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A Systematic Review on the Burden of Non-nutritional Causes of Anemia among Pregnant Women in India

Research Article

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Abstract

Introduction: Anemia is significant public health problem of multifactorial causation. Nutritional causes such as iron, folate, vitamin B12, vitamin A deficiencies, and protein-energy malnutrition can result in anemia. The non-nutritional causes of anemia include genetic disorders such as hemoglobinopathies, infectious diseases, and various other chronic diseases. Non-nutritional causes of anemia constitute a significant burden in world and also in India. This review aimed to study the burden of different non-nutritional causes of anemia among pregnant women in India.

Methods: PubMed and Google Scholar were searched for studies reporting on the prevalence of non-nutritional causes of anemia among pregnant women in India, published from 2012 to 2024. The systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Result: A total of 297 studies were identified, of which 27studies were included in the systematic review. The prevalence of beta-thalassemia disease was 2.1%, beta-thalassemia trait ranged from 0.7 to 8.5%, sickle cell disease from 0.7 to 1.6%, and sickle cell trait from 0.2 to 15.6% amongst pregnant women. The prevalence of malaria was in the range of0.8 to 29.3%, among pregnant women in India.

Conclusion: Non- nutritional causes of anemia constitute a significant burden amongst pregnant women in India. Non-nutritional causes of anemia need to be addressed to achieve targets of control of anemia. There is a need for more scientifically sound basic research investigating the prevalence of different non-nutritional causes of anemia in pregnancy.

Keywords: Anemia Burden; Hemoglobinopathies; Thalassemia; Sickle Cell Disease; Pregnant Women; India

Introduction

Anemia is one of the most important public health problems in many developed and as well as developing countries, including India. Anemia in pregnancy is associated with maternal and fetal complications such as low birth weight, preterm delivery, impaired neurological development of the child, maternal mortality, and morbidity.[1] The World Health Organization (WHO) defines anemia in pregnancy as a condition in which the haemoglobin concentration in the blood falls below 11 g/dl. It results in reduced oxygen-carrying capacity of the blood andthe inability to fulfil the physiological needs of the individual. [2] WHO estimates the prevalence of anemia among pregnant women is 41.8% globally. [3] The National Family Health Survey (NFHS-5) 2019 – 2021 in India estimated the prevalence of anemia among pregnant women to be 52.2%. [4]

The causes of anemia are multifactorial and include both nutritional and non-nutritional causes. Nutritional causes such as iron, folate, vitamin B12, vitamin A deficiencies, and protein-

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energy malnutrition can result in anemia, as these nutrients are needed for the synthesis of hemoglobin in the body. Iron deficiency is known to be the most common cause of nutritional anemia during pregnancy. The non-nutritional causes of anemia include genetic disorders such as hemoglobinopathies (thalassemia, sickle cell disease) and hemophilia, infectious diseases (malaria, tuberculosis, soil-transmitted helminths), and various other chronic diseases.[5]

Hemoglobinopathies including thalassemia and sickle cell disease (SCD) are the most common single-gene disorders (autosomal recessive)and constitute a significant health problem in certain parts of the world, including India.[6] Thalassemia is a blood disorder characterized by inherent defects in the synthesis of globin chains of the hemoglobin. This impairs normal hemoglobin synthesis, thereby affecting the production of red blood cells (RBCs), resulting in anemia. Communities like Sindhis, Punjabis, Gujaratis, Bengalis, Mahars, Kolis, Saraswats, Lohanas, and Gaurs have shown higher frequencies of carrier state of beta-thalassemia. [7] SCD is a genetic blood disorder in which an abnormal hemoglobin S is produced, making RBCs more susceptible to destruction in the small blood vessels. This increased destruction of RBCs is implicated in the pathogenesis of anemia associated with SCD. SCD is known to be prevalent in certain tribal communities of southern, eastern, and western states of India.[8]

Infectious diseases particularly malaria and tuberculosis, and soil-transmitted helminth infestations have been recognized as important health problems in tropical and sub-tropical regions of India. The malarial parasite multiplies inside the human RBCs, leading to their destruction, causing anemia.15 Studies have reported a strong association between tuberculosis and anemia, but the direction of this relationship and the exact mechanism are not known.[9] Soil-transmitted helminth infestations lead to severe anemia through intestinal blood loss and by causing deficiencies of various micronutrients.[10] Chronic diseases are associated with inflammation resulting from infectious causes, metabolic causes, autoimmunity and other causes. Inflammation results in cytokine-mediated increase in hepcidin levels in the body. Hepcidin is a protein molecule that inhibits intestinal absorption of iron and it is released primarily by the liver.[11]

For developing strategies to control the non-nutritional causes of anemia in pregnancy, we need to estimate the magnitude of the problem posed by them. There have been limited studies conducted in India to assess the prevalence of non-nutritional causes of anemia among pregnant women. Also, there are no previous systematic reviews addressing this question. Therefore, this review aimed to estimate the burden of different non-nutritional causes of anemia among pregnant women in India.

Methodology

Search strategy: This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. PubMed and Google Scholar were searched for relevant published articles. The following keywords were used for the literature search – prevalence Anon-nutritional causes of anemia, pregnancy, prevalence of infectious diseases (Malaria, Tuberculosis and helminths), hemoglobinopathies, chronic diseases (Liver and kidney) and all combination of these words. All relevant studies published from 2012 to 2024 were identified during the search process. To increase the width of the search, the list of references of all relevant studies found in the above search was also screened.

Eligibility Criteria

Inclusion criteria: This systematic review included all observational studies conducted in India that assessed the prevalence of non-nutritional causes of anemia such as hemoglobinopathies (beta-thalassemia disease, thalassemia trait, sickle cell disease, and sickle cell trait),hemophilia, infectious diseases (malaria,tuberculosis, soil-transmitted helminths),chronic liver disease, and chronic kidney disease, which were published in different peer-reviewed journals during the last 10 years from 1st January 2012 to 30thJanuary 2022. The search was run again on 31st August 2024 to include all available evidence. Only studies published in English language were included. There were no restrictions specified for the study setting, study duration, and outcome assessment technique.

Exclusion criteria: Studies without full text, commentaries, duplicated studies, anonymous reports, and irrelevant data were excluded.

Search Methods: Two reviewers independently searched PubMed and Google Scholar using the keywords such. After removing the duplicates, the identified studies were first screened by title and abstract. Those studies found relevant on title and abstract screening were considered for full-text evaluation by applying the inclusion and exclusion criteria. The screening was done by two independent reviewers, and any disagreement between them was resolved through discussion with help from a third reviewer.

Study quality assessment: The quality of the included studies was assessed using JBI tool (https://jbi.global/sites/default/files/2020-08/Checklist_for_Prevalence_Studies.pdf). Quality assessment of the studies was done by two independent reviewers with disagreements resolved through discussion.

Data extraction: Data from the studies considered for inclusion in the review were extracted onto Microsoft excel. The following data were extracted –author's name, publication year, study design, study area/setting, study period, sample size, age distribution of the participants, presence and severity of anemia, prevalence of non-nutritional causes of anemia such as hemoglobinopathies (thalassemia, sickle cell disease) and hemophilia, infectious disease (malaria, tuberculosis, helminths) chronic liver disease, and chronic kidney disease among the study participants. Data extraction was done by two independent reviewers, with disagreements resolved through consensus.

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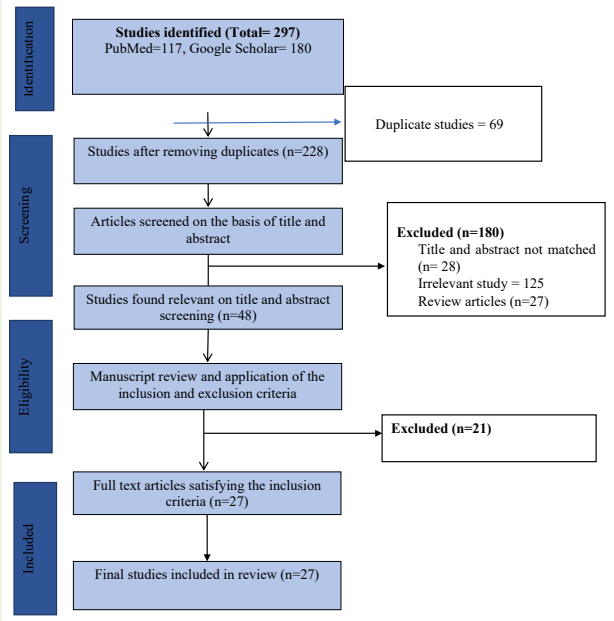

Figure 1: Prisma Flow Diagram.

Results

Selection of the studies

A total of 297 studies were identified by a literature search on two databases. Out of all the studies identified 69 were duplicates. After the removal of the duplicates 228 studies were subjected to title and abstract screening, during which 180 studies were excluded because they were found irrelevant. Forty-eight studies were assessed for eligibility by full-text evaluation by applying the inclusion and exclusion criteria. Twenty-one studies were found ineligible and the remaining 27studies were included in the current review. (Figure 1).

Characteristics of the included studies

A out of twenty-seven studies were included in the review. Six were community-based studies, and the twenty-one remaining studies were hospital-based. A total of seventeen studies reported the prevalence of hemoglobinopathies (Table 1). Only one study conducted in West Bengal reported the prevalence of beta-thalassemia disease. Fifteen studies reported the prevalence of beta-thalassemia trait, four studies were conducted in Maharashtra, and two each conducted in Karnataka, Madhya Pradesh, West Bengal, and one each in Gujarat, Rajasthan, Odisha, Punjab and New Delhi. Three studies reported the prevalence of sickle cell disease, one each was conducted in Maharashtra, Madhya Pradesh, Gujarat. Six studies, one each conducted in West Bengal, Odisha, Maharashtra, Punjab, Madhya Pradesh, Gujarat reported the prevalence of sickle cell trait. Ten studies reported the prevalence of infectious diseases among pregnant women. Eight studies reported malaria prevalence, of them one study was conducted in two states – Andhra Pradesh and Chhattisgarh, three studies were from Chhattisgarh, two studies were from Madhya Prades hand one each from Jharkhand and Rajasthan. One study from Puducherry reported tuberculosis prevalence among pregnant women. One study conducted in Maharashtra reported the prevalence of soil transmitted helminth infestation anemia status in included studies.

Table 1: Prevalence in % of Infectious Diseases Among Pregnant Women in India from 2012 – 2024.

State	Infectious Diseases	Prevalence
Chhattisgarh	Malaria (Highest)	29.3
Chhattisgarh	Malaria (Lowest)	0.8
Puducherry	Tuberculosis	1.8
Maharashtra	Soil-Transmitted Helminths	6.5

Anemia status in included studies

The studies reported a wide variation in anemia across various states of India, particularly in studies focusing on hemoglobinopathies. In Punjab, 38.7% of the pregnant women were found to be anemic, In Maharashtra, one study noted that all pregnant women had microcytic anemia, In Karnataka, 46.7% of the women were anemic, whereas another study from the state showed a lower prevalence of 22.7%. A study from Madhya Pradesh reported 47% anemia prevalence, with another study from the same state reporting 42.8%. Other states such as New Delhi, Maharashtra, Gujarat, Jodhpur, and West Bengal did not report anemia prevalence in the studies. The prevalence of anemia in the infectious diseases was notably high. Madhya Pradesh reported 79% anemia, while Andhra Pradesh and Telangana had an even higher rate of 92.4%. Rajasthan recorded 88.3% anemia prevalence, and Jharkhand reported 86%. Chhattisgarh had 73.2% anemia and another study did not report anemia. In Puducherry, 63.3% of the population was anemic. These figures suggest a significant burden of anemia across different states, particularly in areas affected by infectious diseases.

Burden of hemoglobinopathies among pregnant women

We included seven teen studies that estimated the prevalence of hemoglobinopathies among pregnant women in India. The only identified study that reported the prevalence of beta-thalassemia disease reported a 2.1% prevalence in West Bengal. Among the included studies, the prevalence of beta-thalassemia trait was the highest at 8.5% in Karnataka, and the lowest was reported in a study in Maharashtra (0.7%). The prevalence of sickle cell disease reported in the studies were between 0.7 – 1.6%. Thehighest prevalence of sickle cell trait (15.6%) was reported among tribal populations of Gujarat. Punjab reported the lowest prevalence of sickle cell trait (0.2%).

Burden of infectious diseases

We included ten studies that reported the prevalence of infectious diseases among pregnant women in India. As shown in (Table 1**)** out of the eight studies that estimated the prevalence of malaria infection, the highest (29.3%) and the lowest (0.8%) prevalence were reported in Chhattisgarh. One study reported the prevalence of tuberculosis to be 1.8% among pregnant women in Puducherry. One study reported a 6.5% prevalence of

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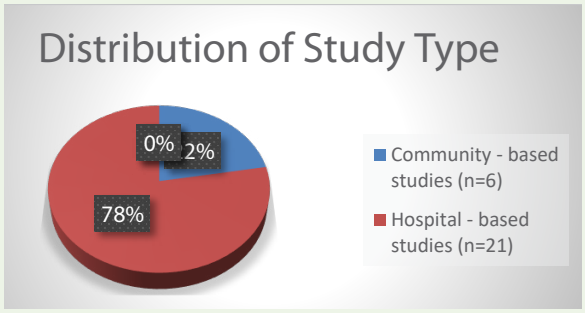

Figure 2: Study Type Distribution.

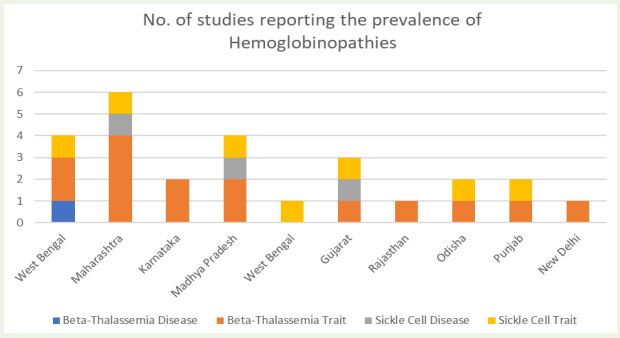

Figure 3: No. of studies reporting the prevalence of Hemoglobinopathies among pregnant women in India from 2012-2024

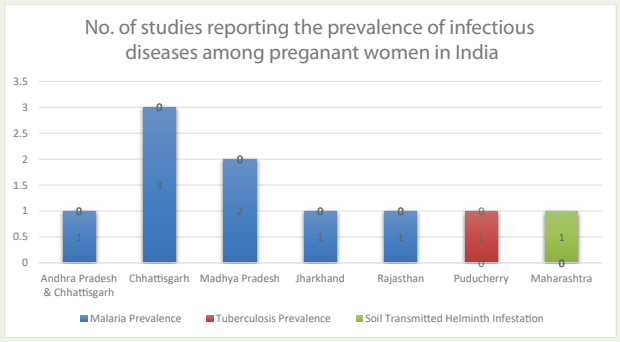

Figure 4: No. of studies reporting the prevalence of infectious diseases among pregnant women in India from 2012-2024.

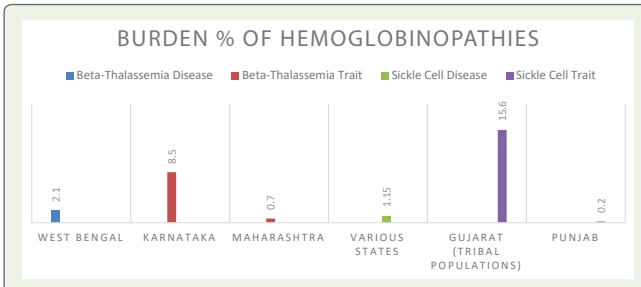

Figure 5: Burden of hemoglobinopathies in % among pregnant women in India from 2012-2024.

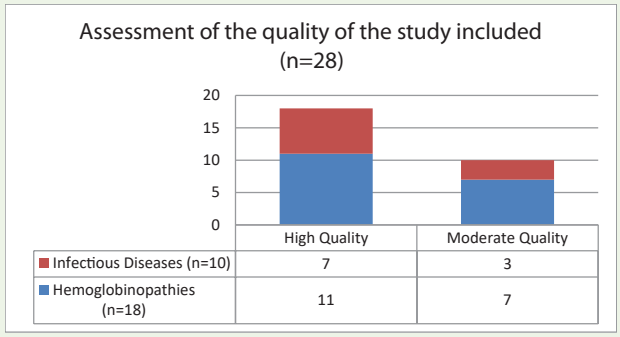

Figure 6: Assessment of the quality of the study included in the study.

soil-transmitted helminth infestation among pregnant women in Maharashtra.

The burden of chronic disease (chronic kidney disease, chronic liver disease) among pregnant women

We failed to identify any study reporting the prevalence of chronic diseases (chronic kidney disease, chronic liver disease) among pregnant women in India.

Study Quality Assessment

Out of the twenty-eight studies included, eighteen (64.2%) were rated as high-quality studies, and the remaining ten (35.7%) were rated to be of moderate quality. Out of the eighteen studies reporting on hemoglobinopathies, eleven studies were assessed to be of high quality and the remaining seven were of moderate quality. Out of ten studies reporting on infectious diseases, seven were of high quality and the remaining three studies were of moderate quality as can be seen in (Figure 7).

Discussion

This systematic review attempted to assess the burden of various non-nutritional causes of anemia. The burden of beta-thalassemia disease of 2.1% andbeta-thalassemia trait ranged from 2.2 to 8.5%. Studies from other countries reported the prevalence of beta thalassemia disease 3.6% in Lao, 3.8% in Thailand, 1.3% in China and 0.5% in Bangladesh. Similarly, the prevalence of beta thalassemia trait reported in the included studies was similar to that reported in Pakistan (6%) and Indonesia (5.7%).[39-42]The prevalence of sickle cell disease in our review ranged from 0.7 to 1.6% and that of Sickle cell trait from 1.5 to 15.6%.Other countries like Africa and United Kingdom estimated around 1% sickle cell disease prevalence among pregnant women which is similar to that reported in studies from India.[43,44]

Not many studies have been conducted to assess the prevalence of hemoglobinopathies among Indian pregnant women. Most of the studies conducted were hospital-based or conducted in specific population groups with small sample sizes. India has a diverse population and consanguineous marriage is common in many cultural groups in India, leading to hemoglobinopathies

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Table 2: Description of the included studies which assessed the prevalence of hemoglobinopathies among pregnant women in India

Author's name and Publication year	Type of the study, Study setting	Place of the study	Sample size of the study	Result (Prevalence %)
Mishra K et al, 2024 [12]	Cross Sectional hospital-based study	Peripheral hospital Punjab	928	2.04% hemoglobinopathies 1.4% β-thalassemia trait 0.1% thalassemia trait (Hb E) 0.2% sickle cell trait 0.1% Hb J 0.2% Hb D Punjab
Patel K et al 2024 [13]	Hospital-based cross-sectional study	Tertiary-care hospital Gujarat	716	8.1% Hemoglobinopathies 5.8% β-thalassemia trait 1.1% Hb D Punjab trait 0.6% Hb S trait 0.2% Hb E trait 0.1% Hb D Iran trait
Chouhan AS et al 2024 [14]	Cross-sectional hospital-based study	Department of Pathology of a tertiary care centerJNMC, Sawangi (Meghe), Wardha Maharashtra	312	3.8% β-thalassemia trait
Dharmarajan S et al, 2021 [15]	Cross-sectional hospital-based study	4 government hospitals, in Pune, Maharashtra	2107	6.3% undiagnosed hemoglobinopathy 3.3% β-thalassemia trait 1.7% sickle cell trait
Gosavi M et al 2021 [16]	Cross-sectional hospital-based study	Tertiary Care Hospital Karnataka	441	4.3% hemoglobinopathies 3.6% β-thalassemia trait
Chauhan A et al 2018 [17]	Cross sectional hospital-based study	Tertiary Care Referral Hospital, Maharashtra	6972	0.86% hemoglobinopathies. 0.1% sickle cell disease 0.7% β-thalassemia trait
Safia R et al 2018 [18]	Cross-sectional hospital-based study	Tertiary Health CareCentre New Delhi	174	2.2% β-thalassemia trait
Desai G et al 2017 [19]	Retrospective hospital-based cohort study	Maternal health carecentre, Jhagadia block Gujarat	10519	1.2% sickle cell disease 15.6% sickle cell trait
Chakraborty S2016 [20]	Cross-sectional hospital-based study	Bankura Sammilani Medical College Hospital, Bankura West Bengal	3500	7.8% hemoglobinopathies 4.5% β-thalassemia trait 2.8% HbE carrier 0.3% HbS carrier
Gupta V et al2015 [21]	Cross-sectional hospital-based study	Departments of Pediatrics, and Obstetrics and Gynecology, Umaid Hospital, Dr. Sampurnanand Medical College, Jodhpur	1500	5.9% β-thalassemia trait
Balgir S et al 2015 [22]	Cross sectional hospital-based study	Department of Obstetrics and Gynecology, NSCB Medical College and Hospital, Jabalpur, Madhya Pradesh	416	47.1% Anemia 12.2% hemoglobinopathies 1.6% sickle cell disesase 7.45 sickle cell trait 2.8% β-thalassemia trait 0.2% hemoglobin E trait
Bhukhanvala DS et al, 2013 [23]	Cross sectional hospital-based study	Maternity hospital of Surat city, West Bengal	3009	3.3% β-thalassemia trait 1.5% sickle cell trait
Kulkarni P et al, 2013 [24]	Cross sectional hospital-based study	Primary Health Centre South Bengalore, Karnataka	210	8.5% β-thalassemia trait
Gosh N et al, 2013 [25]	Cross sectional community-based study	Naxalbari block of Siliguri subdivision, Darjeeling district, West Bengal	188	2.1% β-thalassemia disease
Balgir R et al, 2013 [26]	Cross sectional hospital-based study	Division of Human Genetics, Regional Medical Research Centre (Indian Council of Medical Research), Bhubaneshwar Odisha	178	5.6% β-thalassemia trait 5.6% sickle cell trait 1.1% hemoglobin E trait 0.6% sickle cellE-disease 0.6% hemoglobin H disease
Baxi X et al, 2012 [27]	Cross sectional hospital-based study	Disha Fertility and Surgical center, Indore, Madhya Pradesh	1006	2.7% β-thalassemia trait 0.6% other hemoglobin variants
Satpute SB et al, 2012 [28]	Cross sectional hospital-based study	Civil Hospital, Sangli Maharashtra	1279	3.1% β-thalassemia trait

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Table 3: Description of the included studies which assessed the prevalence of infectious diseases among pregnant women in India

Author's name and Publication year	Type of the study	Place of the study	Sample size of the study	Result (Prevalence %)
Jain V et al, 2023 [29]	Community-based study	Baihar and Birsa blocks of district Balaghat, Madhya Pradesh	1728	23.4% Malaria
Garg S et al,2020 [30]	Cross sectional study Community-based	Baster, Sarguja, Bilaspur, Raipur and Durg,Chhattisgarh	21572	0.8% Malaria
Corrêa et al,2017 [31]	Cross sectional study Community-based	Forested areas of Chhattisgarh, Andhra Pradesh and Telangana	563	29.3% Malaria
Bardajı´A, 2017 [32]	Cross sectional study Hospital-based	Bikaner, Rajasthan	1982	1.3% Malaria
Sohail M et al,2015 [33]	Cross sectional study Community-based	Sadar Hospital, Hazaribag districts of Jharkhand	1271	5.4% Malaria
Ihtesham Aatif Qureshi et al, 2014 [34]	Cross sectional study Hospital-based	Malaria endemic village, Andhra PradeshChattisgarh	1222	20.6% Malaria
Ahmed et al, 2014 [35]	Cross sectional study Hospital-based	Jabalpur City, Katni (semi-rural) and Maihar (rural) hospitalMadhya Pradesh	506	7.5% Malaria
Singh N et al, 2012 [36]	Cross sectional study Hospital-based	Chhattisgarh (formerly the eastern part of Madhya Pradesh)	2696	1.3% Peripheral parasitemia
Vijayageetha et al, 2019 [37]	Mixed method study Hospital-based	Puducherry district of South India	4203	1.8% Tuberculosis
Gaidhane S, et al, 2024 [38]	Cross Sectional study Community-based	Rural areas of Wardha district of Maharashtra	534	6.55% Soil Transmitted Helminths

Table 4: Quality assessment of studies reporting the prevalence of hemoglobinopathies among pregnant women in India

Study	1	2	3	4	5	6	7	8	9	Study Quality
Mishra K et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Patel K et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Chouhan AS et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Dharmarajan S et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Gosavi M et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Chauhan A et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Safia R et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Desai G et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Chakraborty S et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Gupta V et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Balgir S et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Bhukhanvala DS et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Kulkarni P et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Gosh N et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Balgir S et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Baxi X et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Satpute SB et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High

Quality of studies was assessed using JBI tool (https://jbi.global/sites/default/files/2020-08/Checklist_for_Prevalence_Studies.pdf).
1. Was the sample frame appropriate to address the targetpopulation?2. Were study participants sampled in an appropriate way?3. Was the sample size adequate?4. Were the study subjects and the setting described in detail?5. Was the data analysis conducted with sufficient coverage of the identified sample?6. Were valid methods used for the identification of the condition??7. Was the condition measured in a standard, reliable way for all participants?8. Was there appropriate statistical analysis?9. Was the response rate adequate, and if not, was the low response rate managed appropriately?

being concentrated in certain geographical areas and among certain population groups. Hence the findings of these studies may not be generalizable at the population level. This evidence suggests the need for more studies, especially community-based large studies, in more representative population groups to estimate the actual prevalence of different hemoglobinopathies among pregnant women in the country.

The review reported the prevalence of malaria in the range of0.8 to 29.3% among pregnant women in India.[27-33] Other countries reported prevalence of malaria rangingfrom 18–40% in Burkina-Faso, 32% in Zambia, 29% in Congo, 27% in Uganda, 13% in Tanzania, 12% in Liberia and 4% in Ethiopia.(45–49) Previous studies show that the prevalence of malaria is lower in Asian countries as compared to Africa. It was found to be

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Table 5: Quality assessment of studies reporting prevalence of infectious diseases among pregnant women in India

Study	1	2	3	4	5	6	7	8	9	Study Quality
Jain V et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Garg S et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Correa et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Bardaji et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Sohail M et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Qureshi A, I et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Ahmed et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Singh N et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Vijayageetha et al	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High
Gaidhane S et al	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate

Quality of studies was assessed using JBI tool (https://jbi.global/sites/default/files/2020-08/Checklist_for_Prevalence_Studies.pdf).
1. Was the sample frame appropriate to address the targetpopulation? 2. Were study participants sampled in an appropriate way?3. Was the sample size adequate?4. Were the study subjects and the setting described in detail?5. Was the data analysis conducted with sufficient coverage of the identified sample?6. Were valid methods used for the identification of the condition?7. Was the condition measured in a standard, reliable way for all participants?8. Was there appropriate statistical analysis?9. Was the response rate adequate, and if not, was the low response rate managed appropriately?

around 6% in Laos and 0.4% in Afghanistan.[50, 51]Within India, there is wide geographical variations in the prevalence of malaria among pregnant women,likely attributable to the wide variations in geography, terrain and climatic conditions including precipitation. Most of the studies that reported the prevalence of malaria among pregnant women were conducted in Chhattisgarh and neighboring states which are endemic for malaria. Studies assessing the prevalence of tuberculosis and other infectious causes of anemia in pregnancy were limited. There is need for nationally representative studies that assess the prevalence of different infectious causes of anemia so as to take appropriate measures to tackle them.

India, over the last fifty years has implemented several national-level programs to supplement IFA in pregnancy. However, anemia levels continue to remain high. In addition to measures to address the nutritional causes of anemia, there is a need to pay due attention to the non-nutritional causes of anemia. The National guideline on Prevention and Control of Hemoglobinopathies was launched in the year 2016 which provides a strategic framework for the prevention and management of hemoglobinopathies in the country. The National Vector Borne Disease Control Programme (NVBDCP) of the Government of India and the National Strategic Plan for Malaria Elimination in India 2017–2022 attempts to eliminate malaria in a phased manner in the country. The recently launched Anemia Mukt Bharat (AMB) strategy has introduced a 6*6*6 intervention strategy highlighting the need for addressing non-nutritional causes of anemia to reduce the burden of anemia in India. One of the six interventions under the AMB strategy is to intensify awareness, screening, and treatment of non-nutritional causes of anemia with special focus on malaria and hemoglobinopathies in the endemic pockets of the country. There is a need for integrating various programs and guidelines addressing non-nutritional causes for the effective control of anemia in the country. Existing platforms in health care centers, anganwadi centers, VHNDs, Nutrition week, and World Thalassemia Day can serve as avenues to create awareness about non-nutritional causes of anemia. Frontline workers like ASHAs, ANMs, and health workers need to be trained in screening for carrier status of hemoglobinopathies, prevention and care of disease, and counseling diseased/carrier couples and their families.

Strength

To best of our knowledge the first systematic review to summarize the evidence from published studies on the prevalence of non-nutritional causes of anemia among pregnant women in India. The review included all the studies published during the last 12 years.

Limitation

The number of studies eligible for inclusion in this review was limited, which might have affected the estimates of burden different non-nutritional causes of anemia among pregnant women in India. Moreover, most of the studies were hospital-based and concentrated in specific geographical regions or population groups leading to the non-generalizability of findings of the study. No studies were available that assessed the prevalence of chronic liver disease and chronic kidney disease among pregnant Indian women.

Conclusions

The prevalence of different non-nutritional causes of anemia among pregnant women varied highly from region to region. Small sample sizes and varied study designs challenged drawing of valid conclusions. There is need for more studies with robust designs and adequate sample sizes to assess non-nutritional causes of anemia among pregnant Indian women. Non-nutritional causes other than hemoglobinopathies and malaria have not been adequately investigated. Thus, the study advocates the need for better prevalence

Estimation from nationally representative studies to enhance our understanding of the burden of different non-nutritional causes of anemia among pregnant women in India.

Additional File

Search strategy: PubMed Search: Hemoglobinopathies:

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1. (((thalassemia [Title/Abstract])) AND (pregnant [Title/Abstract])) AND (India[Title/Abstract]) (13) 2. (((Sickle cell disease [Title/Abstract])) AND (pregnant[Title/Abstract])) AND (India[Title/Abstract]) (5) 3. (((hemophilia[Title/Abstract])) AND (pregnant[Title/Abstract])) AND (India[Title/Abstract]) (NIL)

Infectious Diseases: 1. (((malaria[Title/Abstract])) AND (pregnant[Title/Abstract])) AND (India[Title/Abstract]) (36) 2. (((tuberculosis[Title/Abstract])) AND (pregnant[Title/Abstract])) AND (India[Title/Abstract]) (26) 3. (((helminths[Title/Abstract])) AND (pregnant[Title/Abstract])) AND (India[Title/Abstract]) (3)

Chronic disease: 1. (((chronic kidney disease [Title/Abstract])) AND (pregnant[Title/Abstract])) AND (India[Title/Abstract]) (4) 2. (((chronic liver disease [Title/Abstract])) AND (pregnant[Title/Abstract])) AND (India[Title/Abstract]) (3)

Google Scholar: Hemoglobinopathies; thalassemia sickle cell disease "Pregnant women" India (2940)

Infectious Diseases: Malaria Pregnant women India (18,000), Tuberculosis Pregnant women India (17,700)

India helminths "Pregnant women" (5,500)

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