Postpartum depression: relation with plasma vasopressin at 6-8 weeks postpartum: a longitudinal correlational study

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Article

Keywords: Postpartum Depression, Edinburgh Postnatal Depression Scale, Vasopressin, Primiparity

Posted Date: May 24th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1292376/v2>

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Abstract

Background

Postpartum depression is the most important postpartum mood disorder due to its significant effects on infant and family health. Arginine vasopressin (AVP) has been suggested as a hormonal agent involved in depression. The purpose of this study was to investigate the relationship between plasma concentrations of AVP and Edinburgh Postnatal Depression Scale (EPDS) score.

Methods

This longitudinal correlational study was conducted in 2016–2017 in Darehshahr Township, Ilam Province, Iran. In the first phase, 303 pregnant women who were at 38 weeks, met the inclusion criteria, and were not depressed (according to their Edinburgh Postnatal Depression Scale scores) were included in the study. In the 6–8 weeks' postpartum follow-up, using the Edinburgh questionnaire, 31 depressed individuals were diagnosed and referred to a psychiatrist for confirmation. The maternal venous blood samples of 24 depressed individuals who still met the inclusion criteria and 66 randomly selected non-depressed subjects was obtained by the researchers to measure AVP plasma concentrations with ELISA assay.

Results

The mean plasma concentration of AVP was significantly higher in the depressed group (41.35 ± 13.75 ng/ml) than in the non-depressed group (26.01 ± 7.83 ng/ml) ($P < 0.001$). In a multiple logistic regression model for various parameters, increased Vassopressin levels were associated with increased odds of postpartum depression (OR = 1.15, 95% CI = 1.07–1.24, $P = 0.000$). Furthermore, multiparity (OR = 5.45, 95% CI = 1.21–24.43, $P = 0.027$) and no exclusive breastfeeding (OR = 13.06, 95% CI = 1.36–125, $P = 0.026$) associated with increased odds of postpartum depression. Gender preference (having a baby non-desired and desired sex) decreased odds of postpartum depression (OR = 0.13, 95% CI = 0.02–0.79, $P = 0.027$ and OR = 0.08, 95% CI = 0.01–0.5, $P = 0.007$).

Conclusion

AVP may be a contributor to clinical postpartum depression by affecting the hypothalamic-pituitary-adrenal (HPA) axis activity. Furthermore, primiparous women had significantly lower EPDS scores.

Introduction

Postpartum depression (PPD) is defined as an episode of major depression that is temporally related to the birth of a child (1). In 2013, the American Psychiatric Association renamed the disorder to "Perinatal

disorder", stating that the onset of the mood disorder may be during pregnancy or within the first 4 weeks after birth (2). PPD is different from postpartum blues, which is a mild mood disorder and often occurs within the first 3 to 5 days after delivery (3). Postpartum depression has many negative effects on the mother and newborn; problems that may be brought for the child include developmental disorders, verbal, cognitive, and social problems, and the subsequent appearance of behavioral disturbances in the child (4–7). The causes of PPD are not fully understood (8, 9).

The American College of Obstetricians and Gynecologists believes that perinatal depression affected one out of every seven women (10). Its prevalence in Iran is reported to be 22% at 6–8 weeks postpartum and 18% at 12–14 weeks postpartum (11). Although many studies have been working on the possible causes of PPD, it remained unclear.

Many studies have investigated the role of vasopressin in the occurrence of major depression at a time other than the postpartum period (12–16). Vasopressin gene is located on chromosome 20 (17, 18), and its function is regulated by two types of receptors (V1 and V2) (19). Increased activity of the hypothalamic-pituitary-adrenal axis in patients with major depression is one of the well-known factors that increase the secretion of corticotropin-releasing hormone (CRH), leading to an increase in corticotropin and cortisol (20, 21). On the other hand, pregnancy depression is a disorder caused by severe stress conditions, in response to which vasopressin plays a major role (22, 23). This hormone, in combination with CRH, can stimulate the release of adrenocorticotropin hormone (ACTH) from the anterior lobe of the cerebellum and eventually cause the release of cortisol/corticosterone from the adrenal gland. Animal studies have shown that in depressed cases, vasopressin, instead of CRH, has a major stimulatory role on ACTH secretion (24). There is evidence indicating that such a role for vasopressin is also conceivable in humans; For example, in depressed individuals, the number of CRH-secreting neurons increase in the paraventricular nucleus (PVN), which can coexist with vasopressin (25).

Given the high prevalence of postpartum depression among mothers, it seems necessary to investigate its relationship with vasopressin, which is closely related to the known pituitary-hypothalamic axis in depression. No literature review has directly examined the relationship between vasopressin and postpartum depression. This study aimed to investigate the relationship between the Edinburgh Postnatal Depression Scale score and the mother blood vasopressin levels at 6–8 weeks postpartum.

Material And Methods

The present longitudinal correlational study was conducted between 2016–2017 after approval of the Research Council of Tarbiat Modares University, Tehran, Iran, obtaining permission from the medical ethics committee of School of Medical Sciences (registration number: IR.TMU.REC.1394.182), and presenting a letter of introduction to the rural and urban health comprehensive centers of Darrehshahr city (affiliated to Ilam University of Medical Sciences, Ilam, Iran). Pregnant women were first briefed about the study objectives and confidentiality of maternal and neonatal information, then their informed consent was obtained.

The required sample size to study on pregnant women at 38 weeks of gestation was estimated as 303 individuals, with 95% confidence interval and 5% accuracy and based on the prevalence of depression among Iranian pregnant women (26). For assessment relationship between plasma vasopressin and EPDS score at 6 to 8 weeks postpartum, the sample size was calculated as 95 persons, based on a minimum correlation of 0.3 between vasopressin and the EPDS score, with 95% confidence interval (so $Z = 1.96$), $\beta = 0.2$ and 10% sample loss. 303 eligible pregnant women in the gestational age of 38 weeks were selected using convenience sampling. For this sample size calculation was used 95% confidence interval, P-value 5%. All 303 subjects were selected from among those who were referred to health comprehensive centers for prenatal care and were not depressed according to their EPDS score (less than 13).

The study inclusion criteria were singleton pregnancy, no systemic diseases such as lupus and diabetes mellitus, no pregnancy complications (diabetes, preeclampsia, ...), no previous history of psychological problems, Iranian nationality, no use of antidepressants, hormonal contraceptive pills, or sleeping pills within two weeks prior to venous blood sampling, good marital relationship with the spouse, no expressed significant economic problems, no family history of depression or other mental illnesses. The study exclusion criteria were high physical activity (like sport), stressful conditions or using alcohol within 12 hours before sampling, insufficient sleep the night before sampling, abnormal blood pressure during sampling or at postpartum period, instrumental vaginal delivery, congenital malformations of the newborn, complications during childbirth (vaginal delivery or cesarean section) leading to treatments such as blood transfusion, resuscitation, hospitalization in the ICU or CCU, or transfer to the operating room.

Methods of data collection included observation, examination (weight, height, BMI, and other criteria in prenatal care forms such as blood pressure, fetal heart rate, fundal height, and warning signs during pregnancy), and patient interview. The patient interview conducted using a questionnaire in three sections of personal information, obstetrics and medical history, and laboratory results. All the data were finally recorded in a checklist. Gestational age was calculated from the first day of the last menstrual period (LMP), or the first trimester ultrasound (if uncertain about LMP). Weight, blood pressure, and heart rate of the fetus were measured by the same person using a digital scale, digital barometer, and fetal heart detector (Sonicaid). The Edinburgh Postnatal Depression Scale is the instrument used to measure postnatal depression. Another questioner used in this study is the translated version of the EPDS in Persian (Iranian language), the acceptability, reliability, and validity of which has been verified in Montazeri et al study (11).

The mothers were controlled according to the routine prenatal care program until delivery. All study population ($n = 303$) were once again assessed with the Edinburgh Questionnaire during 6 to 8 weeks after delivery, and if they received a score of 13 or higher, they were referred to a psychiatrist to confirm their depression. Thirty-one of them scored 13 or more, and postpartum depression of 29 subjects was confirmed by the psychiatrist. Sixteen non-depressed subjects and also five depressed women, did not meet one of the inclusion criteria or were excluded from the study. Finally, venous blood samples were

took from all 24 depressed and 66 randomly selected non-depressed individuals 6 to 8 weeks after delivery at 9–9:30. Blood samples were taken after 15 min rest. The samples were added to EDTA-containing chilled plastic tubes and immediately kept at 4°C within 30 minutes, plasma separation carried out. Samples were centrifuged at 3000 rpm for 10 minutes at 4°C. The produced plasma was frozen at a temperature of -80°C until analysis. After transferring to endocrinology and metabolism laboratories of Shahid Beheshti University of Medical Sciences, Tehran, plasma vasopressin level was measured by the ELISA method, using Human Anti-Diuretic Hormone (ADH) ELISA kit (ZellBio GmbH, Ulm Germany), with a sensitivity of 0.5 ng/ml. plasma osmolality was not measured because it doesn't have effect on plasma AVP levels (16). Afterwards, participating mothers were divided into depressed and non-depressed groups. The relationship between blood vasopressin levels and the Edinburgh Postnatal Depression Scale scores and other variables affecting this relationship was investigated. The normal distribution of variables in each group was assessed using the Kolmogorov-Smirnov test. A chi-squared test was used for qualitative variables, the Mann-Whitney test was used for non-normally distributed variables, and the Independent-sample T test for normally distributed variables. The relationships among the variables in the present study were separately assessed in each group using, regression, and Pearson's ordinal correlation tests. For all statistical tests, the level of significance was considered as $P < 0.05$. Data analysis was done using SPSS software version 21.

Result

Demographic and background data for the two groups are presented in Table 1. Ninety participants were included in our study at 6–8 weeks postpartum. In all, 24 (26.66%) women had depression and 66 (73.33%) women had not depression. The mean age ($\pm$ S.D.) of all subjects was 26.58 ($\pm$ 4.20) years. The mean age ($\pm$ S.D.) was 28.96 ($\pm$ 4.88) years in depressed group and 29.71 $\pm$ 5.55 years in Non-depressed group. The mean BMI $\pm$ S.D. in all subjects was 26.58 $\pm$ 4.20 kg/m²m². All subjects did not drink or smoke.

Table 1
Demographic and clinical characteristics of subjects (n = 90)

Characteristics		Individual status		P-Value
		Depressed (n = 24)	Non Depressed (n = 66)	
		(N) %	(N)%	
Mother's education	Less than high school diploma	4 (16.7)	8 (12.1)	0.37
	High school diploma	12 (50)	25 (37.9)	
	University	8 (33.3)	33 (50)	
Husband's education	less than high school diploma	4 (16.7)	9 (13.6)	0.79
	High school diploma	11 (45.5)	27 (40.9)	
	University	9 (37.5)	30 (45.5)	
History of Abortion	Yes	1 (4.2)	8 (12.1)	0.43
	No	23 (95.8)	58 (87.9)	
Maternal gender preference	Desired sex	4(33.3)	20(41.7)	0.63
	Non desired sex	8 (66.7)	28 (58.3)	
Baby gender	Male	11 (45.8)	34 (51.5)	0.63
	Female	13 (54.2)	32 (48.5)	
Mode of delivery	NVD	9 (25)	27 (75)	0.77
	CS	15 (27.8)	39 (72.2)	
Parity	Nulliparous	9 (37.5)	39 (59.1)	0.06
	Multiparous	15 (62.5)	27 (40.9)	
Breastfeeding status at 6–8 week	No Exclusive Breastfeeding	6 (25)	2 (3)	0.004
	Exclusive Breastfeeding	18 (75)	64 (97)	
Living area	City	17 (70.8)	51 (77.3)	0.53
	Village	7 (29.2)	15 (22.7)	

Prevalence of Postpartum Depression

A total of 303 women at 38 weeks of pregnancy from the rural and urban health centers met the inclusion criteria. All the participants filled out the Edinburgh Postnatal Depression Scale questionnaire at 6–8 weeks postpartum. In our study a score of 13 or above was used as a cut-off point for detection women at risk for postpartum depression. Thirty-one women (10.23%) scored 13 or more on the EPDS. After referral these women to a psychiatric, twenty-nine out of 31 women were diagnosed with depression by the psychiatrist (9.57%). The mean score of EPDS scale was higher in depression women (16.46 ± 3.10) as compared with non-depression women (6.12 ± 13.32). Finally, based on our findings after confirmation of PPD by the psychiatrist, the prevalence of PPD was 9.57%.

Relationship between Plasma Concentrations of Arginine Vasopressin and the EPDS Score

According to the Independent-sample T test, the mean plasma concentrations of arginine vasopressin was significantly higher in the depressed group (41.35 ± 13.75 ng/ml) than in the non-depressed group (26.01 ± 7.83 ng/ml) ($t(28.6) = 5.16, P < 0.001$). The Pearson correlation test showed a positive significant relationship between plasma concentrations of AVP and EPDS Score in the depressed group ($P < 0.001, r = 0.65$).

Relationship between other factors and depression

The association between mode of delivery ($P = 0.77$), gender of baby ($P = 0.63$), living area ($p = 0.53$), level of education in mothers ($P = 0.37$), educational level of husband ($P = 0.79$), preference of gender ($P = 0.63$) by mother before pregnancy, parity ($P = 0.06$), gender of baby ($P = 0.63$), history of abortion ($P = 0.43$), breastfeeding status ($P = 0.004$) and PPD was quantified by Chi-Squared test. Among all above variables, only breastfeeding status was related to PPD ($P = 0.004$) (Table 1). A decrease in depression was found at 6–8 weeks postpartum in women who exclusively breastfed ($P = 0.02$). Women who exclusively breastfed were divided into depressed and non-depressed groups. We ran a Mann-Whitney U test because of abnormal distribution of AVP levels in non-depressed group to evaluate the difference in the concentration of AVP in depressed and non-depressed women who had exclusively breastfeeding. The mean rank of plasma AVP concentrations in depressed group and non-depressed group were 66.73 ng/ml and 37.78 ng/ml; the AVP plasma concentrations in the two group differed significantly ($U = 282, Z = -4.64, P < 0.001$). An independent T-test was conducted to compare mean of maternal age in depressed and non-depressed groups. There was not a significant difference in the mean of maternal age between depressed (28.96 ± 4.88) and non-depressed groups (29.71 ± 5.55); respectively, $t(88) = 0.58, CI95\%, P = 0.55$.

The Factors Associated with Postpartum Depression

To assess association between variables including, plasma vasopressin levels, parity, BMI, preference for neonatal sex, type of delivery, gender of the baby, parity, maternal age, history of abortion, women's education level, husband's education level and breastfeeding status with depression we use binary logistic regression. After analysis, plasma vasopressin levels, parity, preference for neonatal sex and breastfeeding status were statically significant. In the final prediction model, depression was significantly

higher in people with higher plasma vasopressin levels after delivery (OR = 1.15, 95% CI = 1.07–1.24, $P < 0.001$). Multiparous women (OR = 5.45, 95% CI = 1.21–24.43, $P = 0.027$) and ones exclusively did not breastfeed (OR = 13.06, CI = 1.36–125, $P = 0.026$) were more likely to be depressed. Also postpartum depression was significantly higher in women who did not have a gender preference than ones who had a baby of the nondesired (OR = 0.13, 95% CI = 0.02–0.79, $P = 0.027$) and desired (OR = 0.08, $P = 0.007$, 95% CI = 0.01–0.5) sex (Table 2)

Table 2
Logistic regression analysis of factors affecting postpartum depression

Predictors		Adjusted OR	CI95%	P-value
Vassopressin		1.15	1.07–1.24	< 0.001
Parity	Primiparous	1		
	Multiparous	5.45	1.21–24.43	0.027
Breastfeeding	Exclusive	1		
	Non exclusive	13.06	1.36–125	0.026
Maternal gender preference	No preference	1		
	Desired sex of the baby	0.08	0.01-0.0.5	0.007
	Nondesired sex of the baby	0.13	0.02–0.79	0.027

R² = 0.41

Discussion

To our best knowledge, no previous study assessed the relationship between plasma concentrations of arginine vasopressin (AVP) and postpartum depression (PPD). Based on our findings, the prevalence of PPD was 9.57% at 6–8 weeks postpartum (the depression confirmed by a psychiatrist). Among the study population, 53.3% were primiparous and 46.7% were multiparous, while among the depressed people, 37.5% were primiparous and 62.5% were multiparous. In the logistic regression, primiparous status was a significant negative predictor of depression. Some studies show that primiparas are more anxious during pregnancy rather than in the postpartum period. Our study also confirms that primiparas are mostly happy with the birth of a newborn and having a new family member, which reduced the EPDS score. In a study by Righetti-Veltima et al (1997) in Geneva on the risk factors and predictive signs of postpartum depression at three months after delivery, multiparas reported more difficult pregnancies and higher anxiety and were less involved in the perinatal preparation program (27). Figueiredo and Conde (2011) reported that parity has a significant impact on postpartum anxiety and depression. According to their study, second-time parents showed more anxiety and depression symptoms than first-time parents in the second and third trimesters and also 3 months after childbirth, but not at birth (28). The results of these two studies were in line with our results. O'Hara et al (1982) reported that pregnant women and

primiparous women experienced more depressive symptoms, marital distress, and psychological problems than non-pregnant women (29). In Kaij et al study (1996), symptoms of depression decreased (using the Edinburg postnatal depression scale) with an increasing number of children (30). Gotlib et al (1989) showed that multiparity was a risk factor for depression during pregnancy, but not in the postpartum period (31). Wenzel et al (2005) claimed that there was typically no relationship between parity and depression during pregnancy and postpartum (32), which is consistent with the study of Lashkaripour et al (2012) (33). Four above studies showed that there is no clear and well-established conclusion regarding the relationship between primiparous status and postpartum depression. These conflicting results among studies can be due to different tools used for postpartum depression assessment or different times of evaluation. There are also unclear results about the role of other factors affecting the relationship between parity and postpartum depression, such as parents' education level, socioeconomic factors, and maternal age. We excluded people who were economically disadvantaged to control this variable.

Sixty women (66.6% of all women) had a sex preference. Of these women, 40% had a baby of the non-desired sex that only 20% of them developed PPD. In general, only 16.6% of all women who developed PPD, had a baby the non-desired sex. The majority of depressed women had not gender preference. According to our finding, depression in two group of whom whether their baby had the same gender as they desired before birth (or not), was less than the group of women who did not have preference about the sex of the baby. Preference for the sex of the baby boy is still common in countries such as India, China and have harmful effects on pregnant women. This gender preference of the baby boy is deeply rooted in cultural issues. In these societies, the girl is considered an economic consumer of the family, because most girls get married and because of paying dowry to them, economically to the family (34, 35). In one study, having a baby of the nondesired sex increased the risk of developing postnatal depression (36). The result of these studies contradict our result (Table 2). However, Dhillon and MacArthur in the opposite direction of these studies, identified maternal gender preference in Asian women in the UK was no association with PPD (37).

Within the total sample at 6–8 weeks postpartum, 82 women breastfed exclusively (91.1%), 8 women did not initiate or ceased exclusive breastfeeding. In our study, exclusive breastfeeding included Labbock and Krasovec's level 1 and 2 (38). A number of studies have revealed no relationship between breastfeeding and postpartum depression (39). In contrast, a number of researches have showed that breastfeeding may protect against postpartum depression (40, 41). These results are consistent with those from the present study suggesting exclusive breastfeeding may help to reduce mother's postpartum depression. In our study, women who breastfed at 6–8 weeks postpartum had lower scores when compared to women did not initiate or ceased exclusive breastfeeding.

In this study, the mean plasma concentration of AVP was significantly higher in the depressed group than in the non-depressed group; there was a significant positive correlation between mean plasma concentration of AVP and EPDS score. Worldwide epidemiological studies show that depression occurs in women twice as much as men and peaks during the first years postpartum. They also show that the

incidence of all mental illnesses increases in the postpartum period (42). One theory argues that the genes involved in postnatal changes in the brain, if not altered normally, increase the risk of postpartum depression. These genes include a subset of maternal genes that mediate signaling pathways of the vasopressin (42) such as hypocretin receptors. Neuromedin S (Nms) also affects this signaling, acting as a mediator in the activity of enkephalin and dynorphin, and plays a key role in the action balance of different neuropeptides (43). No studies have yet examined the relationship between vasopressin serum level and postpartum depression.

Previous studies on non-pregnant populations are as follows. In a 2006 review article, Keck concluded that a dysfunction in the vasopressin (AVP) and corticotropin-releasing factor (CRF) systems is involved in the pathogenesis and etiology of depression and anxiety (44). In chronic stress, vasopressin is steadily elevated in CRH neurons, so that even a slight irritation may lead to a severe AVP/CRH secretion. This can contribute to the development of dysphoric symptoms and may even be a factor responsible for the onset of major or temperament depression (45). The number of CRH neurons, expressing the vasopressin level, increases in depressed human PVN (46). Elevated AVP mRNA level in the SON in depressed individuals (47) also leads to an increase in plasma vasopressin (24), which is related to suicide risk (48), and altered attention and arousal in memory processes in depressed patients (49). In contrast, Wang et al (2008) found no difference in vasopressin mRNA expression in the SON or PVN of depressed individuals compared to the control group, which may be due to the mere presence of melancholic depressed individuals in this study (50). Brunner et al (2002) found no association between vasopressin concentration in plasma and cerebrospinal fluid (CSF) among depressed and non-depressed individuals. The two were also not different in those who attempted suicide compared to other people. This study is not in line with the results of our study. It might be due to a low sample size and diagnostic heterogeneity in the patient and control groups, which did not allow them to investigate the pathogenetic role of vasopressin (51).

Griebel et al (2003) stated that although CRF has been recognized as a key regulator of the stress system, there is evidence that the vasopressinergic system may play an equal role in regulating stress responses, so vasopressin V (1b) receptor antagonists may be potential treatments for depression. Their results confirmed the efficacy of using SSR149415, which was the first selective, orally active vasopressin V (1b) receptor antagonist in the treatment of depression and anxiety disorders caused by traumatic events (52). Vasopressin V (1b) receptor is required for normal response of the cerebellum and adrenal during chronic stress (53). Muller et al (2000) study on mice showed a selective compensatory activation of the hypothalamic vasopressinergic for maintaining basal ACTH secretion and HPA system activity in heterozygous and homozygous *Crhr1* mutants (*Crhr1*^{-/-}) in basal and stress conditions. Deficiency of CRH receptor 1 (CRHR1) severely impairs the stress response of the hypothalamic-pituitary-adrenocortical (HPA) system and reduces stress-related behavior in mice (54)

In this study, all subjects were controlled as much as possible for the involvement of other factors affecting plasma vasopressin concentration. The results of this study support the role of vasopressin in the pathogenesis of postpartum depression. Since postpartum depression is classified as a sub-type of

major depressive disorder, we also support the possible role of vasopressin in major depression. For the first time in the world, we examined the relationship between plasma concentrations of arginine vasopressin (AVP) and the EPDS Score at 6 to 8 weeks postpartum, revealing a significant positive relationship between plasma concentrations of AVP and the EPDS Score.

Study Limitations

This study provides useful data of the relationship between plasma vasopressin and postpartum depression. However, the present study has some limitations. First, we know that it would be better to evaluate levels of plasma concentrations of vasopressin by Radioimmunoassay (RIA) because no study had not used the enzyme-linked immunosorbent assay (ELISA kit) to measure vasopressin. Therefore, more studies are suggested in order to support our results. However, we could not do it because of lack of access to Human Vasopressin Radioimmunoassay (RIA) kits in Iran, which is a limitation of our study.

Conclusion

After a careful review of previous studies on vasopressin and postpartum depression, we can claim the present study is the first in Iran and the World to have specifically addressed the relationship between maternal plasma vasopressin levels and postpartum depression. Our study can be the basis for further and more precise studies. According to the present study results, mean plasma vasopressin was higher in the depressed group compared to the non-depressed group. Also, among the depressed who exclusively breastfed the mean plasma concentrations of AVP was higher. In the present study, the relationship between vasopressin level and EPDS score was positive. Hence, plasma concentrations of AVP was Positive predictor of EPDS score. Being a primiparous, exclusive breast-feeding and having preference for sex of the baby among women before pregnancy were negatively related to postpartum depression. Vasopressin appears to be related to postpartum depression by contribute to the dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. It is recommended that future studies be conducted with larger sample sizes and longer follow-up periods.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board and the Ethics Committee of Tarbiat Modares University of Medical Sciences (IR.TMU.REC.1394.182) approved the study protocol. All procedures were in accordance with the ethical standards of the Regional Research Committee and with the Declaration of Helsinki 1964 and its later amendments. After explaining the study's purposes, a written consent and a verbal assent were collected from all participants. They were informed that their participation was voluntary, confidential and anonymous, and that they had the right to withdraw from the research at any time.

Consent for publication

Not applicable.

Availability of data and materials

The data sets used and analyzed for the current study are available upon reasonable request.

Competing interests

The authors declare no conflicts of interest.

Authors' contributions

M.K, Sh.JS and S.Z contributed to the conception and design of the study; M.K.Sh.JS, S.Z, A.S,H.D and Kh.A did the literature search; A.K, S.Z and Sh.JS performed the statistical analysis; M.K, S.Z., Sh.JS, A.S,H.D and Kh.A wrote the first draft of the manuscript. All authors contributed to the manuscript revision, and read and approved the submitted version

Acknowledgements

We acknowledge Dr, Mehdi Hedayati, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, for conducting the ELISA analysis of vasopressin and midwives of urban health comprehensive centers of Darehshahr city and all participating mothers in our research.

Funding

This investigation was supported by grants from the Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.

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