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Compliance with Iron Supplementation Consumption in Pregnant Women on Hematological Profiles and Ret-He

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ABSTRACT

Fetal growth will increase the mass of maternal and fetal erythrocytes resulting in an increase in iron requirements, causing a decrease in maternal iron stores. A decrease in iron in the body will disrupt the formation of hemoglobin, because one of the components that forms it is heme which contains iron. the aim of our research is to study the compliance of pregnant women in consuming iron supplements regarding hematological features and body iron reserves through the Ret-He examination. This research is a cross-sectional study in 30 pregnant women for complete blood count (CBC), Ret-He and estradiol. There were differences in the concentrations of Hgb and MCHC (P-value < 0.05) and there were no differences in the concentrations of Hct, RBC, MCV, MCH, RDW, Ret-He and estradiol (P-value > 0.05). It was found that there was a relationship between estradiol and Hgb (P-value = 0.047; r = 0.366). Pregnant women who do not comply with taking iron supplements experience a decrease in Hgb and MCHC. The decrease in Hgb levels is strongly correlated with E2 levels in pregnant women who adhere and do not comply with iron supplementation.

INTRODUCTION

Pregnancy is known to induce iron deficiency anemia due to increased iron requirements (Georgieff 2020). These changes occur due to physiological changes during pregnancy and one of them is hormonal factors (Pascual and Langaker 2023). One of the hormones that plays a role in controlling metabolism during pregnancy is estradiol (E2). Plasma E2 levels increase gradually as pregnancy progresses (Liebmann et al. 2022).

Fetal growth will increase the mass of maternal and fetal erythrocytes resulting in an increase in iron requirements, causing a decrease in maternal iron stores (Nugraha et al. 2019). If this condition is left unchecked, pregnant women will experience iron deficiency and even develop iron deficiency anemia. Therefore, if this condition does not receive special attention, it can disrupt the development of the fetus which can lead to congenital defects, prematurity, low birth weight (LBW), anemia in babies and even death of the baby.

The need for iron in the first trimester is 800 µg/day and increases to 7500 µg/day with the estimated need for iron during pregnancy being 1000 to 1200 mg (Nugraha et al. 2023). Therefore, pregnant women are required to consume foods with high iron content. To compensate for this need, pregnant women will be given iron supplementation.

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However, there are still many pregnant women who do not comply with iron consumption, which can have an impact on reducing pregnant women's iron stores. A decrease in iron in the body will disrupt the formation of hemoglobin, because one of the components that forms it is heme which contains iron (Ems, Lucia, and Huecker 2023). Hemoglobin synthesis in cases of iron deficiency anemia can affect erythrocyte morphology, which can result in changes in hematological examination (Warner and Kamran 2017).

In this regard, the aim of our research is to study the compliance of pregnant women in consuming iron supplements regarding hematological features and body iron reserves through the Ret-He examination.

MATERIALS/METHOD

Research design and sampling

This research is a cross-sectional study. A total of 30 pregnant women were taken from the Jagir Community Health Center (Puskesmas), Surabaya, Indonesia. The inclusion criteria for pregnant women in this study were the woman's informed consent to participate in the research and being declared healthy by the midwife. The exclusion criterion is a leukocyte count of more than 13 x 103/µL. Data collection was carried out during May 2023. The research was approved by the research ethics commission of Nahdlatul Ulama University Surabaya with No. 0074/EC/KEPK/UNUSA/2023. The confidentiality of subjects' personal information is protected throughout the study.

Examination methods

Compliance with iron supplement consumption was carried out using a questionnaire. Blood samples from pregnant women were collected from the antecubital fossa vein, 6 mL of venous blood was taken from each pregnant woman. A total of 3 mL of blood was put into a tube containing K2-EDTA and sent for complete blood count (CBC) examination using a Hematology Analyzer (XN-300 Series, Sysmex Corporation, Kobe, Japan) includes inspection hemoglobin (Hgb), hematocrit (Hct), red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) dan red cell distribution width (RDW). Ret-He using a Hematology Analyzer (XN-Series 1000, Sysmex Corporation, Kobe, Japan).

The remaining 3 mL was put into a plain tube and left for at least 1 hour at room temperature until it coagulated, then centrifuged at 3000 rpm for 15 minutes at room temperature. The serum obtained was stored in closed Eppendorf tubes and kept frozen at -20°C until samples were collected for analysis. Serum was used to examine E2 levels using the enzyme-linked immunosorbent assay (ELISA) method (Bioassay Technology Laboratory, Shanghai Korain Biotech Co., Ltd., Shanghai, China). Measurements were carried out according to the manufacturer's instructions.

Statistic analysis

Data are presented as mean and standard deviation (SD). Samples with normal distribution were statistically analyzed using difference tests and correlation tests. All statistical tests used IBM SPSS statistics for Windows version 21.0 (IBM Corp., Armonk, NY, USA). A p-value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

A total of 30 pregnant women participated in this research with an average age of respondents of 28 (18 – 42) years. Maternal age in the first trimester of pregnancy was 7 people (23.3%), in the second trimester there were 12 people (40.0%), and in the third

trimester there were 11 people (36.7%). There were 18 pregnant women who complied with taking iron supplements (60.0%) and 12 people who did not comply with iron consumption (40.0%). The profile of hematology examination results can be seen in Table 1.

Table 1. Comparison of hematological parameters in pregnant women who adhere and do not comply with consuming iron supplements

Hematological Parameters	**Take Iron Supplements**	**Do Not Take Iron Supplements**	**p-value (2-tailed)**
Hgb (g/dL)	12,4 ± 0,7	11,4 ± 1,4	0,018*
Hct (%)	35,0 ± 2,2	33,1 ± 3,3	0,063
RBC (x 10^6/µL)	4,08 ± 0,36	3,96 ± 0,38	0,386
MCV (fL)	85,7 ± 3,7	84,0 ± 9,4	0,487
MCH (pg)	30,4 ± 1,6	29,0 ± 4,0	0,203
MCHC (%)	35,4 ± 0,8	34,5 ± 1,4	0,030*
RDW (fL)	44,1 ± 3,4	44,4 ± 4,0	0,803
Ret-He (pg)	32,9 ± 2,9	30,4 ± 5,3	0,151
Estradiol (pg/mL)	410,98 ± 170,57	311,27 ± 180,58	0,137

* p-value < 0,05

The results of hematology examination showed a decrease in hemoglobin and MCHC levels. As we know, iron is a component that forms hemoglobin, especially heme (Nugraha 2017). Heme synthesis occurs in the cytosol and mitochondria of erythrocytes, synthesis begins with glycine and succinyl coenzyme A and ends with the production of the protoporphyrin IX ring. (Sciences 1958). The binding of protoporphyrin with Fe^{2+} ions forms the final heme molecule. This final heme will then bind to the globin chain which then forms hemoglobin (Ahmed, Ghatge, and Safo 2020; Farid and Lecat 2019).

MCHC (mean corpuscular hemoglobin concentration) shows the amount of hemoglobin per unit volume. The MCHC value is determined through calculations by dividing the hemoglobin level (g/dL) by the number of erythrocytes (/µL) then multiplying by 100 (Kong et al. 2020; Sarma 1990). Thus, decreasing hemoglobin levels and a persistent number of erythrocytes will affect the MCHC value.

We found a decrease in Hgb and MCHC in pregnant women who did not consume iron, but there was no indication of iron deficiency as seen from Ret-He measurements. Ret-He is a reliable marker of cellular hemoglobin content and can be used to identify the presence of iron deficiency states (Uçar et al. 2019). In iron deficiency anemia, it generally begins with iron deficiency first and then develops into anemia (Warner and Kamran 2017). Maybe iron profile measurements need to be carried out because they are considered more sensitive (Pasricha et al. 2021).

We also tested the relationship between E2 and Hgb, Hct, RBC and Ret-He. E2 is a hormone made naturally in the human body by the ovaries (Thesen, Morck, and Zagermann 2022). A study conducted by Takakura et al (2022) reported that increasing E2 levels induces hemodilution thereby reducing Hgb, Hct and RBC (Takakura et al. 2022). If seen from the statistical tests in Table 2, E2 only correlates with Hgb (r=0.366; p=0.047) and does not correlate with hematocrit (r=0.339; p=0.067), RBC (r=0.258; p=0.169), and Ret-He (r=0.225; p=0.231).

Table 2. Correlation of Estradiol with Hgb, Hct, RBC and Ret-He

	Parameter			
	Hgb (g/dL)	**Hct (%)**	**RBC (x 10^6/µL)**	**Ret-He (pg)**
Correlation	0.366	0.339	0.258	0.225
p-value (2-tailed)	0.047	0.067	0.169	0.231

CONCLUSIONS

Pregnant women who do not comply with taking iron supplements experience a decrease in Hgb and MCHC. The decrease in Hgb levels is strongly correlated with E2 levels in pregnant women who adhere and do not comply with iron supplementation.

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