recurrence may be as high as 40% (von Dadelszen & etal., 2011).

REFERENCES

- ACOG. (2013). Hypertension in Pregnancy Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. [Executive Summary]. The American College of Obstetricians and Gynecologists, 122 (5), 1122-1131.
- Bartsch, E& Medcalf, KE& Park, AL& Ray, JG. (2016) High Risk of Pre-eclampsia Identification Group. Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and metaanalysis of large cohort studies. BMJ 353:1753.
- Baum, M& Schiff, E& Kreiser, D& Dennery, PA& Stevenson, DK& Rosenthal, T& Seidman, DS. (2000) End-tidal carbon monoxide measurements in women with pregnancy-induced hypertension and preeclampsia. Am J Obstet Gynecol. 183 (4):900-3
- Brantsæter, AL. & Myhre, R. & Haugen, M. & et al. Intake of probiotic food and risk of preeclampsia in primiparous women: the norwegian mother and child cohort study. (2011) Am J Epidemiol. 174 (7):807-15.

- Butalia, S. & Audibert, F. & Côté, AM. & Firoz, T. & Logan, AG. & etal. Hypertension Canada's 2018 Guidelines for the Management of Hypertension in Pregnancy. (2018) Can J Cardiol. 34 (5):526-531. doi: 10.1016/j.cjca.2018.02.021.
- Chames, MC. & Haddad, B. & Barton, JR. & et al. Subsequent pregnancy outcome in women with a history of HELLP syndrome at < or = 28 weeks of gestation. (2003)*Am J Obstet Gynecol.* 188 (6):1504-7
- Chappell, LC& Duckworth, S& Seed, PT& Griffin, M& Myers J, & etal. (2013) Diagnostic accuracy of placental growth factor in women with suspected preeclampsia: a prospective multicenter study. Circulation. 5;128 (19):2121-31. doi: 10.1161/CIRCU-LATIONAHA.113.003215.
- Ciftci FC& Caliskan, M& Ciftci, O& Gullu, H& Uckuyu, A& etal. (2014) Impaired coronary microvascular function and increased intima-media thickness in preeclampsia. J Am Soc Hypertens. 8 (11):820-6. doi:10.1016/j.jash.2014.08.012.
- Cnossen,SJ& Morris, RK& Riet, G& Mol, WJ& Joris AM. et al. (2003) Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. Can Med Assoc J 2008;178 (6):701–711
- Conde-Agudelo, A& Villar, J& Lindheimer, M. (2004) World Health Organization systematic review of screening tests for preeclampsia. Obstet Gynecol. doi: 10.1097/01. AOG.0000147599.47713.5d
- Coomarasamy, A. & Honest, H. & Papaioannou, S. & et al. Aspirin for prevention of preeclampsia in women with historical risk factors: a systematic review. Obstet Gynecol. 101 (6):1319-32
- Dadelszen, PV. & Payne, B. & Li, J. & Ansermino, JM. & Broughton, PF. & et al. Prediction of adverse maternal outcomes in pre-eclampsia: development and validation of the fullPIERS model. (2011) *Lancet.* 377 (9761):219-27.
- Dawonauth, L& Rademacher, L& L'Omelette, A& Jankee, S& Yan, M. et al. (2014) Urinary inositol phosphoglycan-P type: Near patient test to detect preeclampsia prior to clinical onset of the disease. A study on 416 pregnant Mauritian women. J Reprod Immunol 101:148–152
- Duckitt, K& Harrington, D. (2005) Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies BMJ.330 (7491): 565. doi: 10.1136/ bmj.38380.674340.E0
- Friedman, SA. & Lubarsky, SL. & Lim, KH. (2001) Mild Gestational Hypertension and Preeclampsia. Sibai BM, (Ed). In *Hypertensive Disorders in Women*. (9-23) Philadelphia: W.B. Saunders.
- Hoodbhoy Z, Hasan BS, Mohammed N, Chowdhury D. (2018) Impact of pre-eclampsia on the cardiovascular health of the offspring: a cohort study protocol. BMJ Open. Sep 26;8 (9):e024331. doi: 10.1136/bmjopen-2018-024331.
- Khalil, G& Hameed, A. (2017) Preeclampsia: Pathophysiology and the Maternal-Fetal Risk. J Hypertens Manag 3:024. doi.org/10.23937/2474-3690/1510024
- LaMarca, B& Cornelius, D& Wallace, K. (2013) Elucidating immune mechanisms causing hypertension during pregnancy. Physiology (Bethesda).28 (4):225-33. doi: 10.1152/physiol.00006.2013
- Levine, RJ& Lam, C& Qian, C& Yu, KF& Maynard, SE& etal. CPEP Study Group. (2006) Soluble endoglin and other circulating antiangiogenic factors in preeclampsia. N Engl J Med. 7;355 (10):992-1005.

- Levine, RJ& Maynard, SE& Qian, C& Lim, KH& England, LJ& etal. (2004) Circulating angiogenic factors and the risk of preeclampsia. N Engl J Med. 12;350 (7):672-83.
- Maine Medical Center (2017) (Accessed at https://mainehealth.org/-/media/mainehealth/ pdfs/clinical-guidelines-and-resources/obstetrical-perinatal-guidelines/hypertensive-disorders-in-pregnancy- (1).pdf?la=en on 10-02-2019)
- Malik, A& Jee, B& Gupta, S.K. (2019) Preeclampsia: Disease biology and burden, its management strategies with reference to India Pregnancy Hypertension 15, 23–31
- Maynard, SE& Min, JY& Merchan, J& Lim, KH& Li J, etal. (2003) Excess placental soluble fms-like tyrosine kinase 1 (sFlt1) may contribute to endothelial dysfunction, hypertension, and proteinuria in preeclampsia. J Clin Invest. 111 (5):649-58.
- Mirković, L& Nejković, L& Micić, J. (2018) A new pathophysiological concept and new classification of pre-eclampsia Vojnosanit Pregl. 75 (1): 83–94.
- Naljayan, MV& Karumanchi, SA. (2013) New developments in the pathogenesis of preeclampsia. Adv Chronic Kidney Dis. 20 (3):265-70. doi: 10.1053/j.ackd.2013.02.003.
- Palei, AC& Spradley, FT& Warrington, JP& George, EM& Granger JP. (2013) Pathophysiology of hypertension in pre-eclampsia: a lesson in integrative physiology. Acta Physiol 208, 224-233
- Phipps E, Prasanna D, Brima W, Jim B. (2016). PreeclampsiaUpdates in Pathogenesis, Definitions, and Guidelines. Clin J Am Soc Nephrol. 6;11 (6):1102-13. doi: 10.2215/ CJN.12081115.
- Ramos JGL, Sass N, Costa SHM. Preeclampsia. (2017) Rev Bras Ginecol Obstet. Sep;39 (9):496-512. doi: 10.1055/s-0037-1604471.
- Roberge, S. & Demers, S. & Nicolaides, KH. & Bureau, M. & etal. Prevention of pre-eclampsia by low-molecular weight heparin in addition to aspirin: a meta-analysis. (2015) Ultrasound Obstet Gynecol.
- Sibai, BM. & Caritis, SN. & Thom, E. & et al. Prevention of preeclampsia with low-dose aspirin in healthy, nulliparous pregnant women. The National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. (1993) N Engl J Med.329 (17):1213-8.
- Soydemir F& Kenny L. (2006) Hypertension in pregnancy. Current Obstetrics & Gynaecology doi:10.1016/j.curobgyn.2006.09.007
- Sullivan, CA. & Magann, EF. Perry, KG. et al. The recurrence risk of the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP) in subsequent gestations. (1994)*Am J Obstet Gynecol.* 171 (4):940-3.
- Tannetta, D& Sargent,I. (2013) Placental Disease and the Maternal Syndrome of Preeclampsia: Missing Links? Curr Hypertens Rep. 15 (6): 590–599. doi: 10.1007/s11906-013-0395-7
- Ukah, UV& Payne, B & Côté, AM & Hoodbhoy, Z& Dadelszen, P. (2016) Risk factors and predictors of pre-eclampsia Magee LA, Dadelszen PV, Stones W, Mathai M. The FIGO Textbook of Pregnancy Hypertension (75-100). Printed in the UK by CPI Group.
- Uzan, J& Carbonnel, M& Piconne, O& Asmar, R& Ayoubi JM. (2011) Pre-eclampsia: pathophysiology, diagnosis, and management. Vasc Health Risk Manag. 7:467-74. doi: 10.2147/VHRM.S20181.
- Vadillo-Ortega, F. & Perichart-Perera, O. & Espino, S. & et al. Effect of supplementation during pregnancy with L-arginine and antioxidant vitamins in medical food on pre-eclampsia in high risk population: randomised controlled trial. (2011) *BMJ*. 19. 342:d2901.

- Vahdat, M& Kashanian, M& Sariri, E& Mehdinia, M. (2012) Evaluation of the value of calcium to creatinine ratio for predicting of pre-eclampsia. J Matern Fetal Neonatal Med 25 (12):2793–2794 doi: 10.3109/14767058.2012.712561
- Venkatesha, S& Toporsian, M& Lam, C& Hanai, J& Mammoto, T& et al. (2006) Soluble endoglin contributes to the pathogenesis of preeclampsia. *Nat Med.* 12 (6):642-9
- Villar, J. & Abdel-Aleem, H. & Merialdi, M. & et al. World Health Organization randomized trial of calcium supplementation among low calcium intake pregnant women. (2006) Am J Obstet Gynecol. 194 (3):639-49.
- Walker, CK. & Krakowiak, P. & Baker, A. & Hansen, RL. Ozonoff, S. & Hertz-Picciotto, I. Preeclampsia, placental insufficiency, and autism spectrum disorder or developmental delay. (2015)*JAMA Pediatr*. 169 (2):154-62
- Wright, D. & Rolnik, DL. & Syngelaki, A. & de Paco, MC. & Machuca M, et al. Aspirin for Evidence-Based Preeclampsia Prevention trial: effect of aspirin on length of stay in the neonatal intensive care unit. (2018) Am J Obstet Gynecol. Jun. 218 (6):612. e1-612.e6.