



Antenatal Depressive Symptoms and Neurodevelopment Outcomes in Children at 30 Months. A Study From South India

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Background: Prevalence of antenatal depression in low and middle income countries is high. However studies examining the association between maternal antenatal depression and early childhood development from these countries are scarce. The objective of the study was to examine the association between antenatal depressive symptoms assessed serially during pregnancy and child neurodevelopment outcomes in mother-child dyads part of a randomized control trial of maternal B12 supplementation during pregnancy.

Method: Subjects were 203 women who had participated in the placebo-controlled, randomized trial of vitamin B12 supplementation during pregnancy and 6 weeks post-partum on whom serial assessments of depressive symptoms in each of the trimesters were available. Cognitive, receptive language, expressive language, fine motor skills and gross motor skills were assessed at 30 months using the Bayley's Scale of Infant Development-3rd edition (BSID-III). Antenatal depressive symptoms were assessed at three trimesters using the Kessler's 10 Psychological Distress Scale (K10). Women were classified into three categories: not depressed (K10 <6 in all trimesters), with intermittent depressive symptoms (K10 ≥6 in at least one trimester) and with persistent depressive symptoms (K10 score ≥6 in at least 2 trimesters).

Results: 112 (55.2%) of the women did not have depressive symptoms, 58 (28.6%) had intermittent depressive symptoms and 33 (16.2%) had persistent depressive symptoms. The children of women with intermittent antenatal depressive symptoms scored lower on the receptive language domain on BSID-III compared to children of women who were not depressed on univariate analysis, but not on bivariate regression analysis. Women with persistent depressive symptoms had lower educational attainment ($p = 0.004$), lower social support ($p = 0.006$) and used more emotional coping strategies ($p = 0.005$) compared to the not depressed group.

Conclusions: A significant number of women in south India had antenatal depressive symptoms. Findings from this study suggest a possible association between antenatal depressive symptoms and receptive language in children. Larger studies including women with clinical depression are needed to confirm these findings.

Keywords: antenatal depressive symptoms, neurodevelopment, language, education, social support, coping

INTRODUCTION

Higher maternal stress and anxiety during pregnancy are associated with poorer cognitive development in infants (1) and young children (2). Children of women with persistent depression during pregnancy had higher odds of developmental delays at 18 months on the Denver Developmental Screening Test (adjusted odds ratio 1.34, 95% CI 1.11, 1.62) (3). In a prospective study of 1030 mother-child pairs from the US, children of women with depression at mid-pregnancy had lower scores on Peabody Picture Vocabulary Test (PPVT) at 30 months (4). In contrast, in a study among US Caucasian women, a mild to modest level of a composite score of maternal depression measured at 24 weeks of pregnancy was associated with higher cognitive scores on Bayley's Scale of Infant Development (BSID) II in children ($n = 82$) at 24 months (5). A recent study concluded that antenatal anxiety but not depression was associated with poorer cognitive outcomes in 3 year old children (6).

The prevalence of antenatal depressive symptoms is high among women in the Asian subcontinent (7, 8). However, studies examining the association between maternal antenatal depression and early childhood development from resource-poor settings are scarce. In a study from Ethiopia, depressive, anxiety and somatic symptoms during pregnancy were associated with poorer infant motor development on BSID-III in infants at 12 months but this association became non-significant after adjusting for socioeconomic, maternal and pregnancy related factors (9).

A recent review highlighted the mutual influence of maternal antenatal depression and nutritional status and their effect on child neurocognitive development (10). The authors recommend including both exposures in study designs to determine their relative and/or additive impact on child neuro development. The effects of maternal Iron Deficiency Anemia (IDA) and Common Mental Disorders (CMD) during pregnancy on child development found that a combined effect of maternal IDA and CMD resulted in a larger reduction in the cognitive domain on BSID III, than the individual effects (11). Vitamin B12 and its metabolites have also been linked to maternal depression and child neurodevelopment (12). The GUSTO study (13) examined the relationship of plasma folate and B12 levels to antenatal depression in 709 women in Singapore. They observed that plasma folate, but not B12 levels, was significantly lower in those with probable depression. Neurodevelopmental outcomes were measured on 443 children from this cohort at 2 years using BSID III (14) and compared across groups based on maternal B12 status, deficient (<148 pmol/L), insufficient (148–220.9 pmol/L) and sufficient (>221 pmol/L). Infants of mothers with

vitamin B12 deficiency had 0.42 SD lower scores on the cognitive domain of BSID III when compared to infants of mothers with sufficient levels of B12. There was no additive effect of antenatal depression on cognitive outcomes.

The effects of maternal antenatal depression on child cognitive or temperamental outcomes could be trimester specific due to programming effects depending on the developmental age and sensitive periods (15). In addition, chronic maternal depression has been linked to poorer neurodevelopmental outcomes (3, 16). Hence it is important to assess maternal depression at multiple time points during pregnancy.

Results from previous studies that examined the effects of depressive symptoms during pregnancy on child cognitive outcomes are inconsistent. The majority of these studies have measured depression at only one time point during pregnancy. A recent study that investigated prenatal/post natal trajectories of maternal anxiety measured at multiple time points during pregnancy and in the post natal period found that only high persistent anxiety was predictive of developmental delay in children at 3 years (17). It is also seen in previous studies that maternal nutrition, especially vitamin B12, its metabolites and folate could have an association with maternal depression and child neurodevelopment. Thus examining the impact of maternal antenatal depressive symptoms and nutritional status on child cognitive outcomes is particularly relevant to low and middle income countries (LMIC) as the rates of antenatal depression and inadequate nutritional status during pregnancy are high. We performed a double-blind, placebo-controlled trial of oral vitamin B12 during pregnancy and early lactation in South Indian women (18). As part of this trial, antenatal depressive symptoms were measured at three trimesters in pregnancy. The objective of the present study was to examine the association between antenatal depressive symptoms, assessed serially during pregnancy and neurodevelopment outcomes in children. We hypothesized that children born to mothers with persistent depression will perform poorer on BSID-III compared to mothers who did not report any depressive symptoms during pregnancy. In addition, we also compared the plasma levels of B12 and its metabolites during pregnancy in women with and without depressive symptoms.

MATERIALS AND METHODS

Women and children who enrolled in the parent placebo-controlled, randomized trial of vitamin B12 supplementation during pregnancy and 6 weeks post-partum were eligible for inclusion in this study. The parent randomized controlled trial

was registered at clinicaltrials.gov as NCT00641862. The present study was approved by the Institutional Ethics Committee, St. John's National Academy of Health Sciences, Bangalore and the Institutional Review Board of the Harvard T. H. Chan School of Public Health. The recruitment site was Hosahalli Hospital, a government hospital serving an underserved community from urban Bangalore. Eligibility for the parent trial included women

aged ≥18 years who had registered for antenatal care at/before 14 weeks gestational age. Excluded were women with multiple gestations, chronic medical conditions, those who anticipated moving out of the area before study completion, those who tested positive for hepatitis B (HepBsAg), HIV or syphilis (VDRL) infections, and those who were already taking daily vitamin supplements in addition to folate and iron. The women were scheduled to be screened by Kessler psychological distress scale K-10) during the three trimesters in the parent trial. Women with severe depressive symptoms (K-10 scores ≥ 20) were referred to a government psychiatric facility for further evaluation and treatment. The present study used a convenient sample from the parent trial that consisted of women who were assessed for depressive symptoms at a minimum of 2 out of 3 time points during the antenatal period (Figure 1).

The women were approached for the 30 month cognitive assessment of their children and consent was sought. 203 mother-child pairs participated in the study. After written informed consent was obtained for the assessment, a study research assistant reviewed the baseline socioeconomic and demographic data that was collected upon initial entry into the study (Table 1).

Assessment of Child Neurodevelopment

The Bayley Scales of Infant Development, 3rd edition, (BSID-III) was used to assess infant neurodevelopment status at 30 months of age ± 2 weeks. The scales assess five domains: cognitive, language (receptive and expressive), motor (fine and gross), social-emotional, and adaptive (conceptual, social, practical). The latter two domains were not assessed as they were deemed not culturally appropriate. BSID III is a widely used instrument for the measurement of neurocognitive assessment in children at this age (5, 9, 11, 14). The instructions for the test items were

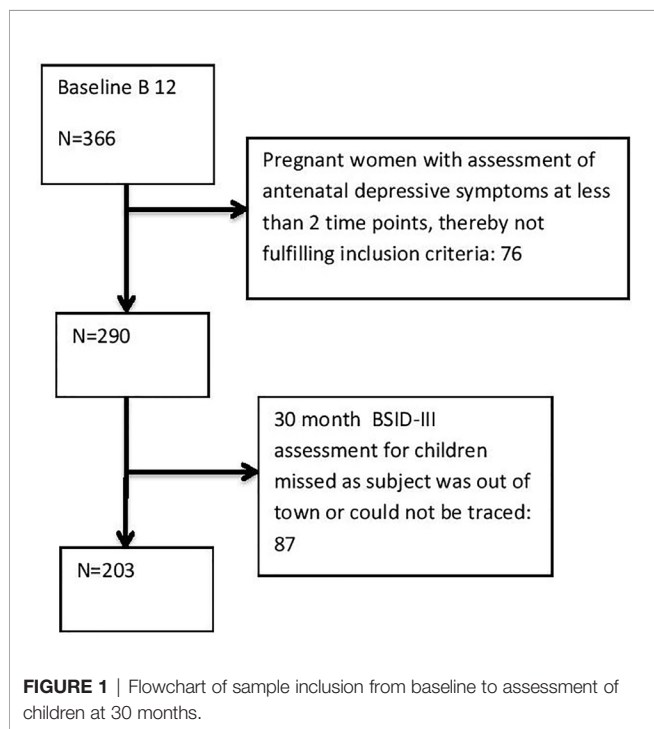


TABLE 1 | Socio-demographic characteristics, birth outcomes and K10 scores of pregnant women whose children underwent BSID-III testing at 30 months of age.

Parameters	Not Depressed (n = 112)	Intermittently Depressed (n = 58)	Persistently Depressed (n = 30)	p value
Age, (years)	27.4 ± 3.8 ¹	26.4 ± 3.6 ¹	26.8 ± 3.3 ¹	0.18
Level of education				0.004
Up to middle school	16 (15.8) ²	15 (28.3) ²	14 (46.7) ²	
High school	50 (49.5) ²	28 (52.8) ²	11 (36.7) ²	
Post high school	35 (34.7) ²	10 (18.9) ²	5 (16.7) ²	
Monthly household income, INR	7000 (5000,10000) ³	8000 (5000,10000) ³	5500 (4000,9250) ³	0.30
Maternal employment				0.99
Employed	13 (13) ²	7 (13) ²	4 (13) ²	
Unemployed	88 (87) ²	46 (87) ²	26 (87) ²	
Parity				0.64
0	56 (54.4) ²	39 (73.6) ²	19 (63.3) ²	
≥ 1	47 (45.6) ²	14 (26.4) ²	11 (36.7) ²	
Sex of the baby				0.76
Male	45 (46) ²	25 (51) ²	12 (43) ²	
Caesarian section	32(28.6) ³	12(20.7) ³	8(26.7) ³	0.51
Gestational age at birth	39.2(38.4,39.6) ²	39.2(38.1,39.6) ²	39.0(38.2, 40.0) ²	0.83
Infant birthweight (kg)	3.0 (2.5,3.25) ³	2.85 (2.53, 3.23) ³	2.75 (2.5,3) ³	0.36
IUGR	31(27.7) ²	19(32.8)	12(40)	0.65
Mean (SD) K 10 score	1 (0.1) ³	4 (3,5) ³	9 (6,12) ³	<0.001

¹Mean ± SD.

²N(%).

³Median (Q1, Q3).

IUGR, intrauterine growth retardation (birth weight less than the 10th percentile of norms for gestational age).

translated into the local language (Kannada). Two master's level psychologists experienced in child developmental testing, trained in the administration and scoring of BSID-III by an international expert (DB) and blind to group assignment administered the tests. We used raw scores from BSID-III for comparing the groups since age-specific norms are not available for Indian children. The BSID-III raw scores were adjusted for the children's gestational age at birth.

Assessment of Psychological Factors

Kessler Psychological Distress Scale

Depressive symptoms were assessed using Kessler Psychological Distress Scale (K-10). The K-10 consists of 10 items based on a 4-week recall period with each item having five response categories and is scored from 0 to 4 (19). In the present study, we administered a translated version of K-10 in local language (Kannada) used in previous studies of assessment of antenatal depressive symptoms (7, 20). In a previous study among South Indian pregnant women, K-10 was found to be good screening instrument for identifying antenatal depression in South India at a cutoff score ≥ 6 (sensitivity = 100%, specificity = 81.3%, and area under the curve = 0.95). A high degree of correlation was also found between Edinburgh Postnatal Depression Scale (EPDS) and K10 scores (Spearman's $r = 0.67$; $p < 0.01$) (20). It was noted in the study that participants had difficulty in comprehending some of the items on EPDS and the use of different response options per item question on the EPDS as compared with the same Likert structure for all item options on the K10. For these reasons, we chose to use K10 as the demographic characteristics of the participants in the present study were similar to the population in the original study that compared K10 and EPDS. Women who had K-10 scores ≥ 6 in 2 or more trimesters of pregnancy were categorized as persistently depressed. Women with K10 scores < 6 at all trimesters belonged to the non-depressed category, and women with K10 scores ≥ 6 in any one trimester were defined as intermittently depressed.

Social Support Scale

A questionnaire in local language was used to measure a broad range of social support available to the woman (21). The questionnaire consisted of 12 items; six reflecting instrumental and six reflecting emotional support with options ranging from definitely not enough (score = 1) to definitely enough (score = 4). This scale was administered in the second trimester.

Coping Checklist

This 70 item scale scored dichotomously as "yes" or "no" indicating the presence or absence of a particular coping behavior (22). The test retest reliability was 0.74. The scale gives information on whether the person uses problem solving coping or emotional coping strategies and has been used in the Indian setting in a variety of populations including women (23). This scale was administered in the second trimester.

Assessment of Dietary Intake During Pregnancy

A pretested interviewer-administered Food Frequency Questionnaire (FFQ) (24) was used to assess habitual dietary intake during the three

trimesters. Standard measures were placed before the respondent to quantify the portion size of each food item when administering the FFQ by trained interviewers. Nutrient information was obtained for 27 macronutrients and micronutrients. We compared energy, carbohydrate, protein, and fat intakes and micronutrients riboflavin, vitamin B6, vitamin B12, folate, and iron intake averaged over three trimesters across the three groups of women.

Assessment of Biochemical Parameters During Pregnancy

Details of biochemical assays have been previously described (18). Briefly, 10 ml of blood was obtained from the women by venipuncture at 12 weeks (baseline), 24 weeks and 33 weeks of pregnancy. The plasma and RBCs were separated and stored at -80°C until analysis. Plasma vitamin B12 was measured by electrochemiluminescence (Roche Diagnostics Mannheim, USA). The intraday and interday assay CVs for vitamin B12 were 0.54% and 2.44% respectively. Plasma total homocysteine (tHcy) and methyl malonic acid (MMA) were estimated by GC-MS (model 3800; Varian, Palo Alto, CA, USA). The interday assay CVs for tHcy and MMA were 5.04% and 5.57% respectively and the intraday assay CVs were 5.60% and 6.92%, respectively. Erythrocyte folate was measured by a competitive immunoassay with direct chemiluminescence detection on an automated immunanalyzer (ADVIA Centaurs, Tarrytown, New York, USA). The intra-assay and inter-assay variabilities were 1.9% and 5.2%, respectively. The following cutoff values were used: low vitamin B12 as < 150 (pmol/L), elevated MMA as > 0.26 ($\mu\text{mol/L}$) and elevated tHcy as > 15.0 ($\mu\text{mol/L}$).

STATISTICAL ANALYSIS

We used SPSS Version 22 for all analyses. Continuous data were described using mean \pm SD and categorical data using n (%). The normality of the data was examined by graphically evaluating Q-Q plots. Kruskal Wallis test was used to compare the three groups of women on biochemical parameters, psychological and cognitive measures as they were skewed. Post-hoc comparisons were done using Mann-Whitney U-test with Bonferroni adjusted p values. Bivariate linear regression analysis was performed if the initial non-parametric comparisons were statistically significant. Regression coefficients (β) and corresponding 95% confidence interval (95% CI) are reported. The level of significance used for statistical significance was $P < 0.05$.

RESULTS

Of the 365 women who were recruited in the parent trial, 203 mother-child dyads were eligible for the present study (**Figure 1**). There were no differences in the socio demographic characteristics or baseline biochemical characteristics of the women included in the study and those who were excluded (data not shown). One hundred and twelve women (55.2%) did not report depressive symptoms in any of the trimesters (not depressed group), while 58 women

(28.6%) reported depressive symptoms at one trimester (intermittent depressed group) and thirty three women (16.2%) had depressive symptoms in at least 2 trimesters (persistent depressed group).

Women with persistent depressive symptoms had a lower educational attainment compared to the other two groups of women (Table 1). Maternal age, family income, parity, maternal employment, sex of the infant and birth outcomes that included mode of delivery, birth weight, gestational age at birth and intrauterine growth restriction were not associated with the presence of persistent depressive symptoms during pregnancy (Table 1). Dietary intakes were not significantly different between the three groups of women (data not presented).

Nutritional markers during pregnancy (vitamin B12, MMA, tHcy, erythrocyte folic acid and Hb) across the three trimesters were not significantly different among the three groups of women (Table 2).

The number of women who had low scores on social support scale was significantly higher in the persistently depressed group. Women with persistent depressive symptoms used more emotional coping mechanisms compared to women in the not depressed group (Table 3).

The receptive language sub-domain score was significantly lower in children of women with intermittent depressive symptoms compared to children of women with no depressive symptoms and was similar to the score of children of women with persistent depressive symptoms (Table 4). However, the difference in receptive language scores on BSID-III was not significantly different between the three groups of women in a bivariate linear regression analysis ($B = 1.42$, 95% CI: $(-0.43, 3.28$ for “no depression” vs “intermittent depression” and $B = 1.87$, 95% CI: $-0.61, 4.34$ for “persistent depression” vs “intermittent depression”) after adjusting for total scores for coping and social support.

DISCUSSION

We found that a significant proportion of pregnant women in South India had depressive symptoms across multiple time points of assessment during pregnancy. Antenatal maternal depressive symptoms were associated with poorer child performance on receptive language domain on BSID-III on univariate analysis, though this association did not emerge on a bivariate regression analysis. Women with persistent depressive

TABLE 3 | Psychological characteristics of the three groups of pregnant women whose children underwent BSID-III testing at 30 months of age.

Variables	Not Depressed (n = 112)	Intermittently Depressed (n = 58)	Persistently Depressed (n = 30)	p value
Social Support (Social support scale)				
Instrumental	1 (0.9) ¹	5(8.6) ¹	4(13.3) ¹	0.02
Emotional	2 (1.8) ¹	3 (5.2) ¹	9 (30) ¹	<0.001
Total	2 (1.8) ¹	6 (10.3) ¹	7(23.3) ¹	0.01
Coping mechanisms (Coping Checklist)				
Problem solving	5 (4,7) ²	6 (4,7) ²	5 (4,7) ²	0.58*
Emotional	21 (18,24) ²	23 (20,25) ²	23 (21,26) ²	0.01*
Seeking social support	5 (3,5) ²	5 (4,5) ²	5 (4,5) ²	0.91*
Total	31 (28,34) ²	33 (29,36) ²	33 (30,36) ²	0.03*

¹N(%) of subjects who scored below median.

²Median (Q1, Q3) values across trimesters.

p value from Chi square test.

*p value from Kruskal Wallis test.

TABLE 4 | BSID III subdomain scores at 30 months of the children of the three groups of pregnant women based on depressive symptoms.

Domain	Not Depressed (n = 112)	Intermittently Depressed (n = 58) Median (Q1, Q3)	Persistently Depressed (n = 33)	p value
Cognitive	72 (69, 75)	71.5 (69.75, 73)	71 (69, 75)	0.62
Receptive language	38 (34, 41)	35.5 (32, 39)	37 (34, 40)	0.04
Expressive language	37 (34, 38)	35 (32, 38)	36 (33, 38)	0.10
Fine motor skills	47 (45, 49)	46 (44, 48)	47 (44, 49)	0.22
Gross motor skills	68 (64, 69)	67 (62, 69)	66 (63, 68)	0.29

p value from Kruskal Wallis test.

symptoms had lower educational attainment and reported lower social support (instrumental and emotional) and used more emotional coping strategies compared to women who were not depressed or who were intermittently depressed. There were no significant differences in average dietary intakes across the three trimesters of pregnancy among the three groups of women. There were no significant differences in plasma B12, elevated tHcy, MMA, erythrocyte folate levels and anemia among the three groups of women.

A high prevalence rate of antenatal depressive symptoms in our study is consistent with earlier observations among pregnant women from low and middle income countries (LMIC) (7, 8).

TABLE 2 | Biochemical characteristics of pregnant women whose children underwent BSID-III testing at 30 months of age.

Variables	Not Depressed (n = 112)	Intermittently Depressed (n = 58)	Persistently Depressed (n = 30)	p value
Vitamin B12 pmol/L	149.7(104.3,204.1)	166.3 (118.1,261.7)	148.1 (112.4,188.9)	0.16
MMA 0.26 μmol/L	0.4 (0.3,0.6)	0.4 (0.2,0.7)	0.4 (0.2,0.6)	0.94
tHcy 15.0 μmol/L	7.6 (4.4,11.7)	7.6 (5.0,11.5)	8.21 (5.5, 11.8)	0.67
Erythrocyte folic acid, nmol/L	457.9 (385.2, 552.58)	494.3 (401.7, 609.4)	507.6 (409.6, 605.7)	0.40
Hemoglobin g/dl	11.0 (10.0,11.7)	11.2 (10.5, 11.9)	11.0 (10.0,11.7)	0.24

Median (Q1, Q3) values across trimesters.

MMA, methylmalonic acid.

Our finding that women with persistent depressive symptoms were less educated than women in the not depressed group is in agreement with earlier studies that noted that depressive symptoms are greater in pregnant women with low educational achievements (25, 26). Less social support in general and less emotional support in particular was associated with persistence of depressive symptoms as noted in previous studies (27, 28). In a community based study from Pakistan, it was observed that availability of social support from extended family network was associated with a decreased risk for depression during pregnancy and in the peri-natal period (29). This ability to draw support from family members is also linked to level of maternal education as women with higher educational attainment seemed to be better equipped to garner support from key family members (30).

Our findings of a possible association between maternal antenatal depressive symptoms and poorer receptive language domain scores on BSID-III in children at 30 months are in agreement with several earlier studies. Studies done in the US, Ethiopia and Ireland also noted an association between antenatal depression and poorer cognitive performance of children, but these effects were largely attenuated when adjusted for various socio demographic characteristics (4, 9, 31). In the present study, we did not do a longitudinal assessment of maternal post natal depressive symptoms which could have impacted child cognitive functions. Several studies have noted that postnatal maternal depression could have an adverse influence on child cognitive outcomes due to poorer mother child interaction and less cognitive stimulation at home (32–34). A longitudinal study with a larger sample size that measures both antenatal and post natal depressive symptoms may be able to reliably assess the cause and effects of maternal depression on cognitive performance of children.

In the present study, the effect of maternal antenatal depressive symptoms on receptive language domain was seen only among children of women who had intermittent depressive symptoms, compared to children of mothers who had no depressive symptoms or persistent depressive symptoms. This is in contrast to an earlier study that noted a higher risk of development delay in children born to women who had depressive symptoms at two time points in pregnancy compared to children of mothers with depression at any one time point during pregnancy (3). However, in this study the cognitive measures were based on the mothers' self-report and maternal mood could have biased parental report on cognitive outcomes in children. The association between poorer performance on receptive language domain and intermittent maternal antenatal depressive symptoms as opposed to persistent maternal antenatal depressive symptoms suggests a possibility of trimester specific effect of maternal antenatal depressive symptoms on child cognitive outcomes (15). While fetal brain development occurs throughout pregnancy, recent neuroimaging studies have shown that there is a spurt in fetal brain development in the third trimester of pregnancy that includes the beginning of myelination, neuronal organization, spinogenesis and synaptogenesis and increase in brain volume (35, 36). In a recent study, we observed that some maternal nutrient markers in the third trimester as compared to the first and second trimesters were associated with amplitude of P300, a neurophysiological marker of cognitive function in children at 72

months (37). However, in the present study, our sample was limited to allow for examining trimester specific associations between antenatal depressive symptoms and child cognitive outcomes.

We did not find any difference in vitamin B12 levels, elevated tHcy, and MMA, and erythrocyte folate levels and anemia among the three groups of women. We also did not find any significant differences in dietary intake among the three groups of women. Recent systematic reviews of the associations between maternal nutritional biomarkers and depression and/or anxiety during pregnancy found that there was a high variability in the associations and opined that further studies in nutrient deficient populations were needed to draw firm conclusions (38, 39).

The findings from the present study of an association between maternal antenatal depressive symptoms and poorer performance in the receptive language domain should be interpreted with caution as BSID III was not adapted for use in the Indian setting and age specific norms are not available. A recent study (40) from Nepal found that the distribution of scores on BSID III were similar to the US norms, except for the language domain. However, in the present study we did not intend to assess individual children for developmental delays and earlier studies have used BSID III raw scores to examine the impact of antenatal factors on child cognitive performance (14, 41).

The major strength of our study is that we assessed depressive symptoms at each of the three trimesters of pregnancy. The neurodevelopment assessments were carried out by trained child psychologists with considerable experience in the administration of BSID-III. We also captured several psychosocial variables linked to maternal antenatal depressive symptoms such as social support and coping mechanisms. The use of a screening measure to assess maternal depression as opposed to a clinical assessment of depression is an important limitation. We could not access the details of the treatment offered to women who were referred to a government facility for treatment of severe depressive symptoms.

CONCLUSIONS

A significant proportion of pregnant South Indian women had antenatal depressive symptoms. We found a modest association between maternal depressive symptoms and impairment in receptive language domain in children on a univariate analysis, but could not be confirmed on bivariate regression analysis. The possible negative association between antenatal depressive symptoms and receptive language domain assumes importance given the sub-optimal cognitive outcomes in children from LMIC. With high prevalence of prenatal depression in low and middle income countries and the relatively large population of children in these countries, the effects of prenatal depressive symptoms on child cognitive outcomes could be magnified, thus contributing to a significant burden to the society. Future longitudinal studies with a larger sample size will be helpful to examine this association between antenatal depressive symptoms and child cognitive outcomes.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Ethics Committee, St. John's National Academy of Health Sciences, Bangalore and the Institutional Review Board of the Harvard T. H. Chan School of Public Health. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

KS, AK, and CD conceptualized the project. AR conducted the psychological assessments and collected data. KS and ST were responsible for setting up the study. DB and ST supervised

cognitive and psychological assessments. TT designed the statistical analyses. ST, EV, and KS wrote the paper. KS had the primary responsibility for the final content. All authors contributed to the article and approved the submitted version.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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