Original Article

Association between Gestational Diabetes Mellitus and Postpartum Depression among Women in Eastern India: A Cohort Study

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Abstract

Background: The study was planned to evaluate the association between Gestational Diabetes Mellitus (GDM) and Postpartum Depression (PPD) in a rural population of Odisha, Eastern India. **Material and Methods:** Pregnant women in the first trimester were recruited and followed up till six weeks of postpartum. Gestational Diabetes Mellitus was assessed with 75 grams glucose challenge test and PPD was assessed at six weeks after delivery with Edinburgh Postnatal Depression Scale. Statistical difference between variables was assessed using Chi-square test, Fischer's exact test, and unpaired *T*-test. Covariates were adjusted using bivariate and multivariate logistic regression to estimate the association between GDM and PPD. **Results:** Out of 436 pregnant women recruited, 347 (89.6%) remained in the study. Prevalence of GDM was 13.9% (95% CI: 10.7–17.3) and PPD was 9.8% (95% CI: 6.6–12.9). Incidence of PPD in the GDM group was 14.58% (95% CI: 4.2–24.9) and in women without GDM was 9.06% (95% CI: 5.76–12.3). However, the association was not significant on multivariate logistic regression (Risk Ratio (RR) = 1.56, 95% C.I: 0.61–6.16; *P*-value = 0.35). **Conclusion:** This study demonstrated that women with GDM were at higher risk of developing PPD suggesting that an "at risk" approach should be implemented for screening.

Keywords: Depressive disorders, diabetes, post-natal, pregnancy

Introduction

Pregnancy and postpartum can be associated with psychological changes ranging from mild forms of mood changes to severe psychotic disorders.[1,2] Postpartum depression (PPD) is one of the most common psychiatric disorders associated with pregnancy and child birth.[3–5] In a systematic review and meta-analysis of Indian studies, pooled prevalence of PPD was reported to be 19%.[6] Studies from other developing countries have also reported varying prevalences from 8% to 60%.[7–9]

Postpartum depression can have grave consequences on the woman herself and the newborn. Hence, identifying the risk factors is important to adopt "at risk" approach for screening and timely management of PPD.[10] Though specific aetiology of PPD is not known, many social, biological, psychological factors like social support, stressful events during pregnancy, domestic violence, and presence of chronic conditions during or before pregnancy including gestational diabetes mellitus, sex of child, preexisting depression, or psychiatric illnesses have been reported to be associated with the development of PPD.[8,11]

A bidirectional link between diabetes and depression in general population is well established. In India, the prevalence of depression in diabetic patients ranged from 2% to 84% according to a systematic review.[12] Thus, it is postulated that

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the occurrence of GDM could also be associated with the development of psychiatric conditions including PPD. With increasing prevalence of diabetes, in general population and GDM, studying this association becomes even more significant. Studies evaluating the strength of the association between GDM and PPD have shown inconsistent results. Gestational Diabetes Mellitus precipitates the chances for PPD by inducing disturbances in the hypothalamic–pituitary–adrenal axis, inflammatory changes, and disorders in serotonergic regulation. A recent meta-analysis of 18 studies showed that the presence of GDM increased the risk of PPD by 1.5 times.[13] While few studies in the meta-analysis reported a significant positive association between GDM and PPD, others failed to find any. However, the estimated effect size would possibly be confounded as covariates were not adjusted for and also due to multi-etiological causation of PPD.[14,15] Many of these studies were not prospective and thus could not account for the effect of preexisting diabetes mellitus or psychiatric illness before pregnancy. Moreover, 14 of 18 studies were limited to USA and Europe and none of them were from Southeast Asia.

To fill the critical gap in literature, we did this prospective study to evaluate the independent temporal association between GDM and PPD in a rural population of Eastern India.

Materials and Methods

Study population

This prospective cohort study was conducted among pregnant women residing in a rural block (Tangi) of a coastal district (Khordha) of Odisha, Eastern India. Tangi block has a population of nearly 1,69,000 and has 69 inhabited villages. Women in reproductive age group are provided antenatal services at the village level through outreach sites on fixed days and through domiciliary visits by community nurses called Auxiliary Nurse Midwife and community health volunteers called Accredited Social Health Activist (ASHA). Women also avail the services directly from six Primary Health Centers and one Community Health Center (CHC) located in the study area. Auxiliary Nurse Midwife and ASHA keep track of any new pregnancy in the area through routine domiciliary visits and also when the women visit outreach centers or health facilities. Pregnant women identified during this process formed our study population. Women in the first trimester of pregnancy without any preexisting history of diabetes or depression and who can comprehend the interview questions were the eligible participants. They were explained the study procedures using a participant information sheet and written informed consent was obtained. The study was approved by the Institutional Ethics Committee of All India Institute of Medical Sciences, Bhubaneswar (Reference number: T/IMF/17-18/26).

We planned to recruit 491 pregnant women according to the sample size estimate assuming the prevalence of GDM as 19%[6] and prevalence of PPD among pregnant women with GDM as 30% and 15% among those without GDM and further accounting for a 20% loss to follow up at a power of 80% and significance level of 95%.

Data collection

Recruitment was done from ANC outpatient department at CHC and community visits on all days from August 2018 to January 2019 and follow-up was completed by September 2019. Follow-up was ensured by telephonic consultations and house visits of the participants. Data was collected at four visits during antepartum and postpartum periods. During the first study visit (<12 weeks of gestation), sociodemographic details were collected and women were assessed for diabetes, depression, high blood pressure, thyroid status, history of chronic morbidities (diabetes mellitus, hypertension, hypothyroidism, chronic obstructive pulmonary disorder), anaemia, body mass index, previous obstetric history and outcome of each pregnancy and addiction history. During second visit (24–32 weeks gestation), pregnant women who screened negative for diabetes were again assessed for diabetes at the CHC. The third and fourth visits were community based. Third visit was made after the term of pregnancy and details related to the outcome of pregnancy were collected (date of delivery, birth weight, mode of delivery, gender of the newborn, birth weight). Fourth visit was made at six weeks postpartum to assess PPD.

Measures

Antepartum and PPD was assessed with the Edinburgh Postnatal Depression Scale (EPDS). Edinburgh Postnatal Depression Scale is a widely validated tool for screening depression during antepartum and postpartum period and consists of 10 items to be rated on a four-point scale ranging from 0 to 3; thus, possible score ranges from 0 to 30. Based on previous studies, the cut-off for the diagnosis of depression was taken as a score above 12.[16] Gestational Diabetes Mellitus was diagnosed using 75 grams glucose challenge test as recommended in the national guidelines for diagnosis and management of gestational diabetes mellitus.[17] Seventy-five grams of glucose was given in 300 ml of water irrespective of fasting stage and blood glucose was measured by glucometer using reagent strips after two hours. The blood glucose level of ≥140 mg/dl after two hours of glucose load was taken as cut off for diagnosis of GDM. Hemoglobin was measured using an automated hemoglobinometer (HemoCue Hb 301) and hemoglobin <11 gm% was considered as anaemia. Thyroid hormones were measured in automatic biochemistry analyzer and cut-off was set as per the manufacturer's instruction. Both the glucometer and hemoglobinometer were calibrated as per the manufacturer's instructions to maintain quality reporting. The serum was separated from blood collected from participants by centrifugation and tests for serum Thyroid Stimulating Hormone (TSH) were performed by chemiluminescence method in Siemens Advia Centaur XP immunoassay analyzer. Serum Ultra TSH done here is a third generation test, based on the principle of a solid phase enzyme-linked immunosorbent assay and offers a sensitivity of 0.05 μIU/ml. All the parameters were assayed on the same

day of sample collection under standard assay protocol using reagents and reference intervals from Siemens Healthcare Diagnostics Inc., USA. To diagnose hypothyroidism, an adult euthyroid reference interval of 0.55–4.78 μIU/mL was taken as per the TSH3-Ultra product insert. Quality control was maintained by using Bio-Rad internal quality control samples daily and external quality control by monthly samples from the Association of Clinical Biochemists of India prepared by Christian Medical College, Vellore.

Study variables

Presence of GDM was exposure variable and presence of PPD was outcome variable. Age, parity, bad obstetric history, hypothyroidism, anaemia, presence of other comorbidities, socioeconomic status, and sex of child were considered as covariates.

Statistical analysis

The data were entered in Microsoft Excel 2013. All the statistical analysis were done in Stata 17.0. Results of descriptive analysis (sociodemography, antenatal characteristics, and risk factors) were presented as means or proportions. Statistical difference between variables was assessed using Chi-square test and Fischer's exact test for categorical variables and unpaired *T*-test for continuous variables. Association of PPD with various factors (sociodemography, antenatal characteristics, and risk factors) was done with bivariate logistic regression. Variables found significant with bivariate analysis (*P*-value <0.25) were included in multivariate logistic regression model. Variables with *P*-value <0.05 on multivariate regression were considered significant.

Results

Out of 436 pregnant women recruited in the study, 98 (20.4%) could not complete the assessment for either GDM or PPD. Baseline characteristics of 347 women who remained in the study were similar in every respect to women who were lost to follow-up [Table 1]. Mean (± S.D.) age of the study participants was 23.9 (±3.7) years. The age of the participants ranged from 15 to 36 years. Mean (± S.D.) years of completed schooling among the study participants was 8.6 (±3.2) years. At the time of recruitment; 4.8% of women reported having a preexisting chronic condition, while 28% were diagnosed to be underweight and 47.7% were anaemic. Hypothyroidism during pregnancy was diagnosed among 31.4% women. Baseline characteristics of study participants are outlined in Table 1.

At the time of recruitment, 7.8% (95% CI: 5.3–10.3) of the participants were diagnosed with antepartum depression. About 13.9% (95% CI: 10.7–17.3) of the participants were diagnosed with GDM. About 9.8% (95% CI: 6.6–12.9) of the participants were diagnosed with PPD using Edinburgh Postnatal Depression scale [Table 2].

Prevalence of PPD in women with GDM was 14.58% (95% CI: 14.4–14.59) and 9.06% (95% CI: 5.76–12.3) in women without GDM. Participants with GDM were found to be 1.6 times more prone to develop PPD. However, the association was not statistically significant (RR: 1.61, 95% CI: 0.74–3.49, *P*-value: 0.23) [Table 2]. Among those who had antepartum depression, the risk of PPD was two times higher but the association was not statistically significant. (RR = 1.95, 95% C.I: 0.63–6.09, *P*-value: 0.25).

In bivariate logistic regression, the presence of any chronic disease, anaemia and ante-natal depression, were found to have a *P*-value of <0.25 and thus included in multivariate model. However, on multivariate logistic regression, these variables were not found to be significantly associated with PPD. In multivariate logistic regression model, women with GDM had a higher risk of PPD but the association was not significant after adjusting for covariates (RR = 1.56, 95% C.I: 0.61–6.16; *P*-value = 0.35) [Table 3].

Discussion

The present prospective cohort study was done to explore the association between GDM and PPD. We tried to establish the temporality by recruiting pregnant women during the antenatal period and followed them up till postpartum period. In the present study, 20% of the participants were lost to follow-up. Most of the post-partum mothers were residing at their maternal home and could not be contacted telephonically in the follow-up visits owing to high loss to follow-up. Literature suggests that >20% loss to follow-up can impart potential bias to the study results.[18] However, it was seen in our study that there was no statistically significant difference among various attributes in participants who were lost to follow-up and those who were not.

The mean age of pregnant women in our study was 23.9 years which was almost similar to other studies done on pregnant women for the estimation of GDM.[19,20]

In this study, 13.9% (95% CI: 10.7–17.3) of the participants were diagnosed with GDM using 75 grams glucose challenge test. A meta-analysis showed that the prevalence of GDM in Asia was 11.5% (95% CI: 10.9–12.1). The difference might be attributed to the varied diagnostic criteria, study settings, and screening procedures adopted in the included studies of meta-analysis.[21]

According to a meta-analysis, women diagnosed with GDM were at higher risk of developing antepartum depression.[22] Also, the American College of Obstetricians and Gynaecologists recommends that all the pregnant women should be screened for depression at least once during pregnancy or in the postpartum period.[23] In the present study, at the time of recruitment, 7.8% (95% CI: 5.3–10.3) of the participants were diagnosed with antepartum depression and at six weeks of delivery, 9.8% (95% CI: 6.6–12.9) were diagnosed with PPD using Edinburgh Postnatal Depression scale. In our study, PPD was not significantly associated with any of the select variables. According to a meta-analysis,[6] the overall pooled estimate of the prevalence of PPD in India

Table 1: Distribution of the participants by sociodemographic and clinical characteristics at baseline

Characteristic	Category	Original Cohort *n*=436	Participants followed up *n*=347	Participants lost to follow-up *n*=89	*P*
Age (in years)	<19	33 (7.6)	29 (8.4)	4 (4.5)	0.37
20-25	263 (60.2)	208 (59.9)	55 (61.8)		
26-30	121 (27.8)	93 (26.8)	28 (31.5)		
>30	19 (4.4)	17 (4.9)	2 (2.2)		
Mean age in years (SD)		23.9 (3.65)	23.9 (3.78)	24.1 (3.12)	0.64
Education	Illiterate	15 (3.4)	10 (2.9)	5 (5.6)	0.20
	Literate	421 (96.6)	337 (97.1)	84 (94.4)	
Occupation	Employed	30 (6.9)	24 (6.9)	6 (6.7)	0.95
	Homemaker	406 (93.1)	323 (93.1)	83 (93.3)	
Median family income (IQR)		12,000 (9,000 to 20,000)	12,000 (8,000 to 20,000)	12,000 (9,000 to 18,000)	0.92
Socioeconomic status	Upper Middle /Middle	285 (65.4)	229 (65.9)	56 (62.9)	0.58
	Lower Middle/ Lower	151 (34.6)	118 (34.1)	33 (37.1)	
Type of family	Nuclear	33 (7.6)	29 (8.4)	4 (4.5)	0.27
	Extended	403 (92.4)	318 (91.6)	85 (95.5)	
Median number of members in the family		6	5	6	0.45
Mean age of head of household (SD)		56.9 (11.86)	56.4 (12.07)	58.9 (10.85)	0.07
Gender of Head of household	Male	364 (83.5)	285 (82.1)	79 (88.8)	0.13
	Female	72 (16.5)	62 (17.9)	10 (11.2)	
Education of head of household	Illiterate	118 (27.1)	95 (27.4)	23 (25.8)	0.77
	Literate	318 (72.9)	252 (72.6)	66 (74.2)	
Mean years of schooling of head of household		4.3 (3.75)	4.3 (3.78)	4.2 (3.10)	0.74
Distance of residence from CHC (in km)		8.81 (7.21)	8.87 (7.48)	8.55 (6.09)	0.71
Mean age at marriage (SD)		20.6 (3.1)	20.6 (3.1)	20.9 (3.5)	0.49
Primi-gravida		203 (46.5)	159 (45.8)	44 (49.4)	0.54
Planned pregnancy	Yes	286 (65.5)	225 (64.8)	61 (68.5)	
	No	150	122	28	0.51
Underweight (weight <45 kg)		122 (28.0)	102 (29.4)	20 (22.5)	0.19
Anaemia		186 (42.7)	150 (43.2)	36 (40.4)	0.63
Hypothyroidism		137 (31.4)	110 (31.7)	27 (30.3)	0.80
History of any chronic disease (prepregnancy)		21 (4.8)	16 (4.6)	5 (5.6)	0.69

Table 2: Prevalence and association of Gestational Diabetes Mellitus and Postpartum depression (*n*=346)

Characteristic	Number	Prevalence/ Estimate	95% C.I.
Gestational Diabetes Mellitus	48	13.9	10.7-17.3
Postpartum Depression			
Overall	34	9.8	6.6-12.9
In women with GDM (*n*=48)	7	14.6	4.2-24.9
In women without GDM (*n*=298)	27	9.1	5.76-12.3
Risk Ratio (of PPD in women with GDM and without GDM)		1.61	0.63-6.09

was 19% (95% CI: 17–22). Different time periods varying from two weeks to one year of pregnancy, urban and rural study settings, and different scales of assessment were used in meta-analysis, which might attribute to the higher difference in prevalence from our study.

Existing literature suggests that the diagnosis of a woman with GDM will increase their susceptibility to either depression or anxiety.[24] In this study, the prevalence of PPD was around 1.6 times higher among women with GDM than women without GDM. The association after adjusting for all the covariates was not statistically significant. The results of our study are similar to a retrospective cohort study wherein participants diagnosed with GDM had nearly two-fold higher risk of developing PPD.[25] A meta-analysis showed that women diagnosed with GDM had significantly increased risk of PPD (RR - 1.59) and suggested that an assessment of PPD should be done in women with GDM.[13]

A cohort study has demonstrated that women with higher glucose levels during pregnancy are more prone to develop PPD. It was also seen in the study that EPDS scores were significantly higher at one month and three months' postpartum period.[26] Hence, healthcare providers can be trained to screen women with GDM for PPD during follow-up visits in the early post-natal period. After appropriate training, front-line healthcare workers can also assess the risk for PPD during scheduled visits in the post-natal period as a part of home-based newborn care program.[27] Women with GDM can be counseled about the importance of adherence to treatment for GDM and

Table 3: Association of Postpartum depression with selected variables

Variable	Unadjusted OR(95% CI)/	Adjusted OR(95% CI)/
Age (in years)	1.45 0.14, 0.9-2.4	1.33 0.26, 0.80-2.22
Mean years of schooling	1.01 0.79, 0.9-1.14	-
Education of the participant	1.0 0.29, 0.08-0.16	-
Occupation of the participant	1.2 0.8, 0.27-5.38	-
Total family income	1.0 0.44, 0.99-1.00	-
Socioeconomic status	0.67 0.33, 0.30-1.49	-
Type of family	0.6 0.41, 0.20-1.92	-
Gender of head of household	1.2 0.67, 0.50-2.92	-
Chronic diseases* (before pregnancy)	0.44 0.23, 0.12-1.66	0.44 0.24, 0.11-1.70
Hypothyroidism	0.88 0.75, 0.41-1.92	-
Anemia	0.64 0.22, 0.31-1.30	0.63 0.22, 0.31 - 1.31
GDM	1.71 0.23, 0.70-4.18	1.56 0.35, 0.62-3.91
Ante-natal depression	1.95 0.25, 0.63-6.09	1.94 0.26, 0.61-6.16
Parity	1.1 0.83, 0.53-2.20	-
Presence of female child in the family	1.6 0.33, 0.63-3.94	-
Pregnancy	1.00 0.99, 0.48-2.10	-
Type of delivery	0.82 0.63, 0.37-1.83	-
Low-birth weight	0.72 0.42, 0.32-1.61	-
Gender of the child	1.15 0.69, 0.57-2.35	-

*Chronic diseases (before pregnancy) - Diabetes, Hypertension, Hypothyroidism, COPD

also about the warning signs and symptoms of PPD. They can be educated about the need to approach health facilities on development of any signs or symptoms. This multipronged provider-based and client-based approach along with the linkage of front-line healthcare workers can help to identify those at risk of PPD and offer timely interventions to those in need.

Our study had various strengths. Participants who were lost to follow-up were similar to the original cohort, thus reducing the effect of selection bias. We excluded participants with preexisting diabetes and psychiatric conditions and thus were able to establish a causal association. In the present study, we could not attain statistical significance though the effect size was similar to previous studies. As the loss to follow-up was high, generalizability and external validity of the study will be limited.

Conclusion

This cohort study demonstrated that women with GDM were at higher risk of developing PPD. Hence, "at risk" approach in routine ante-natal care can be implemented and all pregnant women with GDM can be screened for PPD. To establish the conclusive association of GDM and PPD and its dependent factors in the Indian population, further research involving in-depth analysis in various sites and a larger sample is required.

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Conflicts of interest

There are no conflicts of interest.

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