Review Article

The risk of antenatal depression among the iron-deficient anaemic pregnant women: An evolving correlation

Roopa Satyanarayan Basutkar [a], Pooja Sudarsan [a], Chris Elizabeth Vinod [a], Resia Varghese [a], Divya Perumal [b], P. Sivasankaran [a, *]

[a] Department of Pharmacy Practice, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Ooty, 643001, The Nilgiris, India
[b] Department of Obstetrics and Gynecology, Govt. District Headquarters Hospital, Ooty, 643001, The Nilgiris, India

ABSTRACT

Depression is one of the most common turmoil encountered by pregnant women. Mothers' suffering from antenatal depression holds a greater risk in developing postpartum depression. This increases the need for early detection of antenatal depression which could reduce further complications. Although there are several aetiologies for antenatal depression, iron deficiency anaemia (IDA) proves to be an emerging correlation. It is hypothesised that an altered myelination induced by iron deprivation dysregulates the release of neurotransmitters such as serotonin and dopamine, leading to depression. Of the four literature studies reviewed, two studies portrayed an association between IDA and antenatal depression. The remaining two literature studies showed the relation between antenatal depression and its complications in the infants. In this review article, we intend to establish an association between IDA and antenatal depression.

© 2019 Sir Ganga Ram Hospital. Published by Elsevier, a division of RELX India, Pvt. Ltd. All rights reserved.

1. Introduction

Depression is a chronic illness with a high prevalence in women compared with men, and it is the second leading cause of disability, globally.[1] The prospect of depression escalates during antenatal period of pregnancy but often goes undiagnosed and untreated, thus risking the quality of life.[2] The American Congress of Obstetricians and Gynaecologists (ACOG) had stated that about 14–23% of pregnant women exhibit symptoms of depression.[3] According to the World Health Organization (WHO), around 10% of women in their antenatal period and 13% of women in their postnatal period exhibit depression and it is found during all three trimesters of pregnancy globally.[4] If this condition is left untreated, it could lead to poor self-care by not attending the antenatal clinics and negligence in food habits. There is an elevated peril for obstetric complications such as premature birth and low birth weight and certain morphological changes in the foetus that delay the development. The mother-child bonding is hampered in this course because of changes in neurobiological mechanisms which involve monoaminergic and glutamatergic systems and disturbed functioning of hypothalamic-pituitary-adrenal (HPA) axis with its hippocampal activation. Irregularities have also been found in other zones of the neuroendocrine system and neural regions of the brain which are involved in postpartum depression and compromised neonatal health outcomes.[2,5] Certain inclining factors that include low educational accomplishment, socioeconomic status, past medical records of depression, miscarriage and nutritional deficiencies such as iron deficiency anaemia (IDA) could express a bleak impact on antenatal depression.[6]

The transport of oxygen to the various parts of the body is regulated by iron and iron-containing proteins. The homoeostasis of the body is balanced by iron which is dysregulated during anaemia and energy depletion.[7,8] It is deliberated as a defensive element against depressive symptoms, especially in the antenatal period.[9,10] Studies on the effect of physiological variables such as IDA on antenatal depression are very few. The distribution of iron in the brain occurs heterogeneously, and iron is stored in proteins such as ferritin. Iron is a cofactor for the process of myelination by the oligodendrocytes. Altered myelination and neurotransmitter metabolism caused by IDA

* Corresponding author. Dept. of Pharmacy Practice, JSS College of Pharmacy, Udhagamandalam, 643 001, The Nilgiris, Tamilnadu, JSS Academy of Higher Education and Research, Mysuru, India.
E-mail addresses: roopasatyanarayan@gmail.com (R.S. Basutkar), poojasud96@gmail.com (P. Sudarsan), christyelza@gmail.com (C.E. Vinod), resiavarghese@gmail.com (R. Varghese), drdivyaperumal450@gmail.com (D. Perumal), ponnusankarsivas@gmail.com (P. Sivasankaran).

is hypothesised to cause depressive symptoms. Hypomyelination could lead to an alteration in the uptake and degradation of the neurotransmitters such as tryptophan hydroxylase (serotonin) and tyrosine hydroxylase (norepinephrine and dopamine) which may retool the brain function. Another hypothesis suggests that IDA could also affect the metabolism of energy in the brain parenchyma because of reduced oxygenation.[11]

According to the WHO, about 14% of the developed countries and 51% of the developing countries are affected with anaemia and in India, around 65–75% are said to be affected.[12] IDA is prevalent amongst pregnant women in their second trimester than in their first and third trimesters.[13] Iron also catalyzes the synthesis of various neurotransmitters, including serotonin, norepinephrine and dopamine.[11,14] Deficiency in the bioavailability of iron could lead to frailty in these neurotransmitters, thereby causing impairment in the cognitive functioning of the brain.[9] Preterm deliveries, low birth weight and neonatal anomalies are associated with serious mortality risks mainly in iron-deficient mothers in their second trimester of pregnancy.[10]

The Edinburg Postnatal Depression Scale (EPDS), now commonly known as the Edinburg Depression Scale (EDS), is the most widely used screening tool for depression during pregnancy. It is a 10-item self-assessment scale that helps in detecting the risk of depression among pregnant women.[15,16] It is a simplified scale that relates the depressive episodes over the past seven days, and in some cases, the tool can be repeated even after two weeks. The EDS has also been validated for its efficacy in finding the possibility of antenatal depression.[17,18]

The management of antenatal depression in its advanced stages mainly includes antidepressants and electroconvulsive therapy which is known for its foetal risks. Hence, it is important to detect antenatal depression at its earlier stages.[19] This review was organised to arbitrate the association between depression and IDA in pregnant women.

2. Methods

2.1. The criteria for considering studies for this review

2.1.1. Inclusion criteria
Our search involved observational studies (cross-sectional, cohort) in which the presence of antenatal depression was proved in pregnant women with IDA. We also included studies that project the complications of untreated antenatal depression on the infant's motor and cognitive development. Maternal iron stores or current use of iron supplementation was a required criterion. Our focus was on pregnant women who were assigned to antenatal care and then followed up within a year postpartum to assess the complications in infants. Pregnant women in any trimester of pregnancy were included. The primary 'outcome', specifically antenatal depression, had to be measured using a validated EDS which is a standard tool to measure maternal depression.

2.1.2. Exclusion criteria
Randomised controlled trials (RCTs) and interventional studies were not included for review. Studies on postpartum depression and articles in foreign languages were excluded. Studies that had measured physical symptoms of anaemia such as fatigue other than depression were not included in the review.

2.2. Types of outcome measures

2.2.1. Primary outcome
Assessment of antenatal depression in pregnant women with IDA was evaluated using the EDS.

2.2.2. Secondary outcome
The foetal complications or abnormalities in the study population were evaluated.

2.3. Search methods for identification of studies

2.3.1. Electronic searches
The articles for review were extracted from databases such as PubMed, Scopus, Google Scholar and the Cochrane CENTRAL. The references enlisted in all the included studies were cross checked in various online databases, and furthermore, additional articles were included.

2.3.2. Keywords
The search terms included were "IDA" or "haemoglobin" or "ferritin" or "mean cell haemoglobin concentration" or "mean cell haemoglobin volume" or "transferrin saturation" or "haematocrit" or "anaemia in pregnancy" or "antenatal depression" or "post-partum depression" or "perinatal depression" or "maternal behaviour" or "pregnancy complications" or "prenatal diagnosis" or "Edinburgh Postnatal Depression Scale" or "major depressive episode" or "psychiatric rating scales" or "common mental disorders".

2.4. Data collection

2.4.1. Selection of studies
The search was conducted from 25th October 2018 to 29th December 2018, and studies conducted over last eight years were selected for review. Eligibility screening was carried out with the pooled articles by three independent reviewers (P.S., R.V. and C.E.V.). The screening was conducted based on the inclusion and exclusion criteria using the online Rayyan portal. No restrictions were placed on the trimester of pregnancy, the duration of the study or the country where the study was conducted.

We assessed the duplicated studies, and then the full-text articles of the included studies were retrieved and independently reviewed by three reviewers (P.S., R.V. and C.E.V.). The disagreements and conclusions were discussed and sorted out by a fourth independent reviewer R.S.B.

2.4.2. Data extraction
Information was extracted using the Joanna Briggs Institute (JBI) data extraction form specific for experimental/observational studies by two independent reviewers C.E.V. and R.V. It includes title of the study, author name, country setting, study design, sample size, type of intervention, source of data and population, domain tested, iron status measures, scales used (i.e. EPDS, Bayley's), results and conclusions.

2.4.3. Quality assessment and appraisal
The articles selected for review were appraised using the quality assessment tool (QAT) created by the National Institute of Health (NIH) for cross-sectional and observational studies. Two independent reviewers (P.S. and R.S.B.) assessed the internal validity of included studies using the QAT. The items in the checklist were evaluated as "yes", "no" and others (cannot determine/not applicable/not reported). The overall quality was rated as poor/fair/good. Studies by Dama et al.[20] and Yilmaz et al.[21] were rated as good; however, the study by Tran[22] was fair in quality as some criteria were not met. The study by Tran[23] which assessed the association between antenatal depression and infant motor development was of good quality. All disagreements were discussed with a third reviewer S.P.

3. Results

Three databases engendered about 470 articles from Cochrane CENTRAL, PubMed and Scopus. Further search in Google Scholar resulted in 17 articles which were found to be duplicates of the ones obtained from the aforementioned databases. The articles were screened based on the inclusion and exclusion criteria; 459 articles from a total of 487 articles were excluded, of which 103 were RCTs, 26 were interventional studies, 255 were unrelated studies (no relation with IDA or antenatal depression), 71 were studies on postpartum depression (PPD), 3 were in foreign language and 1 was a reverse causality study. Of the remaining 28 articles, 24 were excluded because of duplication. The review was conducted based on the conclusions of the four articles short listed after the literature search. The whole process is illustrated as a flowchart in Fig. 1.

3.1. Association between IDA and antenatal depression

Two studies were examined to look into the association between IDA and antenatal depression. These studies have used haemoglobin or ferritin levels to diagnose IDA and the EDS as a screening tool for depression or common mental disorders (CMDs) among women of different trimesters of pregnancy. Both studies have shown a positive correlation between IDA and depression. Dama et al.[20] conducted a retrospective cross-sectional study in women during their middle to late pregnancy. Participants with a ferritin <12 ng/L showed an increase in the mean EDS scores ($p = 0.03$) and a likely chance of developing antenatal depression by 45%. Yilmaz et al.[21] had conducted a bivariate correlation analysis between haemoglobin levels and EDS score. A significant negative correlation was found between the two, with r = -0.185 and $p = 0.000$.

3.2. Antenatal depression and complications in infants

Two studies were identified to explain some of the complications prevalent among infants of mothers who had suffered from antenatal depression. Tran[22] found adverse cognitive behaviour in infants whose mothers had suffered from CMD and IDA during their antenatal period. The regression value (r) was found to be -4.80 in participants who had antenatal CMD. Tran et al.[23] postulated how antenatal IDA and CMD would affect the motor development of six-month-old infants and examined the effects of antenatal IDA and CMD on motor development six-month-old infants. M(BSID-Modified) score decreased with an increase in maternal EDS scores by a regression coefficient of -0.60. Most of these infant anomalies are left unnoticed in developing countries; thus, the conduct of such studies is needed for early recognition and treatment. The summary of the studies reviewed is illustrated in Tables 1 and 2.

3.3. Assessment of bias in the included studies

Being a retrospective study, possibility of reverse causality with the variables was not assessed in the study by Dama et al.[20] and also participants referred for mental health concerns were recruited; hence, it is not applicable for generalised pregnant population. Yılmaz et al.[21] did not report serum ferritin level, and randomisation of study population was not carried out. Heterogeneity was not found in this study because patients were from similar socioeconomic status. Indirect effects of certain risk factors such as infant birth weight and postpartum CMD on the outcome were not measured in the study by Tran[22] Tran[23] did not measure several potential antenatal factors that can influence the outcome, and missing of data was also reported. The Bayley Scales of Infant Development (BSID) was not validated; thus, comparisons across the exposure group could not be performed in this study. Pilot studies had been conducted for each variable, but evidence was not properly mentioned. Loss to follow-up was relatively high for studies by Tran[22] and Tran[23] We found that outcome assessors were aware about the exposure status of participants in all the 4 studies; hence, it led to information bias. We used the guidance of Conducting Systematic Reviews and Meta Analysis of Observational Studies of Etiology (COSMOS-E) for assessing the risk of the included studies, and it is illustrated in Table 3.[24]
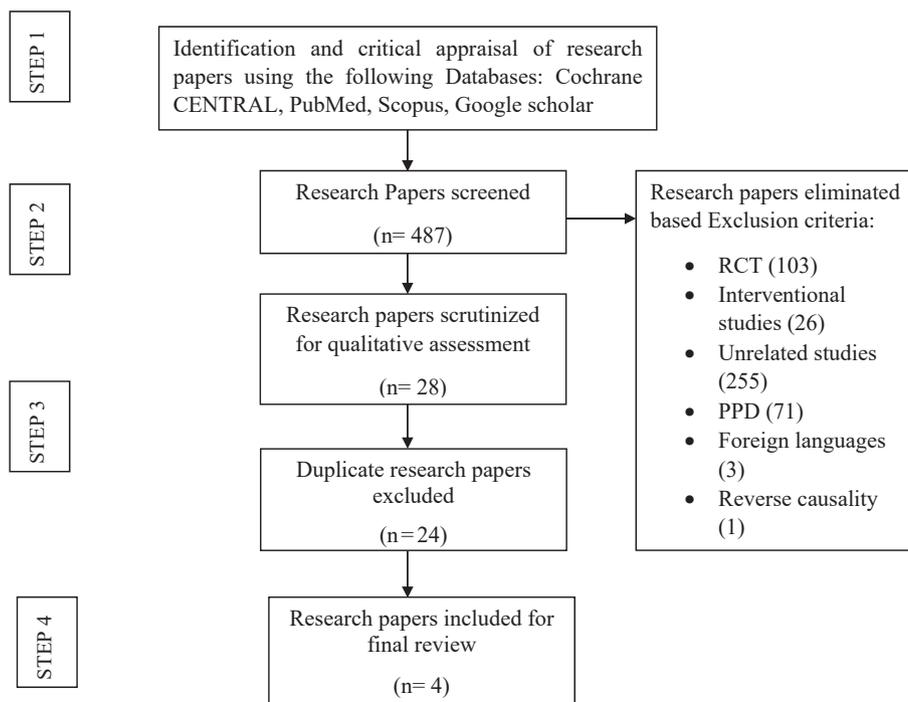

Fig. 1. Flow diagram of screening process.

Table 1
An overview of the methodology and outcomes of various studies.

Author, year	Country	Study design	Sample size	Domain tested	Outcome	Limitations
Dama et al, 2017[20]	Canada	Retrospective cross-sectional	142	Antenatal depression	Antenatal depression	Sample consisted of women who were referred for mental health concerns. The EDS is a questionnaire, not a diagnostic tool, and it is a retrospective study.
Yılmaz et al, 2016[21]	Turkey	Cross-sectional	450	Antenatal depression	Antenatal depression	Sample size was not sufficient; the EDS is only a tool.
Tran et al, 2013[22]	Vietnam	Prospective population-based	497 mother-infant pairs	Child's cognitive status, antenatal depression	Infant cognitive abnormalities	The relation between maternal IDA and child's cognitive behaviour through direct and indirect pathways was undistinguishable; loss to follow-up was relatively high.
Tran et al, 2014[23]	Vietnam	Prospective population-based	418 mother-infant pairs	Antenatal anaemia and CMD, infant motor development	Infant developmental abnormalities	The EDS is only a screening tool; ferritin levels could remain low during the later stages of pregnancy and at the time of inflammation.

EDS, Edinburg Depression Scale; IDA, iron deficiency anaemia; CMD, .

Table 2
Summary of the studies related to IDA and antenatal depression.

Author, year	Parameters measured	p-value	r-value and/or odds ratio, 95% CI	Findings
Dama et al, 2017[20]	EDS (cut-off score $\geq$12), ferritin <12 g/L	$p = 0.030$	Adjusted OR = 2.51 95% CI (1.14—5.52); unadjusted OR = 2.57 95% CI (1.21—5.44)	Iron deficiency is associated with higher levels of depression during pregnancy.
Yılmaz et al, 2016[21]	Hb < 11 g/L, EDS score 11 (anaemic group); Hb $\geq$ 11 g/L, EDS score 7 (non-anaemic group), MCV, Hct	$p = 0.000$	r = −0.185	Anaemia is associated with higher depressive symptoms during pregnancy.
Tran et al, 2013[22]	Hb < 11 g/dL, serum ferritin <15 ng/mL, EDS, Bayley Scale.	$p = $ NA	r = −4.80 95% CI (9.40 to −0.20)	Antenatal IDA and congenital muscular dystrophy have an adverse effect on child's cognitive development.
Tran et al, 2014[23]	Hb < 11 g/dL, ferritin <15 ng/mL, EDS score $\geq$4	$p = $ NA	r = −0.60 95% CI (−1.07 to −0.13)	Antenatal anaemia & common mental disorders have negative impact on infant motor development.

NA, not available; r, regression coefficient; OR, odds ratio; CI, confidence interval; Hb, haemoglobin; EDS, Edinburgh Depression Scale; MCV, mean corpuscular volume; Hct, haematocrit; IDA, iron deficiency anaemia.

4. Discussion

This is the first narrative review to investigate the association between IDA and depression during antenatal period which strengthens the need for the same. Totally, four studies were analysed to inspect the prevalence of antenatal depression in pregnant women with IDA using the EDS. This review included observational studies that were conducted in various ethnic groups, thereby ensuring heterogeneity in the data presented. Various aspects were taken into account while investigating the effects of anaemia and common mental disorders presented during antenatal period on the infant's development using suitable scales. All four studies had limitations, especially with the EDS by virtue of that being a screening tool and not a diagnostic tool.

Insufficient sample size had affected the ability to comprehend an association between maternal common mental disorders and infant's development. Two of the four studies showed a relation between anaemia and antenatal depression. The other two studies emphasised on the risks/complications associated with antenatal depression.

The prime goal of the study by Dama [20] was to investigate the relation between IDA and depression in women of mid to late pregnancy using retrospective sources with a sample size of 142 females using a cut-off score $\geq$12 on the EDS. The study was successful in stating the relation between IDA and depression as it could rule out the other confounding factors that could have also lead to depression. Cloning of these findings is required, even though it can be advantageous for the clinicians. A major limitation in this study was the sample; it consisted of women who were referred for mental health concerns, and the data were retrospective.[20] Yılmaz [21] had conducted the study by using the cross-sectional study design to check whether anaemia is highly associated with depressive symptoms during pregnancy or not. They included women of last trimester pregnancy, and their findings suggest that anaemia in the antepartum period, determined by low haemoglobin concentration and low mean corpuscular volume (MCV), can be considered as a factor that increases the risk of antenatal depressive symptoms. Ferritin, a confirmatory parameter in the diagnosis of IDA, was not measured in this study. This study also demonstrated a correlation between severity of depression and the haemoglobin levels, that is, when there was a significant decrease in the haemoglobin level, with an increase in the EDS score and vice-versa.[21] Tran used a prospective population-based study to check the negative impact of antenatal anaemia and congenital muscular dystrophy on a six-month-old infant's cognitive behaviour using Bayley Scales of Infant and Toddler Development-Third Edition (BSID-III).[22] Systematic recruitment was done for sampling, and path analysis techniques were used to actuate the effects of confounding factors on the main outcome. However, they concluded that risk factors can affect directly and indirectly the infant's cognitive development. The relation between maternal IDA and child's cognitive behaviour through direct and indirect pathways being undistinguishable and loss to follow-up could be considered as the major limitations in this study.[22] A study by Tran was conducted to find the impact of direct and indirect effects associated with IDA and common mental disorders presented during pregnancy on child's motor development.[23] Of 497 eligible participants, 418 mother-infant pairs had given complete data which underwent analysis. The study data intimated that anaemia in late pregnancy is associated with infant motor development.

Table 3
Risk of bias assessment of the included studies.

Dama, 2017[20]		
Methods	Retrospective cross-sectional	
Participants	142	
Outcome	Antenatal depression	
Bias	Author's judgement	Support for judgement
Causal relationship (confounding bias)	Low risk	Being a retrospective study, possibility of reverse causality with the variables was not assessed.
Selective sampling (selection bias)	Unclear risk	Participants referred for mental health concerns were recruited, and hence, it is not applicable for generalised pregnant population.
Outcome assessors were aware of the exposure status of the study participants (information bias)	Unclear risk	Outcome assessors should have been unaware of the exposure status of the study participants.
Yılmaz et al, 2016[21]		
Methods	Prospective cross-sectional study	
Participants	450	
Outcome	Antenatal depression	
Bias	Author's judgement	Support for judgement
Selective reporting (reporting bias)	High risk	Serum ferritin level was not reported.
Sampling (selection bias)	Low risk	Randomisation of study population was not done.
Homogeneity (selection bias)	High risk	Heterogeneity was not present because patients are from similar socioeconomic statuses.
Outcome assessors were aware of the exposure status of the study participants (information bias)	Unclear risk	Outcome assessors should have been unaware of the exposure status of the study participants.
Tran et al, 2013[22]		
Methods	Prospective population-based study	
Participants	497	
Outcome	Infant cognitive development	
Bias	Author's judgement	Support for judgement
Indirect effects (confounding bias)	Unclear risk	Indirect effects of certain risk factors such as infant birth weight and postpartum CMD on the outcome were not measured.
Outcome assessors were aware of the exposure status of the study participants (information bias)	Unclear risk	Outcome assessors should have been unaware of the exposure status of the study participants.
Other bias	Low risk	Loss to follow-up was relatively high (23.9%)
Tran et al, 2014[23]		
Methods	Prospective cohort	
Participants	497	
Outcome	Infant motor development	
Bias	Author's judgement	Support for judgement
Incomplete covariates (confounding bias)	Unclear risk	Several potential antenatal factors that can influence the outcome were not measured.
Outcome assessors were aware of the exposure status of the study participants (information bias)	Unclear risk	Outcome assessors should have been unaware of the exposure status of the study participants.
BSID was not validated, thereby limiting the comparisons within the groups (information bias)	Low risk	Proper evidence for the pilot study should have been given.
Missing data (selection bias)	Unclear risk	Around 92 participants of 418 had missing data during W2, W3 and W4.
Other bias	Low risk	Loss to follow-up (15.9%)

CMD, common mental disorder; BSID, Bayley Scales of Infant Development.

Results showed the need of effective antenatal care and optimisation of child's development.[23] Physical and mental health problems for mothers in their antenatal period leads to developmental delays in the infants because of foetal programming and adverse pregnancy outcomes such as preterm birth. The results from the studies also specified that the effect of postpartum CMD on infant outcomes was statistically insignificant.

As antenatal depression is a poorly researched topic, only few studies with heterogeneity in its methodology have been included for review. Studies in which antenatal depression assessed using other depressive scales and those studies that measured reverse causality were not included for review. These are some of the major limitations with this review. The strengths of this review include that it is the first review which measures the relationship between IDA and antenatal depression among pregnant women. The results from the risk of bias assessment table can be used to conduct future studies in a better way. It postulates the need for further research on antenatal depression among iron-deficient pregnant women. The result from this review is generalisable to any population. To conclude, we have recognised the possible relation present for IDA to cause depressive symptoms during the antenatal period which if left unnoticed could affect the maternal mental health and also the foetal cognitive development. Deficiency of standardised diagnostic tools in the aforementioned studies expresses the need for further research in this area. This could be kept as the main focus for any future updation as the literature keeps progressing.

5. Conclusion

The research articles included in this review showcase the relationship between IDA and antenatal depression. Also, they express the complications observed in the maternal health outcome and infant's cognitive and motor development. Because antenatal depression is a major risk factor for postpartum depression, it needs to be identified in the early stages and necessary measures must be taken for its prevention. Because the scale used to assess the depression symptoms is not a diagnostic tool, future research studies must aim for better understanding in this field.

Contributions of authors

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmrp.2019.07.003.

References

1. Albert PR. Why is depression more prevalent in women ? *J Psychiatry Neurosci.* 2015;40(4):219–221.
2. Kinser PA, Thacker LR, Lapato D, et al. Depressive symptom prevalence and predictors in the first half of pregnancy. *J Women's Health.* 2018;27(3): 369–376.
3. ACOG. *Depression and Postpartum Depression: Resource Overview* [Internet]. Acog.org.; 2019. cited 18 March 2019]. Available from: https://www.acog.org/Womens-Health/Depression-and-Postpartum-Depression?IsMobileSet=false
4. WHO. *Maternal Mental Health* [Internet]. Who.int.; 2019. cited 18 March 2019]. Available from: https://www.who.int/mental_health/maternal-child/maternal_mental_health/en/
5. Evans J, Heron J, Francomb H, Oke S, Golding J. Cohort study of depressed mood during pregnancy and after childbirth. *BMJ.* 2001;323(7307):257–260.
6. Leigh B, Milgrom J. Risk factors for antenatal depression, postnatal depression and parenting stress. *BMC Psychiatry.* 2008;8:24.
7. Basutkar RS, Tsundue T, Shiva H, Rose A, Ponnusankar S. Vitamin D supplementation in patients with iron deficiency anaemia: a Systematic Review and a Meta-Analysis. *Syst Rev Pharm.* 2019;10(1):01–10.
8. Basutkar RS, Eipe T, Tsundue T, Perumal D, Ponnushankar S. Reduced vitamin D levels and iron deficiency anaemia in pregnant women: an evolving correlation. *J Young Pharm.* 2019;11(1):92–96.
9. Noemia LM, Carmen VL. Ferritin: could be a health indicator. *J Fam Med Dis Prev.* 2018;4(2):1–8.
10. Sifakis S, Pharmakides G. Anemia in pregnancy. *Ann N Y Acad Sci.* 2000;900: 125–136.
11. Beard JL, Connor JR. Iron status and neural functioning. *Annu Rev Nutr.* 2003;23: 41–58.
12. Vanamala VG, Rachel Aruna, Pakyanadhan Sushil, Somavathi. Incidence and outcome of anemia in pregnant women: a study in a tertiary care centre. *Int J Reprod Contracept Obstet Gynecol.* 2018;7(2):462–466.
13. Kumar KJ, Asha N, Murthy DS, Sujatha M, Manjunath V. Maternal anemia in various trimesters and its effect on newborn weight and maturity: an observational study. *Int J Prev Med.* 2013;4(2):193–199.
14. Bodnar Lisa M, Wisner Katherine L. Nutrition and Depression: implications for improving mental health among childbearing-aged women. *Biol Psychiatry.* 2005;58(9):679–685.
15. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. *Br J Psychiatry.* 1987;150: 782–786.
16. Montazeri A, Torkan B, Omidvari S. The Edinburgh Postnatal Depression Scale (EPDS): translation and validation study of the Iranian version. *BMC Psychiatry.* 2007;7:11.
17. Kozinszky Z, Dudas RB. Validation studies of the Edinburgh postnatal depression scale for the antenatal period. *J Affect Disord.* 2015;176:95–105.
18. Choi SK, Kim JJ, Park YG, Ko HS, Park IY, Shin JC. The simplified Edinburgh Postnatal Depression Scale (EPDS) for antenatal depression : is it a valid measure for pre-screening? *Int J Med Sci.* 2012;9(1):40–46.
19. Payne Jennifer L, Meltzer-Broody Samantha. Antidepressant use during pregnancy: current controversies and treatment strategies. *Clin Obstet Gynecol.* 2009;52(3):469–482.
20. Dama M, Van Lieshout RJ, Mattina G, Steiner M. Iron deficiency and risk of maternal depression in pregnancy: an Observational Study. *J Obstet Gynaecol Can.* 2018;40(6):698–703.
21. Yılmaz E, Yılmaz Z, Çakmak B, et al. Relationship between anemia and depressive mood in the last trimester of pregnancy. *J Matern Fetal Neonatal Med.* 2017;30(8):977–982.
22. Tran TD, Biggs B-A, Tran T, et al. Impact on infants' cognitive development of antenatal exposure to iron deficiency disorder and common mental disorders. *PLoS One.* 2013;8(9). e74876.
23. Tran TD, Tran T, Simpson JA, et al. Infant motor development in rural Vietnam and intrauterine exposures to anaemia , iron deficiency and common mental disorders: a prospective community-based study. *BMC Pregnancy Childbirth.* 2014;14:8.
24. Dekkers O, Vandenbroucke J, Cevallos M, Renehan A, Altman D, Egger M. COSMOS-E: guidance on conducting systematic reviews and meta-analyses of observational studies of etiology. *PLoS Med.* 2019;16(2). e1002742.

Abbreviations

ACOG: American Congress of Obstetricians and Gynaecologists
WHO: World Health Organisation
HPA: Hypothalamic-pituitary-adrenal axis
IDA: Iron deficiency anaemia
EPDS: Edinburg Postnatal Depression scale
EDS: Edinburg Depression Scale
JBI: Joanna Briggs Institute
QAT: Quality Assessment Tool
NIH: National Institute of Health
RCT: Randomised controlled trials
PPD: Postpartum depression
CMD: Common mental disorders
BSID-M: Bayley Scales of Infant Development
COSMOS-E: Conducting Systematic Reviews and Meta Analysis of Observational Studies of Etiology
MCV: Mean corpuscular volume
Hct: Haematocrit
PS: Pooja Sudarsan
RV: Resia Varghese
CV: Chris E Vinod
RB: Roopa Satyanarayan Baustkar
SP: S Ponnusankar