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Analysis of Ferritin Serum in Anemia Pregnant Woman

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ABSTRACT

Anemia remains a common comorbidity complicating over 28% of pregnancy in Indonesia by 2023, Iron deficiency anemia is the most common, and to date, ferritin serum has been used as a diagnostic marker, but has not been routinely examined in pregnant women, thus hindering the accurate diagnosis of iron deficiency anemia in pregnant women. Our study aimed to examine ferritin serum among pregnant women, as well as, to investigate the prevalence of iron deficiency anemia in the Dalu Sepuluh Health Center of Deli Serdang Regency. A total of 60 pregnant women were randomly selected to participate in this cross-sectional study. We found that iron deficiency anemia was most common in pregnant women aged 20 – 35 years old (75%), with second-trimester pregnancy (36.7%), multigravida, and multiparity. Interestingly, 57% of pregnant women were considered malnourished (upper arm circumference of < 23.5 cm) which was found in 36.7% of primigravida and is associated with moderate iron deficiency anemia (71.4%), marked with < 30µg/L ferritin serum ($p < 0.05$). Cut-off point of serum ferritin was 28.98 ng/dL with a sensitivity of 92% and a specificity of 91.4%, indicating that the body's iron levels are in low condition. This study indicated that lower levels of ferritin serum are associated with anemia in pregnant women. We suggested that ferritin serum be put as a mandatory routine examination in pregnancy.

Keywords: *Ferritin Serum, Iron Deficiency Anemia, Nutritional Status, Prevalence, Pregnant Women*

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INTRODUCTION

Increased blood supply is required to facilitate fetal growth during pregnancy. Unfortunately, a pregnancy that is complicated by anemia hinders sufficient fetal growth as the red blood cells containing haem are not adequate. The nature of the pregnancy itself puts pregnant women at an increased risk of developing anemia, as the demand for hemoglobin, iron, and overall circulation are known to be higher during pregnancy. The World Health Organization (WHO, 2016) defines anemia as a condition in which the number, size, and concentration of hemoglobin is below the cut-off value leading to decreased capacity of oxygenation throughout the tissues.

Anemia has been remained a major global health issue in highlighted the global prevalence of anemia in pregnant women at around 40%, with the highest burden in low- and middle-income countries. Factors contributing to this include such as iron deficiency, responsible for about 50–60% of anemia cases during pregnancy, Infections such as malaria and hookworm, and Dietary deficiencies in folate, vitamin B12, and vitamin A (Zhou et al., 2024).

The prevalence of pregnancy with anemia in Indonesia reached 48.9% in 2018 and decreased to 27.7% in 2013 (BKPK, 2018). The Indonesian Health Survey in 2023 mentioned that nearly 28% of pregnancy cases were complicated by anemia or the same as 3 out of 10 pregnant women with anemia. Furthermore, up to 17% of these pregnant women were chronically malnourished (Kemenkes, 2024). When these numbers are compared to the global prevalence, the trend was also seen to decrease by 9% from the initial prevalence of 37% in 2019 (WHO, 2019).

Anemia in pregnant women can lead to fatigue, increased susceptibility to infections, and higher risks of complications during childbirth. Severe anemia is associated with maternal mortality due to conditions like postpartum hemorrhage. It also reduces work capacity and overall quality of life, reflecting broader health disparities in affected populations(Zhou et al., 2024). Meanwhile for the fetus, maternal anemia increases the risk of preterm delivery, low birth weight, and perinatal mortality. Insufficient iron during gestation can impair fetal brain development, leading to long-term cognitive and developmental issues. These outcomes not only affect individual families but also contribute to broader public health challenges and economic burdens Other theories also say that persistent anemia during pregnancy increases the risk of abortion, intrauterine growth defect, premature labor, infection, premature rupture of the membrane, antepartum bleeding, prolonged labor, uterine subinvolution which may lead to postpartum hemorrhage, and puerperium infection, as well as decreased production of breast milk (Kemenkes, 2024).

Studies showed that anemia during pregnancy is more likely to be caused by iron deficiency. Iron is an essential element in forming hemoglobin. Iron deficiency anemia is most commonly marked by the reduction of ferritin, an intracellular protein that serves as the reservoir of iron, ready to release iron when needed. In addition, ferritin also plays a role in regulating iron homeostasis and as a depiction of iron stores and systemic inflammation in the body (Oh, Lee, Kim, & Lim, 2018).

Ferritin is synthesized in the liver and spleen, where its production is regulated at the post-transcriptional level through interaction with iron-responsive elements in the mRNA so that the rate of intracellular ferritin synthesis remains constant (Oh et al., 2018). Large amounts of ferritin are intracellular, and only a small fraction of total body ferritin is found in serum. Some of it is carried into the circulation derived from dead cells and actively secreted in the absence of apoptosis, so it can be used roughly as a surrogate for whole-body iron storage provided that the rate of iron flux in and out of the circulation is constant (Kell & Pretorius, 2014).

Based on several studies, it is known that normal serum ferritin in pregnant women ranges > 30 µg / L (Milman N, Agger AO, 1992 and Kaufer & Casaneuva, 1990). Although hemoglobin and ferritin concentrations are both markers of iron deficiency, there are differences between them. Hemoglobin level is the last marker of iron deficiency but cannot reflect tissue iron status. However, serum ferritin (SR) is generally considered the best measure of iron deficiency in pregnancy. Decreased serum ferritin levels are an early marker of iron deficiency, and are not affected by recent iron consumption. (Adediran et al., 2011)(Santosa, Siahaan, Amri, & Yuwono, 2022). Some studies explain that the rise and fall of serum ferritin is related to Haemoglobin. Therefore, it is necessary to know how serum ferritin levels in anemic pregnant women.

RESEARCH METHODOLOGY

This type of research is analytic observational with a cross-sectional design. The population of all pregnant women with anemia from 2022 to 2023 was 149 people. Calculate the sample size using the Slovin formula obtained by 60 respondents. Inclusion criteria are pregnant women with anemia, exclusion of pregnant women with other diseases such as infection, TB, malaria, hypertension, diabetes, etc. Sampling was carried out using Random Sampling. The research location was in the working area of Puskesmas Dalu Sepuluh, Deli Serdang Regency. The research activities were carried out for six months, assisted by trained health cadres to measure LILA (upper arm circumference) and Prodia Medan laboratory officers who played a role in taking blood samples of pregnant women. The hemoglobin examination was conducted using the cyanmethemoglobin method using a spectrophotometer. The serum ferritin examination was conducted using the ELISA (enzyme-linked immunoassay) method because has high sensitivity and specificity, ability to measure low levels of ferritin and standardized and widely used in research and clinical settings. This method is common in research and diagnostic laboratories for precise quantification.

Blood collection for this examination was carried out in the morning, then blood samples were taken to the laboratory. Before blood sampling, informed consent was obtained from the respondents. Bivariate tests were performed using Chi-Square. The study was conducted after obtaining approval from the Ethics Committee of the Poltekkes Kemenkes Medan with number 201.1706.

RESULT AND DISCUSSION

Result

Based on our study conducted in the working area of Puskesmas Dalu Sepuluh Deli Serdang Regency on pregnant women who come to visit health facilities to get ANC (Ante Natal Care) services such as Puskesmas, Polindes, Midwife Independent

Practice, and Posyandu, the age of pregnant women stratified by their gestational age is shown in Table 1 below.

Table 1. Age of pregnant women stratified by the gestational age (trimester) at Puskesmas Dalu Sepuluh

Age (years)	**Gestational age (trimester)**						**Total**	
	I		**II**		**III**			
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
< 20	2	3,3	1	1,7	5	8,3	8	13,3
20 – 35	6	10	22	36,7	17	28,3	45	75
>35	0	0	5	8,3	2	3,3	7	11,7
Total (n)	8	13,3	28	46,7	24	40	60	100

Based on Table 1, it can be seen that of the 60 respondents, the majority of pregnant women with anemia were aged in the range of 20 - 35 years (75%) and the gestational age in the second trimester (36.7%). The proportion of pregnant women aged > 35 years who made ANC visits was the smallest proportion at 11.7%. Likewise, anemic pregnant women aged <20 years were still found at 13.3% and their gestational age was in the third trimester. The next table describes the age of mothers based on pregnancy count as follows.

Table 2. Age of pregnant women stratified by their pregnancy count at Puskesmas Dalu Sepuluh

Age (years)	**Pregnancy count**						**Total**	
	primi		**multi**		**grande**			
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
< 20	6	75	2	25	0	0	8	100
20 – 35	14	31,1	30	66,7	1	2,2	45	100
>35	0	0	6	85,7	1	14,3	7	100

Based on Table 2, it is known that pregnant women with the age of < 20 years the majority have a history of primigravida pregnancy (first-time pregnancy) by 75%. Meanwhile, among pregnant women aged 20 - 35 years, the majority had a history of multigravida pregnancy (3 - 4 pregnancies) 66.7%, as well as at the age of the mother > 35 years was 85.7%. Therefore, it is necessary to know how the history of pregnancy with childbirth (parity) which will explain whether there is a match between the pregnancy history of pregnant women based on parity as in Table 3 below.

Table 3. Pregnancy and parity count at Puskesmas Dalu Sepuluh

Pregnancy counts	Parity counts								Total	
	0		1		3 – 4		>4			
	n	%	n	%	n	%	n	%	n	%
primigravida	18	90	2	10	0	0	0	0	20	100
Multigravida	5	13,3	16	42	17	44,7	0	0	38	100
Grandemulti gravida	0	0	0	0	1	50	1	50	2	100

Based on Table 3, it is known that 90% of pregnant women with a history of primigravida pregnancy have no history of giving birth (nullipara). For pregnant women with a history of multigravida pregnancy the majority have given birth 3 - 4 times (multiparous) amounting to 44.7% and only a small portion of 13.3% have never given birth to a child either alive or dead. Likewise, with grand multigravida, pregnant women both have parity 3 - 4 times or > 4 (grand multipara) around 50%. Table 4 describes the nutritional status of pregnant women using the LILA measure based on pregnancy counts as follows.

Table 4. LILA measure based on the pregnancy counts at Puskesmas Dalu Sepuluh

LILA (cm)	Pregnancy counts						Total	
	primi		multi		grande			
	n	%	n	%	n	%	n	%
< 23,5	4	57	3	43	0	0	7	100
≥ 23,5	16	30	35	66	2	4	53	100

Based on Table 4 above, it is known that pregnant women with LILA size < 23.5 cm are mostly with a history of primigravida pregnancy (57%). LILA size > 23.5 cm was found in the majority of pregnant women with a history of multigravida pregnancy (66%) and a small portion of only 4% with grand multigravida. Furthermore, table 5 explains the size of LILA with the degree of anemia based on the results of Hb measurement of pregnant women as in Table 5 below.

Table 5. LILA measure and severity of anemia at Puskesmas Dalu Sepuluh

LILA (cm)	Severity of anemia						Total	
	light		moderate		heavy			
	n	%	n	%	n	%	n	%
< 23,5	2	28,6	5	71,4	0	0	7	100
≥ 23,5	23	43,4	30	56,6	0	0	53	100

Based on Table 5, it is known that in pregnant women with LILA size < 23.5 cm, about 71.4% experienced moderate anemia. Meanwhile, about 56.6% of pregnant women with LILA > 23.5 cm experienced anemia. The average Hb of pregnant women was 9.71 g/dl with ±0.8949, where the lowest Hb was 7.5 g/dl and the highest was 10.9 g/dl. Table 6 below describes the serum ferritin levels of pregnant women with the degree of anemia of pregnant women. This study only measured serum ferritin in anemic pregnant women. Pregnant women who were not anemic haven't been sampled in this study, so the result just showed serum ferritin in anemia pregnant women.

Table 6. Serum ferritin levels and severity of anemia at Puskesmas Dalu Sepuluh

Serum Ferritin	Severity of anemia						Total	
	light		moderate		heavy			
	n	%	n	%	n	%	n	%
≥ 30 µg/L	9	100	0	0	0	0	9	100
< 30 µg/L	16	31,4	35	68,6	0	0	51	100

Based on Table 6, it is known that serum ferritin levels of pregnant women ≥ 30 µg/L 100% have mild anemia. In contrast serum ferritin levels of pregnant women < 30 µg/L about 68.6%. The average serum ferritin level of pregnant women with anemia is 29.11 µg/L ± 1.9621. The minimum value of serum ferritin levels of anemic pregnant women in the study ranged from 26.50 µg/L and a maximum of 35.67 µg/L. Based on the Chi-Square test results, it is known that $p < 0.05$ indicating that there is a significant relationship between serum ferritin levels and the degree of anemia in pregnant women.

Discussion

One interesting thing from Table 1 is that there are still pregnant women aged < 20 years at 13.3% and > 35 years at 11.7% with gestational age in the second and third trimesters. The largest proportion of pregnant women who experienced anemia in the second trimester of pregnancy was 46.7%. It can be assumed that there is a tendency to increase the incidence of anemia as the gestational age increases. The second trimester of pregnancy has a higher chance of anemia compared to those in the first and third trimesters. This is because there is an increase in plasma volume, while hemoglobin and hematocrit levels decrease during the first trimester and reach their lowest levels at the end of the second trimester and will increase again during the third trimester of pregnancy (Ayensu, Annan, Lutterodt, Edusei, & Peng, 2020). Therefore, this is the right time to give/consume iron supplementation at a dose of 30 mg/day as the gestational age enters the 12th week (beginning of the second trimester), when the iron requirement for pregnancy begins to increase. (Kemenkes RI, 2023);(Melati Davidson, Tampubolon, Berlyana Bornensiska, Satya Wacana, & Studi Ilmu Keperawatan Universitas Kristen Satya Wacana, 2022). Administration of iron at a dose of 60 to 120 mg/day is an exception if indicated based on laboratory results of anemia that have been set at each stage of gestation, namely trimester I < 11gr / dl, trimester II < 10.5 gr/dl and trimester III < 11 gr/dl (Kemenkes RI, 2023). The dose should be decreased to 30 mg/day if the hemoglobin concentration is within the normal range for the stage of pregnancy (Kemenkes RI, 2023).

The possibility of anemia occurring in respondents in this study can be caused by several things including respondents' non-compliance in taking Fe tablets, and concurrent consumption of Fe tablets with food or drinks that inhibit Fe absorption by the body(Nartey et al., 2023). In addition, pregnant women who are too young (< 20 years) and too old (> 35 years) have a risk of being prone to anemia. This is in line with the results of Riskesdas in 2013 and the results of Sari, et al's research which found that too young and old age are at risk for anemia(Badan Penelitian Dan Pengembangan

Kesehatan Republik Indonesia, 2018); (Sari, Fitri, & Dewi, 2021). Another assumption is that pregnant women at the age of lower than 20 years may be divided by iron consumption with the fetus so that it is not sufficient because biologically the body still needs adequate iron for the growth of the mother, as well as at the age of > 35 years, it is thought that they have entered the early degenerative phase, so that body functions are not optimal and experience various health problems that require iron as part of the body's immunity (Sari et al., 2021).

Likewise in Table 2, it can be explained that the risk of anemia is high in multigravida pregnancies, this is due to the possibility of pregnant women having experienced anemia in previous pregnancies. In addition, as in Table 3, it was found that most pregnant women with multigravida had a history of multipara and grand multipara. We assumed that biological conditions like this require high iron intake, so that high parity coupled with close or frequent pregnancy spacing causes iron reserves in the body to automatically decrease because the pregnancy will attract and absorb more iron supplies in the body, thus anemia in pregnant women will continue to recur. The results of this study are in line with other studies which found that pregnant women with parity 3 and above are more prone to anemia than parity 0. The risk of blood loss will affect hemoglobin so that Hb levels decrease in mothers who often give birth with the assumption that the amount of iron decreases by up to 250 mg each time they give birth.(Indriani, 2019);(Ririn Riyani, Siswani Marianna, & Yoanita Hijriyati, 2020);(Wahyuni, Farianingsih, & Rohmatin, 2023).

This study found the largest proportion of pregnant women with primigravida (57%). According to the author's assumption, it is likely that most primigravida are in the age group < 20 years. This is likely due to the mother's experience in the first pregnancy that has never experienced before, besides the previous nutritional status, the emotional and health of the mother plays a role in the adequacy of iron needed during pregnancy and ultimately determines the quality of the baby when born as well as subsequent growth and development. The results of this study are in line with other studies that found the risk of chronic malnutrition to be more prevalent in primigravida women aged <20 years. (Indriani, 2019);(Ririn Riyani et al., 2020);(Wahyuni et al., 2023);(Farahdiba, 2021).

Our study is in line with the Indonesian Health Survey in 2023 which highlighted that chronic malnutrition plays an important role in increasing the risk of anemia (BKPK, 2024). Other studies pointed out that pregnant women with chronic malnutrition generally have a higher risk of anemia than mothers who do not experience it. This is due to an imbalance in macronutrient and micronutrient intake. Micronutrients, especially iron, that are not fulfilled in women with chronic malnutrition cause the expansion of blood cells during pregnancy is not optimal. Lack of other micronutrients such as vitamin C, vitamin B9, and B12 can hamper iron absorption. If some of the vitamins above can be fulfilled, the iron absorption process is more effective so that it can increase hemoglobin levels in the blood (Farahdiba, 2021). Pregnant women who did not experience chronic malnutrition, but are too young or too old, are also multigravida multipara, or grand multipara, are also exposed to increased risk of anemia regardless of their nutritional status. It can be seen that pregnant women with anemia in this study are most likely due to iron deficiency in the body. This study is in line with other studies that show a tendency to decrease serum ferritin levels in iron deficiency anemia (Tarancon-Diez et al., 2022);(W.H.O Geneva, 2020). This study is in line with the cut off point of serum Ferritin value if < 15 – 30 ng/mL is considered a strong indication of iron deficiency anemia. Ferritin levels below this range indicate low iron reserves in the body (Omuse, Chege, Kawalya, Kagotho, & Maina, 2022).

In this study showed that cut-off point of serum ferritin was 28.98 ng/dL with a sensitivity of 92% and a specificity of 91.4%, which means if the serum value of ferritin is between 28.98 – 30 µg/mL, it is likely that the person has iron deficiency anemia. Based on cut – off point in this study showed that cut off point of serum ferritin, its sensitivity was quite high (92%) and its specificity in the range of 89 – 92%, indicating that the body's iron levels are in low condition. This is in line with another study that found that the most optimal serum ferritin cut off is <45µg/L, with a sensitivity of 85% and a specificity of 92%(Jäger et al., 2024).

Serum ferritin levels under normal circumstances are a sensitive marker for iron status in the body. However, in inflammatory conditions, ferritin is also an acute phase reactant that can increase in response to inflammation, in which case it will be difficult to assess iron stores, for example in chronic kidney disease, and chronic heart failure then iron deficiency is very high. Therefore, in these conditions, the cut-off of serum ferritin level is different from normal which is < 100 µg/L (Tarancon-Diez et al., 2022);(W.H.O Geneva, 2020);(Galetti et al., 2021). Examination of serum ferritin levels is based on WHO recommendations serum ferritin is used as a good marker of iron stores and can be used to diagnose iron deficiency in apparently healthy individuals. Serum ferritin levels in children with infection or inflammation, i.e. below 30 µg/L, adults < 70 µg/L can be used to indicate iron deficiency (W.H.O Geneva, 2020).

Iron metabolism is primarily aimed at hemoglobin formation. The main source for reutilization is mainly from old erythrocyte hemoglobin that is destroyed by macrophages of the reticuloendothelial system. Under balanced conditions, 25 ml of erythrocytes, equivalent to 25 mg of iron, are phagocytosed by macrophages every day, but just as many erythrocytes will be formed in the bone marrow or iron will be released by macrophages into the blood circulation every day. Iron from food sources absorbed by the duodenum ranges from 1-2 mg, that much can also be lost due to skin desquamation, sweat, urine, and feces (Bouri & Martin, 2017);(Kotla, Dutta, Parimi, & Das, 2022).

Iron deficiency anemia is anemia caused by reduced body iron reserves. This situation is characterized by decreased transferrin saturation, and reduced bone marrow ferritin or hemosiderin levels, causing iron deficiency which consists of three stages, starting from the mildest stage, namely the platen stage (iron depletion), then the latent stage (iron deficient erythropoesis) and the iron deficiency anemia stage (iron deficiency anemia). The first stage has a decrease in serum ferritin of less than 12µg/L and iron in the bone marrow is empty or one positive, while other components such as total iron binding capacity (TIBC), serum iron (SI), transferrin saturation, RDW, MCV, hemoglobin, and blood cell morphology are still within normal limits, and is called the iron depletion stage. The second stage has a decrease in serum ferritin, serum iron, transferrin saturation, and iron in the empty bone marrow, but TIBC increases >390 µg/dl. Other components are still normal and are called iron deficiency erythropoiesis. The third stage is called iron deficiency anemia, which is a severe stage of iron deficiency and is characterized in addition to decreased serum ferritin and hemoglobin levels (Tarancon-Diez et al., 2022);(W.H.O Geneva, 2020);(Peng & Uprichard, 2017);(Huang, Li, & Tsai, 2023). Based on the explanation above, it can be understood that if pregnant women experience iron deficiency, the body cannot produce enough hemoglobin. Meanwhile, hemoglobin plays a role in transporting oxygen to be distributed to all body tissues so that its needs are not adequately met, which in turn can inhibit the growth of the fetus inside (Bouri & Martin, 2017).

CONCLUSION

The results of this study found that there was a tendency for decreased serum ferritin levels in pregnant women with anemia. The higher the degree of anemia, the lower the serum ferritin level. This study showed cut-off point of serum ferritin was 28.98µg/dL, described a fairly high sensitivity and specificity diagnosing that anemia pregnant women have iron deficiency Especially in pregnant women with too young or old age, and a history of multiple pregnancies and childbirth are at higher risk of developing anemia during pregnancy. This study recommends that examination of body iron reserves through serum ferritin is needed to confirm iron deficiency anemia in pregnant women as per WHO recommendations.

By measured serum ferritin will provide a clear picture of iron status, it allows healthcare providers to implement timely and appropriate interventions. This not only safeguards maternal health but also ensures optimal fetal development, reducing risks for both mother and baby. Integrating serum ferritin analysis into standard prenatal care can significantly enhance health outcomes and improve the overall quality of maternity services.

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