

ANEMIA IN EACH TRIMESTER WITH LOW BIRTH WEIGHT : A SYSTEMATIC LITERATURE REVIEW

Dewi Murtiningsih¹, Nidatul Khofiyah², Dewi Rokhanawati³

^{1,2,3} Magister Midwifery Program, Faculty of Health Sciences, Universitas 'Aisyiyah Yogyakarta

***corresponding author : dewimurtiningsih10@gmail.com**

Abstract

Low birth weight has negative impacts towards the baby's health, both short and long term. This occurs by several factors and one of the highest one is caused by anemia. There is substantial evidence of a U-shaped curve that shows the lowest hemoglobin concentration in pregnancy of the second trimester. The effect anemia in pregnancy and the incidence of low birth weight have different results in each trimester. The aim of this study was to analyze further effect of anemia in the respective trimester towards low birth weight. This review has eight stages, including identifying midwifery problems, determining the priority of problems and research questions, determining the framework, searching for literature, selecting articles, critical assessment, data extraction and mapping. Furthermore, with research articles from 2 databases (Pubmed and ScinceDirect) with quantitative methods. Anemia in the first trimester does not affect the occurrence of low birth weight if it does not continue to the later trimester. But anemia in the second and third trimesters potentially affect low birth weight and premature birth, with highest risk if it occurs in the third one. Conclusion: Abnormal hemoglobin concentrations in pregnant women can cause poor neonatal outcomes, namely as low birth weight.

Keywords: anemia, low birth weight

1. INTRODUCTION

Low birth weight according to the World Health Organization (WHO) is less than 2,500 grams (5.5 pounds) at birth. The incidence of LBW in the world reaches more than 20 million babies, this figure represents 15.5% of all births with 95.6% received from developing countries. The percentage of low birth weight in developing countries is 16.5%, this number is double the percentage of low birth bodies in developed countries which is 7% [1]. Developing countries that have the highest birth rates are born from the continents of Asia and Africa, namely from Asia at 18.3% and Africa 14.3% [2], and large bodies born low in Indonesia today are 6.2% [3]. Low birth weight has a negative impact on baby's health, both short and long term. Babies born with low birth weight have higher perinatal mortality and morbidity than children with normal birth weight, ranging from low cognitive [4]. which appears as adults [2]. One of the causes of anemia is anemia. According to the WHO classification, pregnant women are included in the anemia criteria if the hemoglobin concentration is less than 11.0 g / dl in the first and third trimesters and the hemoglobin concentration is less than 10.5 g / dl in the second trimester [5]. This classification difference occurs due to physiological factors, namely plasma volume which increases 10-15% at the age of a pregnancy of 6-12 weeks and increases faster afterwards until 30-34 weeks' gestation[6]. Hb and hematocrit concentration (Hct) usually decreases during the first trimester and reaches the lowest level at the end of the second trimester then increases again during the third trimester of pregnancy [5].

Mothers who experience anemia during pregnancy have a 14 times greater chance of giving birth to babies with low birth weight than pregnant women without anemia [2]. The percentage of pregnant women who experience anemia in Indonesia is 48.9%, the majority of anemia occurs in

pregnant women aged 15-24 years (84.6%). The government has given a policy so that every pregnant mother consumes iron tablets to prevent anemia, namely at least 90 tablets during her pregnancy, but the coverage rate is still low (38.1%), so the prevalence of anemia is still high in each trimester [3]. In one study it was found that the prevalence of anemia increased in continuing pregnancies namely 11.9% in the first trimester 11.9%, 32.1% in the second trimester, 33% in the third trimester and 26.1% in labor[7]. There is substantial evidence for a U-shaped curve that displays higher hemoglobin concentrations in early pregnancies (12-16 weeks) and at the end of pregnancy (≥ 37 weeks) compared to mid-pregnancy (28-33 weeks) [8]. The association of anemia with the incidence of LBW has different results in each trimester [5]. This is the interest of researchers to analyze further the relationship between anemia in each trimester of pregnancy with the incidence of low birth weight.

2. MATERIAL AND METHOD

The researcher screens 1041 literature reviews from two databases (PubMed and ScienDirect) for review. 9 articles taken in a systematic Literature Review using quantitative research methods with quality journals Q1, Q2 and Q3. This population in the Systematic Literature Review is pregnant women in the first, second and third trimesters who are anemic and not anemic to find out the relationship of anemia in each trimester of pregnancy with the incidence of low birth weight. This Systematic Literature Review is adjusted to the Systematic Literature Review steps, namely 1) Identification of problems, 2) Prioritizing problems and research questions, 3) Creating Frameworks, 4) Literature searching, 5) Selecting articles, 6) Making critical appraisal, 7) Extracting selected paper data, 8) Collecting data dan Mapping data.

Identify problems

Problem Identification: Problems that often occur in pregnant women include the high anemia in pregnancy which can lead to low birth weight babies. Mothers who experience anemia during pregnancy have a 14 times greater chance of giving birth to babies with low birth weight [2]. The incidence of LBW in the world reaches more than 20 million babies and infants born with low birth weight have higher mortality and perinatal morbidity [1].

Research Questions

What is the relationship between anemia in each trimester of pregnancy and the incidence of babies with low birth weight?

Creating Frameworks

| Element | Inclusion | Exclusion |
|-----------------------|---|--|
| Population | Pregnant women with normal and abnormal hemoglobin concentrations | Pregnant women with complications and multiple pregnancies |
| Exposure/Event | Hemoglobin concentration | |
| Outcomes | Risk factors for anemia, anemia with low birth weight, impact of low birth weight | |
| Study Design | Case control; Cross Sectional; Cohort | |

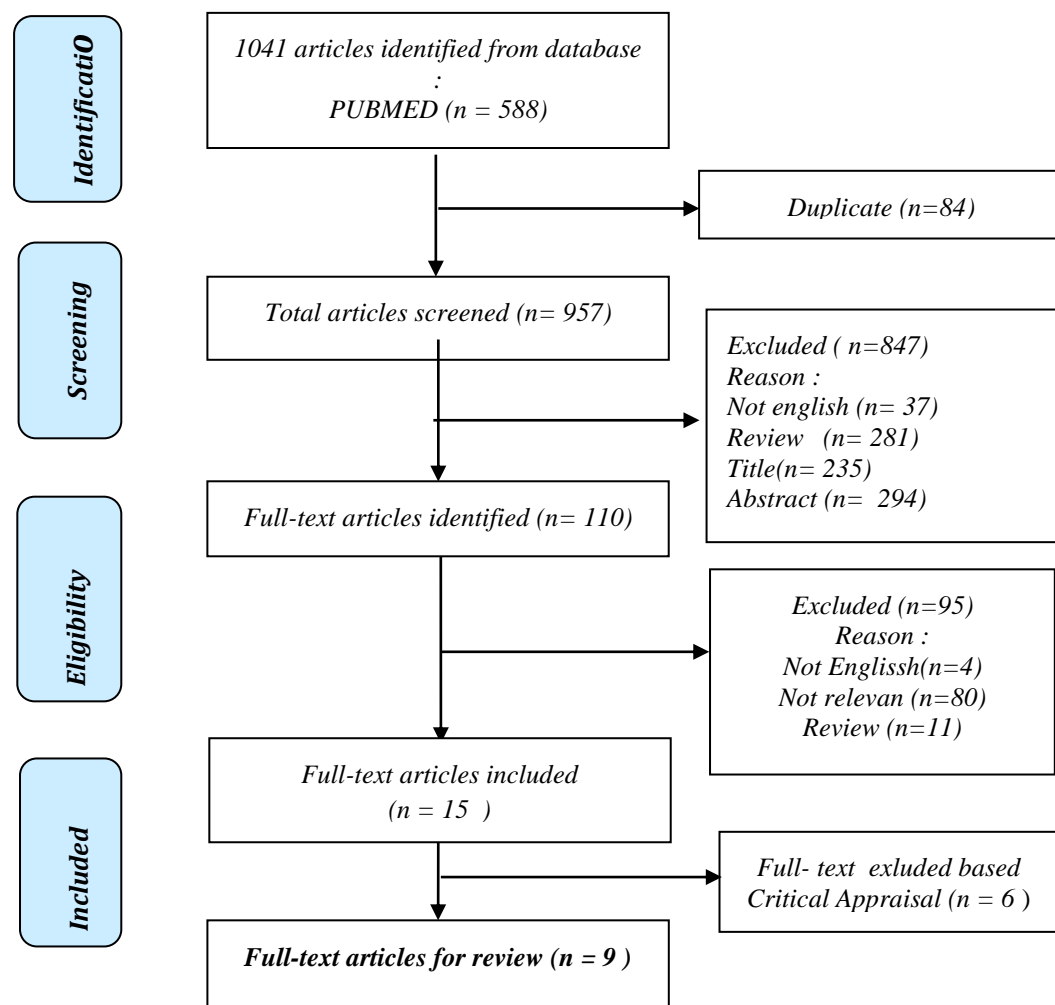
Literature searching

Article searches were obtained from the PubMed and Science direct databases, by searching articles for the past 10 years, starting in 2009 until 2018. Search only included articles provided in full text and "human species".

Selecting articles

In the article search, 1041 articles were identified, after being filtered by review, English-language articles, title suitability, and abstracts, 110 articles were based on inclusion and exclusion criteria. Full text that is appropriate the theme of the researcher was 15, then critical appraisal was carried out and 9 articles were obtained for final review

PRISMA FLOW DIAGRAM



Making critical appraisal

Critical appraisal is done by tools Joanna Briggs of Joanna Briggs Institute. From 15 articles, 9 articles of good quality were obtained.

Extracting data

Nine articles that are suitable and of good quality are then extracted from the data to find out in detail and classify several points of the article, such as the research country, research objectives, methods used, and the results or findings of the research conducted.

Collecting data and Mapping data

9 selected articles came from articles from 2009-2018, articles in the systematic literature review used quantitative research methods with cross sectional research designs of 4 articles, namely articles 2, 3, 4, and 8, cohort research designs of 3 articles, namely articles 1,5,9 and retrospective designs of 2 articles, namely article 6,7. Articles come from various countries: 3 from India, 1 from Ethiopia, 2 from Iran, 1 from the Netherlands, and 2 from Turkey. This Mapping literature the author classifies articles into 3 main points, namely: Anemia factors in pregnancy are in the articles 1,2, 4, 6,7,8. Anemia in each trimester of pregnancy for low birth weight is found in articles 2,3,5 6,7,8,9. The impact of LBW is in the article 1,2,3,5.

3. RESULTS AND DISCUSSION**a. Risk factor of anemia**

The prevalence of anemia in pregnancy varies in each article, ranging from 20.2% - 55%. A very high prevalence rate is found in a study in eastern India which states that the prevalence of anemia is very high reaching almost 91% with 35.1% of mothers having less weight and 32.8% of mothers having anemia with less weight [4]. More than half of pregnant women experience anemia since the beginning of pregnancy. A higher percentage of anemia was seen in the second trimester and the lowest in the third trimester, more than a third of pregnant women remained anemic for three trimesters and less than 30% of pregnant women were not anemic for three trimesters [9], whereas in the pregnant women group anemia showed a decrease in hemoglobin concentration in the second trimester and increased hemoglobin concentration in the first and third trimesters [5]. There is a U-shaped curve that displays higher hemoglobin concentrations in early pregnancy (12-16 weeks) and at the end of pregnancy (≥ 37 weeks) compared to mid-pregnancy (28-33 weeks) [8] [10]. This is caused by plasma volume increasing by 10-15% at 6-12 weeks 'gestation and increasing rapidly after 30-34 weeks' gestation[6], in line with the article which states that Hb and Hematocrit (Hct) concentrations are usually decreases during the first trimester and reaches the lowest level at the end of the second trimester and increases again during the third trimester of pregnancy. The decrease in hemoglobin concentration in the second trimester was more evident in mothers who were not anemic than anemic mothers [5].

The high prevalence of anemia in pregnant women is caused by several risk factors, including gestational age at the first ANC. This statement is in line with research that states that LBW is more common in pregnant women who do not do ANC [11], in developing countries about one third of pregnant women do ANC for the first time after 20 weeks of pregnancy, mild anemia is noted at gestational age ≤ 20 weeks does not affect birth outcomes, but if recorded after 20 weeks' gestation can increase the risk of newborn death, while moderate / severe anemia if recorded at gestational age ≤ 20 weeks will increase the risk of neonatal death and low birth weight and if recorded after 20 weeks' gestation, it will increase the risk of newborn death. Recording the condition of the pregnant woman at the time of ANC, so that when a pregnant woman performs

ANC at the beginning of pregnancy then results show that she is anemic, she is expected to be able to improve her anemic condition [4]. As many as 28.3% of pregnant women in Indonesia have their pregnancies examined at 4 months or more, so that if anemia occurs in the first trimester of pregnancy, anemia will not be detected so that it continues in the next trimester [4] [11]. The coverage of iron tablet consumption in Indonesia is also still low, which is 38.1% [3]. This condition is a risk factor for anemia because 80% of women will receive IFA supplements or iron tablets through the ANC and IFA related to decrease in anemia by 185. Non compliance with IFA is a factor in the occurrence of anemia [11]. Maternal age is a risk factor of anemia [12], in Indonesia the highest prevalence of anemia in pregnancy at the age of 15- 24 years (84,6%) [3]. In adolescence tends to occur anemia because of unpreparedness of mothers in accepting pregnancy and including the implementation of Antenatal care [13]. In addition to young age, anemia also occur a lot in old age whereas the health level of uterus has decrease and the mother has blood loss in previous labor and menstruation [9]. Indeks of low Body Mass ($<18 \text{ kg} / \text{m}^2$) can cause iron deficiency and other micronutrients, causing high anemia levels. High BMI also has a greater adverse impact on maternal health and affects neonatal health through changes in glucose homeostasis, which leads to fetal macrosomia and other pathophysiological mechanisms [4], so it is necessary to maintain maternal weight at the limit normal. Improving maternal nutrition can provide greater benefits to increase birth weight [4]. It is estimated that the increase in birth weight on average 100 g babies is associated with a reduction in neonatal mortality of 30-50% [11]. Women with high parity can also cause anemia, because iron reserves are reduced due to repeated pregnancies [7] [14]. LBW is more common in infants whose parents have a lower education level compared to secondary education or higher education, because education affects the mother's knowledge and attitudes towards her condition [11].

Anemia in each trimester and Low Birth Weight

Low Birth Weight incidence increases with increasing severity of anemia in each trimester. Anemia in the first trimester increases the risk for cesarean section. Prevention of anemia in the first trimester is very important to reduce the rate of cesarean section. This condition can occur if anemia continues in the second and third trimesters [7], this result is supported by an article stating that low hemoglobin concentrations in the first trimester are the factors that most influence LBW [15]. A different statement was obtained from another article stating that in the first trimester anemia did not affect the incidence of low birth weight because anemia would improve in the second and third trimesters if handled appropriately [10] [4]. Anemia in the second and third trimesters will increase the incidence of low birth weight and preterm birth [7], according to another article that mentions an increased incidence of preterm birth and low birth weight seen if the mother has anemia in the second and third trimesters. Decreasing hemoglobin in women in the second trimester is physiological, but will continue with low birth weight babies if not handled properly, so iron supplementation earlier and maintaining optimal Hb (10-12 g / dl) during pregnancy has overall results better regarding preterm birth and low birth weight [10].

Anemia can directly cause the growth of the baby in the womb to be bad because of inadequate oxygen flow to the placental tissue which causes low infant weight and maternal nutritional deficiencies [11], in line with Menon's research that babies born of pregnant women who are not anemic in the second trimester have greater weight, height, and head circumference compared to babies who are anemic [16] and pregnant women who are not anemic are associated with birth weight values higher babies [5]. The impact of anemia in the third trimester is the occurrence of low birth weight. This condition is due to rapid fetal growth occurring in the third

trimester of pregnancy, so that in the third trimester increases the need for iron and other micronutrients [5]. In addition, anemia in the third trimester is also the pathophysiology of premature and neonatal death [14]. Anemia causes chronic hypoxia in the mother and the baby has fetal distress, this condition increases the release of corticotropin hormone (CRH) which causes premature birth and increases infection in the mother [17]. Different results were found in another article stating that there was no correlation between fetal weight and anemia in the second and third trimesters, this researcher revealed that treatment of anemia before and in the early stages of pregnancy correlated directly with better fetal outcomes [15]. Maternal hemoglobin concentrations of 10-13 gr / dl are considered optimal concentrations for fetal growth and fetal well-being and are associated with the lowest risk of low birth weight. But there is an interesting thing that mothers who are not anemic or with high hemoglobin concentrations in each trimester of pregnancy can give poor perinatal results and mothers who are anemic or low hemoglobin concentrations in each trimester of pregnancy can provide good perinatal results [7]. This can be seen in the article fetus and restrict fetal growth [4]. Increased blood viscosity at high hemoglobin concentrations can also create placental infarction. Placental infarction can cause intrauterine growth retardation and perinatal death. Second, excessive iron intake can contribute to oxidative stress, which can cause lipid peroxidation and damage to placental cell DNA. Third, excess iron can produce free radicals [7] and damage the systemic response to inflammation and infection [8]. Anemia in each trimester of pregnancy can also provide the possibility of giving birth to a baby with a normal birth weight. When the hemoglobin concentration decreases, there will be an increase in the total number of erythrocytes, but the plasma volume during pregnancy is estimated to increase more than the increase in the number of erythrocytes, perfusion or flow to the placenta is better, supported by decreased blood viscosity so that gas exchange and nutrition the fetus becomes smoother [7].

Impact of Low Birth Weight

The impact of low birth weight can occur both short and long term. Children with low birth weight have higher perinatal mortality and morbidity than children with normal birth weight [4]. The rate of newborn deaths, neonatal deaths, and low birth weight babies increased with increasing anemia severity and with a lower BMI. LBW is at high risk for becoming a dwarf adult [4]. About 8% of newborns have an APGAR score of less than 8 if born to mothers with anemia, this occurs because of poor placental and neonatal development due to previous anemia which causes an inadequate supply of oxygen to the fetus [12]. LBW babies also cause, psychological immaturity so that the level of emotional and social interaction is bad when adult. This is in line with research that states that babies of pregnant women who are not anemic in the third trimester have higher alertness and social interaction abilities than babies who are anemic [16]. In addition, the adverse effects of low birth weight can cause cognitive impairment, low IQ, neurodevelopmental disorders that cause mental retardation, impaired growth and many chronic diseases that appear later [4] [15].

4. CONCLUSION

Anemia in each trimester of pregnancy has a different effect on the incidence of low birth weight. The severity of anemia will affect the severity of low birth weight, because anemia causes an inadequate supply of oxygen to the fetus. Anemia in the first trimester does not affect the incidence of low infant weight as long as an immediate supplement is added to blood, but can affect pregnancy if anemia continues until the second and third trimesters, anemia in the second and third trimesters can affect premature and low birth weight. But the most influential for LBW is all in the third trimester where fetal growth is maximal at the end of the trimester. Abnormal

Hemoglobin concentration (anemia and high hemoglobin concentration) increases the risk of adverse birth outcomes such as low birth weight (LBW), so it is very important to check hemoglobin concentration in the mother to be able to achieve normal hemoglobin concentration during pregnancy.

5. ACKNOWLEDGMENTS

The author would like thank to Nidatul Khofiyah, S.Bid.,Bd.,MPH and Dewi Rokhanawati, SSiT.,MPH as the supervisor in completing the systematic Literature Review.

REFERENCES

- [1] UNICEF. Low Birth weight: Country, regional and global estimates. UNICEF; New York, NY, USA: 2004
- [2] Aboye, W (2018) 'Prevalence and associated factors of low birth weight in Axum town, Tigray, North Ethiopia.', BMC research notes. BioMed Central, 11(1), p. 684. doi: 10.1186/s13104-018-3801-z.
- [3] Riskesdas (2018) Hasil Riset Kesehatan Dasar
- [4] Patel, A (2018) 'Maternal anemia and underweight as determinants of pregnancy outcomes: cohort study in eastern rural Maharashtra, India.', BMJ open, 8(8), p. e021623. doi: 10.1136/bmjopen-2018-021623.
- [5] Moghaddam Tabrizi, F. and Barjasteh, S. (2015) 'Maternal Hemoglobin Levels during Pregnancy and their Association with Birth Weight of Neonates.', Iranian journal of pediatric hematology and oncology, 5(4), pp. 211–7. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/26985354> (Accessed: 10 December 2018).
- [6] Chesley, L. C. (1972) 'Plasma and red cell volumes during pregnancy.', American journal of obstetrics and gynecology, 112(3), pp. 440–50. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/4551251> (Accessed: 10 December 2018).
- [7] Vural, T (2016) 'Can anemia predict perinatal outcomes in different stages of pregnancy?', Pakistan Journal of Medical Sciences, 32(6), pp. 1354–1359. doi: 10.12669/pjms.326.11199.
- [8] Dewey, K. G. and Oaks, B. M. (2017) 'U-shaped curve for risk associated with maternal hemoglobin, iron status, or iron supplementation', The American Journal of Clinical Nutrition, 106(Supplement 6), p. 1694S–1702S. doi: 10.3945/ajcn.117.156075.
- [9] Haidar, J. (2010) 'Prevalence of anaemia, deficiencies of iron and folic acid and their determinants in Ethiopian women.', Journal of health, population, and nutrition, 28(4), pp. 359–68. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20824979> (Accessed: 7 December 2018).
- [10] Ganesh Kumar, S (2010) 'Determinants of low birth weight: A case control study in a district hospital in Karnataka', The Indian Journal of Pediatrics, 77(1), pp. 87–89. doi: 10.1007/s12098-009-0269-9.
- [11] Balarajan, Y., Subramanian, S. V. and Fawzi, W. W. (2013) 'Maternal Iron and Folic Acid Supplementation Is Associated with Lower Risk of Low Birth Weight in India', The Journal of Nutrition, 143(8), pp. 1309–1315. doi: 10.3945/jn.112.172015.
- [12] Ahankari, A. S (2017) 'Risk factors for maternal anaemia and low birth weight in pregnant women living in rural India: a prospective cohort study', Public Health, 151, pp. 63–73. doi: 10.1016/j.puhe.2017.06.023.
- [13] Alizadeh. (2014) 'Impact of maternal hemoglobin concentration on fetal outcomes in adolescent pregnant women.', Iranian Red Crescent medical journal. Kowsar Medical Institute, 16(8), p. e19670. doi: 10.5812/ircmj.19670.
- [14] Bencaiova, G. and Breymann, C. (2014) 'Mild anemia and pregnancy outcome in a Swiss collective.', Journal of pregnancy. Hindawi Limited, 2014, p. 307535. doi: 10.1155/2014/307535.

- [15] Bakacak, M (2015) 'The effect of maternal hemoglobin concentration on fetal birth weight according to trimesters.', *The journal of maternal-fetal & neonatal medicine: the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians*, 28(17), pp. 2106–10. doi: 10.3109/14767058.2014.979149.
- [16] Menon, K. C(2016) 'Effects of anemia at different stages of gestation on infant outcomes.', *Nutrition (Burbank, Los Angeles County, Calif.)*, 32(1), pp. 61–5. doi: 10.1016/j.nut.2015.07.009.
- [17] Allen, L. H. (2009) 'Provision of Multiple Rather Than Two or Fewer Micronutrients More Effectively Improves Growth and Other Outcomes in Micronutrient-Deficient Children and Adults', *The Journal of Nutrition*, 139(5), pp. 1022–1030. doi: 10.3945/jn.107.086199.
- [1]