Review Article: Systematic Review, Meta-Analysis, Integrative Review, Scoping Review

RISK FACTORS FOR THE ANEMIA IN PREGNANT WOMEN: A LITERATURE REVIEW

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Abstract
Background: Anemia in pregnancy is still a global public health problem and is the largest contributor to morbidity and mortality. Some studies report that risk factors for anemia vary from place to place, so more in-person observations are needed regarding anemia risk factors.
Objectives: This study aimed to determine the risk factors of anemia in pregnant women. Methods of using literature review studies.
Design: This study design is a literature review to search and review article from database and the theory which is descriptive.
Data Sources: Search for scientific articles using the Mendeley application by entering the keyword "*Risk Factors, Anemia, Pregnancy*" with Published year 2018-2021, English and Indonesian, full text, National journal has ISSN and open access.
Review Methods: The literature review method using narrative review based on inclusion criteria, namely articles discussing anemia in pregnant women, published in 20158-202, International and National Publications, having ISSN National Journals, Articles using English, original articles, full text and open access. While the Exception Criteria for Articles other than English, type of research literature review and RCT, articles are then collected and a journal summary is made containing the name of the researcher, the year the journal was published, the title of the study, the method and a summary of the results or findings. The summary of research journals is entered into a table according to the format, and 10 articles are eligible.
Results: From the 10 selected articles, it can be concluded that the risk factors for anemia, especially in developing countries, are multifactorial, including micro-iron deficiency, folate, and vitamins A and B12 as well as anemia due to parasitic infections such as malaria and hookworms or chronic infections such as TB, HIV, parasites. intestines, infection of working mothers (farmers), contaminated drinking water sources, consumption of coffee/tea and diet. Meanwhile, other factors in Indonesia are unfavorable geographical location, level of education, lack of public awareness of health, socio-economic situation, parity (number of children), and chronic energy shortages (KEK).
Conclusion: Anemia is still a global health problem and still has to be addressed, especially in developing countries. Therefore, efforts are needed to better understand the main causes of anemia, including iron deficiency as well as other nutritional deficiencies, diseases, and Hb disorders related to anemia so that appropriate action can be given. Biochemical measurement of micronutrients (especially iron and Vitamin A), inflammatory signs in addition to hematological index when assessing anemia clinically are also urgently needed

Keywords: *Risk Factors, Anemia, Pregnancy.*

INTRODUCTION

Anemia in pregnancy is still a public health problem globally and is the largest contributor to morbidity and mortality (A. et al., 2005; Black et al., 2013; Brabin et al., 2001; Haider & Bhutta, 2017; Keats et al., 2019; Means, 2020; Stephen et al., 2018).

The World Health Organization (WHO) reports about 32.4 million pregnant women suffer from anemia worldwide, with the highest prevalence in Africa (44.6%) followed by Asia with a prevalence of 39.3% (World Health Organization, 2015a).

Anemia is a decrease in the number and size of red blood cells (hemoglobin / Hb concentration) below the set limit value, resulting in a lack of ability for blood to transport oxygen throughout the body (L.T. et al., 2017; Osman et al., 2020; Stephen et al., 2018; WHO, 2006, 2012). About 20% of maternal deaths are caused by anemia and most occur in developing countries. (Black et al., 2013; Kefiyalew et al., 2014; Osman et al., 2020; Stephen et al., 2018). Gestational anemia significantly affected 32.4 million (38.2%) pregnant women. This health problem is most severe in Southeast Asia (48.7%) and Africa (46.3%) (Osman et al., 2020; Stevens et al., 2013; WHO, 2006).

Basic Health Research (2013) reported that the incidence of anemia in pregnant women in Indonesia amounted to 37.1%. (Badan Penelitian dan Pengembangan Kesehatan, 2013) Increased to 48.9% in 2018 (RISKESDAS, 2018).

While the incidence of anemia in Biak Numfor Regency in 2018 was 81% of 3,087 pregnant women, and in 2019 amounted to 79 (%) of 3,063 pregnant women (*Profil Dinas Kesehatan Kab. Biak Numfor*).

It is reported that 40% of the most common cases of anemia are caused by iron deficiency or about 1.24 billion people worldwide are affected by iron deficiency anemia, but this causative factor is different in each community group and each region (de Leeuw et al., 1966; Means, 2020; Osman et al., 2020; WHO, 2006).

Anemia that occurs in pregnant women has a devastating impact on health, social, and economic status, leading to an increased risk of lack of physical activity, increasing the risk of premature birth, low birth weight, intrauterine fetal death, neonatal death, maternal death, and consequently infant mortality, especially in mothers with severe anemia (Ayano, 2018; Ezzati et al., 2004; Figueiredo et al., 2018; Gedefaw et al., 2015; Haider et al., 2013; Osman et al., 2020; Rahman et al., 2016; Sharma et al., 2020; Zhang et al., 2009).

The study findings report that the risk factors for anemia vary from place to place so more deep observation is needed related to the risk factor of anemia (Osman et al., 2020; WHO, 2006).

Based on the above problems, the researcher wants to examine more deeply related risk factors for anemia in pregnant women by using literature studies.

METHODS

Design

The design of this research is Literature Review or literature review. The nature of this study is descriptive analysis, which is the regular parsing of data that has been obtained, then given understanding and explanation in order to be well understood by readers.

Search Methods

Literature review is compiled through the search of research articles that have been published both nationally and internationally.

The population and sample were pregnant women with anemia.

Search for scientific articles using the Mendeley application by entering the keyword *"Risk Factors, Anemia, Pregnancy"* with Published year 2018-2021. Articles selected based on:

a. Inclusion Criteria
1. Article discussing anemia in pregnant women;
2. Published year 20158-2021;
3. International and National Publications;
4. Have an ISSN for National Journal;
5. Articles using English; and
6. Original articles, full text and open access.

b. Exclusion Criteria
1. Articles other than English; and
2. Types of review literature research and RCT.

Search Outcome

From the search obtained 4,124 articles after filtering the year that is 2018-2021 obtained 990 articles, then selecting the category of journals, duplication, open access, research design taken is mix methods study, cross sectional study, correlation analysis, and qualitative study obtained 90 articles.

The final process is to conduct journal selection based on inclusion criteria obtained by 10 journals that are eligible for review. Article Search Strategy can be seen in figure 1.

Quality Appraisal

This literature review is synthesized using narrative methods by grouping similar extraction data according to the results measured to answer the purpose. Research journals that fit the inclusion criteria are then collected and made journal summaries including the name of the researcher, the year of publication of the journal, the title of the study, methods and summary of results or findings (Fadlallah et al., 2019; Pesut et al., 2020).

The summary of the research journal is entered into the table in accordance with the format mentioned above. To further clarify abstract analysis and full text the journal is read and observed. The journal summary is then conducted an analysis of the content contained in the purpose of the research and the results / findings of the study.

Analysis of the contents of the journal, then coded into the contents of the journal reviewed based on the outline or core of the study is done by parsing in a sentence then if it has been collected then searched for similarities and differences in each study and then discussed to draw conclusions.
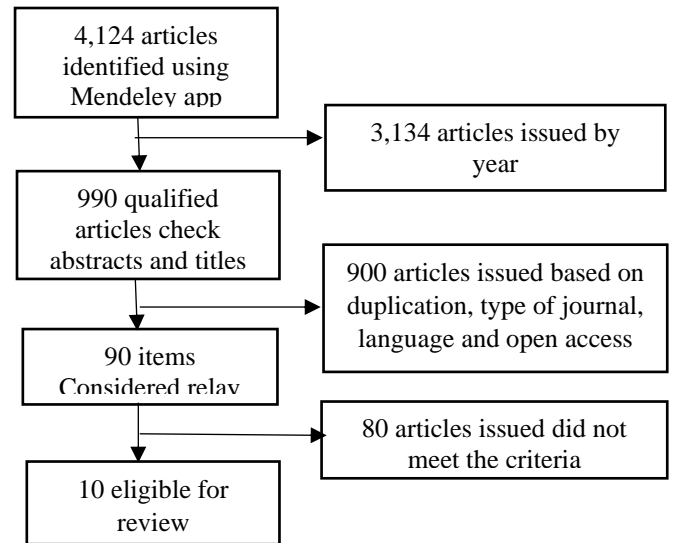

Figure 1. Article Search Strategy.

Data Abstraction

Researchers accompanied by two supervisors simultaneously review and read the full article, then discuss to agree on the decision of the article that is adjusted to the criteria of inclusion.

Data Analysis/ Synthesis

After the researchers conducted filtering such as duplication, year of publication, the type of research found ten articles were selected based on inclusion criteria that discussed risk factors for anemia in pregnant women. The filtering process can be seen in Figure 1.

RESULTS

From the search for articles using the Mendeley application, results can be seen on table 1 extraction result of research.

Table 1. Extraction of Research Results.

Title	Author/Year	Type of Research and Sample	Data Analysis	Result
Risk factors of anemia among pregnant women attending antenatal care in health facilities of Eastern Zone of Tigray, Ethiopia	(Berhe et al., 2019)	Control case studies. Sample 600 pregnant women in 2017/2018.	Bivariate and multivariate logistic regression analysis	Risk factors for ane during pregnancy a significantly intesti parasites, occupatio (farmers), unprotec (polluted) drinking sources, drinking c with or immediately daily meals and die
Risk Factors for Anemia in Pregnant Women (Study In The Working Area of Slawi Kab. Tegal Health Center)	(Fatkhiyah, 2018)	Observational research with case control design. Sample 60 pregnant women divided into 2 groups.	Chi square	There is a positive association of parity the incidence of an pregnancy.
Prevalence and risk factors of anemia among ever-married women in Jordan	(Arabyat et al., 2019)	Cross sectional. Representative sample of married women aged 15-49 years tested for hemoglobin levels in JPFHS 2012.	Univariate and multivariate logistic regression	Knowledge is relate incidence of anemi
Spatial distribution and determinant factors of anaemia among women of reproductive age in Ethiopia: a multilevel and spatial analysis	(Kibret et al., 2019)	Observational. 645 cluster of enumeration area (EA).	Multivariable logistic regression model	Factors of risk for a are demographics, l education, low inco women living in rur areas.
Anemia in pregnant women participants of the First 1000 Days of Life Program in Agats, Asmat, Papua: Prevalence and analysis of risk factors	(Astari et al., 2018)	Descriptive observational. Sample 230 pregnant women.	Univariate, bivariate, and multivariate.	Risk factors for ane pregnant women in include the geograp location of Asmat, l level of public educ lack of health work health care facilities of public attention t health, low socioec conditions, and nutr status of pregnant w
Prevalence and Determinant of The Incidence of Anemia pregnant women	(Harna et al., 2020)	Cross sectional. Sample 94 pregnant women.	Descriptive and presented in the form of frequency and cross tabulation	Factors that affect t incidence of anemi pregnant women ar gestational age, KE and parity.
Anaemia in Pregnancy: Prevalence, Risk Factors, and Adverse Perinatal Outcomes in Northern Tanzania	(Stephen et al., 2018)	Cohort study. Sample 539 pregnant women.	Proportions were used for categorical variables and mean or median with respective measures of dispersion for numerical variables. Odds Ratio (OR) with 95%	The mother's low le education is a facto associated with ane during pregnancy.

			Confidence Interval (CI)	
Prevalence, risk factors and associated adverse pregnancy outcomes of anaemia in Chinese pregnant women: a multicenter retrospective study	(Lin et al., 2018)	Retrospective study. Sample 44,002 pregnant women.	Bivariate and multivariate logistic regression analyses	Anemia is significa associated with mat age of 35, family m income, rural living BMI.
Prevalence of anaemia, risk of haemo concentration and risk factors during the three trimesters of pregnancy	(Arija, 2018)	Longitudinal study. Sample 11,259 women whose pregnancies.	Chi-squared test	The risk factor of a too young and old.
Knowledge and Attitude of Pregnant Women in Rural Tanzania on Prevention of Anaemia	(Margwe & Lupindu, 2018)	Cross-sectional. Sample of 354 pregnant women	Fisher's exact test, multivariable logistic regression	Knowledge and atti related to anemia

DISCUSSION

Anemia is a worldwide public health problem, particularly in developing countries that can affect human health, development, social and economic health (Black et al., 2013; Kassebaum et al., 2016; Mbule et al., 2013; Stephen et al., 2018; Stevens et al., 2013; Vaz-Tostes et al., 2016; WHO, 2011; WHO and UNICEF, 2004). The goal of the study was to identify risk factors for anemia by considering as many factors as possible.

The results of the journal review identified several risk factors of anemia namely micronutrient deficiency of iron, folate, and vitamins A and B12 and anemia due to parasitic infections such as malaria and hookworms or chronic infections such as TB, HIV, intestinal parasites, maternal work (farmers), contaminated drinking water sources, drinking coffee/tea and diet are major risk factors for anemia in developing countries (Berhe et al., 2019; Foote et al., 2013; Hoffmann et al., 2015; Metz, 2008; Ononge et al., 2014; Stephen et al., 2018; WHO, 2005 Zhang *et al.*, 2009; Hirani and Karmaliani, 2013; Stephen *et al.*, 2018; Dogra, 2020).

While in Indonesia the risk factor of anemia is the unfavorable geographical location, education level, lack of public attention to health, socio-economic circumstances, parity (number of children), adequacy of iron consumption, and KEK status

(Amallia et al., 2017; Astari et al., 2018; Fatkhiyah, 2018; Harna et al., 2020; Irwanti et al., 2019; Pasmawati & Hatma, 2019; Ristica, 2013; Satriani et al., 2019; Tanziha et al., 2016). In addition to factors above culture is a contributing factor to the occurrence of anemia (Afiyah Sri Harnany, 2006; Contento, 2008).

Several vitamins play a role in iron metabolism, including riboflavin (B2), pyridoxine (B6), cobalamin (B12), and folate. Deficiency of this nutrient has been linked to the incidence of anemia, but the extent of this vitamin's role in anemia is not yet clearly known (Arredondo et al., 2006).

Deficiency of vitamin B12 (cobalamin) and folate can cause macrocytic anemia that can affect DNA synthesis and cell division in the bone marrow (megaloblastic changes), such as hypersegmentated neutrophils (Arredondo et al., 2006; Chaparro & Suchdev, 2019; Fishman et al., 2000; Hacibekiroglu et al., 2015; Jafari et al., 2013; Wieringa et al., 2016).

In general, iron deficiency is a cause of anemia, although deficiencies in other nutrients and vitamins can also cause anemia, including deficiencies in vitamins A, B12, B6, C, D, and E, folate, riboflavin, copper, and zinc. Some of these vitamins such as vit A, B6, and B12, folic acid, and riboflavin are needed by the body to produce red blood cells normally. While other nutrients, such as vitamins C and E, can protect

red blood cells as anti-oxidants. (Chaparro & Suchdev, 2019; Losken et al., 2005).

Malaria caused by the Plasmodium parasite can cause severe anemia, in addition to other complications including death. (Baird, 2007; Barcus et al., 2007; M. et al., 2007; Sohail et al., 2015; World Health Organization, 2016).

P. falciparum malaria during pregnancy is the leading cause of maternal and fetal morbidity and mortality. Although P. vivax infection receives less attention from P. falciparum infection, both play an important role in causing anemia in the mother and cause BBLR type of infection to always coexist. (Duffy et al., 2001; Hamer et al., 2009; Sohail et al., 2015).

Parasites require iron for growth, and malaria significantly disrupts iron metabolism in a variety of ways including through hemolysis, heme release, damaged erythropoiesis, increased iron in macrophages, and decreased iron absorption. (Sohail et al., 2015; Spottiswoode et al., 2014) .

Anemia is the most common hematological disorder among patients infected with HIV. The disease is usually characterized as normochromic and normocytic anemia with low reticulocyte counts, normal iron storage, and impaired EPO responses.

The prevalence of anemia in HIV-positive people increases along with the development of the disease caused by several factors either indirectly or directly related to the virus. HIV infection causes chronic disease acute phase response, increased hepcidin and AI, and altered iron metabolism (Minchella et al., 2015; Redig & Berliner, 2013; Sohail et al., 2015).

Intestinal parasites (hookworms, Ascaris lumbricoides, Trichuris trichiuria) are a risk factor for anemia in pregnancy, this is in line with research conducted in Vietnam (Kramer & Kakuma, 2012), Nigeria (Idowu et al., 2005), Benin (Ouédraogo et al., 2012), Ethiopia (Haidar & Pobocik, 2009), Gilgel Gibe area (Getachew et al., 2012), Southeastern Ethiopia (Kefiyalew et al., 2014), Southern Ethiopia

(Lebso et al., 2017), and in Northwestern Ethiopia (Asrie, 2017).

Intestinal parasites cause blood loss, so the mother and fetus are at high risk of anemia. This is because worms in the intestine can cause intestinal necrosis and blood loss due to attachment to the intestinal mucosa (Brooker et al., 2008; World Health Organization, 2015).

Pregnant women who work as farmers are at risk of anemia, which is associated with a lack of information about balanced nutritional intake during pregnancy, economic factors that impact on not being able to access and utilize health services. (EDHS, 2016; Kassa et al., 2017; Xu et al., 2016).

Sources of water that are not clean (polluted), can cause various infections that affect the reduction of iron and other micronutrients and can cause anemia (Berhe et al., 2019).

Consuming coffee/tea after meals or immediately after meals, anemia can affect the presence of anti-nutritional factors such as tannins and caffeine, which are found in tea and coffee, respectively (Baig-Ansari et al., 2008; Obse et al., 2013; Taylor & Meyers, 2012).

Tea and coffee can decrease iron absorption by 60% and 50% respectively (Allen, 2000; Anderson & Fitzgerald, 2010). The effect of tea on the absorption of non-hem iron is thought to stem from the formation of an insoluble tannate iron complex (Obse et al., 2013).

In some studies, the level of education has been reported to have an effect on the reduced risk of anemia. Educated pregnant women have a better income so that it affects the food to be consumed so that they do not experience nutritional anemia (Tanzania Bureau of Statistics, 2010).

It was further reported in Ethiopia that the prevalence of anemia was higher in uneducated pregnant women (Melku et al., 2014). Secondary and higher education levels are also associated with maternal compliance in terms of exclusive breastfeeding, ANC visits in accordance with the recommendations given (Tanzania Bureau of Statistics, 2010).

Income levels also affect the incidence of anemia, this is because low income leads to an inability to consume nutritious foods. A study in Ethiopia showed that women with low incomes are more at risk of suffering from anemia than women with higher incomes (Bekele et al., 2016; Gedefaw et al., 2015; Stephen et al., 2018).

Parity is a factor in the occurrence of anemia in pregnant women, this is associated with the theory that a mother who often gives birth has a risk of anemia in subsequent pregnancies if she does not pay attention to nutritional needs, because during pregnancy nutrients will share for the mother and the fetus they contain. The more often a woman gives birth, the greater the risk of blood loss and has an impact on decreasing Hb levels. Each time a woman gives birth, the amount of iron lost is estimated at 250mg (Pasmawati & Hatma, 2019).

Adequacy of iron consumption related to the occurrence of anemia is due to the need for iron in pregnancy increased, especially in the final trimester, in the process of maturation of iron red blood cells taken from plasma transferin which is the iron reserve in serum. (Pasmawati & Hatma, 2019).

Pregnant women with an arm circumference (LILA) of less than 23 cm are at risk of anemia. (Milman et al., 2000). The upper arm is the measure used for nutritional status assessment, with the normal limit being 23 cm for adult women, while the lesser arm circumference is also associated with undernutrition status. This is in line with the results of studies reported in eastern Ethiopia and western Ethiopia, Kenya, Nepal, and India (Alene & Mohamed Dohe, 2015; Mondal et al., 2006; Osman et al., 2020). With the similarity of reported research results, malnourished pregnant women are at higher risk of anemia.

Culture is one of the factors of anemia. Culture is the experience of people from the moment they are born, culture is also shared knowledge and shared meaning, where the meaning indicates the complexity of belief or knowledge and the connection of values or feelings with beliefs (Contento, 2008). The results of health ethnographic research in 2012 on 12 ethnicities in Indonesia showed that maternal and child health problems are still very concerning.

In Mexico, pregnant women and after childbirth are prohibited from eating foods that are "cold". In Indonesia alone pregnant women and after childbirth are prohibited from eating eggs, meat, shrimp, sea fish and catfish, conch, lembayung leaves, bitter melon, pineapple, brown sugar, and foods fried with oil (Harnany, 2006).

So that by knowing the risk factors for anemia, health workers can implement policies that focus more on the risk group and perform treatment for insufficient iron and provide appropriate iron supplements. With proper treatment is expected to reduce the number of deaths and the number of pains caused by anemia.

CONCLUSION

Anemia is still a global health problem and still has to be addressed especially in developing countries. So, efforts are needed to better understand the main causes of anemia including iron deficiency as well as other nutritional deficiencies, diseases, and Hb disorders associated with anemia so that appropriate measures can be given. Biochemical measurements of micronutrients (especially iron and Vitamin A), signs of inflammation, in addition to the hematological index when assessing anemia clinically are also urgently needed.

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DECLARATION OF CONFLICTING INTEREST

This comprehensive summary or systematic review is independent writing, so there is no conflict of interest in the writing.

AUTHOR CONTRIBUTION

Nurnaningsih: Designed the study, collected and analyzed articles, and contributed to the completion of a systematic review.

Mardiana Ahmad: Contribution as a supervisor guide and discuss the final results of the review literature manuscript.

Isharyah Sunarno: Contribution as a supervisor involved in planning and supervision in the completion of the literature review.

Nur Aliya Arsyad: Contributed to the preparation of the final manuscript.

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