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Title: Maternal depressive symptoms are not associated with child anaemia: A cross-sectional population study in Peru, 2015

Running title: Maternal depression and children anaemia

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Data Availability Statement:

The data that supports the findings of this study are available from the "Instituto Nacional de Estadística e Informática de Perú (INEI)" at <http://inei.inei.gob.pe/microdatos/>, "Consulta por encuesta" section. Data name: ENCUESTA DEMOGRÁFICA Y DE SALUD FAMILIAR- ENDES.

Abstract

Introduction: Approximately, one in three Peruvian children aged 6 to 59 months old have anaemia. Maternal depression, which may be disabling and affect the proper care of children, is associated with chronic malnutrition in their offspring. Therefore, the aim of this study is to evaluate if there is an association between depressive symptoms of mothers with the presence of anaemia in their children.

Methods: Analytical cross-sectional study of the Peruvian Demographic Health Survey 2015, which is nationally representative. Depressive symptoms were measured with the Patient Health Questionnaire-9 (PHQ-9) using a score of 10 as cut-off. The presence of anaemia was measured using HemoCue® and was considered positive when the hemoglobin was less than 11 g/dL.

Results: Crude and adjusted prevalence ratios (PR and aPR) were calculated with 95% confidence intervals, using generalized linear models of the Poisson family. We analyzed 6,683 mother-child binomials. The prevalence of anaemia in the children and depressive symptoms in women were 28.7% [95% CI: 27.3-30.2] and 6.9% [95% CI: 6.1-7.9], respectively. We found no statistically significant association between these variables in the bivariable analysis or in the different multivariable models (aPR: 1.05, 95% CI: 0.85-1.30). The sample did not have moderate or severe malnutrition.

Conclusions: There is no statistically significant difference between the prevalence of anaemia in children of mothers with or without depressive symptoms. We recommend continuing research in this field to determine more associate factors to childhood anaemia in order to improve primary prevention interventions. Ideally, conducting longitudinal studies such as prospectives cohorts to determine risk factors should be done.

Key words: *depressive symptoms; anaemia; children health; Peru (MeSH NLM)*

Introduction

Anaemia in children is a major public health issue (Kassebaum et al., 2016). In Peru, although this pathology has had a decreasing trend, its prevalence has been estimated at 32.6% in 2015 (Instituto Nacional de Estadística e Informática - INEI, 2016). Children with anaemia are more likely to have long-term health problems, such as impaired immune system development, poor cognitive development and poor physical growth which are ultimately associated with an impairment of the academic and labor performance in later life (McCann & Ames, 2007; Sachdev et al., 2005). The problem is multifactorial and has been associated with several variables, such as maternal education, income, maternal anaemia, lack of prenatal care during the first trimester of pregnancy, irregular intake of iron supplements during pregnancy, home birth, chronic malnutrition in children, among others (Velásquez-Hurtado et al., 2016; Woldie et al., 2015).

Major depression, another significant global health issue, is a common psychiatric disorder mainly in women (Kessler, 2003) with a particularly high prevalence during and after pregnancy (Bennett et al., 2004). Pregnancy has been reported as a period associated with the onset, recurrence or exacerbation of depressive symptoms (Nonacs & Cohen, 2004). The prevalence of depression during pregnancy in developing countries is 25% and that of postpartum depression is approximately 28% (Stewart et al., 2003). In addition, women who develop depression during pregnancy may continue to have symptoms even for five years after childbirth (Najman et al., 2000).

Maternal psychiatric disorders (e.g. depression) can negatively affect the health of their offspring. Studies have shown the association between maternal psychiatric disorders with consequences on their children, such as chronic malnutrition, impaired cognitive development and low life satisfaction (Bennett et al., 2015; Van der Waerden et al., 2015; Wemakor, 2016; Ashaba et al., 2015; Harpham et al., 2005). Nonetheless, there are studies that show the opposite, which makes the subject somewhat controversial. In an analysis of the longitudinal study Young Lives, researchers found an association of maternal psychiatric disorders with chronic malnutrition in India, however, they did not find this association in Ethiopia, Vietnam or Peru (Harpham et al., 2005). Studies conducted in European countries (Grote et al., 2010) and United States (Ertel et al., 2010) found no association between maternal depression and chronic malnutrition, but found an association between depression and increased height-for-age in American children. The authors attributed this to the fact that maternal depression could be linked to

overnutrition (Surkan et al., 2008). However, results of another study conducted in Brazil in 2016, showed that overnutrition (as obesity) in children was not associated with maternal depression (Brentani & Fink, 2016).

Chronic malnutrition and anaemia are diseases often found together in children of low income countries. The former is usually characterized by a deficit of micronutrients such as zinc, iodine, iron, folic acid and hydroxocobalamin (Branca & Ferrari, 2002; Wang et al., 2015). Deficiencies iron, folic acid and hydroxocobalamin are known to be common causes of anaemia (Janus & Moerschel, 2010). Chronic malnutrition and anaemia share many risk factors and children at risk of stunting is also at risk of anaemia and viceversa (Anticona & San-Sebastian, 2014; Reinhardt & Fanzo, 2014; Hussien et al., 2019; Rahman et al., 2019; Belachew & Tewabe, 2020).

The association of chronic malnutrition in children with both maternal depression and anaemia suggests the possible association between the latter two. Table 1 summarizes the studies that have evaluated association between chronic malnutrition in children with maternal depression. However, we have not found studies that analyze this possible link. Therefore, the aim of this study is to evaluate if there is an association between the variables studied in a population-based sample of Peruvian women and their children.

Materials and Methods

Study Design

We conducted an analytical cross-sectional study using data from “Encuesta Demográfica y de Salud Familiar” – ENDES (Peruvian Demographic Health Survey - DHS) of 2015. ENDES is an annual survey with a probabilistic multi-stage sampling that includes a representative sample of the Peruvian population. It is carried out by field workers trained in assessing hemoglobin values through HemoCue® and interviewing the participants using standardized questionnaires, which include the Patient Health Questionnaire-9 (PHQ-9) (INEI 2016).

Study Population

We used data from Peruvian women aged 18 to 49 years old residing or spending the night before the interview at the surveyed household, as well as the data from their children aged 6 to 59 months old.

We excluded pregnant women, women who were not native Spanish speakers and those who did not complete the PHQ-9. We also excluded children with no hemoglobin values registered and those categorized as wasted (moderate and severe acute malnutrition, weight-for-height Z score < -2 standard deviations). We decided to exclude acutely malnourished children because this condition is commonly associated with other diseases that could acutely modify hemoglobin values, such as dehydration caused by diarrheal diseases (Thakur et al., 2014; Leidman et al., 2018; Díez & Marrodán, 2018; Belachew & Tewabe, 2020). In the case of women having more than one eligible child aged 6 to 59 months, we considered data from their eldest child in order to avoid duplicate observations for the same mother.

Variables

Children hemoglobin adjusted to altitude

ENDES field workers used the HemoCue® portable equipment to measure hemoglobin. This method uses capillary blood and it is acceptable for anaemia screening, since values are comparable to those resulting from standard laboratory techniques (Mills et al., 1989; Sanchis-Gomar et al., 2013). Anaemia in children aged 6 to 59 months old was considered when the hemoglobin level was below 11 g/dL according to the Technical Standards for Anaemia of the Peruvian Ministry of Health 2016 (Ministerio de Salud – MINSA, 2016). Furthermore, the ENDES provides corrected hemoglobin values (for altitude above sea level). The correction was performed using the CDC/PNSS and Dirren formula (Dirren, 1994).

Maternal Depressive Symptoms

ENDES uses the Spanish translated version of the PHQ-9 (INEI, 2016) consisting of nine items with scores from 0 to 3 (range: 0 to 27) to evaluate depressive symptoms in the last two weeks. The score is sorted by this instrument as follows: from 0 to 4 for the presence of minimal or none depressive symptoms, from 5 to 9 for mild symptoms, from 10 to 14 for moderate symptoms, from 15 to 19 for moderately severe symptoms and from 20 to 27 for severe symptoms. For our study, we considered the variable as dichotomous using a cut-off of ≥ 10 , based on a

meta-analysis, in which that cut-off provided a sensitivity of 88% and a specificity of 92% for major depression (Gilbody et al., 2007). In addition, this questionnaire has a Chilean validation (Baader et al., 2012) and a cultural adaptation by a board of experts in Peru (Calderón et al., 2012). The collection of PHQ-9 data was carried out by staff duly trained in its administration.

Covariates

The study included sociodemographic variables such as age of the mother (in years) and age of the child (in months) divided into tertiles, child sex, maternal partnership status (categorized as “mother with partner” if married or cohabiting with a partner; otherwise “mother without partner” if separated, divorced or widowed), area of residence (whether urban or rural), natural region (Lima, coast excluding Lima, highlands and jungle), socioeconomic status (wealth index quintiles for consumer durables and dwelling characteristics), maternal education (no formal instruction, primary, secondary and higher education), health insurance (type of insurance the mother/family has) and food or nutritional support of any social program run by the Peruvian government (“Qali Warma”/“Vaso de Leche” National School Nutrition Program and “Wawa Wasi”/“Cuna Más” Child Care Social Program). Furthermore, we included health variables such as alcohol or cigarette consumption (self-reported as any consumption in the last 12 months), iron supplementation in the child (yes vs no), anaemia in the mother (hemoglobin <12 g/dL, determined by HemoCue® and adjusted for altitude), low birth weight (weight <2,500 grams at birth), chronic malnutrition (stunting, height-for-age Z-score 2 standard deviations below the population mean) and if the children received any preventive treatment against intestinal parasites in the last 12 months).

Statistical Power Calculation

To calculate the statistical power, we used Epidat 4.2 (“Xunta de Galicia”/Pan American Health Organization). For the calculation, we considered chronic malnutrition as a “proxy” for anaemia in the children. It was calculated based on the results of a previous cohort study (Santos et al., 2010), in which the frequency of chronic malnutrition was three times higher in children of depressed mothers than in children of non-depressed mothers. According to this, for convenience, we considered a difference to be detected of at least 10% in proportions of the outcome

variable for exposed and non-exposed children. Considering that the prevalence of anaemia in Peruvian children is 32.6% (INEI, 2016), we used estimated values of 37% vs. 27% in children of mothers with and without depressive symptoms, respectively. In addition, considering that the prevalence of depression in Lima is 10% approximately, (estimating that the prevalence in women is higher than the general population of 6.4%, according to the study) (Fiestas et al., 2014) a ratio of sample sizes of 9 to 1 (non-exposed/exposed) was used. Considering a 95% confidence level, we obtained a power of 99% to detect that difference in a sample of 6,000 mother-child pairs.

Data Analysis

We carried out the analysis using Stata 13.0 statistical package (College Station, Statacorp, TX, US), considering the ENDES 2015 (INEI, 2016) multistage design (using *svy* option). Sampling weights indicated by ENDES were used. All analyses were carried out based on a significance level of 5%.

For the descriptive analysis, we calculated the proportions of depressive symptoms in mothers and anaemia in children. The proportions of the other variables were also calculated. In the bivariable analysis, we analyzed the association between depressive symptoms in mothers with anaemia in children using the Pearson's Chi-square test. For the analysis of the other categorical variables, the Chi-square test was used as well.

We used generalized linear regression models using the Poisson family and link log to calculate the crude and adjusted prevalence ratios (PR and aPR) with their respective confidence intervals at 95%. We evaluated the multicollinearity of the variables with the "variance inflation factor". The multivariable models were constructed after confirming no evidence of multicollinearity.

For the multivariable model, we added potential confounding factors, cumulatively, in blocks. We considered variables of the mother and child according to previous literature (Velásquez-Hurtado et al., 2016; Woldie et al., 2015; Wieringa et al., 2016; Demirchyan et al., 2016; Khan et al., 2016; Ayoya et al., 2013; El Kishawi, 2015;

Habid et al., 2016). Age and sex were the first adjusted variables. Then, we added sociodemographic variables (socioeconomic status, health insurance, natural region), variables concerning maternal characteristics (marital status, anaemia and age of the mother) and health-related variables of the child (chronic malnutrition, history of anti-parasitic treatment and previous iron supplementation).

As additional analyses, we graphically evaluated if there was any correlation between the main variables as numeric (Hemoglobin level and depressive symptoms score) (figure shown in Supplementary material).

Finally, we carried out an exploratory subgroup analysis for potentially effect-modifying variables: socioeconomic status, rurality and geographic region (Kassebaum et al., 2014; Kassebaum et al., 2016).

Ethical aspects

The dataset did not contain personally identifiable information of the participants. It is publicly available on the website of the INEI: <http://inei.inei.gob.pe/microdatos/> (INEI 2016).

Results

From the 9,222 6 to 59 months old children with mothers aged 15 to 49, we excluded 1,282 children for not being the eldest child and 1,119 pairs that met our exclusion criteria. We included 6,683 mother-child binomials in the data analysis (Figure 1).

In our sample, we found a prevalence of anaemia in the children of 28.7% [95% CI: 27.3-30.2]. The prevalence of maternal depressive symptoms was 6.9% [95% CI: 6.1-7.9]. The average age of the mothers was 30.8 (S.D. 2.9) years old and that of the children was 34.7 (S.D. 4.6) months old. Most women lived in urban areas and had

completed secondary education. The prevalence of chronic malnutrition in children was 12.8 % [CI 95%:11.7-14.0]. Half of them received iron supplements and the third part received preventive antiparasitic treatment. The characteristics of mothers and their children are detailed in Table 2.

In the bivariable analysis, we found no statistically significant difference between the prevalence of anaemia in children whose mothers had or did not have depressive symptoms (28.6% vs 28.7%, $p=0.974$). On the other hand, among the variables of the children, we found an association of the anaemia in the children with chronic malnutrition, iron supplementation, antiparasitic treatment and participation in the “Qali-Warma” social program, whilst among the variables of the mother, we found association with the socioeconomic status, education level and alcohol and cigarettes consumption in the last 12 months and anaemia (Table 3).

In the multivariable analysis, we found no association between the anaemia in the children and maternal depressive symptoms in the different models adjusted by sociodemographic and clinical variables (Table 4).

No correlation was found among the main variables when plotted (Supplementary material). Additionally, there was no association between the variables in the stratified analysis according to the socioeconomic status, rurality and natural region.

Discussion

The aim of this study was to evaluate if there is an association between maternal depressive symptoms and anaemia in their children aged 6 to 59 months old in Peru. Contrary to our initial hypothesis, we found no statistically significant differences between the prevalence of anaemia in children of mothers with or without depressive symptoms.

Numerous studies have found an association between maternal depression and the presence of problems in the development of the children. There are studies that link maternal depression with poor maternal childcare (McLearn et al., 2006; Lovejoy et al., 2000) which can lead to chronic malnutrition. One study found an association between risk of maternal mental disorders with chronic and acute malnutrition, poor cognitive development and low life satisfaction in children from Vietnam, Ethiopia and India (Harpham et al., 2015). Particularly, previous studies have found an association between maternal depression with cognitive development deficits in the child in France, chronic malnutrition in the children in Ghana and acute malnutrition in the children in Vietnam and India (Harpham et al., 2005; Van der Waerden et al., 2015; Wemakor et al., 2016). Recent studies still find a persistent link between mental health in mothers and children growth faltering (Ashaba et al., 2015; Kaaya et al., 2016; Motlathledi et al., 2017; Rotheram-Fuller et al., 2018). These studies suggest a strong influence of maternal mental health in children health, mainly in nutritional aspects.

A study in Cambodia relates a high prevalence of nutritional deficits such as deficiency of vitamin A, B9, B12, zinc and especially iron with a higher prevalence of anaemia in children (Wieringa et al., 2016). On the other hand, a study in a rural region of Armenia established a relationship of poor diet with anaemia in children up to 5 years old (Demirchyan et al., 2016). In addition, several studies in Bangladesh, Haiti, Pakistan and Gaza have established an association between chronic malnutrition and anaemia in children (Khan et al., 2016; Ayoya et al., 2013; El Kishawi, 2015; Habid et al., 2016). The evidence already mentioned shows an association between chronic malnutrition and anaemia in the children; as well as the biological plausibility in which a poor diet would lead to anaemia due to lack of nutritional contribution.

Despite this, we found no association between these variables and could be explained by uncontrolled or unrecognized confounders (Maldonado et al., 1993), the cross-sectional nature of our study or chronic malnutrition may not really be associated with psychiatric disorders (Harpham et al., 2005).

One important unevaluated confounding factor could be breastfeeding duration. Breastfeeding creates a bond between the mother and child, and could be bidirectionally associated with maternal depression (Castro &

Figueiredo, 2015; McElderry & Napolitano, 2016; Pope & Mazmanian, 2016; Silva et al., 2017; Raheem et al., 2019). Additionally, breastfeeding duration can impact the probability of developing anaemia (Dalili et al., 2015). Another issue in developing countries could be the extension of exclusive breastfeeding duration in children older than six months. Studies have shown that prolonging exclusive breastfeeding beyond six months of age is a risk factor for anaemia in the children (Meinzen-Derr et. al., 2006; Pasricha et al., 2010). The association between prolonged exclusive breastfeeding and anaemia could be partially due to confounding by socioeconomic status. It would have been ideal to control for the potentially confounding effect of breastfeeding on our association of interest; however, we were unable to evaluate this variable. We believe it would be important to consider controlling for its effect in future studies.

In the bivariable analysis, we found that several factors were associated with the outcome. Among these factors, societal forces (such as socioeconomic status, maternal education, rurality and natural region) seem to have an important influence on anaemia in children, which is consistent with previous evidence from Peru (Velásquez-Hurtado et al., 2016). It could be possible that in the Peruvian setting, since it is a developing and unequal society, these factors are primary drivers of anaemia, irrespectively of the mental status of the mother. It would be interesting to replicate this study in developed and developing countries to see if maternal depressive symptoms have a different effect on childhood anaemia, according to the characteristics of the setting.

We have found twenty-four studies including a mother-child pairs from 20 countries performed an analysis between maternal depression or depressive symptoms and impaired child growth (Table 1). Regarding the prevalence of maternal depression in our sample, it was lower than in many of the reviewed studies. This variation might be explained because we used an observational instrument for screening depressive symptoms, as it did by Neamah et al. (Neamah et al., 2018) and Motlhatlhedhi et al. (Motlhatlhedhi et al., 2017). Other studies have applied different methods for depression screening and found significant and non-significant results with children nutritional status (Ashaba et al., 2015; Fisher et al., 2015; Brentani & Fink, 2016; Wemakor & Mensah, 2016; Moreira et al., 2017; Saeed et al., 2017; Girma et al., 2019; Anato et al., 2020). Only one design that considered major depression diagnosis found association with chronic malnutrition in children at 3 and 6 months old (Adewuya et al., 2008). The relationship between children stunting and maternal depressive symptoms is evident

with prevalence of chronic malnutrition around 20 to 40 % (Anato et al., 2020; Girma et al., 2019; Nguyen et al., 2013; Black et al., 2009; Stewart et al., 2008; Harpham et al., 2005), like our nutritional proxy prevalence (28.6%). Just two longitudinal research from Bangladesh (Nasreen et al., 2013) and England (Husain et al., 2012) found non-significant findings with these variables.

Limitations and strengths

Our study has limitations. Due to the cross-sectional design, we cannot assure that maternal depressive symptoms actually preceded anaemia. In addition, the hemoglobin levels were not assessed with a blood sampling laboratory test and it was also not possible to include other related and important hematologic values (corpuscular constants, transferrin, ferritin, etc.). Nonetheless, the study used a validated and accurate method for large epidemiological studies. (Mills et al., 1989; Sanchis-Gomar et al., 2013). We were not able to assess the presence of important confounders such as no social support, psychiatric illnesses different to depression, medication to treat depression and breastfeeding duration.

Additionally, there was no clinical depression diagnosis, but depressive symptoms were assessed by a demographic screening method that has acceptable sensibility and specificity values. (Gilbody et al., 2007; Baader et al., 2012; Calderón et al., 2012).

In addition, our study also has important strengths. Multiple studies evaluated the association of different maternal variables with anaemia in their children; however, as far as we know, there is no other study that has raised our research question. In addition, our study was carried out using a nationally-representative sample.

Conclusion

We found no statistically significant difference between the prevalence of anaemia in children of mothers with or without depressive symptoms. Further longitudinal research is needed to confirm or refute our results. We recommend continuing research in this field to better understand anaemia in order to prevent it and its consequences.

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Disclosures

We declare no conflicts of interest.

Key messages

- Childhood anaemia is still prevalent as a global health issue.
- Maternal depression may affect negatively in growth and development of children.
- Prior evidence suggests that there might be an association between maternal depression and childhood anaemia.
- Prospective studies should be made in order to uncover more childhood anaemia risk factors

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Table 1. Studies of maternal depression and children stunting: methods, analysis and results comparison.

Study	Country, study design and sample size	Depression prevalence and measure	Chronic malnutrition or stunting prevalence and measure	Findings	Confounding factors
Anato et al., 2020	Ethiopia, cross-sectional, N=232	22.8%, EPDS using a cut off of ≥ 13	30.6%, WHO growth standards: height-for-age z-score	Significant findings: stunting, OR = 2.55, 95% CI: 1.24- 5.25	Multivariate analyses adjusted for maternal wealth index, education, occupation, family size, level of household food security, workload
Girma et al., 2019	Ethiopia, case-control, N=234	26.9%, SRQ-20 using a cut off of ≥ 6	33.3%, WHO growth standards: height-for-age z-score	Significant findings: stunting, OR = 3.24, 95% CI: 1.14- 9.21	Multivariate analyses adjusted for maternal education, liquid waste disposal site, maternal knowledge about child feeding, wealth index, child sex and history of diarrhea, birth order
Neamah et al., 2018	Tanzania, longitudinal, N=1,031	2% for moderate-to-severe and 6.1% for mild depressive symptoms, PHQ-9 using a cut off of ≥ 9 and 5 for moderate-to-severe and mild symptoms	34.1%, WHO growth standards: height-for-age z-score	Non-significant findings: stunting, RR = 1.07, 95% CI: 0.73- 1.56	Models controlled for maternal age, education, child age, vitamin A random assignment, wealth quintiles
Moreira et al. 2017	Brazil, longitudinal, N=1,381	19.8% for 2 or 3 years postpartum, EPDS using a cut off of ≥ 12	6%, WHO growth standards: height-for-age z-score	Non-significant findings: stunting, OR = 0.96, 95% CI: 0.51- 1.80	Multivariate analyses adjusted for maternal age, number of children, monthly family income, child age and sex, birth weight
Motlhatlhedhi et al., 2017	Botswana, case-control, N=171	21.6%, PHQ-9 using a cut off of > 10	49.1%, WHO growth standards: height-for-age z-score	Significant findings: stunting, OR = 4.33, 95% CI: 1.89- 9.89	Unadjusted analysis, no covariates included in models
Saeed et al., 2017	Pakistan, cross-sectional, N=325	40.3%, AKUADS using a cut off of ≥ 20	36.6%, WHO growth standards: height-for-age z-score	Significant findings: stunting, OR = 3.15, 95% CI: 1.91- 5.18	Multivariate analyses adjusted for maternal age, education, occupation, household income, child sex and age
Brentani & Fink, 2016	Brazil, cross-sectional, N=798	12.5%, EPDS using a cut off of > 13	7.3%, WHO growth standards: height-for-age z-score	Non-significant findings: stunting, B=0.017, SE=0.034	Multivariate analyses adjusted for maternal age, marital status, wealth index, child sex and age, twin child, prematurity, small gestational age

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Table 1. Studies of maternal depression and children stunting: methods, analysis and results comparison. (continued)

Study	Country, study design and sample size	Depression prevalence and measure	Chronic malnutrition or stunting prevalence and measure	Findings	Confounding factors
Wemakor & Mensah, 2016	Ghana, cross-sectional, N=384	27.8%, CES-D using a cut off of ≥ 16	16.1%, WHO growth standards: height-for-age z-score	Significant findings: stunting, OR = 2.48, 95% CI: 1.29- 4.77	Models controlled for maternal age, marital status, household wealth, child birth weight, sex and age
Ashaba et al., 2015	Uganda, case-control, N=166	27.7%, depression diagnosis using MINI	75%, WHO growth standards: height-for-age z-score	Significant findings: stunting, OR = 2.40, 95% CI: 1.11- 5.18	Models were adjusted for maternal age, education, marital status, occupation, source of income, number of children
Fisher et al., 2015	Vietnam, longitudinal, N=211	33.6%, depression diagnosis using the SCID-I	15.6%, WHO growth standards: height-for-age z-score	Significant findings: stunting, OR = 1.65, 95% CI: 1.10–2.49	Covariates included maternal age, marital, educational and occupational status, household wealth, parity, child age and sex and health, duration of breastfeeding and intimate partner relationship
Nasreen et al., 2013	Bangladesh, longitudinal, N=652	14.1% at 2-3 months and 31.7% at 6-8 months postpartum, EPDS using a cut off of ≥ 10	58.4% at 2-3 months and 70.7% at 6-8 months age, WHO growth standards: height-for-age z-score < -2	Non-significant findings: stunting, B=0.154, SE=0.090	Models were adjusted for maternal age, maternal height, maternal nutritional status, wealth index, parity, number of children, child sex, height and weight at birth and age 2-3 months, head circumference at birth, infant's illness at 6–8 months, and maternal perceptions of the infant's temperament as fussy/difficult and unpredictable
Nguyen et al., 2013	Bangladesh, Vietnam, Ethiopia; cross-sectional; N=4,400; 4,029; 3,000	49%, 31%, 39%; SRQ-20 using a cut off of 7	40%, 17%, 44%; WHO growth standards: height-for-age z-score	Significant findings: stunting, OR = 1.21, 95% CI: 1.03- 1.41	Multivariate analyses adjusted maternal age, education, height/body mass index, wealth index, child age and sex, illness as diarrhea or upper acute respiratory infection, low birth weight
Husain et al., 2012	England, longitudinal, N=237	26.5%, EPDS using a cut off of ≥ 12	1%, WHO growth standards: height-for-age z-score	Non-significant findings: stunting, β : 0.03 (-0.30, 0.37)	Covariates included maternal age, more than 2 children, parity, planned pregnancy, marital status, education, child birth weight

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Table 1. Studies of maternal depression and children stunting: methods, analysis and results comparison. (continued)

Study	Country, study design and sample size	Depression prevalence and measure	Chronic malnutrition or stunting prevalence and measure	Findings	Confounding factors
Ertel et al., 2010	USA, longitudinal, N=872	8% antenatal and 7.9% postpartum depression, EPDS using a cut off of ≥ 13 or 15	4.2%, WHO growth standards: height-for-age z-score	Non-significant findings: antenatal depression OR: -0.01, 95% CI: -0.19- 0.17 Significant findings: postpartum, OR:0.29, 95% CI: 0.11- 0.47	Multivariate analyses adjusted for maternal age, ethnicity, household income, height, pregnancy weight gain, gestational age at birth and birthweight for gestational age, breastfeeding duration, age of introduction of solid foods, child sex and age
Grote et al., 2010	Belgium, Germany, Italy, Poland, Spain; longitudinal; N=929	11%, EPDS using a cut off of ≥ 13	6.4%, WHO growth standards: height-for-age z-score	Non-significant findings: stunting β : 0.01 (-0.45, 0.47)	Covariates included country, feeding type, single mother, mother's age, birth order, body mass index of mother, stress in pregnancy, caesarean section, pregnancy not wished, anthropometric measure, smoking
Santos et al., 2010	Brazil, longitudinal, N=3,792	17.9%, EPDS using a cut off of ≥ 13	3.6%, WHO growth standards: height-for-age z-score	Non-significant findings: stunting, OR: 1.0, 95% CI: 0.6- 1.5	Multivariate analyses adjusted for maternal height, maternal weight, wealth index, education, maternal occupation, marital status, paternal occupation, recent infant diarrhea, recent infant fever, child age, sex and weight-for-age z-score at first postnatal weighing
Black et al., 2009	Bangladesh, cross-sectional, N=221	52.9% at 6 months and 51.5% at 12 months postpartum, CES-D using a cut off of ≥ 16	18% at 6 months and 36.9% at 12 months age, WHO growth standards: height-for-age z-score	Significant findings: 12-month height-for-age z-score, adjusted β : -0.01 ($p = 0.01$), unadjusted OR: 2.2, 95% CI: 1.3–3.8.	Covariates included maternal education and wealth index, poverty status, child sex, birth order, receipt of zinc or iron, maternal perceptions of infant temperament and months of breastfeeding
Adewuya et al., 2008	Nigeria, longitudinal case-control, N=876	14.6%, Major depression diagnosis using the DSM-III-R (SCID-NP)	13.3% at 3 and 16.6% at 6 months age, WHO growth standards: < 5th percentile of height-for-age	Significant findings: stunting at 3 months; OR: 3.3, 95% CI: 1.03–10.5; at 6 months, OR: 3.3, 95% CI: 1.2–9.6.	Unadjusted analysis, no covariates included in models

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Table 1. Studies of maternal depression and children stunting: methods, analysis and results comparison. (continued)

Study	Country, study design and sample size	Depression prevalence and measure	Chronic malnutrition or stunting prevalence and measure	Findings	Confounding factors
Stewart et al., 2008	Malawi, cross-sectional, N=501	29.9%, SRQ-20 using a cut off of 8	24.8%, WHO growth standards: mean height-for-age z-score	Significant findings: height-for-age z-score, β : -0.27 ($p = 0.01$)	Multivariate analyses adjusted for maternal height and weight, wealth index, occupation, education, marital status, paternal occupation, recent infant diarrhea, recent infant fever, child age and sex
Surkan et al., 2008	Brazil, cross-sectional, N=595	55.5%, CES-D using a cut off of ≥ 16	24.6%, WHO growth standards: height-for-age z-score < -2	Significant findings: stunting, OR: 1.8, 95% CI: 1.1–2.9	Model covariates included the infant sex, birth weight and age, breastfeeding duration, maternal education, sanitation score, socioeconomic status, living conditions, number of children
Harpham et al., 2005	Ethiopia, cross-sectional, N=1,722	33%, SRQ-20 using a cut off of 7–8	38%, WHO growth standards: height-for-age z-score < -2	Non-significant findings: stunting, OR: 0.9, 95% CI: 0.7–1.2	Unadjusted and adjusted models by covariates included maternal age and education, child sex, age and birth weight and household composition, wealth index and geographical location
Harpham et al., 2005	India, cross-sectional, N=1,823	30%, SRQ-20 using a cut off of 7–8	27%, WHO growth standards: height-for-age z-score < -2	Significant findings: stunting, OR: 1.4, 95% CI: 1.2–1.6	Unadjusted and adjusted models by covariates included maternal age and education, child sex, age and birth weight and household composition, wealth index and geographical location
Harpham et al., 2005	Peru, cross-sectional, N=1,949	30%, SRQ-20 using a cut off of 7–8	25%, WHO growth standards: height-for-age z-score < -2	Non-significant findings: stunting, OR: 1.1, 95% CI: 0.9–1.4	Unadjusted and adjusted models by covariates included maternal age and education, child sex, age and birth weight and household composition, wealth index and geographical location
Harpham et al., 2005	Vietnam, cross-sectional, N=1,570	21%, SRQ-20 using a cut off of 7–8	16%, WHO growth standards: height-for-age z-score < -2	Non-significant findings: stunting, OR: 1.3, 95% CI: 0.9–1.7	Unadjusted and adjusted models by covariates included maternal age and education, child sex, age and birth weight and household composition, wealth index and geographical location

AKUADS, Aga Khan University Anxiety and Depression Scale; β , mean; B, unstandardized regression coefficient; CES-D, Center for Epidemiological Studies Depression Scale; CI, confidence interval; DMS-III-R (SCID-NP), Diagnostic and statistical manual of mental disorders, third edition, revised Structured Clinical Interview – non-patient version; EPDS, The Edinburgh postnatal depression scale; MINI, Mini International Neuropsychiatric Interview; N, sample; OR, odds ratio; p, p value; PHQ-9, Patient Health Questionnaire-9; RR, risk relative; SCID-I, Structured Clinical Interviews for the Diagnostic and statistical manual of mental disorders, fourth edition axis 1 diagnoses; SE, standard error; SRQ-20, 20-item Self-Reporting Questionnaire; WHO, World Health Organization.

Table 2. Characteristics of mothers and children of ENDES 2015 (N = 6,683)

Characteristics	n	%
Mother age in tertiles (years)		
[18-27]	2,442	34.4
[28-33]	2,120	31.8
[34-49]	2,121	33.8
Mother has a partner	5,636	83.3
Area of residence		
Urban	4,907	76.2
Rural	1,766	23.8
Natural region		
Lima	771	28.1
Coast (excluding Lima)	2,167	28.2
Highlands	2,047	27.1
Jungle	1,688	16.7
Socioeconomic status (Quintiles)		
Poorest	1,433	19.7
Poor	1,964	25.0
Medium	1,477	21.7
Rich	1,085	18.6
Richest	724	14.9
Maternal education		
No formal instruction	95	1.4
Primary	1,370	20.5
High school	3,254	47.6
Higher education	1,964	30.4
Health insurance	5,488	81.1
Cigarette consumption in the last 12 months	447	7.6
Alcohol consumption in the last 12 months	4,072	68.8
Maternal anaemia (Hb <12 g/dL) ^a	1,333	20.4
Depressive symptoms in the last 14 days	461	6.9
Child's age in tertiles (months)		
[06-26]	2,231	33.0
[27-44]	2,347	34.7
[44-59]	2,105	32.3
Low birth weight	387 ^b	5.9
Children chronic malnutrition	893	12.8
Children iron supplementation	3,512	48.7
Preventive antiparasitic treatment	2,254 ^b	31.6
“Vaso de Leche” / “Qali Warma” nutritional program	2,271 ^b	33.2
“Wawa wasi” / “Cuna Más” social program	276 ^b	5.3
Anaemia in the child (Hb <11 g/dL) ^a	2,082	28.7

^a Hemoglobin measured by HemoCue[®] and adjusted by altitude.

^b Totals may not add up due to missing values.

Hb: Hemoglobin

Table 3. Bivariable analysis according to the diagnosis of anaemia in the children, Peru 2015 (N = 6,683)

Characteristics	Anaemia in the child				p
	No		Yes		
	n	%	n	%	
Maternal depressive symptoms ^a					0.974
No	4,274	71.3	1,948	28.7	
Yes	327	71.4	134	28.6	
Mother age in tertiles					
[18-27]	1,620	68.7	822	31.3	0.008
[28-33]	2,133	70.7	666	29.3	
[34-39]	1,315	74.4	594	25.6	
Area of residence					<0.001
Urban	3,455	72.9	1,452	27.1	
Rural	1,146	66.0	630	34.0	
Natural region					<0.001
Lima	587	76.6	184	23.4	
Coast (excluding Lima)	1,593	74.5	584	25.5	
Highlands	1,287	64.4	760	35.6	
Jungle	1,134	67.9	554	32.1	
Mother has a partner					0.283
No	730	73.1	317	26.9	
Yes	3,871	70.9	1,765	29.1	
Socioeconomic status (quintiles)					
Poorest	902	65.0	531	35.0	<0.001
Poor	1,256	66.2	708	33.8	
Medium	1,046	71.8	431	28.2	
Rich	808	73.9	277	26.1	
Richest	589	83.9	135	16.1	
Maternal education					
No formal instruction	66	67.6	29	32.4	<0.001
Primary	920	69.2	450	30.8	
High school	2,188	69.0	1,066	31.0	
Higher education	1,427	76.3	537	23.7	
Health insurance					0.598
No	838	72.1	357	27.9	
Yes	3,763	71.1	1,725	28.9	
Maternal anaemia					0.014
No	4,333	71.8	1,919	28.2	
Yes	268	64.1	163	35.9	
Consumption of alcohol in the mother ^b					<0.001
No	1,285	66.8	713	33.2	
Yes	2,927	73.9	1,145	26.1	
Consumption of cigarettes in the mother ^b					0.002
No	4,260	70.6	1,974	29.4	
Yes	339	79.7	108	20.3	

(continued on next page)

Table 3. Bivariate analysis according to the diagnosis of anaemia in the children (N = 6,683) (continued)

Characteristics	Anaemia in the child				<i>p</i>
	No		Yes		
	n	%	n	%	
Child's sex					0.009
Male	2,332	69.5	1,138	30.5	
Woman	2,269	73.2	944	26.8	
Child's age in tertiles (months)					
[06-26]	1,114	53.4	1,117	46.6	<0.001
[27-44]	1,768	77.2	579	22.8	
[44-59]	1,719	83.2	386	16.8	
Chronic malnutrition (child)					0.001
No	4,042	72.1	1,748	27.9	
Yes	559	65.7	334	34.3	
Iron supplementation (child)					<0.001
No	2,376	77.2	795	22.8	
Yes	2,225	65.0	1,287	35.0	
Preventive antiparasitic treatment (child)					<0.001
No	2,842	68.2	1,521	31.8	
Yes	1,715	77.8	539	22.2	
Low birth weight					0.311
No	4,328	71.1	1,962	28.9	
Yes	269	74.0	118	26.0	
“Vaso de Leche” / “Qali Warma” nutritional program					0.008
No	3,087	72.6	1,323	27.4	
Yes	1,512	68.6	759	31.4	
“Wawa wasi” / “Cuna Más” social program					0.925
No	2,525	65.3	1,532	34.7	
Yes	171	65.6	105	34.4	

^a Evaluated by PHQ-9 (using a cut-off score of 10 or more).^b Self-report for the last 12 months.

Table 4. Multivariable analysis between depressive symptoms in the mother and anaemia in the children, Peru 2015.

	Crude		Model 1 ^b		Model 2 ^c		Model 3 ^d		Model 4 ^e	
	PR	95% CI	aPR	95% CI	aPR	95% CI	aPR	95% CI	aPR	95% CI
Depressive symptoms ^a										
No	1	Ref	1	Ref	1	Ref	1	Ref	1	Ref
Yes	0.99	0.79 – 1.25	1.11	0.88 – 1.37	1.09	0.87 – 1.35	1.08	0.87 – 1.33	1.05	0.85 – 1.30

^a Evaluated by PHQ-9 (using a cut-off score of 10 or more).

^b Model 1: Adjusted for age and sex of the children.

^c Model 2: Adjusted for Model 1 + natural region, socioeconomic status and health insurance.

^d Model 3: Adjusted for Model 2 + mother age, mother has a partner and anaemia in mother.

^e Model 4: Adjusted for Model 3 + chronic malnutrition, preventive antiparasitic treatment and iron supplementation in the child.

PR, prevalence ratio; aPR, adjusted prevalence ratio