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Homocysteine and serotonin: Association with postpartum depression

S. Aishwarya [a], Soundravally Rajendiren [a,*], Shivanand Kattimani [b], Pooja Dhiman [a], S. Haritha [c], P.H. AnanthaNarayanan [a]

[a] Department of Biochemistry, JIPMER, Puducherry 605006, India
[b] Department of Psychiatry, JIPMER, Puducherry 605006, India
[c] Department of Obstetrics and Gynecology, JIPMER, Puducherry 605006, India

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ABSTRACT

Postpartum depression (PPD) is a disorder of multifactorial origin with significant consequences on both maternal and child health. One of the biological factors implicated is perturbed methionine–homocysteine metabolism. Since this metabolic pathway plays a significant role in myelination of nerve fibers, the growth and development of the child would also be adversely affected. We carried out this study in 103 women (58 with PPD and 45 without PPD) who delivered their child in our institute from December 2010 to November 2011. The study group was evaluated for PPD using Edinburgh postnatal depression scale with a cut-off score of 10. Assessment of fetal well being was done by APGAR score assessed immediately after birth. Serum folic acid, vitamin B12, homocysteine and serotonin was done by ELISA. We found significantly elevated levels of homocysteine in women with PPD as compared to those without PPD, both at 24–48 h as well as six weeks after delivery, although no associations were found with folate and vitamin B12 levels. Also, there was a significant negative correlation between serum homocysteine and serotonin levels in the postpartum depression group with a significant negative correlation between homocysteine and serotonin. Our study showed a significantly lower APGAR score in the infants born to mothers with PPD. Our study also shows that homocysteinemia is associated with PPD whether at the first week or sixth week, while low serum serotonin may play a role in depression during the first week, but may not have a role in depression status at the sixth week. Also, PPD in the mother is related to a low APGAR score in infants born to these mothers emphasizing the significance of both mental as well as nutritional status of the mother.

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1. Introduction

Postpartum depression (PPD) is a debilitating, multidimensional health problem affecting 10–15% of new mothers and has serious consequences for women, child and the family (Martin and Silverstein, 2009). PPD can develop in a woman during pregnancy, few months after having the baby, from miscarriage, or weaning the child from breastfeeding (NWHIC, 2002). Various biological, genetic, hormonal and psychosocial factors interact in order to provoke depression. One of the biological factors for PPD may be higher levels of homocysteine. The methionine–homocysteine metabolic pathway plays a major role in the methylation reactions involved in the biosynthesis of monoamine neurotransmitters (Folstein et al., 2007; Kim et al., 2008). Deficiency of these vitamins can lead to decrease in methionine levels with relative increase in homocystenine. Hyperhomocystenimia as such can affect the neurotransmitter (serotonin, dopamine and catecholamine) pathways that are involved in mood and behavioral changes. However, in this context there is a scarcity of studies with conflicting results and none with reference to homocysteine and PPD. A study by Abou-Saleh et al. (1999), reported a strong association between low folate levels and depressed mood at day seven after delivery whereas Rouillon et al. (1992) found no relationship between PPD and folate levels on the third day of delivery. Another important fact to be borne in mind while discussing maternal nutritional and mental status is the effect of these factors in the development and growth of the child. Recently the role of folate and vitamin B12 have been studied in child development (Molloy et al., 2008). The probable role played by vitamin B12 and folate may be their involvement in methionine–homocysteine metabolism, which is essential for the myelination of brain (Drar et al., 2008).

Hence the present study has been planned with the objectives to assess and compare the levels of homocysteine and its vitamin determinants in depressed and non depressed women during the 24–48 h postpartum period and at six weeks to evaluate whether

* Corresponding author. Tel.: +91 9442214256.
E-mail addresses: aiswarya.say@gmail.com (S. Aishwarya), soundy27@yahoo.co.in (S. Rajendiren), drshivanand@hotmail.com (S. Kattimani), harithas@hotmail.com (S. Haritha), phananthanarayanan@gmail.com (P.H. AnanthaNarayanan).

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the above said factors can predict the development of depression during the postpartum period and to find if serotonin levels have an association with homocysteine and its vitamin determinants in the study subjects. Also, effect of maternal depression was assessed by comparing APGAR scores for the infants born to these mothers.

2. Materials and methods

2.1. Study design and subjects

This study was conducted at the Department of Biochemistry, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, in collaboration with the Department of Obstetrics & Gynecology and Department of Psychiatry from December 2010 to November 2011. The study was approved by the Institute Research Council and Institute Human Ethics Committee. Women who delivered their child in JIPMER from December 2010 to November 2011 formed the subjects of the study. Those who were able to read either English or Tamil were included for screening purpose. A written informed consent was obtained from each subject. Detailed demographic and clinical data about each subject were collected after delivery. Psychosocial factors considered included socioeconomic status, number of children, marital harmony, and educational status of patient and her family. Women with previous history of any endocrine dysfunction associated with parameters of PPD, psychotropics drugs, neurological disorder, previous history of depression or any psychiatric illness and any complications during pregnancy were excluded from the study. Also, women with any illness in the third trimester were also excluded from the study.

2.2. Screening for presence of postpartum depression

The study group was evaluated for identifying PPD at 24–48 h after delivery and a second time at six weeks after the delivery, using Edinburgh postnatal depression scale (EPDS) Tamil/English Version. EPDS is a well validated scale consisting of questions related to depressive symptoms and each symptom is rated for its severity on four point Likert scale. Total score of EPDS can range from 0 to 30 and a cut-off score of 10 and above has shown good sensitivity and specificity to detect PPD (Adewuya et al., 2006; Teissedre and Chabrol, 2004; Adouard et al., 2005; Altshuler et al., 2008). No interventions were done during the period between assessments.

2.3. Assessment of fetal well being

APGAR score was assessed immediately after birth and at first day. Measurement of vitamin B12, folate, homocysteine and serotonin: five ml of blood sample was collected from all subjects at each time of assessment. The serum was separated by centrifuging the blood at 5000 rpm for 10 min at room temperature and stored it at −40 °C for the analysis of parameters. Serum folic acid, vitamin B12 and homocysteine were measured using direct competitive immunoassay by chemiluminescent technology in The ADVIA Centaur, Siemens Health care Diagnostic. Assay of serum serotonin was done by a commercial ELISA kit method.

2.4. Statistical analysis

To analyze and compare the groups, both descriptive and inferential statistics were used. The continuous data were assessed for the normality and accordingly appropriate parametric or non-parametric tests were used. To compare the variables which follow normal distribution, independent student's *t*-test were used and for non normal distribution, Mann–Whitney *U* test was used. The comparisons of categorical data between the groups were compared by using χ^2-test. For association studies Pearson correlation analysis was used. Receiver operator curve (ROC) analysis was performed to assess the predictive power of the study parameters and Youden index (sensitivity + specificity − 1) was resorted as a measure of accuracy. All statistical analysis was carried out at 95% confidence interval and the p value < 0.05 considered as significant finding. All statistical work was carried out by using SPSS version 16.

3. Results

One hundred and three subjects participated in the study out of which 58 were women with PPD and 45 were without PPD. Table 1

Table 1
Socio demographic characteristics of women with PPD and women without PPD.

Sl. no.	Characteristics		Total (*N*) 108	PPD *N* (%) 58	Non-PPD *N* (%) 45
1	Age (years)	<20	4	0(0)	4(9)
		20–25	78	51(88)	27(60)
		26–30	21	7(12)	14(31)
		>30	0	0(0)	0(0)
2	Gender of child	Male	46	27(46.5)	19(42)
		Female	56	31(53)	25(55)
		Both male and female (twins)	1	0(0)	1(2)
3	Parity	Primiparous	78	33(57)	45(100)
		Multiparous	24	24(43)	0(0)
4	Education	Elementary	10	5(8.6)	5(11.1)
		Secondary	65	40(69)	25(55.6)
		Collage	28	13(22.4)	15(33.3)
5	Socioeconomic status*	Low	36	15(25.9)	21(46.7)
		Moderate	67	43(74.1)	24(53.3)
		High	0	0(0)	0(0)
6	Employment	Employed	17	9(15.5)	8(17.8)
		Unemployed	86	49(84.5)	37(82.2)
7	Diet	Veg	11	7(12)	4(9)
		Non-veg	92	51(88)	41(91)

PPD, postpartum depression.
* Statistical significance.

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