SYSTEMATIC REVIEW

Prevalence and Determinants of Anemia among Women of Reproductive Age in Developing Countries

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ABSTRACT

Anemia is one of the major causes of maternal mortality and morbidity across the globe, affecting around two-thirds of pregnant women in developing countries. The objective of this study was to synthesise study findings regarding the prevalence and determinants of anemia among women of reproductive age in developing countries. A total of 28 articles were reviewed by two authors for preliminary screening after removing overlapping information. Finally, 15 studies conducted from 2000 to 2015 were included in the review. The average prevalence of anemia was found to be 46.5% with a range of 18.1% to 75% in different studies. Factors such as increased maternal age, low education, high parity, poor socio-economic status, poor nutritional status, and certain diseases have been found as important determinants of anemia. There is a need to improve the socio-economic status, literacy, diet and general health of poor women in developing countries.

Key Words: *Anemia, Prevalence, Determinants, Developing countries.*

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INTRODUCTION

Anemia is a major public health concern among women of reproductive age, leading to high maternal and infant morbidity and mortality. Anemia occurs when the number and size of red blood cells or hemoglobin concentration falls below an established cut-off value, consequently impairing the capacity of the blood to transport oxygen around the body.[1] Its adverse health outcomes affect people from all age groups, particularly women of reproductive age.[2] According to World Health Organization (WHO), around 528.7 million (29.4%) women of reproductive age are anemic worldwide, of which 20.2 million women are severely anemic.[3] In addition, anemia affects nearly two-thirds of pregnant women from developing countries.[4] More specifically, South-East Asia demonstrates a high burden of anemia among women of reproductive age (41.9%), followed by African and Eastern Mediterranean regions.[3] In Pakistan, more than half of the population (51%) of women of reproductive age is anemic. The burden of anemia in non-pregnant women is relatively lower as compared to pregnant women.[5] According to a recently conducted National Nutritional Survey-2018 in Pakistan, around 41.7% of women of reproductive age are anemic, with a slightly higher proportion in rural (44.3%) as compared to urban settings (40.2%).[6]

This survey highlights iron deficiency as the most common type of anemia among Pakistani women, occurring in 18.2% of women of reproductive age, with greater prevalence in rural settings (18.7%) compared to urban population (17.4%).[6] More specifically, Sindh province of Pakistan has the highest proportion of iron deficiency anemia, with 23.8% of all women of reproductive age being affected, followed by Balochistan (19.0%) and Punjab (18.7%) provinces.[6] A recent study conducted in a rural district of Pakistan found that 77% of reproductive-aged women are anemic, including 7.8%, 48.7% and 20.8% classified as severely, moderately and mildly anemic, respectively.[7]

Multiple factors may cause anemia among women of reproductive age including unhealthy diet, deficiencies of micronutrients mainly iron, certain vitamins (B12 and folate) and some chronic disease states.[8,9] Normal physiological changes of pregnancy, hemoglobinopathies, malaria, HIV, and hookworm infestation may also contribute to anemia.[9,10] The prevalence of anemia is significantly higher in developing countries due to insufficient diet and low intake of vitamins, iron and folic acid.[4,11] Additional factors that predispose women to anemia include differences in lifestyles, socio-demographic factors, hygiene conditions, and genetic susceptibility.[4,11]

There is a complex impact of anemia on the health of women and children.[12] The consequences of anemia vary according to the type and severity of anemia among

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both pregnant and non-pregnant women of reproductive age.[13,14] Anemia can lead to multiple adverse consequences among women, ultimately harming their productive and reproductive capabilities.[15] Anemia reduces the energy of mothers and capacity for work, which can further compound the issue by affecting household food security and income.[16] In addition, severe anemia during pregnancy impairs oxygen delivery to the fetus and interferes with normal intrauterine growth, thereby resulting in intrauterine growth retardation, low birth weight, and neonatal deaths.[17] Several studies have shown that anemia among pregnant women may result in poor maternal and fetal outcomes such as low-birth-weight, prematurity, intrauterine fetal death, abortion, perinatal mortality, postpartum hemorrhage, and puerperal pyrexia.[5,18] A review of observational studies showed a linear association between maternal anemia and maternal mortality, with 10 g/L increase in maternal hemoglobin associated with a 29% reduction in maternal mortality.[19] Research indicates that 25% of low birth weight, 44% of preterm deliveries, and 21% of perinatal mortality are attributable to anemia during pregnancy in low-income countries.[20]

Studies have been conducted to estimate the prevalence and magnitude of anemia among pregnant women and its associated factors in developing countries.[4,5,21-24] Given the burden and impact of anemia on women and their children, there is a need for a systematic review of the prevalence and determinants of anemia among the women of reproductive age in developing countries.

This systematic review will assist in the redesigning of public health programmes aimed to reduce the high disease burden of anemia occurring mainly in developing countries.

METHODOLOGY

An electronic systematic literature search was carried out on the prevalence and determinants of anemia among women of the reproductive age group in developing countries. The criteria to define a developing country were chosen by guidelines based on World Bank's 2016 country classification.[25] To address our study question, a study was considered eligible for inclusion if it was a primary research paper in a peer-reviewed journal, published in English, and described primary epidemiological research from 2000 to 2015 concerning the prevalence and determinants of anemia in developing countries. The eligibility criteria were grouped into four major categories including population, intervention, outcome, and settings as depicted in Table I. A systematic search of published articles was conducted in 2017. We searched a range of electronic bibliographic databases: PubMed through the National Center for Biotechnology Information (NCBI), Medline and Embase through Ovid, Cochrane Library through Wiley Interscience, Google Scholar, SCOPUS through Elsevier, and Science Direct from 2000 to 2015. Within these databases, we searched relevant journals such as The Lancet, Blood Journal, British Medical Journal, Gastroenterology Journal, Nature, PLOS-Medicine, Journal of Clinical and Diagnostic Research, The New England Journal of Medicine, Nature & Nature Medicine, Clinical Infectious Diseases, and Annals of Internal Medicine.

Two authors undertook the literature search independently and scanned the results for potentially relevant studies then retrieved the full articles. The primary outcome of the analyses was anemia; and definitions of anemia varied slightly across studies. However, these definitions were generally in agreement with WHO definitions for anemia, which are Hb <12.0 g/dl or Hct <36% among non-pregnant women, and Hb <11.0 g/dl or Hct <33.0% among pregnant women.[26] The search terms were grouped into four major categories of interest: population, intervention, outcome, and settings. We utilised a combination of Medical Subject Heading (MeSH) keywords, and text words, which were clustered into four major categories including population, intervention or exposure, outcome, and settings as shown in Table II. Most common search terms appearing in abstracts and titles included "anemia AND prevalence", "prevalence", “low hemoglobin level", "risk factors", "predictors", "determinants", and "correlates". Further details of search strategy are given in Table II.

The searched articles were first screened by titles, then by abstracts, followed by a full-text assessment. Articles that did not meet inclusion criteria were excluded. As a result, our initial search identified 18,600 citations. However, 15,512 articles had irrelevant titles. Of the remaining 3,088 articles with relevant titles, we reviewed abstracts and found 180 relevant abstracts. Upon reviewing abstracts, 157 articles were removed either because we did not have access to full-text articles or these were the review or secondary articles or their duplicates had also been found in some other databases. Hence, we were able to retrieve full texts from 28 articles, which were assessed by two reviewers for eligibility criteria and quality using Newcastle-Ottawa Scale for different study designs (Table V). Finally, 15 articles met the required criteria for quality with a high score, so were included in the review as shown in Figure 1.

Potentially relevant articles were imported into a single Endnote file, where each study was reviewed. The abstracts which did not explicitly measure the prevalence of anemia and its determinants were discarded. Finally, full-text copies of the remaining relevant articles were obtained and scrutinised. Articles that met our inclusion criteria were abstracted and summarised using a standardised form. In addition, we searched their reference lists for further papers to avoid missing any

relevant articles. Each stage of the process after the initial electronic search was carried out independently by the two authors, and their decisions and abstracted summaries were compared. Any discrepancies between the two reviewers were resolved. The abstracted data included author, reference, year of publication, study design; population-based or hospital-based study; characteristics of the study subjects, definition of anemia; prevalence of anemia, potential confounders or effect modifiers considered; and risk ratio or odds ratio for anemia.

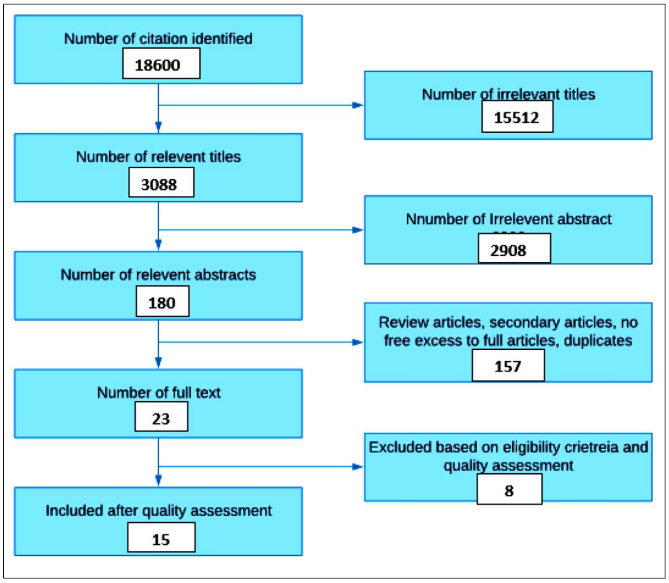

Figure 1: Flow chart summarising the identification and selection of papers for systematic review.

Both authors independently assessed the quality of each study using the different Newcastle-Ottawa Scales for cross-sectional and cohort studies.[27] This scale was used to assess the quality of descriptive (n = 8) and analytical (n = 7) studies by assessing potential sources of bias in the selection, comparability of participants and the assessment of study outcome. Based on this scale, the maximum score for selection was 4 points, while it was 2 points for comparability; and the maximum score for the outcome was 3 points, making a total score of 9. Each study was scored against 9 maximum points and study with higher scores depicted high quality. The majority of the studies generally performed well with an average score of 7; and eight studies attained a score of 8 out of 9, four studies attained a score of 7 out of 9, two studies scored 6 and only one scored 5 out of 9. The quality assessment of all included studies is given in Table V.

Table I: Eligibility criteria to undertake systematic review.

Characteristic	Inclusion criteria	Exclusion criteria
Population	Studies involving women of reproductive age group whose status of anemia had been measured through hemoglobin or hematocrit levels.	Studies including less than 15 years and more than 49 years old females and males of any age group were excluded.
Intervention / exposure	Studies describing the prevalence and determinants or risk factors or predictors of anemia were included.	Studies focusing on interventions for anemia were excluded.
Outcome	Studies describing the anemia as an outcome variable.	Outcomes describing serum Iron or folic acid levels, ferritin levels or hemoglobin electrophoresis were excluded.
Study setting	Studies conducted or implemented in developing countries as per criteria of World Bank.	Studies conducted in developed countries.
Type of studies	Original studies, demographic health surveys, cross-sectional studies, case-control studies and cohort studies.	Experimental or interventional studies focusing on prevention or treatment of anemia.
Duration	Studies published between 1 January 2000 to 31st December 2015.	Studies published before 1 January 2000 and after December 2015.
Language	Studies available in English language.	Studies which were not published in English.

Table II: Search strategy for systematic review.

Population	Married women OR married mother* OR pregnant mother* OR pregnant women OR women OR reproductive-age women OR maternal* [Mesh] AND
Exposure	Predictors OR determinants risk factors OR prevalence OR prevalence AND risk factors OR prevalence AND determinants OR prevalence AND predictors OR socio-demographic factors* OR socioeconomic factors OR dietary factors OR community factors OR socio-demographic determinants OR socio-demographic predictors OR dietary predictors OR access related factors OR reproductive factors OR causes OR nutritional factors OR co-morbid OR diseases AND.
Outcome	Anemia OR hemoglobin levels OR hemoglobin concentrations OR hemoglobin status OR low hemoglobin levels OR low hemoglobin concentrations AND
Setting	Developing country OR developing nation OR least developed country OR least developed nation OR less developed nation OR Third World country OR Third World nation OR under-developed country OR remote region OR low and middle income country OR under-developed nation OR low and middle income nation OR Armenia OR Moldova OR Bangladesh OR Bhutan OR Myanmar OR Indonesia OR Timor-Leste OR Kenya OR Ukraine OR Kiribati OR Uzbekistan OR Kosovo OR Vanuatu OR Pakistan OR Vietnam OR India OR Democratic Republic of Congo OR Ethiopia OR Zambia OR Uganda.

RESULTS

Fifteen articles were published in 2005 or later; and of those, 10 articles were published after 2010. These studies were mainly conducted in South Asia,[4] and Africa,[7] as shown in Table IV. Of the total 15 studies, ten were cross-sectional studies, two were national demographic health surveys, two were cohort studies and one was cluster randomised trial (Table IV). In total, 14 studies provided prevalence or proportion of women with anemia and fifteen studies provided information about determinants of anemia (Table III). Likewise, all of the studies had adjusted for potential confounders (Table IV). Ten studies measured the prevalence of anemia demonstrating an average prevalence to be 46.5%, ranging from 18.1% to 75% in various studies as shown in Table III.[28,29] The determinants of anemia were grouped into three main themes including socio-demographic factors, nutrition-related factors, and comorbid or other factors (Table III).

1. Socio-demographic factors:

Socio-demographic factors included women's age,

Table III: Prevalence and determinants of anemia among women of reproductive-age in developing countries.

Authors	Prevalence of Anemia	Pregnant	Illness	Deficiency of iron	Deficiency of folic acid	Education	Intestinal parasite	Serum folic acid	Serum ferritin	Toiltet use	Family-planning	Age	Parity	Place of residence	Hookworm parasite	Use of ITN to prevent mosquto bite	Tea consumption	Egg consumption	Non-mica foods	BMI	Giving birth within 1 year	Socio-economic factor	Others
Ullah, Irfan, Muhammad Zahid, Muhammad IsmailA Khan, and Mudassir Shah	67.6	✔				✔																✔	
Habib, Muhammad Atif, Camille Raynes-Greenow, Sajid Bashir Soofi, Noshad Ali, Sidrah Nausheen, Imran Ahmed, Zulfiqar Ahmed Bhutta, and Kristen I. Black	18.1				✔								✔								✔		Household food insecurity
Haidar, Jemal	30.4		✔	✔	✔	✔	✔	✔	✔	✔	✔		✔										Malaria, Pneumonia, TB
Anjum, Anam, Maleeha Manzoor, Nadia Manzoor, and Hafiz Abdullah Shakir	75%											✔										✔	
Addis Alene, Kefyalew, and Abdulahi Mohamed Dohe	56.8	✔		✔									✔										
Million Getachew, DelenesawYewhalw, KetemaTafess, YehenewGetachew, Ahmed Zeynudin	53.6	✔	✔											✔	✔	✔							Malaria
Naila Baig-Ansari Salma Halai Badruddin Rozina Karmaliani Hillary Harris Imtiaz Jehan Omrana Pasha Nancy Moss Elizabeth M. McClure Robert L. Goldenberg	75.0 mild 14.8 moderate 0.7 severe	✔															✔	✔	✔				Clay/dirt other non-pica food
Charlotte M, Page, Archana patel, Patricia L. Hibberd	53%	✔											✔										Biomass fuel
Lover AA, Hartman M, Chia KS, Heymann DL	21%					✔															✔		Other fruits, night before Malaria
McClure, Elizabeth M. McClure, Meshnick, Steven R Mungai, Peter Malhotra, Indu King, Christopher L Robert L. Goldenberg Hudgens, Michael G Siega-Riz, Anna Maria Dent, Arlene E	71%		✔												✔					✔			Schistosomiasis, Trichuria, Malaria
Chowdhury, HasinaAkhter Ahmed, KaziRumana Jebunessa, Fatema Akter, Jesmin Hossain, Sharmin Shahjahan MD	37%					✔						✔		✔								✔	Income
Sam Ononge Oona Campbell Florence Mirembe	32.5%			✔																			Malaria infection, Human Immunodeficiency virus infection
Haji Kedir, YemaneBerhane AlemayehuWorku	43.9%	✔																					Chewing khat dietary restriction
Mbule MA, Byaruhanga YB, Kabahenda M, Lubowa A	63.1%																					✔	Ownership of functioning radio
Md. Kamruzzaman Md. Golam Rabbani Aik Saw Md. Abu Sayem Md. Golam Hossain						✔						✔								✔		✔	Muslim

education, parity, current pregnancy status, interpregnancy interval, place of residence, socioeconomic status and religion. Two studies reported women's age to be an important determinant of anemia (Table IV) and with older women more likely to experience anemia.[30,31] Four studies found that women's education was an important determinant of anemia, all of which demonstrated illiterate women were more likely to be anemic as compared to their counterparts.[30-33] Likewise, four studies found strong associations between parity and

Table IV: Descriptions of studies showing statistically significant predictors of anemia among women of reproductive-age in developing countries.

S. No.	Study	Year	Location	Study design	Statistically significant factors
1.	Habib, Muhammad Atif, *et al.* "Prevalence and determinants of iron deficiency anemia among non-pregnant women of reproductive age in Pakistan." Asia Pacific journal of clinical nutrition 27.1 (2018): 195.	2018	Pakistan	A secondary analysis was performed using the National Nutrition Survey in Pakistan 2011- 2012	• Poor consumption of iron and folic acid supplementation during the last pregnancy: AOR 1.31 (95% CI 1.05, 1.64). • A history of four or more pregnancies: AOR 1.30 (95% CI 1.04, 1.60). • Birth interval of <24 months: AOR 1.27 (95% CI 1.06, 1.71). • Household food insecurity: AOR 1.42 (95% CI 1.23, 1.63). • Presence of clinical anemia: AOR 5.82 (95% CI 4.82, 7.02).
2.	Addis Alene K, Mohamed Dohe A. Prevalence of anemia and associated factors among pregnant women in an urban area of Eastern Ethiopia. Anemia. 2014;2014.	2014	Eastern Ethiopia	A community-based cross-sectional study	• Pregnant women in the second trimester: AOR 2.87 (95% CI 1.61-5.17) • Pregnant women in the third trimester: AOR 3.32 (95% CI 1.84-6.00) • No usage of Iron supplementation during pregnancy: AOR 1.54 (95% CI 1.04-2.27) • Having three to five children: AOR 1.95 (AOR 1.19-3.19)
3.	Anjum, Anam, *et al.* "Prevalence of anemia during pregnancy in district Faisalabad, Pakistan." Punjab Univ. J. Zool 30.1 (2015): 15-20.	2015	Faisalabad, Pakistan	Cross-sectional study	The authors did not find any significant factors for anemia.
4.	Ullah, Irfan, *et al.* "Prevalence of anemia in pregnant women in district Karak, Khyber Pakhtunkhwa, Pakistan." International Journal of Biosciences 3 (2013): 77-83.	2013	Khyber Pakhtunkhwa, Pakistan	Cross-sectional study	• Illiterate women (88%) were more anemic than literate women. • Women from low socioeconomic status were more anemic (80%) than the upper class (52%). • Women in the third trimester (81.9%) were more anemic than the first trimester (58.6%).
5.	Haidar J. Prevalence of anemia, deficiencies of iron and folic acid and their determinants in Ethiopian women. Journal of Health, Population, and Nutrition. 2010 Aug 1:359-68(48).	2010	Ethiopia	A cross-sectional community-based study	• Chronic illnesses: AOR 1.11 (95% CI 1.15-1.55) • Deficiency of iron: AOR 0.40 (95% CI 0.35-0.64) • Deficiency of folic acid: AOR 0.50 (95% CI 0.50-0.90)
6.	Getachew M, Yewhalaw D, Tafess K, Getachew Y, Zeynudin A. Anaemia and associated risk factors among pregnant women in Gilgel Gibe dam area, Southwest Ethiopia. Parasites & vectors. 2012;5(1):1.(49)	2012	Gilgel Gibe dam area, Southwest Ethiopia	A cross-sectional community-based study	• Place of residence AOR 1.63 (95% CI 1.02-2.62 p 0.042) • Use of ITN to prevent mosquito bite AOR 2.84 (95% CI 1.33-6.05 p 0.007) • Plasmodium malaria-infected AOR 11.19 (95% CI 3.31-37.7 p 0.01) • Soil-Transmitted Helminth (STH) infections AOR1.82, 95% CI 1.16-2.87 p 0.001)
7.	Baig-Ansari N, Badruddin SH, Karmaliani R, Harris H, Jehan I, Pasha O, et al. Anemia prevalence and risk factors in pregnant women in an urban area of Pakistan. Food and nutrition bulletin. 2008;29(2):132-9.(3)	2008	Hyderabad, Pakistan	A cross-sectional analytic study	• Tea consumption before pregnancy 1-3×/day aPOR 1.9 (95% CI 1.01-3.7) • Tea consumption before pregnancy > 3×/day aPOR 3.0 (95% CI 1.3-8.0) • Egg consumption during pregnancy Never or < 2×/wkaPOR 1.7 (95% CI 1.1-2.5) • Other nonpica food aPOR1.8(95% CI 1.2-2.7) • Clay or dirt aPOR3.7(95% CI 1.1-12.3)
8.	Page CM, Patel A, Hibberd PL. Does smoke from biomass fuel contribute to anemia in pregnant women in Nagpur, India? A cross-sectional study. PloS one. 2015;10(5):e0127890.(23)	2015	Nagpur, India	Cohort study	• Biomass fuel RR 1.44 (95% CI 1.27-1.64) • Parity (n 3+) RR 1.69 (95% CI 0.97-2.92)
9.	Lover AA, Hartman M, Chia KS, Heymann DL. Demographic and spatial predictors of anemia in women of reproductive age in Timor-Leste: implications for Health Program Prioritization. PloS one. 2014;9(3):e91252.(22)	2014	Timoe-Leste	DHS	• Illiteracy AOR 2.04 (95% CI 1.49-2.80 p <0.001) • Birth in previous 1 year AOR 1.80 (95% CI 1.29-2.51 p 0.001) • Other fruits, the night before survey AOR 1.57 (95% CI 1.13-2.20 p 0.009) • Confirmed Malaria Rate AOR 2.25 (95% CI 1.50-3.38 p <0.001)
10.	McClure EM, Meshnick SR, Mungai P, Malhotra I, King CL, Goldenberg RL, et al. The association of parasitic infections in pregnancy and maternal and fetal anemia: a cohort study in coastal Kenya. PLoS Negl Trop Dis. 2014;8(2):e2724.	2014	Coastal Kenya	Cohort study	• Hookworm (>=100 eggs/g) RR 2.37 (95% CI 1.44, 3.91 p 0.0007) • P. falciparum (MS-positive) R2.06 (95% CI 1.24, 3.44 p 0.005) • Low BMI RR 1.25 (95% CI 0.86, 1.81 p 0.2) • Primigravida 0.78 (0.54, 1.11 p 0.2)
11.	Chowdhury HA, Ahmed KR, Jebunessa F, Akter J, Hossain S, Shahjahan M. Factors associated with maternal anaemia among pregnant women in Dhaka city. BMC women's health. 2015;15(1):1.	2015	Dhaka, Bangladesh	Cross-sectional study	• Age OR 0.851 (95% CI 0.759-0.955 p 0.006) • Literacy OR 0.199 (95% CI 0.072-.0.550 p 0.002) • Living area (urban) OR 0.334 (95% CI 0.131-.0.848 p 0.021) • Income OR 0.268 (95% CI 0.095-.0.754 p 0.013)
12.	Ononge S, Campbell O, Mirembe F. Haemoglobin status and predictors of anaemia among pregnant women in Mpigi, Uganda. BMC research notes. 2014;7(1):1	2014	Mpigi, Ugenda	Stepped-wedge cluster-randomised trial	• Malaria ??0.14 (95% CI ?0.27, ?0.01 p 0.20)
13.	Kedir H, Berhane Y, Worku A. Khat chewing and restrictive dietary behaviors are associated with anemia among pregnant women in high prevalence rural communities in eastern Ethiopia. PloS one. 2013;8(11):e78601	2013	Eastern Ethiopia	Cross-sectional study	• ChewiongKhat AOR 1.29 (95% CI 1.02, 1.62)
14.	Mbule M, Byaruhanga Y, Kabahenda M, Lubowa A, Mbule M. Determinants of anaemia among pregnant women in rural Uganda. Rural Remote Health. 2013;13(2259):15-49.	2013	Uganda	Cross-sectional survey	• Ownership of functioning radio OR 2.07 (95% CI 1.29-3.31) • Relative wealth rank OR 2.150 (95% CI 1.280-3.60)
15.	Kamruzzaman M, Rabbani MG, Saw A, Sayem MA, Hossain MG. Differentials in the prevalence of anemia among non-pregnant, ever-married women in Bangladesh: multilevel logistic regression analysis of data from the 2011 Bangladesh Demographic and Health Survey. BMC women's health. 2015;15(1):1.	2011	Bangladesh	Demographic &Heth Survey	• Secondary education OR 0.769 (95% CI 0.919-0.644 p <0.01) • Higher education OR 0.638 (95% CI 0.870-0.468 p <0.01) • Non-Muslim OR 1.506 (95% CI 1.833-1.238 p<0.01) • Currently contraceptive use OR 1.506 (95% CI 1.833-1.238 p<0.01) • Currently breastfeeding OR 1.349 (95% CI 1.833-1.238 p<0.01) • Currently amenorrheic OR 1.635 (95% CI 2.197-1.27 p<0.01) • Wealth index, rich OR 0.7815 (95% CI 0.918-0.664 p<0.01) • Age Group (30-49) OR 1.469 (95% CI 1.723-01.253 p<0.01) • BMI normal OR 0.717 (95% CI 0.827-0.622 p<0.01) • BMI Overweight OR 0.491 (95% CI 0.605-0.368 p<0.01) • BMI Obese OR 0.396 (95% CI 0.584-0.268 p<0.01)

Table V: Quality assessment* of individual studies included in the systematic review.

	Selection	Comparability	Outcome	Overall
Prevalence of Anemia, Deficiencies of Iron and Folic Acid and Their Determinants in Ethiopian Women	3	2	2	7
Anemia and associated risk factors among pregnant women in Gilgel Gibe dam area, Southwest Ethiopia	4	1	3	8
Anemia prevalence and risk factors in pregnant women in an urban area of Pakistan	3	1	3	7
Does Smoke from Biomass Fuel Contribute to Anemia in Pregnant Women in Nagpur, India?	1	1	3	5
Demographic and spatial predictors of anemia in women of reproductive age in Timor-Leste: implications for Health Program Prioritization.	4	1	3	8
The association of parasitic infections in pregnancy and maternal and fetal anemia: a cohort study in coastal Kenya	4	1	3	8
Factors associated with maternal anemia among pregnant women in Dhaka city	3	1	3	7
Hemoglobin status and predictors of anemia among pregnant women in Mpigi, Uganda	2	1	3	6
Khat chewing and restrictive dietary behaviors are associated with anemia among pregnant women in high prevalence rural communities in eastern Ethiopia	4	1	3	8
Determinants of anemia among pregnant women in rural Uganda	4	1	3	8
Differentials in the prevalence of anemia among non-pregnant, ever-married women in Bangladesh: multilevel logistic regression analysis of data from the 2011 Bangladesh Demographic and Health Survey. BMC women's health	4	1	3	8
Prevalence and determinants of iron deficiency anemia among non-pregnant women of reproductive age in Pakistan	4	1	3	8
Prevalence of anemia and associated factors among pregnant women in an urban area of Eastern Ethiopia	3	2	3	8
Anjum, Anam, *et al*. "Prevalence of anemia during pregnancy in district Faisalabad, Pakistan." Punjab Univ. J. Zool 30.1 (2015): 15-20.	2	1	3	7
Ullah, Irfan, *et al*. "Prevalence of anemia in pregnant women in district Karak, Khyber Pakhtunkhwa, Pakistan." International	2	1	3	6

**According to the Newcastle-Ottawa Scale for observational studies in systematic review. Maximum score for selection = 4 stars, maximum score for comparability = 2 stars, maximum score for outcome or exposure = 3 stars, maximum total score = 9.*

anemia as depicted in Table IV. Higher parity with more than three children was found to be positively associated with anemia as compared to the nulliparous women among all reviewed studies.[33-36]

Two studies found a strong positive association between a small inter-pregnancy interval of less than 1 year and anemia (Table IV).[29,32] Six studies showed pregnancy as an important risk factor for anemia with more women found to be anemic in the second and third trimester as compared to the first trimester.[4,33,34,36-38] In addition, three studies indicated that socioeconomic status played a significant role in anemia; and that being poor was found to be a determinant of anemia.[30,31,39] In addition, two studies found a positive and significant association between place of residence and anemia.[31,37] Lastly, one study found that non-Muslims were more at risk for anemia as compared to Muslims (Table IV).[30]

2. Nutrition-related factors:

Most of the studies assessed nutritional factors through biomarkers such as serum iron, folic acid, and serum ferritin. However, some of the studies also assessed nutritional status based on the intake of foods and body mass index (BMI) of the women. Thus, nutrition-related factors included iron deficiency, folic acid deficiency, serum ferritin levels, consumption of eggs and tea, consumption of fruits, history of pica (clay, dirt, or ice) and history of breastfeeding.

Three studies found iron and folic acid deficiency as important factors for anemia, demonstrating iron-deficient and folic acid-deficient women were more likely to be anemic as compared to their counterparts (Table IV).[29,36,40] Moreover, two studies found undernourishment (BMI of <18.5 kg/m^2) as a significant positive factor for anemia (Table IV).[35] Likewise, one study found that a history of pica was strongly associated with anemia with an adjusted odds ratio (OR) of 3.7.4 Similarly, one study conducted in Ethiopia showed chewing khat (chewable tobacco) was also positively associated with anemia (Table IV).[38] Moreover, consumption of fruits/vegetables low in vitamin A was also was associated with anemia in one study conducted in the Democratic Republic of Congo (DRC) (Table IV).[32] One study conducted in Bangladesh indicated breastfeeding as a determinant of anemia among women (Table IV).[30]

3. Comorbid and other factors:

Studies have also assessed important diseases such as malaria, hookworm infestation, and chronic illness as factors contributing to anemia. For example, three studies assessed the association between malaria and anemia; and two of these, found positive significant association with ORs ranging from 2.06 to 11.[19,32,35] In contrast, one of these studies, conducted in Uganda, found an inverse relationship.[39] Similarly, hookworm infestations were positively associated with anemia (OR: 2.37) in studies conducted in Kenya and Ethiopia (Table IV).[35,37] History of chronic illness was associated with anemia in one study conducted in Ethiopia, with an OR of 1.11 (Table IV).[40] Additionally, other factors such as biomass fuel usage, current usage of contraceptive methods and usage of ITN (Insecticide-treated nets) were also positively associated with anemia as show in Table IV.[30,34,37]

DISCUSSION

This review found that most of the available literature on prevalence of anemia and its determinants among women of reproductive age was from Asian and African countries. The prevalence of anemia ranged from 18.1% to 75% among women of reproductive age in developing countries. Anemic women tended to be older, uneducated, poor, undernourished, multiparous, living in rural areas, and have deficiencies in iron and folic acid. Furthermore, having a history of pica, malaria or worm infestation was positively associated with anemia in

developing counties. WHO / UNICEF has suggested that the problem of anemia is of very high magnitude in a community when the prevalence rate exceeds 40% and requires urgent implementation of interventions.[15]

Studies mainly from Bangladesh showed older age as an important and significant determinant for anemia.[30,31] Likewise, women having more children were at risk of anemia, as demonstrated in studies conducted in India and Kenya.[34,35] These findings can be explained by the fact that older and multiparous women are more likely to be anemic due to hemodilution during each pregnancy, which is further aggravated by blood loss during labor.[41] Thus, anemia associated with older women may be due to high fertility rates and increased menstrual blood loss.[42,43] The prevalence of anemia was also slightly higher among multiparous women with narrow birth-spacing, which also concurs with previous studies.[42,43]

Likewise, rural and illiterate women belonging to poor socioeconomic status were found to be more anemic in studies conducted in Ethiopia, Congo, and Bangladesh. It is claimed that educated women are usually more aware of health problems, having knowledge about the availability of healthcare services, and also utilising the information more efficiently than uneducated women.[44] Moreover, high literacy levels tend to positively affect health-seeking behaviours, and education may enhance a woman's control over her fertility.[45] Education may expose women to more health education messages and campaigns, enabling them to recognise their health status or complications and, ultimately, take suitable and timely action.[45] These women might have greater opportunities to receive health information and pay more attention to maternal healthcare; thus, reducing the chances of anemia.[45] Similarly, we found the highest prevalence of anemia among rural women based on the standard of living index. This might be due to the fact that rural poor women lack access to their own resources because of lower rates of extra-household employment and reduced economic power within the household, as supported by one study conducted in India.[46] Moreover, dimensions of autonomy such as freedom of movement, decision-making power and control over finances can also exert a strong influence over service use and service choice in the developing countries.[47]

With respect to the nutritional factors, our study found that iron and folic acid deficiency, low intake of fruits and eggs, high intake of tea, and history of pica were found to be the determinants of anemia. These significant investigations demonstrating poor nutrition associated with anemia, were largely conducted in Ethiopia, Bangladesh, and Pakistan.

The deficiency of iron and folic acid along with low intake of fruits and vegetables, and history of pica denote deprivation of iron and folic acid from the diet of women and merits greater consideration. This is consistent with one of the studies conducted in Ethiopia.[43] Moreover, literature also shows that at least 50% of anemia worldwide results from an iron deficiency, which is mainly caused by a lack of bioavailable dietary iron, increased demand for iron such as during childhood, pregnancy, and lactation, or a combination of the two.[48] Furthermore, poor intake of fruits and a healthy diet might be a proxy for low income, thus preventing these women from purchasing a healthy diet, rich in iron and folic acid.

One study from Pakistan reported an association between pica and anemia among women. Purposeful consumption of nonfood substances such as laundry starch, clay, dirt, or ice is a dietary habit termed as 'pica', in which there is a craving to ingest these substances having no nutritious value.[49] Pica behaviour is found in conjunction with micronutrient deficiencies and the literature has identified two mechanisms by which pica may cause these micronutrient deficiencies. Firstly, pica materials may bind to the mucosal layer of the gut, thereby preventing absorption of micronutrients.[50] Secondly, these materials may also absorb micronutrients in ingested food, preventing them from being metabolised.[51] A meta-analysis also showed strong associations between pica and micronutrient deficiencies, suggesting that pica status could be used as a preliminary clinical indicator for micronutrient deficiency among women.[52] Moreover, it has also been found that consumption of tea has a detrimental effect on iron as intestinal absorption of non-heme food iron may be inhibited by tea, thus causing anemia.[53]

This review also found an association of certain diseases such as malaria, hookworm infestation, and chronic illnesses with anemia. Specifically, studies from Kenya, Ethiopia, Congo, and Uganda showed these associations. Malaria infection in humans by plasmodium species is associated with a reduction in hemoglobin levels causing anemia.[54] Moreover, human hookworm infection has been well establishd to result in intestinal blood loss which, in turn, can contribute to anemia.[55,56] The cause of anemia is multifactorial in African countries such as iron- and folate-deficient diet and infections, such as malaria, hookworm, and human immunodeficiency virus (HIV).[57] Furthermore, these associations between infections and anemia can also be explained by the fact that infection causes anemia through the loss of nutrients, decreased appetite and poor absorption.[58]

To the best of authors' knowledge, this is the first systematic review of prevalence and determinants of anemia among women on reproductive age group, synthesising data, mainly from developing countries. Moreover, most of the studies used standard WHO definitions of anemia, which take into consideration different cut-offs of anemia for pregnant and non-pregnant women.

Despite these strengths, this systematic review has some potential limitations. Firstly, we found mainly cross-sectional studies and only three longitudinal studies in this review, therefore, the temporal relationship between various determinants and anemia could not be determined. Secondly, different studies have found a variety of determinants for anemia, depending upon the differences in the epidemiological and socio-demographic context of those countries; therefore, results may not be generalisable to all settings. Thirdly, this review included papers only in the English language and might have overlooked the important literature published in the local languages. Lastly, we did not study the prevalence and determinants of different types of anemia separately, such as iron deficiency anemia, megaloblastic anemia, and anemia due to hemoglobinopathies.

CONCLUSION

Anemia is a common public health problem among women of reproductive age in developing countries. Determinants such as higher maternal age, low education, high parity, poor socioeconomic and nutritional status, and certain diseases have been found as important determinants of anemia among women of developing countries. Thus, there is a need to improve the diet and general health of women. In addition to improving the access to a healthy and nutritious diet to poor women, women should be given awareness regarding consumption of a healthy diet and family planning. Moreover, along with increasing iron and folic acid, infections such as malaria and hookworm call for a deworming campaign, and distribution of insecticide-treated nets for poor women in developing countries.

AUTHORS' CONTRIBUTION:

SAA: Conceptualised and designed the manuscript, involved in searching various databases for relevant studies and assessed the quality of articles, provided input in developing the figure and tables of the study, drafted the manuscript by providing important intellectual feedback and also gave the final approval of the version to be published.

UK: Involved in searching various databases for relevant articles and assessed the quality of articles as a second reviewer and assessor, provided input in developing the figure and tables of the study, and gave final approval of the version to be published.

AF: Provided expertise in writing the manuscript, reviewed manuscript critically by providing intellectual feedback, and gave final approval of the version to be published.

CONFLICT OF INTEREST:

Authors declared no conflict of interest.

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