ABSTRACT

Purpose This is a prospective pregnancy–birth cohort designed to investigate the effects of depression on socioemotional development of children. Perinatal depression is a risk factor for poor child development and for many it has a recurring chronic course. Thus, the exposure to depression can continue through the early years of the child with detrimental developmental outcomes.

Participants Between October 2014 and February 2016, we recruited 1154 pregnant women from a rural subdistrict of Pakistan. Data include longitudinal and repeated measures of maternal psychosocial measures and child growth, cognitive and socioemotional measures. Follow-up include mother–child dyad assessments at 3rd, 6th, 12th, 24th and 36th months of child age. All these follow-ups are community based at the household level. We have competed baseline assessment.

Findings to date Of the eligible dyes, we followed 885 (76.6%), 929 (91%) and 940 (93.3%) at 3, 6 and 12 months post-childbirth. We include a subsample mother–child dyad DNA and inflammatory biomarkers, 73 and 104, respectively.

Future plans While we continue to do 24-month and 36-month follow-up assessments, we plan to follow these mother–child dyads up to the age of 7–8 years with some children being exposed to at least 1 year of school environment. Investigators interested in learning more about the study can contact (jmaselko@unc.edu) and (siham.sikander@hdrfoundation.org).

INTRODUCTION

Perinatal depression is an episode of depression occurring either during pregnancy, within 1 year after delivery, or both. The prevalence of perinatal depression is high in low/middle-income countries (LMIC), with a prevalence of >30% reported in south Asian countries like Pakistan. While being highly prevalent, it also has a recurring and chronic course. It is more common among poorer women exposed to gender-based risks (eg, intimate partner violence, son preference, role restrictions around housework and infant care) and/or those with a psychiatric history. A number of systematic reviews from LMIC and high income countries (HIC) indicate that child health outcomes are negatively associated with perinatal depression.

For example, recent studies highlight the effects of perinatal depression on child socioemotional and cognitive developmental outcomes. Negative effects of symptoms of depression for the child start as early as in pregnancy and can be observed lasting into adulthood. Reducing perinatal depression and improving outcomes in the next generation is thus a global public health priority.

Although observational evidence shows that reductions in depressive symptomology are associated with improvements in child outcomes, experimental evidence from interventions to mitigate maternal depression has
not been as consistent. Many studies have not found a sustained impact on child outcomes when perinatal or maternal depression was treated. This inconsistency across studies is likely attributable to differences in design features such as length of follow-up, choice of comparison groups, unaddressed endogeneity and enrolment age differences (eg, infants aged 1–18 months). Apart from these limitations, the perinatal mental health interventions themselves are also varied in their content and intensity. There is evidence from LMIC that effective interventions for perinatal depression; the majority of these interventions are front loaded, with booster sessions lasting until at most 3–6 months postnatal, which may not address the recurring nature of depression or its chronicity in the longer term. Finally, evaluations of depression interventions also do not typically account for important contextual factors, such as chronic exposure to intimate partner violence, a known risk factor for poor maternal mental health, which may influence their efficacy.

With this backdrop, we established a pregnancy–birth cohort, called Bachpan (the word Bachpan means childhood in the local Urdu language) cohort study, to follow-up the mother–child dyads through 36 months postnatal and beyond. We recruited both prenatally depressed and non-depressed pregnant women in our cohort to be seen at 3, 6, 12 and 24 months of child age before a final assessment at 36 months (see box 1). The multiple, frequent and long-term mother–child dyad follow-ups will enable rigorous analyses of the relationship between changes in women’s depressive symptoms and child outcomes like the socioemotional, cognitive and growth, in terms of multiple cofactors that mediate the risk and underscore the potentially modifiable risk factors and time varying mechanisms. Alongside the cohort with its child outcomes, a peer-delivered perinatal depression intervention with outcomes of remission/
was invited to participate as part of the non-exposed arm of the cohort, resulting in a 1:1 ratio of prenatally ‘depressed’ and ‘non-depressed’ in the sample. Immediately after the screening, all participants were approached for their baseline assessments. All screening, baseline and follow-up assessments were done by trained research assistants (graduates and maters in social science, psychology and behavioural science).

In all, 1910 pregnant women were approached. Of these, 154 (8%) were ineligible by the criteria above, 25 (1.3%) refused to participate at the eligibility screening stage.

The remaining 1731 (90.6%) eligible pregnant women were screened for depression. In all, we enrolled 1154 pregnant women in the Bachpan cohort study; out of these 570 were depressed and 584 non-depressed according to the PHQ-9 cut-offs mentioned above. Only 11 (0.64%) refused enrolment into the cohort. We dropped/excluded 566 (32.7%) pregnant women who were non-depressed since they were over and above the sample we required (see figure 2).

After collecting prenatal baseline information, each mother–child dyad is followed up at child age 3, 6, 12, 24 and 36 months. The follow-ups are scheduled using the birth dates of the index children from registers of the same LHWs who registered these pregnant women. We intend following this birth cohort at 7–8 years of child age, by that time majority of the children would have had at least 1 year of school exposure.

All follow-up interviews are conducted face-to-face, either at the woman’s home or the LHW’s house. The follow-up rates at 3, 6 and 12 months have been 76.7%, 91% and 93%, respectively. The lower attrition rates thus far are due to the process by which we engage with the community and households through the resident community health workers called LHWs. Coupled by the convenience of being interviewed at participants’ preferred place and time adds to minimising the overall attrition. Lastly, the women who miss any follow-ups are ensured that they are followed up in the subsequent follow-up assessment. The 24-month follow-up will be completed in August 2018 and the 36-month postnatal follow-up assessments are scheduled for August 2019. Baseline characteristics did not differ significantly between those missing and those present at each of the follow-up time points.

**MEASUREMENTS**

Child growth and development and maternal depression at 36 months postnatally are the main outcomes of interest. We also incorporate a comprehensive set of measures of potential exposures, moderators, mediators and confounders relevant to numerous etiological questions of interest that this cohort may address. What follows is the details of the constructs and measures used, broadly divided into two categories (1) maternal and (2) child (see table 1).

**MATERNAL CONSTRUCTS AND MEASURES**

**Sociodemographics**

Information on the women’s age and level of education; their husbands’ occupation, income, assets, economic shocks and debt; and the household structure are assessed. We also ask about the household’s overall socioeconomic status through the LHW-based subjective measure previously used in our studies. It is a 5-point likert scale-based measurement with 1 being richest and 5 being the poorest. LHWs being residents of the same community and the village, where the participants live, have intimate knowledge of the overall socioeconomic status of all the households in their catchment area.

Since socioeconomic measurements are challenging to record accurately, we use this measure especially in combination with debt alongside other measures to help us create accurate categories which are also sensitive to change over time.

**Psychosocial factors**

Perinatal depression was assessed longitudinally using the PHQ-9; we used the ≥10 cut-off for enrolling pregnant women into the trial portion of the cohort. The PHQ-9 inquires about frequency of depressive symptoms in the last 2 weeks. It has been validated and used extensively in
Given that the PHQ-9 is a screening tool, we used the Structured Clinical Interview for DSM IV Disorders (SCID) module for current major depressive episode as a diagnostic tool and to assess the criterion-related validity of using the scores from the PHQ-9 to measure the number of symptoms endorsed by the woman over time. The diagnostic and statistical manual of mental disorders (DSM) IV diagnosis of current major depressive

<table>
<thead>
<tr>
<th>Constructs</th>
<th>Measured/assessed</th>
<th>Antenatal Baseline</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
</tr>
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<tr>
<td>Maternal constructs</td>
<td>Age, education, household structure, household assets household roster, occupation, economic shocks and debt</td>
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<td>Decision-making, autonomy and self-efficacy</td>
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<td>Disability/function</td>
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<td>Intimate partner violence</td>
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<tr>
<td>Other constructs of interest</td>
<td>Family history of mental illness and substance use</td>
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<td>Beliefs, practices, investment and expectations about children</td>
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<tr>
<td>Child health and development</td>
<td>Weight, length/height and head circumference</td>
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<td>Maternal and child biomarkers (subsample)</td>
<td>Hair steroid hormones (mother)</td>
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<td>Genetic</td>
<td>DNA (mother)</td>
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<td>DNA (child)</td>
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episode is generated through the SCID algorithm. SCID is a semistructured interview for the diagnoses of psychiatric disorders. It has been cross-culturally adapted for assessing depression among women during pregnancy and in the postpartum period.42

Perceived stress
Women’s subjective experience of their stress is assessed with the 10-item Cohen’s Perceived Stress Scale (PSS).43 44 It is a tool designed to measure the degree to which situations in one’s life are appraised to be stressful.

Social support
We use three instruments to capture both emotional and instrumental support. The Multidimensional Scale of Perceived Social Support is used as a measure of subjectively assessed social support.45 It has been adapted for Pakistani settings and used extensively in the study area.46 It has 12 items rated on a 7-point likert scale with subdomains capturing perceived support from significant other, family, and friends. We use the Maternal Social Support Index as a measure of instrumental support. It consists of 21 questions which inquire about the availability of support to the woman in her daily tasks.47

An interview regarding who is caring for the child during daily instrumental and social activities, a Day-in-Life (DIL) was developed for the study to assess relative support in caregiving that the depressed and non-depressed groups of mothers’ report.

Maternal self-efficacy
We use the 10-item Maternal Self-Efficacy Scale to assess a woman’s beliefs about her ability to take care of her child compared with other mothers she has seen.48 This tool has been used extensively in research on maternal depression and child development, in both high/low-income countries.49 50

Physical health
Disability
The WHO Disability Assessment Schedule (WHO-DAS) is used to assess women’s disability. It is a 12-item questionnaire that assesses levels of functionality over the last 30 days. Combined with two items about one’s ability to work in the last 30 days, the WHO-DAS generates a total disability score, quality adjusted life years and number of days the respondent is not able to work.52

Height, weight, waist circumference and the blood pressure of women are measured at each encounter. We also assess obstetric history including number of pregnancies, live births and contraception being used or not.

Intimate partner violence (IPV)
We assess IPV using the WHO Violence Against Women Instrument.53 It minimises reporting biases by asking only about specific behaviours perpetrated by a male partner, rather than ascertaining if a woman subjectively perceives she has experienced ‘abuse’ or ‘violence’. The tool addresses three types of violence (1) physical, (2) psychological and (3) sexual, severity, timing and frequency. For the cohort, we adapted the instrument for ease of administration, and only referenced the respondent’s husband as the perpetrator.

Other maternal measures of interest
Women’s history of mental illness, substance abuse among family members, the mother’s engagement in traditional rituals (such as chilla which is a 40-day period when a woman is relieved of household responsibilities after child birth),54 and significant negative life events in the past 1 year.54 We also administer the Client Services Receipt Inventory to record health services sought during the perinatal period. This will enable us to assess cost-effectiveness of the intervention tested in the cohort (see the child constructs and measures section).54 56 We also assess women’s decision-making, autonomy, religiosity, risk taking, bonding with her parents (using the Parental Bonding Instrument [PBI])57 58 and her adverse childhood experiences (including physical and psychological abuse, neglect and several sorts of family dysfunction).59 60

CHILD CONSTRUCTS AND MEASURES
Child nutrition and care
We assess breastfeeding practices in accordance with WHO guidelines, as well as complementary feeding and food diversity, in terms of frequency and quantity.61 62 We also ascertain beliefs, practices and expectations of mothers for their children with respect to vaccination coverage.

Child interaction
Observation of mother–child interaction (OMCI)
We adapted the OMCI, which is a tool to evaluate responsive parenting through direct, 3–5 min OMClis around a picture book activity. OMCI was developed and used in Pakistan for 12, 24 and 48 months old children.63

Home observation for measurement of the environment (HOME) inventory
We use HOME as a measure of maternal responsiveness and the overall conduciveness of the home environment for child rearing. It is an extensively used measure of the child’s family environment64 and it has been validated in Pakistan.65 67

Attachment relationship
We assess the maternal attachment with the child through the 19-item Maternal Postnatal Attachment Scale.68 It has been used extensively across settings.

Child caregiving practices
The DiL tool is a semistructured interview using a narrative elicitation technique, designed to elicit in detail the involvement of the mother as well as other family members in daily care of the infant. The DiL tries to create a narrative about who the child spends time with by


5
taking an account of all the activities done with the child. This begins with the account starting from early morning instrumental tasks such as who wakes, washes and feeds the infant; similarly, the narrative building continues into the afternoon and night until the time the child sleeps again. The household members like the mother, father, mother-in-law, aunt and so on are recorded against each activity and overall impression of time spent without the mother is made; the data thus provide a detailed picture of both whom the infant spends the day with and what kind of support the mother receives and from whom.

**Child growth and development**

We collect anthropometric measurements for physical development (including weight, height and head circumference) based on WHO standards and norms. We also assess diarrheal and acute respiratory illness episodes using WHO definitions.

**Strengths and Difficulties Questionnaire (SDQ)**

The SDQ is a screening tool for child’s socioemotional/behavioural development using parental report of 25 child attributes divided into five subscales: emotional symptoms, conduct problems, hyperactivity, peer problems and prosocial behaviour.69 70 The SDQ has been extensively translated into 50 other languages (including Urdu) and used in LMIC including the study area.71–73

**Ages and Stages Questionnaire (ASQ)**

We also use the socioemotional component of the ASQ (ASQ-SE) during the follow-up assessments as well as at the final outcome assessment at 36 months postnatal.74 75 The ASQ-SE includes a simple set of 25 questions asking the caregiver to report age-appropriate psychosocial milestones.76 It has been widely used.77

**Bayley Scales of Infant and Toddler Development Third Edition (BSID-III)**

We use the BSID-III, which is an individually administered assessment of the child’s achievement of developmental milestones across five areas: cognitive, language, motor, socioemotional and adaptive skills.78 Raw scores in each domain are summarised by chronological age-related scaled scores and composite scores for each domain. The child is assessed with the full test at the 12-month contact and with only the receptive language and fine motor domains at 36 months, due to time demands and also the difficulties involved in administering the language laden instructions in other domains.

**Epigenetics and biomarkers (subsamples)**

We conducted a small nested feasibility study of buccal DNA samples from 73 mothers in the third trimester of pregnancy and the same 73 mother–child dyads at 3 months postchild birth (approximately half from prenatally depressed and half from prenatally non-depressed). We also collected, apart from the above, hair samples from 104 mother–child dyads at 12 months postnatal. These components will enable us to examine epigenetic and hair cortisol (and other biomarkers of stress) among depressed versus non-depressed mothers and their children.
<table>
<thead>
<tr>
<th>Maternal measures</th>
<th>3rd month n=885, % or mean (SD)</th>
<th>6th month n=929, % or mean (SD)</th>
<th>12th month n=940, % or mean (SD)</th>
</tr>
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<tbody>
<tr>
<td>Response rate</td>
<td>76.60%</td>
<td>91%</td>
<td>93.30%</td>
</tr>
<tr>
<td>PHQ-9 scores</td>
<td>5.2 (5.8)</td>
<td>4.8 (5.6)</td>
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</tr>
<tr>
<td>SCID current MDE</td>
<td>15.30%</td>
<td>12.90%</td>
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<td>PSS scores</td>
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<td>19.8 (3.7)</td>
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<td>MSPSS scores</td>
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<td>4.8 (1.3)</td>
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<tr>
<td>MSES scores</td>
<td>37.0 (3.9)</td>
<td>37.4 (3.3)</td>
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<td>MSSI scores</td>
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<tr>
<td>Tasks done alone</td>
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<td>2.8 (1.8)</td>
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<td>Tasks done by someone else</td>
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<tr>
<td>Very satisfied</td>
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<td>NA</td>
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<tr>
<td>Satisfied</td>
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<td>Daily waking, bathing, feeding of the child</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Done by mom alone</td>
<td>87.10%</td>
<td>NA</td>
<td>79.90%</td>
</tr>
<tr>
<td>Shared by grandmother, father or others</td>
<td>9.80%</td>
<td></td>
<td>18%</td>
</tr>
<tr>
<td>Daily interacting, holding, soothing of the child</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Done by mom alone</td>
<td>57%</td>
<td>NA</td>
<td>44.60%</td>
</tr>
<tr>
<td>Done by mom alone shared by grandmother, father or others</td>
<td>30.50%</td>
<td></td>
<td>51.60%</td>
</tr>
<tr>
<td>ASQ-SE scores</td>
<td>NA</td>
<td>9.5 (12.2)</td>
<td>NA</td>
</tr>
<tr>
<td>Height for age z-scores</td>
<td>0.1 (1.8)</td>
<td>0.1 (1.7)</td>
<td>−0.7 (1.3)</td>
</tr>
<tr>
<td>Weight for age z-scores</td>
<td>−1.1 (1.3)</td>
<td>−0.9 (1.2)</td>
<td>−0.8 (1.1)</td>
</tr>
<tr>
<td>Immunisation completion (measles vaccination at 9 months of infant’s age)</td>
<td></td>
<td></td>
<td>97.10%</td>
</tr>
<tr>
<td>BSID scaled scores</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Continued
**Patient and public involvement**
No patients were involved in development of the research questions, design of the study or the recruitment.

**Data management**
All data are collected electronically via tablets and is uploaded daily onto the main server. Quality checks for consistency, accuracy, missing data and other irregularities are conducted weekly. Any issues are shared with the research team and discussed during a weekly field staff meeting. Data are backed up daily to a secondary server. All data are deidentified/anonymised before being shared with coinvestigators. At all stages/levels, data are password protected with multiple layers of authorisation.

Prior to analysis, we upweighted the mothers whose depression levels were <10 on the PHQ-9 in order to make the baseline sample representative of the local population, since only one in three of these women was invited to participate in the study. We generated cluster-specific weights and assigned them to these non-depressed women. Since all of the women who scored a 10 or above on the PHQ-9 were invited to participate, their default weight was 1.

**Findings to date**
In tables 2 and 3, we summarise our key findings to date. To make the 1154 women representative of the local population, since only one in three of these women was invited to participate in the study. We generated cluster-specific weights and assigned them to these non-depressed women. Since all of the women who scored a 10 or above on the PHQ-9 were invited to participate, their default weight was 1.

**Sociodemographics**
The mean age of pregnant women in our cohort is 26.6 years, with an average of 8.1 years of education. Almost all of them being housewives (94%), with a third of these women being pregnant for the first time (the rest have up to four children); 67.2% live in a joint family structure. All of these findings are comparable to what we have seen in our previous studies from the same area and what is reported in the national demographic survey.54 79

**Maternal psychosocial factors**
At baseline, the mean PHQ-9 and PSS scores were 6.7 and 15.8 showing mild levels of depressive symptoms as well as mild levels of perceived stress. While 26.6% were found to have major depressive episode on SCID. Rates of major depressive episode are comparable to our previous studies in the same area.58 54 The stress levels rise marginally while the severity of depressive symptoms go down over time. Overall at baseline (prenatal), 32.8% and 29.2% of women experienced psychological and sexual abuse in the last 12 months, respectively, while 15.9% reported physical violence in the last 12 months. Similarly, a high proportion report experiencing abuse at 12 months postnatal, which other studies also report and is correlated with maternal mental health issues.79 80 The support women have (both physical and instrumental) from prenatal to 12 months postnatal is relatively low.

**CHILD MEASURES**
The rates of exclusive breastfeeding at 3 and 6 months postnatal were 48% and 8.7%, respectively. These figures are comparable to what are reported in national surveys as well as from the study area.1, 79 The mean z-scores for both height-for-age and weight-for-age were poor but slightly better than the overall national trends.79 Similarly, our cohort at 12 months had a very high vaccination coverage of 97%.

In terms of the responsivity, attachment seems to improve over time as shown by the HOME and MPAS mean scores. Interesting to note is that time spent during the day interacting with the child drops as the child grows older (DiL—57% of the time mother interacting, soothing and holding at 3 months vs 44.6% at 12 months), meaning other family members like the grandmother and the father get more involved.

We do not have normative data on cognitive and socioemotional development of children in Pakistan, especially of this age group. Thus, our values will be most useful for making internal group comparisons as well as observing changes over time.
MAIN STRENGTHS AND LIMITATIONS

The main strengths include hypothesis-led investigation, use of robust study design and a multidisciplinary team. Multiple interim assessments in between the third trimester of pregnancy and 36-month postnatal follow-ups provide a rigorous design in analysing the relationship between changes in maternal depressive symptoms and child outcomes. We have taken great care to utilise standardised and validated instruments.

The loss to follow-up rates is relatively low at each assessment wave. However, missing data are common in longitudinal studies, due to attrition or non-response to questionnaire items, and inappropriate handling of missing data can lead to biased statistical interpretation. In addition to likelihood-based statistical methods, which are valid under the missing at random assumption, we will employ multiple imputation to address the issue of missing data, which will help minimise bias and make use of all available data. One of the limitations is not having administered PHQ-9 at 12 months postnatal. Thus, the severity of depressive symptoms across the cohort will not be known—only if they are depressed or not though the diagnostic interview (SCID).

In summary, this pregnancy–birth cohort with a follow-up period of at least 3 years postnatal is well suited to answer multiple research questions broadly related to the topic of maternal depression and child developmental trajectories. We are not aware of any other pregnancy–birth cohort of perinatal depression being followed in other low-resource settings or LMIC. The findings are especially relevant for rural based women and children living in LMIC and low-resource settings.

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Collaborators For any further information or potential collaboration Drs Joanna Maselko (jmaselko@unc.edu) and Siham Sikander (siham.sikander@hdrfoundation.org) can be contacted.

Contributors SS drafted the paper and all authors reviewed and approved it. SS, IA, AR and JM were responsible for the design of the study. SS, IA, LMB, KO, AH and JM were responsible for data gathering instruments. SS and IA were responsible for the conduct of the cohort. JG, AZ and ELT were responsible for database design and management.

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Data sharing statement Currently the data are not available since the cohort is ongoing.

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