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Antenatal depressive symptoms and behavioral outcomes in children at 78 months: A study from South India

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Abstract

Background: Low and middle income countries report a higher prevalence of antenatal depression. The association between antenatal depressive symptoms and behavioral outcomes in children at 78 months in motherchild dyads who participated in a randomized control trial of maternal B12 supplementation during pregnancy was examined in this study.

Methods: Children of 140 women, out of 366 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 done using the Kessler's 10 Psychological Distress Scale (K10), were assessed using the Strength and Difficulties Questionnaire (SDQ) at 78 months.

Results: Thirty seven women (26.4%) reported depressive symptoms at one trimester (intermittent group) and 28 women (20%) had depressive symptoms in at least 2 trimesters (persistent group). On adjusted bivariate regression analysis, children of women with intermittent antenatal depressive symptoms scored lower on the prosocial behavior subscale of SDQ compared to children of mothers with no depressive symptoms (B=;−0.91, 95% CI: −1.65,−0.18; p=0.016).

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CRediT authorship contribution statement

Susan Thomas: Visualization, Writing – original draft. **Tinku Thomas:** Formal analysis. **Anura Kurpad:** Conceptualization. **Christopher P. Duggan:** Conceptualization. **Krishnamachari Srinivasan:** Conceptualization, Visualization, Writing – original draft, Validation.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

Limitations: The use of a screening measure to assess maternal depression, the assessment of the children's behavior based only on the mothers' reports and the small number of women with persistent depressive symptoms in our sample is important limitations.

Conclusions: The possible association between antenatal depressive symptoms and prosocial behavior in children point to the need for routine assessment and intervention for emotional disorders during pregnancy.

Keywords

Antenatal depression; child behavior outcomes; prosocial behaviour; internalizing symptoms; externalizing symptoms

1. Introduction

Antenatal depression is associated with several obstetric risk factors (Ajinkya et al., 2013), and has adverse effects on child development (Deave et al., 2008; Thomas et al., 2020) and emotional and behavioral problems in childhood (Leis et al., 2013), Studies have also reported more behavioral problems in children at 3 years born to mothers with antenatal depression when compared to children of mothers who were never depressed (Rotheram-Fuller et al., 2018) and associations between greater severity of maternal antenatal depression and increased behavior problems in children at mid childhood (Faleschini et al., 2019). However, the findings on the association between antenatal depression and childhood behavioral problems have been inconsistent. A longitudinal study on 7144 women from UK found that antenatal anxiety in late pregnancy and not antenatal depression was associated with behavioral/emotional problems among children at age 4 (O'Connor et al., 2002). A study that examined the association trajectories of maternal depression and child behavior at 5 years found that mothers who had persistently high or persistently intermediate levels of depressive symptoms during pregnancy, and at 4 months, 8 months, one year, 3 years and 5 years postpartum had children with increased levels of emotional and behavioral difficulties, but children of mothers with depressive symptoms only during pregnancy did not have increased levels of emotional or behavioral problems (van der Waerden et al., 2015). The inconsistent findings on the association between antenatal depressive symptoms and childhood behavioral difficulties may be related to the severity of depressive symptoms, the timing and/or persistence of depressive symptoms during pregnancy (de Bruijn et al., 2009; Tharner et al., 2012; Tuovinen et al., 2021).

We had performed a double-blind, placebo-controlled trial of oral vitamin B12 during pregnancy and early lactation in South Indian women (Duggan et al., 2014). 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 behavioral outcomes in children at 78 months.

2. 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 undeserved 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 (K10 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. The details of recruitment and methods are provided in a previous paper (Duggan et al., 2014; Thomas et al., 2020).

The women were approached for behavioral assessment of their children when they were 6 years old and consent was sought. 140 mother-child pairs participated in the study (Fig. 1). 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).

2.1. Assessment of child behavior

Child behavior was assessed by the Strength and Difficulties Questionnaire (SDQ) (Goodman, 1997). The Strengths and Difficulties Questionnaire (SDQ) is a brief emotional and behavioral screening questionnaire for children and young people. The tool comprises of 25 items and is administered to the parent, and yields 5 sub-scales of 5 items each. The sub-scales include: (1) Emotional symptoms (2) Conduct problems (3) Hyperactivity/inattention (4) Peer relationships problem and (5) Pro-social behavior. The Hyperactivity/ inattention sub-scale and the Conduct problems sub-scale are combined to get a score of externalizing symptoms and the Emotional symptoms sub-scale and Peer relationships problems sub-scale are combined to get a score of Internalizing symptoms. The Externalizing and Internalizing symptom scores are combined to get a total difficulties score. The Pro-social behavior is associated with being considerate, sharing, helpful and kind. Higher scores indicate fewer difficulties with prosocial behavior. The questionnaire is found to have strong internal consistency and moderate test retest reliability (Yao et al., 2009). The SDQ is used widely in research in India and is found to be useful for assessing internalizing and externalizing

symptoms among children and adolescents in community based studies (Nair et al., 2017; Singh et al., 2015).

2.2. Assessment of maternal psychological factors

2.2.1. Depressive symptoms—Maternal depressive symptoms during pregnancy 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 (Kessler et al., 2003). In the present study, we administered a translated version of K-10 in local language (Kannada). 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 cut off score ≥6 (sensitivity = 100 %, specificity = 81.3 %, and area under the curve = 0.95) (Fernandes et al., 2011). We have used K10 in earlier studies as a measure of antenatal depression (Lukose et al., 2014; Thomas et al., 2020). In the present study, 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 three trimesters belonged to the non-depressed category, and women with K10 scores ≥ 6 in any one trimester were defined as intermittently depressed.

2.2.2. Social support scale—A questionnaire in local language was used to measure a broad range of social support available to the woman during pregnancy. It was developed as part of an earlier study that examined the relation between parental social support, child's home environment and cognitive performance (Malda, 2009). The items in the SSQ were based on and adapted from existing questionnaires and example items given in articles and book chapters. The items were piloted, translated and adapted to Indian setting. The questionnaire had an alpha coefficient of 0.88 in the original study (Malda, 2009). 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 of pregnancy.

2.2.3. Coping checklist—This 70 item scale scored dichotomously as 'Yes' or 'No' indicating the presence or absence of a particular coping behavior (Rao et al., 1989). 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 (Rao et al., 2003). This scale was administered in the second trimester of pregnancy.

2.2.4. Assessment of home environment—The home environment was assessed using Bradley's home inventory for early childhood (Bradley and Caldwell, 1979), which has been used across cultures to study the effects of home environment on childhood cognitive abilities. It is an observational tool that allows trained observers to quantify observations related to mother-child interactions, family living patterns and habits, orderliness of the physical home environment, and the potential of the observed environment to positively influence development, and has been used in our previous studies of cognitive and neurophysiological outcomes in children of women who were supplemented with

Vitamin B12 during pregnancy (Srinivasan et al., 2017, 2020; Thomas et al., 2019, 2020). The test was administered at 66 months.

2.2.5. Assessment of biochemical parameters during pregnancy—Details of biochemical assays have been previously described (Duggan et al., 2014). 10 mL of blood was obtained from the women by venipuncture at 12 weeks (baseline). The plasma and RBCs were separated and stored at -80C 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.

2.3. Statistical analysis

We used SPSS Version 22 for all analyzes. Continuous data were described using mean ± SD or median (Q1,Q3) 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 (Persistently depressed vs. intermittently depressed vs. non-depressed) on biochemical parameters, psychological and behavioral 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, adjusting for all the parameters that had significant univariate association, along with intervention. Regression coefficients (β) and corresponding 95% confidence interval (95% CI) are reported. The level of significance used for statistical significance was $P < 0.05$.

3. Results

Of the 366 women who were recruited in the parent trial, 140 mother-child dyads who were assessed for depressive symptoms at a minimum of 2 out of 3 time points during the antenatal period and whose children were available for behavioral assessment at 78 months were eligible for the present study. 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). Seventy five women (53.5%) did not report depressive symptoms in any of the trimesters (not depressed group,) while 37 women (26.4%) reported depressive symptoms at one trimester (intermittent depressed group) and 28 women (20%) had depressive symptoms in at least 2 trimesters (persistent depressed group). Among the women with intermittent depressive symptoms, 30 (81.1%) had depressive symptoms in the first trimester. Women with persistent depressive symptoms had a lower educational attainment compared to the other two groups of women (Table 1).

Scores on prosocial behavior domain on SDQ were lower in children born to women with intermittent depressive symptoms [Median (Q1, Q3): 9 (6.5,10); $p < 0.01$] and higher maternal baseline hemoglobin was associated with lower scores on prosocial behavior (Spearman's rank correlation coefficient: −0.17; $p < 0.05$). Higher scores on home environment were associated with lower scores on externalizing symptoms domain on SDQ (Spearman's rank correlation coefficient: − 0.18; $p < 0.05$) and higher scores on problem solving based coping were associated with lower scores on internalizing symptoms domain on SDQ (Spearman's rank correlation coefficient: − 0.20; $p < 0.05$) and total difficulties

score on SDQ (Spearman's rank correlation coefficient: − 0.23; $p < 0.01$). Higher scores on emotional social support were associated with lower total difficulties score on SDQ (Spearman's rank correlation coefficient: − 0.19; $p < 0.05$).

A bivariate regression analysis was conducted to examine the association between the depressive symptoms during pregnancy and child behavior outcomes adjusting for all the parameters that had significant univariate association, along with intervention. The pro-social behavior sub-domain score on SDQ continued to be significantly lower in children of women with intermittent depressive symptoms compared to children of women with no depressive symptoms (Table 2) after adjusting for B12 intervention, maternal hemoglobin in the first trimester, maternal problem solving coping and emotional social support and home environment.

We did not find any association between persistent antenatal depressive symptoms and child behavior outcomes on both univariate and bivariate analyzes.

4. Discussion

A significant proportion of pregnant women in South India in this study had depressive symptoms across multiple time points of assessment during pregnancy. We found that antenatal maternal depressive symptoms were associated with poorer prosocial behavior on SDQ in children at 78 months, both on univariate and adjusted analysis.

Most studies on the association between antenatal depression and child behavior outcomes, noted that antenatal depressive symptoms was associated with more internalizing and externalizing symptoms among children (Faleschini et al., 2019; Rotheram-Fuller et al., 2018). However, a recent meta-analysis that included 8 studies on the association between maternal perinatal depression and anxiety and child and adolescent development found that antenatal depression and/or anxiety were associated with poorer prosocial behavior in children, though the effect sizes were small (Rogers et al., 2020), which is in agreement with our study. Prosocial behavior or acts that benefit others are very important to children and adolescents, as it helps to increase their acceptance by peers and foster affiliation and contribute critically to positive development and well-being (Dirks et al., 2018). Prosocial behavior is critical to development of peer attachment among children and is mediated by empathy (Schoeps et al., 2020), and lack of prosocial behavior could result in lower self-esteem and impede development of healthy relationships in the future (Padilla-Walker and Carlo, 2014). Maternal emotional problems during pregnancy are associated with increased infant stress reactivity which in turn is related to poorer dyadic interaction quality between the mother and child at 5 years (Zietlow et al., 2019). Disorganized attachment (Hayes et al., 2013) and problems in the mother-child interactions (van Doorn et al., 2016) predict poor prosocial behavior during childhood. However, in our sample, intermittent depressive symptoms and not persistent depressive symptoms was associated with poor prosocial behavior in children. This could be due to the less number of women with persistent depressive symptoms in our sample. The association between intermittent depressive symptoms and poor prosocial behavior among children could also be due to trimester specific effects. Some studies have reported that maternal stress during early

pregnancy has a more detrimental effect on child neurodevelopmental outcomes than stress during later pregnancy (Davis and Sandman, 2010). The modest sample size of our study did not allow examination of trimester specific effects of maternal depression on child behavioral outcomes. Larger longitudinal studies with several time points of assessment of depression both during pregnancy and post-partum may help to understand the intrauterine effects of maternal depression on behavioral outcomes in children. Studies that assess the exclusive effects of depression as opposed to anxiety symptoms during pregnancy may also help to understand the association better.

4.1. Strengths

The major strength of our study is that we assessed depressive symptoms at each of the three trimesters of pregnancy. The assessments were carried out by trained child psychologists.

4.2. Limitations

The use of a screening measure to assess maternal depression as opposed to a clinical assessment of depression and the assessment of the children's behavior based only on the mothers' reports are important limitations. In addition, we do not have data on depressive symptoms in mothers during the follow-up period. The small sample size with limited number of women in the persistent depression category is another limitation.

5. Conclusion

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 behavioral outcomes could be high, 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 behavioral outcomes.

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Role of the funding source

The funders have no role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

References

Ajinkya S, Jadhav PR, Srivastava NN, 2013. Depression during pregnancy: prevalence and obstetric risk factors among pregnant women attending a tertiary care hospital in Navi Mumbai. Indian Psychiatry J. 22, 37–40. 10.4103/0972-6748.123615.

Bradley RH, Caldwell BM, 1979. Home observation for measurement of the environment: a revision of the preschool scale. Am. J. Ment. Defic. 84, 235–244. [PubMed: 93417]

Davis EP, Sandman CA, 2010. The timing of prenatal exposure to maternal cortisol and psychosocial stress is associated with human infant cognitive development. Child Dev. 81 (1), 131–148. 10.1111/j.1467-8624.2009.01385.x. [PubMed: 20331658]

de Bruijn ATCE, van Bakel HJA, van Baar AL, 2009. Sex differences in the relation between prenatal maternal emotional complaints and child outcome. Early Hum. Dev. 85, 319–324. 10.1016/j.earlhumdev.2008.12.009. [PubMed: 19162414]

Deave T, Heron J, Evans J, Emond A, 2008. The impact of maternal depression in pregnancy on early child development. BJOG 115, 1043–1051. 10.1111/j.1471-0528.2008.01752.x. [PubMed: 18651886]

Dirks MA, Dunfield KA, Recchia HE, 2018. Prosocial behavior with peers: intentions, outcomes, and interpersonal adjustment. Handbook of Peer Interactions, Relationships, and Groups, 2nd ed. The Guilford Press, New York, NY, US, pp. 243–264.

Duggan C, Srinivasan K, Thomas T, Samuel T, Rajendran R, Muthayya S, Finkelstein JL, Lukose A, Fawzi W, Allen LH, Bosch RJ, Kurpad AV, 2014. Vitamin B-12 supplementation during pregnancy and early lactation increases maternal, breast milk, and infant measures of vitamin B-12 status. J. Nutr. 144, 758–764. 10.3945/jn.113.187278. [PubMed: 24598885]

Faleschini S, Rifas-Shiman SL, Tiemeier H, Oken E, Hivert MF, 2019. Associations of prenatal and postnatal maternal depressive symptoms with offspring cognition and behavior in mid-childhood: a prospective cohort study. Int. J. Environ. Res. Public Health 16, E1007. 10.3390/ijerph16061007. [PubMed: 30897718]

Fernandes MC, Srinivasan K, Stein AL, Menezes G, Sumithra RS, Ramchandani PG, 2011. Assessing prenatal depression in the rural developing world: a comparison of two screening measures. Arch. Womens Ment. Health 14, 209–216. 10.1007/s00737-010-0190-2. [PubMed: 21061137]

Goodman R, 1997. The strengths and difficulties questionnaire: a research note. J. Child Psychol. Psychiatry 38, 581–586. 10.1111/j.1469-7610.1997.tb01545.x. [PubMed: 9255702]

Hayes LJ, Goodman SH, Carlson E, 2013. Maternal antenatal depression and infant disorganized attachment at 12 months. Attach. Hum. Dev. 15, 133–153. 10.1080/14616734.2013.743256. [PubMed: 23216358]

Kessler RC, Barker PR, Colpe LJ, Epstein JF, Gfroerer JC, Hiripi E, Howes MJ, Normand SLT, Manderscheid RW, Walters EE, Zaslavsky AM, 2003. Screening for serious mental illness in the general population. Arch. Gen. Psychiatry 60, 184–189. [PubMed: 12578436]

Leis J, Heron J, Stuart E, Mendelson T, 2013. Associations between maternal mental health and child emotional and behavioral problems: does prenatal mental health matter? J. Abnorm. Child Psychol 42 10.1007/s10802-013-9766-4.

Lukose A, Ramthal A, Thomas T, Bosch R, Kurpad AV, Duggan C, Srinivasan K, 2014. Nutritional factors associated with antenatal depressive symptoms in the early stage of pregnancy among urban South Indian women. Matern. Child Health J. 18, 161–170. 10.1007/s10995-013-1249-2. [PubMed: 23440491]

Malda M, 2009. There is no place like home: On the relation between culture and children's cognition. Ridderkerk, Ridderprint.

Nair S, Ganjiwale J, Kharod N, Varma J, Nimbalkar SM, 2017. Epidemiological survey of mental health in adolescent school children of Gujarat, India. BMJ Paediatr. Open 1, e000139. 10.1136/bmjpo-2017-000139.

O'Connor TG, Heron J, Glover V, Alspac Study Team, 2002. Antenatal anxiety predicts child behavioral/emotional problems independently of postnatal depression. J. Am. Acad. Child Adolesc. Psychiatry 41, 1470–1477. 10.1097/00004583-200212000-00019. [PubMed: 12447034]

Padilla-Walker LM, Carlo G, 2014. The study of prosocial behavior: past, present, and future. Prosocial Development: A Multidimensional Approach. Oxford University Press, New York, NY, US, pp. 3–16. 10.1093/acprof:oso/9780199964772.003.0001.

Rao K, Apte M, Subbakrishna DK, 2003. Coping and subjective wellbeing in women with multiple roles. Int. J. Soc. Psychiatry 49, 175–184. 10.1177/00207640030493003. [PubMed: 14626360]

Rao K, Subbakrishna DK, Prabhu GG, 1989. Development of a coping checklist—a preminary report. Indian J. Psychiatry 31, 128–133. [PubMed: 21927370]

Rogers A, Obst S, Teague SJ, Rossen L, Spry EA, Macdonald JA, Sunderland M, Olsson CA, Youssef G, Hutchinson D, 2020. Association between maternal perinatal depression and anxiety and child and adolescent development: a meta-analysis. JAMA Pediatrics 174, 1082–1092. 10.1001/jamapediatrics.2020.2910. [PubMed: 32926075]

Rotheram-Fuller EJ, Tomlinson M, Scheffler A, Weichle TW, Rezvan PH, Comulada WS, Rotheram-Borus MJ, 2018. Maternal patterns of antenatal and postnatal depressed mood and the impact on child health at three years postpartum. J. Consult. Clin. Psychol. 86, 218. 10.1037/ccp0000281. [PubMed: 29504791]

Schoeps K, Monaco E, Cotolí A, Montoya-Castilla I, 2020. The impact of peer ´ attachment on prosocial behavior, emotional difficulties and conduct problems in adolescence: the mediating role of empathy. PLoS One 15, e0227627. 10.1371/journal.pone.0227627.

Singh K, Junnarkar M, Sharma S, 2015. Anxiety, stress, depression, and psychosocial functioning of Indian adolescents. Indian J. Psychiatry 57, 367. 10.4103/0019-5545.171841. [PubMed: 26813517]

Srinivasan K, Thomas S, Anand S, Jayachandra M, Thomas T, Strand TA, Kurpad AV, Duggan CP, 2020. Vitamin B-12 supplementation during pregnancy and early lactation does not affect neurophysiologic outcomes in children aged 6 years. J. Nutr. 150, 1951–1957. 10.1093/jn/nxaa123. [PubMed: 32470975]

Srinivasan K, Thomas T, Kapanee ARM, Ramthal A, Bellinger DC, Bosch RJ, Kurpad AV, Duggan C, 2017. Effects of maternal vitamin B12 supplementation on early infant neurocognitive outcomes: a randomized controlled clinical trial. Matern. Child Nutr. 13, e12325. 10.1111/mcn.12325.

Tharner A, Luijk MPCM, van Ijzendoorn MH, Bakermans-Kranenburg MJ, Jaddoe VWV, Hofman A, Verhulst FC, Tiemeier H, 2012. Maternal lifetime history of depression and depressive symptoms in the prenatal and early postnatal period do not predict infant-mother attachment quality in a large, population-based Dutch cohort study. Attach. Hum. Dev. 14, 63–81. 10.1080/14616734.2012.636659. [PubMed: 22191607]

Thomas S, Thomas T, Bosch RJ, Ramthal A, Bellinger DC, Kurpad AV, Duggan CP, Srinivasan K, 2019. Effect of maternal vitamin B12 supplementation on cognitive outcomes in south indian children: a randomized controlled clinical trial. Matern. Child Health J. 23, 155–163. 10.1007/s10995-018-2605-z. [PubMed: 30003521]

Thomas S, Vigil E, Thomas T, Bellinger DC, Ramthal A, Kurpad AV, Duggan CP, Srinivasan K, 2020. Antenatal depressive symptoms and neurodevelopment outcomes in children at 30 months. A study from South India. Front. Psychiatry 11. 10.3389/fpsyt.2020.486175.

Tuovinen S, Lahti-Pulkkinen M, Girchenko P, Heinonen K, Lahti J, Reynolds RM, Hamäläinen E, Villa PM, Kajantie E, Laivuori H, Raikkonen K, 2021. Maternal ¨ antenatal stress and mental and behavioral disorders in their children. J. Affect. Disord. 278, 57–65. 10.1016/j.jad.2020.09.063. [PubMed: 32950844]

van der Waerden J, Galéra C, Larroque B, Saurel-Cubizolles MJ, Sutter-Dallay AL, Melchior M, EDEN Mother–Child Cohort Study Group, 2015. Maternal depression trajectories and children's behavior at age 5 years. J. Pediatr. 166, 1440–1448.e1. 10.1016/j.jpeds.2015.03.002.

van Doorn MMEM, Kuijpers RCWM, Lichtwarck-Aschoff A, Bodden D, Jansen M, Granic I, 2016. Does mother–child interaction mediate the relation between maternal depressive symptoms and children's mental health problems? J. Child Fam. Stud. 25, 1257–1268. 10.1007/s10826-015-0309-1. [PubMed: 27004017]

Yao S, Zhang C, Zhu X, Jing X, McWhinnie CM, Abela JRZ, 2009. Measuring adolescent psychopathology: psychometric properties of the self-report strengths and difficulties questionnaire in a sample of Chinese adolescents. J. Adolesc. Health 45, 55–62. 10.1016/j.jadohealth.2008.11.006. [PubMed: 19541250]

Zietlow AL, Nonnenmacher N, Reck C, Ditzen B, Müller M, 2019. Emotional stress during pregnancy – associations with maternal anxiety disorders, infant cortisol reactivity, and mother–child interaction at pre-school age. Front. Psychol. 10, 2179. 10.3389/fpsyg.2019.02179. [PubMed: 31607996]

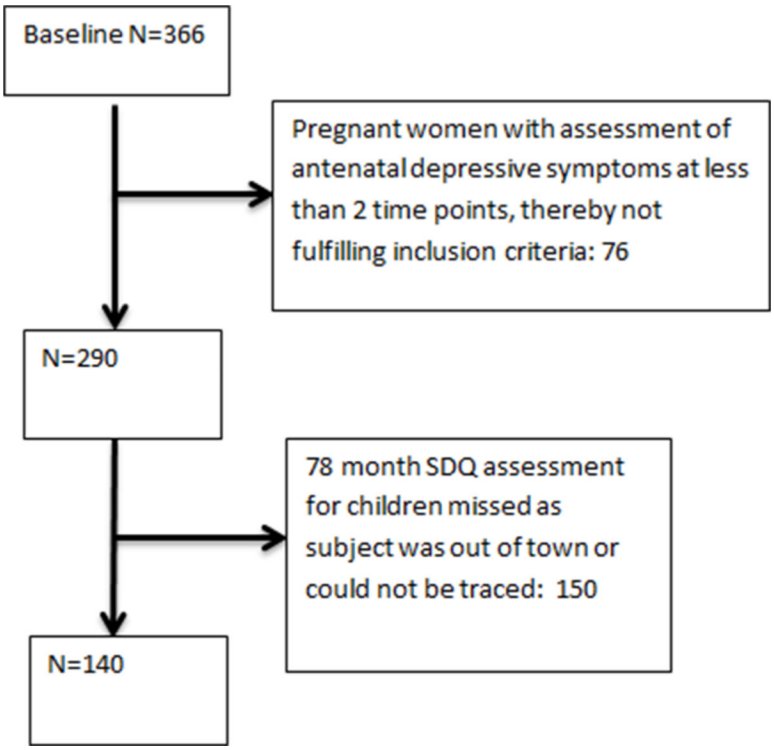

Fig. 1.

. Flow chart of sample inclusion from baseline to assessment of children at 78 months.

Table 1

Socio-demographic characteristics, birth outcomes, baseline K10 scores, home environment inventory scores and baseline biochemical characteristics of women whose children underwent SDQ assessment at 78 months of age.

Parameters	Not Depressed (*n* = 75)	Intermittently Depressed (*n* = 37)	Persistently Depressed (*n* = 28)	*p* value
Age, years	30.23 ± 4.1[1]	30.07 ± 3.5[1]	30.12 ± 4.0[1]	0.97
Level of Education				**0.001**
Up to Middle school	12 (8.6)[2]	12 (8.6)[2]	11 (7.8)[2]	
High school	35 (25)[2]	19 (13.6)[2]	14 (10)[2]	
Post high school	28 (20)[2]	6 (4.3)[2]	3 (2.1)[2]	
Monthly household income (INR)	16500(10000, 22750)[3]	15000(10000, 20000)[3]	14000(10000, 20500)[3]	0.39
Maternal employment				
Employed	29 (20.7)[2]	14 (10)[2]	9 (6.4)[2]	0.89
Parity				
0	41 (29.3)[2]	26 (18.6)[2]	18 (12.8)[2]	0.26
Sex of the baby				
Male	35 (25)[2]	20 (14.2)[2]	10 (7.1)[2]	0.34
Caesarian section	21(15)[2]	10(7.1)[2]	7(5)[2]	0.93
Gestational age at birth	39.3(38.6, 40.3)[3]	39.1(38.1, 40.2)[3]	39.3(38.4,40.0)[3]	0.45
Infant birth weight (kg)	3.0 (2.75,3.25)[3]	2.86 (2.50, 3.25)[3]	2.8 (2.5,3)[3]	0.31
IUGR	18(12.8)[2]	12(8.6)[2]	8(5.7)[2]	0.68
Baseline K10 score	1 (0,3)[3]	8 (6,9)[3]	9 (8,12)[3]	**<0.001**
Home Environment Inventory score at 66 months	34(30,39)	33(30,35)	34(28.5,36)	0.30
Vitamin B12 (pmol/L)	142.07(102.51,203.13)[3]	170.63(127.97, 279.67)[3]	151.66(115.72, 219.50)[3]	0.16
Hemoglobin (g/dL)	11.70(10.80, 12.50)[3]	11.60 (10.85, 12.30)[3]	11.50(10.40,12.28)[3]	0.59

[1]: Mean ± SD

[2]: N(%)

[3]: Median (Q1, Q3)

IUGR: Intrauterine Growth Retardation (birth weight less than the 10th percentile of norms for gestational age).

Table 2

Multivariate analysis of SDQ scores at 78 months.

SDQ Parameters *n* = 140	Presence of depressive symptoms	B	95% CI	p value
Prosocial	Not depressed	Ref	–	–
	Intermittently depressed	−0.91	−1.65, −0.18	**0.016**
	Persistently depressed	−0.25	−1.19, 0.70	0.606
Externalizing	Not depressed	Ref	–	–
	Intermittently depressed	0.05	−1.01, 1.10	0.929
	Persistently depressed	−0.63	−1.98, 0.72	0.359
Internalizing	Not depressed	Ref	–	–
	Intermittently depressed	1.17	−0.04, 2.38	0.059
	Persistently depressed	1.01	−0.55, 2.57	0.202
Total Difficulties	Not depressed	Ref	–	–
	Intermittently depressed	1.23	−0.39, 2.86	0.136
	Persistently depressed	0.39	−1.70, 2.48	0.709

All analyzes are adjusted for intervention, baseline maternal hemoglobin, home environment, maternal problem solving coping and maternal emotional social support.