

Anxiety during Pregnancy and Preeclampsia: A Case-Control Study

Masoumeh Kordi (MSc)¹, Azra Vahed (MSc)^{2*}, Fariborz Rezaee Talab (MD)³, Seyed Reza Mazloum (MSc)⁴, Marzieh Lotfalizadeh (MD)⁵

¹ Assistant Professor, Department of Midwifery, School of Nursing and Midwifery, Mashhad, Mashhad University of Medical Sciences, Mashhad, Iran

² MSc Student, Department of Midwifery, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran

³ Assistant Professor, Department of Neurological Diseases, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

⁴ Instructor of Nursing, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran

⁵ Associate Professor, Department of Obstetrics and Gynecology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

ARTICLE INFO

Article type:
Original article

Article History:
Received: 04-Nov-2015
Accepted: 11-Apr-2016

Key words:
Anxiety
Preeclampsia
Pregnancy

ABSTRACT

Background & aim: Preeclampsia is a common and dangerous complication of pregnancy, the reason for which remains unknown. Multiple factors such as depression, as well as psychological and physical stress may be involved in its development. This study was performed to determine the relationship between anxiety during pregnancy and the incidence of preeclampsia.

Methods: This case-control study was conducted on 150 pregnant women with preeclampsia and 150 healthy pregnant women, who were all referred to health centers and university hospitals of Mashhad in 2014. The diagnosis of preeclampsia was made by systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg accompanied with urinary protein excretion more than 300 mg/24 h. The cutoff point for the presence of anxiety was the score of ≥ 8 ; the score of 8-9 was mild anxiety, and the score of 20 indicated very severe anxiety. Data collection tools included a form of demographic characteristics, clinical and laboratory signs of preeclampsia, depression, anxiety, and stress scale (DASS 21). Independent t-test, Mann-Whitney, Chi-square, and logistic regression model were performed using SPSS, version 16.

Results: We found a significant relationship between anxiety and preeclampsia ($P < 0.001$), such that 26.7% of those with preeclampsia and 10.7% of the control group had anxiety. Participants with anxiety had 2.90 fold increased risk of preeclampsia in comparison with those without it (OR = 2.90, CI95%: 1.46-4.26).

Conclusion: Due to high risk of preeclampsia in women with anxiety during pregnancy, it can be considered as a risk factor for preeclampsia.

► Please cite this paper as:

Kordi M, Vahed A, Rezaee Talab F, Mazloum SR, Lotfalizadeh M. Anxiety during Pregnancy and Preeclampsia: A Case-Control Study. Journal of Midwifery and Reproductive Health. 2017; 5(1): 814-820.

DOI: 10.22038/jmrh.2016.7881

Introduction

Hypertensive disorders in pregnancy are a major cause of maternal and fetal mortality, which complicate about 8% of all pregnancies (1). Preeclampsia is a specific hypertensive disorder of pregnancy that presents after 20 weeks of pregnancy and is reported in 2-7% of pregnancies. The prevalence of preeclampsia varies in different parts of Iran (2). Different studies performed on the prevalence of the

disorder in the country, reported the prevalence rates of 1-8% for this disorder (3).

Despite extensive studies on this disease, its etiology is still unknown; accordingly, it was named as the disease of theories in 1916 (4). Many risk factors such as lifestyle (eating habits, sleeping, resting, physical activity, weight control, and smoking), psychological aspects, high hemoglobin level, and sleep disorders were

* Corresponding author: Azra Vahed, Department of Midwifery, School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran. Tel: 38591511; Email: Vaheda911@mums.ac.ir

considered for this disease (5-8).

Stress during pregnancy may indirectly or directly lead to increased complications of pregnancy. Levels of tumor necrosis factor- α and interleukin-6 pro-inflammatory cytokines are higher in women experiencing stress during pregnancy. On the other hand, the level of paired interleukin-10 (IL-10), which plays an important role in normal pregnancy, diminished in women with preeclampsia. Also, increased levels of corticotropin and increased activity in the sympathetic nervous system (SNS), which are the changes caused by stress, are observed in women with preeclampsia (1, 9).

Psychological aspects lead to overactivation of SNS due to the stimulation of autonomic nervous system that is a risk factor for preeclampsia (10). Previous studies showed that symptoms of anxiety or depression are associated with adverse pregnancy outcomes, such as preterm birth, birth weight less than 2500 gr, and small head circumference (11). However, there are few studies examining the association between psychological factors and preeclampsia. Some studies have shown a positive relationship between maternal psychological factors and preeclampsia (10).

According to the study of Kurki et al. (2000), stress and depression increased the risk of developing this disease 3.2 and 2.5-fold, respectively. Depression and anxiety during pregnancy due to the changes in the secretion of vasoactive hormones or other neuroendocrine transmitters, can lead to an enhanced risk of gestational hypertension (8).

The study of Qiu et al. (2007) demonstrated the relationship of depression and the symptoms of depression with an increased risk of preeclampsia (12). However, the study of Vollebregt et al. (2008) found no association between work stress, anxiety, depression, or anxiety related to pregnancy during the early stages and gestational hypertension or preeclampsia during pregnancy (1). According to the results of Kurki (2000), Vienna (2011), Qiu (2008), and Sigma (2001), pre-eclampsia is associated with anxiety, whereas the studies of Vollebregt (2000) and Anderson (2004) showed no relationship between anxiety and

preeclampsia (1,8, 12-15).

A major problem midwives commonly witness is anxiety in pregnant women. Pregnancy is a stressful situation for most women and the reactions of women are different in this regard (2). There are conflicting results regarding the link between psychological aspects and hypertension, and a small number of studies have evaluated the relationship between psychological aspects and preeclampsia in Iran. Accordingly, we decided to examine the relationship between anxiety and preeclampsia. In so doing, we can prevent or lower the incidence of preeclampsia and promote the chance of giving birth to a healthy neonate.

Materials and Methods

This case-control study, after approval of the Research Ethics Committee of Mashhad University of Medical Sciences, was performed on 300 pregnant women (150 women with preeclampsia and 150 women without preeclampsia) who were referred to 12 health centers and three university hospitals of Mashhad in 2014. The sample size (based on a pilot study) with confidence coefficient of 95% and using the formula of ratio analysis with power of 80 was calculated as 133 cases that was increased to 150 women in each group.

The inclusion criteria included gestational age of 28 to 40 weeks (based on the first trimester ultrasound or the first day of the last menstrual period), maternal aged <18 and >35, singleton pregnancy, no hearing, speech, or mental problems, no diseases, having a body mass index of ≤ 29 , and lack of stressful events during the last six months. The exclusion criteria comprised of withdrawal from participation in the study and use of antihypertensive drugs in the control group. Data collection tools included the demographic characteristics form, clinical and laboratory signs of preeclampsia, and Depression, Anxiety, and Stress Scale (DASS 21).

Prior to performing the study, the researcher introduced herself, explained the objectives and procedure of the study, obtained informed consent, and completed the information through an interview. The content

validity of the demographic characteristics form and clinical and laboratory signs of preeclampsia was confirmed. The validity of the depression, anxiety, and stress scales of Doss was confirmed by Mollahadi in Iranian population (16), and its reliability was established in this study with Cronbach's alpha coefficient of 0.86.

Inventory of depression, anxiety, and stress consisted of 21 items that were categorized into depression (n=7 items), anxiety (n=7 items), and stress (n=7 items). The questionnaire is rated using a 4-point Likert scale ranging from not at all to very high (score 0 to 3). The minimum and maximum possible scores range are 0 to 21, respectively. Since we used the short version of the questionnaire (the long form has 42 items), the scores were multiplied by 2 at the end. The cutoff point used for the presence of symptoms was depression ≥ 10 , stress ≥ 15 , and anxiety ≥ 8 ; the scores of 10-13, 8-9, and 15-18 were indicative of mild depression, anxiety, and stress, respectively. The scores of > 12 , 20, and 34 demonstrated very severe depression, anxiety, and stress, respectively (10). The questionnaire was completed during prenatal visits.

In the control group, at first, among the areas with numbers of 1, 2, and 3 of Mashhad, 12 health centers were randomly selected. Once the control group was determined, the patients referred to the prenatal care were considered to be in proportion to the population of the centers. Furthermore, all the women without preeclampsia, with gestational age of 28 to 40 weeks, who met the inclusion criteria were selected by convenience sampling method.

In the case group, the pregnant women with gestational age of 28 to 40 weeks who met inclusion criteria and were monitored by the health centers during pregnancy or were hospitalized in the maternity wards of Imam Reza (AS), Ghaem, or Hashemi Nejad hospitals who had preeclampsia based on clinical and laboratory signs confirmed by physicians were selected by convenience sampling method. Preeclampsia was diagnosed according to systolic blood pressure of ≥ 140 mmHg or diastolic blood pressure of ≥ 90

mmHg, accompanied by urinary protein excretion of 300 mg/24 h or $\geq +1$ on a urine test strip, which was determined by observation of the criterion and blood pressure readings. These measurements were obtained by the researcher and approved by a gynecologist.

Blood pressure was measured by the researcher, taken from the right hand in a sitting position. If necessary, a urine sample was requested to assess urine protein. The women with no signs of preeclampsia, who were considered as the control group, were observed up to 24 h after delivery to ensure no incidence of preeclampsia and other problems. Those patients diagnosed with preeclampsia were removed from the control group and were entered into the case group. In case of pregnancy-induced hypertension without proteinuria, the patient was excluded from the study.

During the study, we excluded two patients due to preeclampsia, one due to gestational diabetes, and one due to hyperthyroidism. It should be noted that the control group received the questionnaire when they were waiting for prenatal care and sometimes after receiving care. Regarding the case group, they received the questionnaire when the subjects were admitted to the maternity ward, but before delivery. After delivery, the questionnaires were given to the patients about a day after delivery in the absence of patient's companion.

The data was analyzed using descriptive and inferential statistical methods. Mann-Whitney U test was used to compare the quantitative variables between the two groups. Chi-square test was run to compare the qualitative variables between the two groups. Moreover, independent samples t-test was performed to compare quantitative variables with normal distribution, using SPSS version 16. P-value less than 0.05 was considered statistically significant.

Results

The two groups were not significantly different in terms of maternal age ($P=0.310$), educational level ($P=0.083$), job ($P=0.827$). Therefore, the mean age of the mothers was 28.8 ± 5.4 years in the case group and 27.5 ± 4.9

years in the control group. In addition, 36 (24%) subjects in the case group had

Table 1. Distribution of subjects based on parity, gestational age, socio-economic status in the case and control groups

Variables	Groups							Chi-square test
	Case		Control		Total			
	N	%	N	%	N	%		
Parity	0	52	34.7	63	42.0	115	38.3	X ² =4.28 df=2 P=0.118
	1	47	31.3	52	34.7	99	33.0	
	2≤	51	34.0	35	23.3	86	28.7	
	Total	150	100.0	150	100.0	300	100.0	
Gestational Range (week)	28-30	29	19.3	36	24.0	65	21.7	Chi-square test X ² =4.10 df=3 0.250
	31-34	35	23.3	40	26.7	75	25.0	
	35-37	32	21.3	36	24.0	68	22.7	
	38-40	54	36.0	38	25.3	92	30.7	
	Total	150	100.0	150	100.0	300	100.0	
Husband's Employment	worker	29	19.3	15	10.0	44	14.7	Chi-square test X ² =6.76 df=5 P= 0.238
	Free	93	62.0	107	71.3	200	66.7	
	Retired	1	0.7	1	0.7	2	0.7	
	Employee	25	16.7	25	16.7	50	16.7	
	No job	2	1.3	2	1.3	4	1.2	
	Total	150	100.0	150	100.0	300	100.0	

elementary education and 52 (34.7%) in the control group had high school diploma. Furthermore, 141 (94%) patients in the case group and 164 (96%) in the control group were housewives. The two groups were also matched in terms of parity (P=0.118), gestational age (P=0.250), and husband's employment status (P=0.238; Table 1).

Chi-square test results showed that the two groups had significant difference in terms of anxiety (P<0.001; Table 2).

The mean score of anxiety in patients with preeclampsia (case group) was 10.0 ± 6.4, and in

non-preeclamptic women (control group) it was 8.1 ± 5.7 (p=0.006).

Logistic regression was used to determine the association between history of abortion, body mass index, hemoglobin in the second trimester and hemoglobin in the second trimester with preeclampsia. The model results showed the body mass index, hemoglobin in the second trimester and anxiety had significant association with preeclampsia. It can be said that for every one-unit increase in anxiety, the risk of preeclampsia increases as 2.9-fold (Table 3).

Table 2. Distribution of subjects based on anxiety in the two groups

Chi-square test results	Groups						Anxiety
	Total		Control		Case		
	%	N	%	N	%	N	
X ² =12.64	18.7	56	10.7	16	26.7	40	Yes
df=1	81.3	244	89.3	134	73.3	110	No
P<0.001	100.0	300	100.0	150	100.0	150	Total

Table 3. Determining the effects of confounding variables on the exposure odds ratio of risk factors in patients with preeclampsia based on logistic regression model

Variables	Beta coefficient	SD	P-value	OR	95% confidence interval
History of abortion	-0.600	0.361	0.097	0.549	1.089-0.276
Body mass index	0.089	0.036	0.013	1.093	1.019-1.173
Hemoglobin in the second trimester	0.411	0.169	0.015	1.508	1.082-2.101
Anxiety	1.06	0.334	0.001	2.904	1.466-4.263

Discussion

In this study, anxiety was found to be associated with preeclampsia. The findings of this study exhibited that 5.3% of patients with preeclampsia and 0.7% of cases in the non-preeclamptic group suffered from very severe anxiety. The odds ratio of preeclampsia in the case group, when anxiety was detected, was 2.90 times higher than in the control group. Some psychological aspects lead to over-active SNS, which is due to the stimulation of autonomic nervous system and is a risk factor for preeclampsia (10). Depression and anxiety during pregnancy, due to the changes in the secretion of vasoactive hormones or other neuroendocrine transmitters, can lead to an increased risk of gestational hypertension (8).

The study of Kurki et al. (2000) in Finland was performed to determine the relationship between depression and anxiety in early pregnancy and the risk of preeclampsia in nulliparous women. In that study, modified Beck Depression Inventory and a questionnaire for the assessment of anxiety were given to 623 nulliparous women at 8-17 weeks of gestation (mean: 12 weeks) in one-month intervals of prenatal visits as well as during delivery. They found that 28 women (4.5%) had preeclampsia during pregnancy. Depression was observed in 85 (30%) patients and anxiety in 99 (16%) in early pregnancy. The odds ratio for preeclampsia after adjustment for the confounding factors was depression at 2.5 times, and anxiety at 3.2 times more than normal women. Moreover, if they had both factors, the risk for preeclampsia increased 3.1-fold. According to the aforementioned study, depression and anxiety during early pregnancy is associated with the risk of preeclampsia (8). The results of this study are consistent with our study. The study conducted by Kuki was prospective and the Beck Depression Inventory, paired with the researcher-made questionnaire, was used for anxiety. While our study was a case control study and a DASS21 was used, sampling was performed in the third trimester of pregnancy.

In the study of Sikkema et al. (2004), a few women with preeclampsia had severe degrees of anxiety (14). It seemed that the inconsistency between our results and the study of Sikkema

was the low sample size. In the Sikkema study, of the 250 primiparous women, 9 cases had complications with preeclampsia. In the study of Hans et al. (1996), increased peripheral vascular resistance induced by increased levels of catecholamine, as a result of overactivity of SNS, was noted as the reason for increased preeclampsia (17). However, in the study of Parberg et al. (1999), no significant relationship was found between increased levels of catecholamine and preeclampsia (18). Vasoconstriction in preeclampsia may occur in early pregnancy and results in increased uterine vascular resistance in anxious mothers, which can be the cause of preeclampsia (2).

In Teixeira's et al. study (1999), there was a significant relationship between uterine artery resistance index and severity of anxiety (19), which may show a relationship between increased anxiety and abnormal change in uterine artery blood flow. In the study of Vollebregt et al. (2008), no significant relationship was found between work stress, anxiety, and depression during early pregnancy and gestational hypertension or preeclampsia (1). According to the study of Vianna et al. (2011), a positive relationship was reported between stress, anxiety and depression with preeclampsia (13), which is consistent with the results of our study.

According to the study of Qiu et al. (2007), a correlation was reported between depression and anxiety with preeclampsia. Furthermore, the relationship between anxiety and preeclampsia is consistent with the results of our study (12). In the study of Nisell et al. (1989), of 345 patients in the first trimester, no significant difference was found between the score of stress and hypertensive disorders during pregnancy (20). These findings are consistent with our study. In the study of Andersson et al. (2004), no significant relationship was found between anxiety and depression with preeclampsia (15). This difference with our study is likely due to the tools of measuring anxiety.

The strength of this study was sampling from different areas, health centers and hospitals of Mashhad and then matching the two groups as much as possible. The limitation of this study was that for all information about stress, anxiety

and depression, only self-report DASS21 was used without clinical confirmation.

Conclusion

The results of this study indicated that anxiety increases the risk of preeclampsia. Therefore, providing in-service training programs on the methods of reducing anxiety is recommended. Evaluation, identification, and management of anxiety during the perinatal period through learning relaxation techniques and receiving psychological counseling during pregnancy is also suggested.

Acknowledgements

The present study was derived from the corresponding author's M.Sc. thesis project (code: 922863) approved by the Research Council of Mashhad University of Medical Sciences. The authors would like to thank Mashhad University of Medical Sciences for their financial support. They also extend their gratitude to the Deputy of Research and the staff of Mashhad Health Centers.

Conflicts of Interest

There are no conflicts of interest.

References

1. Vollebregt KC, van Der Wal MF, Wolf H, Vrijkotte TG, Boer K, Bonsel GJ. Is psychosocial stress in first ongoing pregnancies associated with pre-eclampsia and gestational hypertension? *BJOG: An International Journal of Obstetrics & Gynecology*. 2008; 115(5):607-615.
2. Alipour M, Feizi Z, Seyedfatemi N, Hosseini F. Correlation between maternal anxiety during pregnancy and incidence of preeclampsia in primigravid women. *Iran Journal of Nursing*. 2006; 19(47):79-88 (Persian).
3. Gharekhani P, Sadatyan SA. *Basics of pregnancy and childbirth*. 1st ed. Tehran: Institute of Light Publishing; 2002 (Persian).
4. Cunningham FG, Leveno KJ, Bloom SL, HauthJC, Rouse DJ, Spong CY. *Williams obstetrics*. 24th ed. New York: McGraw-Hill; 2014.
5. Batool-Anwar S, Malhotra A, Forman J, Winkelman J, Li Y, Gao X. Restless legs syndrome and hypertension in middle-aged women. *Hypertension*. 2011; 58(5):791-796.
6. Monahan FD, Sands JK, Neigh Bors M, Marek JF, Green CJ. *Phipps' medical surgical nursing health and illness perspectives Europ/middle east and African*. 7th ed. St. Louis: St Louismosby Elseviers; 2007. P. 2090.
7. Shojaeian Z, Sadeghian Harat R, Negahban Z. Predictive values of hemoglobin and hematocrit concentration during second trimester in diagnosis of preeclampsia. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2010; 12(4):14-21 (Persian).
8. Kurki T, Hillesmaa V, Raitasalo R, Mattila H, Ylikorkala O. Depression and anxiety in early pregnancy and risk for preeclampsia. *Obstetrics & Gynecology*. 2000; 95(4):487-490.
9. Moafi F, Dolatian M, Keshavarz Z, Alavi Majd H, Dejman M. Association between social support and maternal stress with preeclampsia. *Social Welfare Quarterly*. 2013; 13(48):151-170.
10. Kharaghani R, Geranmaye M, Janani L, Hantooshzade S, Arbabi M, Rahmani Bilandi R, et al. Preeclampsia and depression: a case-control study in Tehran. *Archives of Gynecology and Obstetrics*. 2012; 286(1):249-253.
11. Rezaee R, Framarzi M. Predictors of mental health during pregnancy. *Iranian Journal of Nursing and Midwifery Research*. 2014; 19(7 Suppl 1):S45-50.
12. Qiu C, Sanchez SE, Lam N, Garcia P, Williams MA. Associations of depression and depressive symptoms with preeclampsia: results from a Peruvian case-control study. *BMC Women's Health*. 2007; 7(1):15.
13. Vianna P, Bauer ME, Dornfeld D, Chies JA. Distress conditions during pregnancy may lead to pre-eclampsia by increasing cortisol levels and altering lymphocyte sensitivity to glucocorticoids. *Medical Hypotheses*. 2011; 77(2):188-191.
14. Sikkema JM, de Medina PG, Schaad RR, Mulder EJ, Bruinse HW, Buitelaar JK, et al. Salivary cortisol levels and anxiety are not increased in women destined to develop preeclampsia. *Journal of Psychosomatic Research*. 2001; 50(1):45-49.
15. Andersson L, Sundstrom-Poromaa I, Wulff M, Astrom M, Bixo M. Implications of antenatal depression and anxiety for obstetric outcome. *Obstetrics & Gynecology*. 2004; 104(3):467-476.
16. Mollahadi M, Tayyebi A, Ebadi A, Daneshmandi M. Comparison between anxiety, depression and stress in hemodialysis and kidney transplantation patient. *Journal of Critical Care Nursing*. 2012; 2(4):9-10 (Persian).
17. Schobel HP, Fischer T, Heuszer K, Geiger H, Schmieder RE. Preeclampsia—a state of sympathetic overactivity. *New England Journal of Medicine*. 1996; 335(20):1480-1485.
18. Paarlberg KM, Vingerhoets JJ, Passchier J, Dekker GA, Heinen AG, Geijn HP. Psychosocial predictors of low birth weight: a prospective study. *BJOG: An International Journal of Obstetrics & Gynecology*. 1999; 106(8):834-841.
19. Teixeira JMA, Fisk MN, Glover V. Association

between maternal anxiety in pregnancy and increased uterine artery resistance index, cohort based study. *BMJ*. 1999; 318(7177):153-157.

20. Nisell H, Larsson G, Wager J. The relation between

life stress and hypertensive complications during pregnancy. *Acta Obstet Gynecol Scand* 1989;68(5): 423-7.