



**A STUDY OF MATERNAL PLASMA OXYTOCIN LEVEL AND POSTPARTUM DEPRESSION IN LOW RISK PREGNANT POPULATION: A NESTED CASE-CONTROL STUDY**

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**ABSTRACT**

**Objectives:** To study the correlation between plasma oxytocin levels and Postpartum depression (PPD) among low risk pregnant population. **Methods:** After proper history, 2 ml of blood was collected from each patient. These women were followed up and assessed for PPD at 2 and 6 weeks postpartum using Edinburgh Postnatal Depression Scale (EPDS) and further confirmed by psychiatrist. Those with score  $\geq 10$  were taken as cases (n=30) and score  $< 10$  were taken as controls (n=30). Plasma oxytocin levels were estimated and compared between the two groups using the antenatal blood samples. **Results:** The mean level of plasma oxytocin in the cases was  $247.63 \pm 51.45$  pg/ml and in controls was  $286.31 \pm 49.82$  pg/ml. Statistical significant association between plasma oxytocin levels and PPD was found ( $p=0.005$ ). Nuclear family, higher number of living children, pressure to have a male child, multigravidity and a previous female child were significantly associated with PPD. Caesarean section and longer hospital stay were also significantly associated with PPD. Significant difference was found between breastfeeding activities among women with and without PPD. **Conclusion:** Women with lower plasma oxytocin levels at 34-36 weeks of gestation are prone to develop PPD. Measuring plasma oxytocin levels at 34-36 weeks of gestation in women with the risk factors for PPD can help to reduce maternal morbidity and mortality and the burden of the disease.

**KEYWORDS:** Postpartum depression, Plasma oxytocin levels, Risk factors.

**INTRODUCTION**

Postpartum depression defined as an episode of depressive symptoms within 4-6 weeks postpartum. It is the most common puerperal psychiatric disorder with an overall prevalence of around 10-15%.<sup>[1]</sup> History of major depression multiplies the risk by 25% and past history of postpartum depression increases recurrence rates by 50%.<sup>[2]</sup> Postpartum depression is noticeable symptoms usually are depressed mood, loss of pleasure in day to day activities, sleep disturbances, loss of appetite and energy, feeling of guilt, reduced concentration, irritability, anxiety and suicidal thoughts.<sup>[3]</sup> Postpartum is an emotionally vulnerable time period for major

depressive symptoms, partly caused by the imbalance in the hormonal hemostasis. PPD not only has negative consequences for the mother but also for the child up to 3 years of age like poor infant weight gain, cognitive developmental issues, disturbed motor development, poor language and behavioral development.<sup>[4]</sup>

Risk factors for PPD can be categorized as strong, moderate and small. The strongest correlation exists with depression or anxiety during pregnancy, past history of psychiatric illness, stressful life events and poor social support. Moderate ones include: psychological factors such as maternal neuroticism and marital relationship

whereas the small risk factors are pregnancy and delivery related complications and socio-economic status.<sup>[4]</sup>

The postpartum period is regarded as a period of maturation crisis same like adolescence and menopause. The etiology would range from biochemical to psychosocial and biological too.<sup>[6]</sup> Endocrine factors like hypothalamic-pituitary gonadal axis dysregulation, withdrawal of estrogen and progesterone, increased levels of prolactin, abnormal cortisol levels and reduced thyroid hormone levels have all been implicated.<sup>[6]</sup>

The less studied hormone in PPD is the nonapeptide oxytocin, is synthesized in the paraventricular and the supraoptic nucleus of the hypothalamus. Though traditionally known for its role in labour and lactation, strong association of oxytocin and postpartum maternal adaptation and maternal and infant bonding have been observed.<sup>[7,8]</sup> Higher postpartum maternal infant attachment has been observed in women with oxytocin rise between first and third trimester compared to those women with low or stable levels of oxytocin.<sup>[9]</sup> Lower oxytocin levels in pregnancy especially in the third trimester could result in impaired emotional adaptation and thus predisposition to PPD.

The current burden of PPD in low and middle income countries like India could be very high. Developing countries like India lack a national peripartum mental health registry and thus the actual disease burden is unknown. This scarcity of evidence also hinders the management of postpartum mental illnesses. With this we planned to investigate the relationship between plasma oxytocin and PPD in a bid to provide a new predictive marker or new targets for the diagnosis of PPD, in turn facilitating early treatment modalities.

## METHODS

This study was conducted in the Department of Obstetrics and Gynecology in collaboration with Department of Biochemistry at University College of Medical Science (UCMS) & Guru Teg Bahadur Hospital (GTBH), Delhi, India. Prior institutional ethical committee clearance was taken (IEC-HR/2019/41/73R)

**Table 1: Plasma Oxytocin Levels amongst Cases and Controls.**

Parameters	Case (n = 30)	Control (n = 30)	
	Mean ± SD	Mean ± SD	P-value
Plasma Oxytocin Levels (pg/mL)	247.63 ± 51.45	286.31 ± 49.82	0.011

The socio-demographic profile of cases and controls is depicted in Table 2. 40.0% of the cases and 66.7% of the controls had no living children. 56.7% of the cases and 26.7% of the controls had one child. Statistically significant association was noted between the number of living children and the development of depression with a

200 low risk pregnant women were enrolled at 34-36 weeks of gestation from November 2019 to October 2021.

Women with previous or recent history of anxiety, depression or any chronic illness were excluded from the study.

After an informed and written consent, proper history and examination was done. 2 ml of blood was collected in an EDTA vial at 34-36 weeks of gestation and then centrifuged at 5000 rpm for 5 minutes. Supernatant plasma was divided into aliquots and stored at -70°C till further analysis. Plasma oxytocin levels was estimated by Sandwich ELISA kit (Human Oxytocin Elisa kit from Coon Koon Biotech). All women were assessed by Edinburgh Postnatal Depression Scale (EPDS) Hindi version for postpartum depression. The recommended cut-off point is 9/10. At 2 weeks and 6 weeks postpartum, the women were assessed by EPDS score. An EPDS score of 10 was taken as cases and controls were then selected randomly from the remaining cohort. At 6 weeks postpartum, the antenatal blood samples of both the cases and the controls were analysed for the levels of oxytocin.

## RESULTS

Two hundred low risk pregnant women were screened using EPDS at 2 and 6 weeks postpartum. Out of 200 postpartum women, 30 had a score of 10 or more on the EPDS scale were considered as cases. 30 random women were selected as controls from remaining 170. Maternal plasma oxytocin levels were then measured in these 60 samples and the relationship between plasma oxytocin levels and PPD was studied.

The mean ± (SD) of plasma oxytocin levels (pg/mL) in the cases was 247.63 ± (51.45) and in the controls was 286.31 ± (49.82). The difference was statistically significant between the two groups in terms of plasma oxytocin levels (pg/ml) (p = 0.011) (Table 1).

p value of 0.040. 60.0% of the cases and 16.7% of the controls had a pressure to have a male child and this significantly associated with onset of PPD (p<0.001). Both the groups were comparable in terms of age distribution, education and employment status.

Table 2: Socio-Demographic profile of Cases and Controls.

Parameters	Case Control (n=30) (n=30)		p value
	Mean ± SD	Mean ± SD	
Age (Years)	25.03 ± 3.15	24.40 ± 3.75	0.481
<b>Parameters</b>	<b>Cases</b>	<b>Controls</b>	<b>P value</b>
<b>Education</b>			0.137
Uneducated	6 (20.0%)	2 (6.7%)	
Primary School	2 (6.7%)	1 (3.3%)	
Middle School	7 (23.3%)	8 (26.7%)	
High School	3 (10.0%)	10 (33.3%)	
Intermediate	6 (20.0%)	2 (6.7%)	
Graduation	6 (20.0%)	7 (23.3%)	
<b>Employment Status</b>			1.000
Employed	1 (3.3%)	1 (3.3%)	
Unemployed	29 (96.7%)	29 (96.7%)	
<b>Type of Family</b>			<0.001
Nuclear	21 (70.0%)	1 (3.3%)	
Joint	9 (30.0%)	29 (96.7%)	
<b>Number of Living Children</b>			0.040
None	12 (40.0%)	20 (66.7%)	
1	17 (56.7%)	8 (26.7%)	
2	1 (3.3%)	2 (6.7%)	
<b>Pressure To Have Male Child (Yes)</b>	18 (60.0%)	5 (16.7%)	<0.001

The obstetric profile of cases and controls is depicted in Table 3. 70.0% of the cases and 40.0% of the controls were multigravidas and thus multigravidas were more prone to PPD and statistically significant association was noted between gravidity and PPD (p=0.020).

40% of the cases had a previous female child and only 16.7% of the controls had a previous female child.

Table 3: Obstetric profile of Cases and Controls.

Parameters	Cases	Controls	P value
<b>Gravida</b>			0.020
Primigravida	9 (30.0%)	18 (60.0%)	
Multigravida	21 (70.0%)	12 (40.0%)	
<b>Pregnancy planning</b>			0.166
Planned	23 (76.7%)	27 (90.0%)	
Unplanned	7 (23.3%)	3 (10.0%)	
<b>Previous obstetric history</b>			0.028
None	9 (30.0%)	20 (66.7%)	
Female Child	12 (40.0%)	5 (16.7%)	
Male Child	7 (23.3%)	3 (10.0%)	
Male+Female Child	2 (6.7%)	2 (6.7%)	

Table 4 represents the intrapartum and postpartum details of the cases and controls. 36.7% of the cases had a cesarean section for labour complications (fetal distress, non progress of labour, failed induction) when only 10.0% of the controls had a cesarean section. Statistical significant difference was noted among the cases and controls in terms of mode of delivery. Cesarean section puts women at a risk of development of PPD. There was no statistically significant difference between the cases and controls in terms of distribution of gender of the baby and gender of the baby when desiring a male child.

The mean (SD) of duration of hospital stay (days) among the cases was 3.93 (1.20) and among the controls was 3.00 (0.87) was statistically significant. (p = 0.001).

**Table 4: Intrapartum and Postpartum details of Cases and Controls.**

Parameters	Cases	Controls	P value
<b>Type of labour</b>			0.353
Spontaneous	29 (96.7%)	26 (86.7%)	
Induced	1 (3.3%)	4 (13.3%)	
<b>Duration of labour (Hours)</b>	7.50 ± 2.70	8.13 ± 1.91	0.534
<b>Mode of Delivery</b>			0.015
Vaginal	19 (63.3%)	27 (90.0%)	
Cesarean	11 (36.7%)	3 (10.0%)	
<b>Gender of the baby</b>			0.194
Male	11 (36.7%)	16 (53.3%)	
Female	19 (63.3%)	14 (46.7%)	
<b>Postpartum complication</b>			0.612
None	29 (96.7%)	27 (90.0%)	
PPH	1 (3.3%)	3 (10.0%)	
<b>Duration of hospital stay (Days)</b>	<b>Mean ± SD</b>	<b>Mean ± SD</b>	<b>P value</b>
	3.93 ± 1.20	3.00 ± 0.87	0.001

## DISCUSSION

In this study, the prevalence of PPD in low risk pregnant population was found to be 15% taking EPDS score of 10 or more as a cut-off. Shrestha et al in a prospective observational cohort study noted the prevalence of PPD to be 12%.<sup>[10]</sup>

The plasma oxytocin levels in this study ranged between 95 pg/ml to 398.33 pg/ml. The mean levels of plasma oxytocin in the cases was 247.63pg/ml ( $\pm 51.45$  pg/ml SD) and in controls was 286.31pg/ml ( $\pm 49.82$  pg/ml SD). The levels of plasma oxytocin was significantly associated with postpartum depression (p value=0.011) and were lower at 2 weeks and 6 weeks postpartum. Our findings are similar to those reported by Skrundz et al<sup>[11]</sup> Zolkowitz et al<sup>[12]</sup> Jobst et al<sup>[13]</sup> who reported that lower plasma oxytocin levels in third trimester predispose women to PPD.

Literatures across the world has described various risk factors associated with PPD. Among the socio-demographic risk factors for PPD, age as a risk factor did not correlate with the onset of PPD in our study, the fact is supported by Ghosh et al.<sup>[14]</sup> The composition of the family if nuclear significantly correlated with the development of PPD with a p-value of <0.001. Women belonging to nuclear family are more prone to develop PPD as these women have to manage with little or no help from their family which could contribute to PPD. These results are in congruence to Ghosh et al who found a significant association between PPD and the type of family with women coming from nuclear family at increased risk of PPD.<sup>[14]</sup> Statistically significant association was observed between the pressure to have a male child and PPD (p value <0.001). These findings are consistent with a study by Gupta et al where pressure and expectation to have a male child were significantly associated with PPD.<sup>[15]</sup> Significant association was also noted between the number of living children and PPD with a p value of 0.040. Aggarwal et al noted that

having more than two children were significant risk factors for PPD.<sup>[16]</sup>

Among the obstetric risk factors, number of previous pregnancies and onset of PPD significantly correlated with a p value of 0.020. In congruence with studies multigravidas were more prone to develop PPD probably due to the increased financial burden and responsibilities that come with an increase number of children.<sup>[17,18,19]</sup> Of the cases, 40 % had a previous female child versus 16.7% of the controls had a female child. Gender of the previous child and PPD significantly correlated with each other with a p value of 0.028. Similar findings were noted by Modi VP et al.<sup>[20]</sup>

Various intrapartum and postpartum risk factors for PPD have also been explored in our study. 36.7% of the cases had cesarean delivery as compared to only 10% controls. Statistically significant association was noted between PPD and mode of delivery with a p value of 0.015, in turn contributing to the fact that cesarean delivery may increase the women's risk of developing PPD. These findings are supported by Boyce PM and colleagues who reported that women having cesarean section had six times more risk of developing PPD in comparison to women with spontaneous vaginal or instrumental delivery.<sup>[21]</sup> Prolonged duration of hospital stay significantly increased the risk of development of PPD (p value=0.001), though the literature on the same is limited.

## CONCLUSION

PPD is a recognised cause of increased maternal and neonatal morbidity. Identification of risk factors during routine antenatal visits will detect women requiring early help. In this study, the specificity of plasma oxytocin was 30.0% as the sample size was cut off due to covid pandemic. So to conclude, plasma oxytocin levels done in the late third trimester especially in women with risk factors may help in early identification and treatment of the vulnerable population and save many more maternal

lives. But future studies with adequate sample size are necessary to use plasma oxytocin as a predictive marker.

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