



Differences in Ferritin and Hemoglobin Levels Before and After Administration of Iron Sucrose Injection to Second or Third Trimester Pregnant Women at Araskabu Public Health Center, Deli Serdang

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Abstract

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BACKGROUND: Anemia cases in pregnant women in Indonesia are still high because pregnant women do not routinely take iron supplements or often referred as *Tablet Tambah Darah* because of the side effects it causes. An alternative to this problem is the intravenous administration of iron sucrose.

AIM: The purpose of this study was to determine differences in ferritin and hemoglobin (Hb) levels before and after administration of iron sucrose injection to pregnant women in the second or third trimester at Araskabu Public Health Center, Deli Serdang.

METHODS: This is an analytical study with a Quasi-Experimental Pre-Post Design for Second or Third Trimester Pregnant Women at Araskabu Public Health Center, Deli Serdang which was carried out in April 2022 by blood sampling and administration of iron sucrose injection intravenously, and then blood sampling was repeated 14 days after the injection in May 2022. The subjects in this study were 25 pregnant women aged 20–40 years who had antenatal care selected using the Consecutive Sampling technique. The difference in the mean of ferritin and Hb was analyzed using the paired t-test if the data are normally distributed and the Wilcoxon test if the data are not normally distributed. The results were significant if $p < 0.001$. The Mann–Whitney and Kruskal–Wallis tests were used to examine the difference between two or more sample groups. The results of the analysis were significant if $p < 0.050$.

RESULTS: The mean ferritin level before administration of iron sucrose injection to pregnant women in this study was 18.97 ± 8.284 g/L and the mean ferritin level after iron sucrose injection was 98.95 ± 18.878 g/L. The mean increase in ferritin levels after injection of iron sucrose was 79.97 ± 19.77 g/L. The mean Hb level before administration of iron sucrose injection to pregnant women in this study was 10.13 ± 0.386 g/dL and the mean Hb level after administration was 12.01 ± 0.723 g/dL. The mean increase in Hb levels after injection of iron sucrose was 1.88 ± 0.68 g/dL.

CONCLUSIONS: Iron sucrose injection can significantly increase ferritin and Hb levels.

Introduction

According to the World Health Organization (WHO) 2019, the global prevalence of anemia is 29.9% in women aged 15–49 years and 36.5% anemia is found in pregnant women of reproductive age [1]. Based on *Riset Kesehatan Dasar* (RISKESDAS) data in 2018, the prevalence of anemia in pregnant women in Indonesia was 48.9%, this number increased by 11.8% when compared to the figure in 2013 which was 37.1% [2]. The prevalence of anemia in pregnancy in North Sumatra Province in 2017 was 15–39% [3]. The Medan City Health Service report in 2018 shows data from 39,240 pregnant women, there are 780 pregnant women who experience anemia [4]. Araskabu Public Health Center had the most anemia in 2019 and 2020 were at the Araskabu Public Health Center as much as 13.11% and 11.70%, respectively [5].

Pregnancy causes physiological changes in the mother, thereby increasing the risk of anemia, which is most vulnerable starting at around 20–24 weeks of gestation. During pregnancy, there is a change in erythropoiesis, in which maternal blood volume increases sharply, especially plasma volume. There is an increase in plasma volume during pregnancy as much as 10–15% followed by an increase in erythrocyte volume. However, the increase in erythrocyte volume is not proportional to the increase in plasma volume (hemodilution) causing a decrease in hemoglobin (Hb) concentration and hematocrit. Therefore, anemia is often found in pregnant women [6].

The Hb borderline level is based on the WHO [7] and the Regulation of the Minister of Health of the Republic of Indonesia (PERMENKES no. 21 of 2021), which states that pregnant women with mild anemia have an Hb value of 10.0–10.9 g/dL, moderate anemia are 7.0–9.9 g/dL, and severe anemia are <7.0 g/dL [8]. Iron deficiency is

the most common nutritional deficiency problem and is the main cause of anemia in pregnancy. Iron deficiency anemia is present in 60% of cases and decreases to 42% in patients who have been taken iron supplementation [9], [10]. Iron requirements in the first trimester (with an increase of 0.1 mg/dL) and gradually increase in the second trimester (with an increase of 0.1–0.4 mg/dL) and the third trimester (with an increase of 0.3–0.9 mg/dL) and the postpartum period (with an increase of 1 mg/dL) [6]. Iron deficiency anemia in pregnancy is diagnosed if the blood examination found Hb <11 g/dL followed by iron reserve status (ferritin <30 ug/L).

According to the Regulation of the Minister of Health of the Republic of Indonesia no. 21 of 2021, the handling of pregnant women with anemia is by giving iron supplementation or *Tablet Tambah Darah*. Based on the 2013 RISKESDAS data, the coverage of pregnant women taking iron tablets was 89.1%. Among those who consumed iron, 33.3% consumed at least 90 days during pregnancy [2], [8]. Another treatment is by administration of intravenous iron injection. The types of preparations available are Iron Sucrose, Iron Dextran, Iron Polymatose Complex, Ferric Gluconate and Ferric Carboxymaltose [11]. Parenteral iron rapidly reaches the Hb target with few side effects and should be considered after the first trimester and in patients with bad response [12].

Iron sucrose complex is used intravenously in the treatment of iron deficiency anemia during pregnancy [13]. Iron sucrose is rapidly distributed to the bone marrow for erythropoiesis and the liver and spleen reticuloendothelial system for iron storage [14]. Several studies showed that the mean Hb and serum ferritin levels of the study were 8.54 g/dL and 7.63 ng/mL before treatment, to 12.1 g/dL and 99.0 ng/mL after treatment ($p < 0.0001$). The mean increase in Hb levels was 3.29 g/dL [15]. The study conducted at Dr. Pirngadi Hospital, H. Adam Malik Hospital and Kedai Durian Public Health Center Medan in 2006 showed that administering Venofer 200 mg IV could increase Hb, MCV, and ferritin levels significantly and effectively used as a therapy for iron deficiency anemia [16].

Several studies have shown that this injection therapy can increase Hb and ferritin within 14 days, so that the condition of iron deficiency anemia in pregnant women is resolved more quickly and can provide better maternal and fetal outcomes. In this study, evaluation of Hb and ferritin was carried out before and after administration of intravenous iron sucrose injection treatment in second or third trimester pregnant women.

Methods and Materials

This is an analytical study with a quasi-experimental design to analyze differences in ferritin

and Hb levels before and after administration of iron sucrose injection to pregnant women in the second or third trimester at Araskabu Public Health Center, Deli Serdang. This study started with blood sampling in April 2022, followed by intravenous iron sucrose injection in April 2022, and then re-examinations of the blood 14 days after injection in May 2022.

The subjects in this study were 25 pregnant women aged 20–40 years who underwent antenatal care and met the inclusion criteria, namely, pregnant women in the second or third trimester, pregnancies with a single fetus, pregnant women with Hb levels <11 g/dL, pregnant women with ferritin <30 g/L, willing to participate in the study and signing the informed consent, has no history of hypersensitivity to iron preparations, is not receiving intravenous iron preparations in the previous 2 weeks, and is not included in the exclusion criteria, namely, pregnancy with twins, women with a history of abnormalities previously known blood pressure, women with known renal, hepatic and cardiac disorders, pregnant women with a history of diabetes mellitus, women with spinal cord disease, pregnant women with bleeding, women with infectious, systemic inflammatory diseases, asthma and malignancies, and defect blood samples. The sample was selected using a non-probability sampling method, namely the consecutive sampling technique.

Procedure

3 mL of blood was taken from the Median Cubiti Vein, put into a vacutainer with aseptic precautions where the blood in the tube can last up to 24 h before it reached the laboratory of the Universitas Sumatera Utara Hospital (USU Hospital) Medan by using a cooler box. The blood was examined in the USU Hospital Medan laboratory for Ferritin and Hb examination. Ferritin examination was carried out using the sandwich ELISA technique and an ELISA reader. Serum ferritin was examined using the principle of examination to measure the luminescence of chemical substances that are triggered by electricity using the Sandwich Electro Chemiluminescence Immuno Assay method.

Hb level <11 g/dL was diagnosed as anemia, and then ferritin was examined and treated with iron sucrose injection. These patients were given an intravenous infusion of 200 mg iron sucrose diluted in 100 mL of normal saline over 30 min. The required injection dose was calculated based on the ganzoni formula, namely $(\text{body weight [kg]} \times [\text{target HB} - \text{accurate HB}] [\text{g/dL}] \times 2.4 + \text{iron stores [500 mg]})$. The same was done on day 14 from the start of therapy.

Statistic analysis

The data obtained were analyzed descriptively to see the frequency distribution of the characteristics of the research sample in the second or third trimester

pregnant women who came to the Araskabu Public Health Center, Deli Serdang. Then after obtaining the results of laboratory tests, the data were tabulated to analyze the differences before and after using the paired-t test if the data were normally distributed or Wilcoxon if the data were not normally distributed. The researcher also performed the difference in the mean of ferritin and Hb by using the independent-t test if the data were normally distributed and the Mann-Whitney test if the data were not normally distributed. For categorical data, the Chi-square test was used, and the Fisher Exact test was used if it does not meet the Chi-square test requirements. The results of the analysis were significant if $p < 0.05$, with a 95% confidence level.

Results

The mean ferritin level before administration of iron sucrose injection to pregnant women in this study was 18.97 ± 8.284 g/L and the mean ferritin level after administration of iron sucrose injection to pregnant women in this study was 98.95 ± 18.878 g/L. The mean increase in ferritin levels after injection of iron sucrose was 79.97 ± 19.77 g/L. There was an increase in ferritin levels after giving iron sucrose injection to pregnant women compared to before being given iron sucrose injection and based on the analysis, it was found that there was a statistically significant difference between ferritin levels before and after iron sucrose injection with $p < 0.001$ (Tables 1 and 2).

Table 1: Differences in mean ferritin and hemoglobin levels before and after administration of iron sucrose injection to research subjects

	Before administration of iron sucrose injection	After administration of iron sucrose injection	p-value
Ferritin (µg/L)	18.97 ± 8.284	98.95 ± 18.878	$< 0.001^*$
Hemoglobin (g/dL)	10.13 ± 0.386	12.01 ± 0.723	$< 0.001^{**}$

*Uji Wilcoxon, **Paired-t test

Table 2: The mean increase in ferritin and hemoglobin levels after administration of iron sucrose injection to pregnant women at Araskabu Public Health Center, Deli Serdang

Variable	Min	Max	Median	Mean ± SD
Increased Ferritin Levels (µg/L)	53.61	113.50	82.30	79.97 ± 19.77
Increased Hemoglobin Levels (g/dl)	1.10	3.80	1.80	1.88 ± 0.68

The mean Hb level before administration of iron sucrose injection to pregnant women in this study was 10.13 ± 0.386 g/dL and the mean Hb level after administration of iron sucrose injection to pregnant women in this study was 12.01 ± 0.723 g/dL. The mean increase in Hb levels after injection of iron sucrose was 1.88 ± 0.68 g/dL. There was an increase in Hb levels after administration of iron sucrose injection to pregnant women compared to before being given iron sucrose injection and based on the analysis, it was found that there was a statistically significant difference between Hb levels before and after iron sucrose injection with $p < 0.001$ (Tables 1 and 2).

Pregnant women with ferritin levels < 12 g/L gave the highest increase in ferritin levels, namely 98.88 ± 8.59 g/L after administration of iron sucrose injection, compared to pregnant women with ferritin levels $12-15$ g/L and $16-30$ g/L. The results showed that there was a significant difference in the mean increase in ferritin levels after administration of iron sucrose injection to pregnant women based on ferritin levels before administration of iron sucrose injection with $p < 0.05$ (Table 3).

Table 3: Mean ferritin levels after administration of iron sucrose injection based on ferritin levels

Ferritin Levels	Min	Max	Mean ± SD	p-value*
16–30 µg/L	53.61	112.90	76.83 ± 19.63	0.018
12–15 µg/L	56.30	74.00	63.37 ± 8.51	
< 12 µg/L	88.90	113.50	98.88 ± 8.59	

*Kruskal Wallis test.

Pregnant women with Hb levels of $7-9.9$ g/dL gave the highest increase in Hb levels, namely 2.07 ± 0.77 g/dL after administration of iron sucrose injection, compared to pregnant women with Hb levels of $10-10.9$ g/dL. The test results showed that there was no significant difference in the mean increase in Hb levels after administration of iron sucrose injection to pregnant women based on the level of Hb levels before iron sucrose injection with $p > 0.050$ (Table 4).

Table 4: Mean hemoglobin levels after administration of iron sucrose injection based on hemoglobin levels

Hemoglobin Levels	Min	Max	Mean ± SD	p-value*
10–10.9 g/dL	1.10	3.80	1.82 ± 0.66	0.400
7–9.9 g/dL	1.30	3.56	2.07 ± 0.77	

*Mann Whitney test.

The mean difference in ferritin levels before and after administration of iron sucrose injection was highest in the age group of pregnant women > 30 years, which was 82.86 ± 23.87 g/L, with the multigravida parity group, which was 90.43 ± 15.83 , and based on gestational age in the second trimester was 85.02 ± 23.24 , with the majority of UAC being overweight, which was 90 ± 22.73 . The results of the mean difference test showed that there was no significant difference in the

Table 5: Mean ferritin levels before and after and the difference based on the characteristics of the research subjects

Characteristics	Ferritin levels (µg/L)			p-value
	Before administration of iron sucrose injection	After administration of iron sucrose injection	Differences after and before administration of iron sucrose injection	
	Mean ± SD	Mean ± SD	Mean ± SD	
Age				
≤ genyear	14.08 ± 0.00	70.38 ± 0.00	56.30 ± 0.00	
21–30 year	19.47 ± 8.55	99.32 ± 18.00	80.18 ± 18.27	0.449*
>30 year	19.26 ± 8.67	102.12 ± 20.33	82.86 ± 23.87	
Parity				
Primigravida	20.29 ± 6.43	85.40 ± 11.64	65.11 ± 9.57	
Secondigravida	18.77 ± 9.33	102.01 ± 22.07	83.24 ± 22.19	0.105*
Multigravida	17.34 ± 9.89	107.77 ± 14.56	90.43 ± 15.83	
Grande multigravida	21.77 ± 4.98	93.38 ± 20.46	71.61 ± 25.45	
Gestational age				
Trimester II	21.84 ± 8.59	106.87 ± 22.25	85.02 ± 23.24	0.222**
Trimester III	16.72 ± 7.58	92.73 ± 13.51	76.00 ± 16.35	
UAC				
Underweight	22.28 ± 7.44	99.74 ± 20.44	77.46 ± 21.50	
Normal	16.84 ± 9.04	82.62 ± 16.98	81.48 ± 17.99	0.893*
Overweight	17.08 ± 8.83	99.98 ± 22.09	82.90 ± 22.73	
Obesity	14.09 ± 0.00	88.09 ± 0.00	74.00 ± 0.00	

*Kruskal-Wallis test, **Mann-Whitney test.

mean difference in ferritin levels between before and after administration of iron sucrose injection based on age, parity, gestational age, and UAC with $p > 0.05$ (Table 4).

Table 6: Mean hemoglobin levels before and after and the difference based on the characteristics of the research subjects

Characteristics	Hemoglobin levels (g/dL)			p-value
	Before administration of iron sucrose injection	After administration of iron sucrose injection	Differences after and before administration of iron sucrose injection	
	Mean \pm SD	Mean \pm SD	Mean \pm SD	
Age				
≤ genyear	10.10 \pm 0.00	11.90 \pm 0.00	1.8 \pm 0.00	0.746*
21–30 year	10.10 \pm 0.32	12.06 \pm 0.81	1.96 \pm 0.77	
>30 year	10.21 \pm 0.56	11.91 \pm 0.56	1.70 \pm 0.45	
Parity				
Primigravida	10.08 \pm 0.31	11.72 \pm 0.27	1.63 \pm 0.38	0.713*
Secondigravida	10.19 \pm 0.37	12.15 \pm 0.95	1.96 \pm 0.79	
Multigravida	10.20 \pm 0.45	12.28 \pm 0.58	2.08 \pm 0.78	
Grande multigravida	9.80 \pm 0.56	11.35 \pm 0.07	1.55 \pm 0.49	
Gestational age				
Trimester II	10.10 \pm 0.44	11.91 \pm 0.86	1.81 \pm 0.80	0.434**
Trimester III	10.16 \pm 0.36	12.10 \pm 0.62	1.94 \pm 0.59	
UAC				
Underweight	10.19 \pm 0.49	11.86 \pm 0.36	1.67 \pm 0.33	0.261*
Normal	10.11 \pm 0.34	11.73 \pm 0.65	1.61 \pm 0.43	
Overweight	10.08 \pm 0.34	12.49 \pm 1.03	2.41 \pm 1.00	
Obesity	10.10 \pm 0.00	12.30 \pm 0.00	2.20 \pm 0.00	

*Kruskal Wallis test, **Mann Whitney test.

The mean difference in Hb levels before and after administration of iron sucrose injection was highest in the age group of pregnant women 21–30 years, namely, 1.96 ± 0.77 g/dL, with multigravida parity group, which was 2.08 ± 0.78 , and based on gestational age in the third trimester, namely, 1.94 ± 0.59 , with the majority of UAC being overweight, which is 2.41 ± 1.00 . The results of the mean difference test showed that there was no significant difference in the mean difference in ferritin levels between before and after administration of iron sucrose injection based on age, parity, gestational age, and UAC with $p > 0.05$ (Table 6).

Discussion

Differences in the mean levels of ferritin and Hb before and after administration of iron sucrose injection to pregnant women at Araskabu Public Health Center, Deli Serdang

The outcome obtained was an increase in ferritin levels after administration of iron sucrose injection, from a mean of 18.97 ± 8.284 g/L to 98.95 ± 18.878 g/L, and this increase was statistically significant ($p < 0.001$). According to another study in the group given intravenous iron sucrose injection, 27 patients (48%) showed an increase in serum ferritin levels between 51 and 100 ng/mL. Ten patients (18%) treated with IV iron had an increase in serum ferritin of 101 to 150 ng/mL and 8 patients (14%) had an increase in serum ferritin of more than 200 ng/mL [17]. The study by Bhavi *et al.* showed that in 24 women given intravenous

iron sucrose in 6 slow IV bolus injections on days 1, 4, 8, 12, 15 and 21 with a maximum dose of 200 mg. Serum ferritin was higher in group IV ($p < 0.001$) [13].

The same thing was also found in the study of Cancado *et al.*, where the mean serum ferritin level of the study sample was 7.63 ng/mL (before treatment) to 99.0 ng/mL (post-treatment) ($p < 0.001$) [15]. Meanwhile, according to Gupta *et al.*, those who examined serum ferritin on day 28 after intravenous injection of iron sucrose showed that serum ferritin increased from 4.1 ± 2.5 to 28 ± 26 ng/mL at week 4, with a $p < 0.001$. It was found that serum ferritin increased from 11.9 ± 5.0 to 95.5 ± 38.1 ng/mL for 6.9 ± 1.8 weeks in the iron sucrose injection group [18]. This was not much different from the results found in this study which showed an increase in serum ferritin levels within 14 days after administration of iron sucrose injection. The iron sucrose complex is effective because of its rapid removal from plasma and the availability of iron for erythropoiesis. After a bolus dose of iron sucrose, peak plasma occurs within 10 min. Twenty-four hours after administration showed rapid bone marrow uptake as has been demonstrated by positron emission tomography studies. Studies had shown that 70–97% of iron is used for erythropoiesis, with an elimination rate of only 4–6% [15].

In another study in India by Kriplani *et al.* on 100 pregnant women with initial Hb between 5 and 9 g/dL with a diagnosis of iron deficiency who were given a regimen of intravenous iron sucrose injection at a dose of 200 mg twice weekly, a significant increase in serum ferritin levels (from 11.2 ± 4.7 to 69 ± 23.1 g/L) ($p < 0.001$) [19].

The Hb variable also found a significant increase from 10.13 ± 0.386 g/dL to 12.01 ± 0.723 g/dL after administration of iron sucrose injection ($p < 0.001$). The study in Malaysia by Samsudin *et al.* on pregnant women on the comparison of administration of iron sucrose injection with Low Molecular Weight Iron Dextran (LMWID) found that side effects were reported in five patients receiving LMWID and none in the group treated with iron sucrose injection ($p = 0.024$). The mean increase in Hb levels 2 weeks after treatment was also higher in the group receiving iron sucrose injection compared to LMWID. The group receiving iron sucrose injection showed an increase in Hb of 1.91 ± 1.10 g/dL (from 8.43 ± 1.03 g/dL to 10.29 ± 0.90 g/dL) compared to the LMWID group of 1.39 ± 0.54 g/dL (from 8.61 ± 0.70 g/dL to 9.92 ± 0.88 g/dL, $p = 0.023$). All participants in both groups gave birth on time [20].

The same thing was obtained from the study of Bhavi *et al.*, where there was a higher Hb level in women receiving intravenous iron compared to oral ferrous fumarate 22 ± 11.5 g/L versus 12 ± 9 g/L ($p < 0.0001$). A total of 55% of subjects in the intravenous group had an increase in Hb of more than 20 g/L compared to only 11% of the oral therapy group. A total of 48% of patients in group IV showed an increase in serum ferritin levels

between 51 and 100 ng/mL compared to only 3.5% in the oral group. Intravenous iron sucrose is effective in the correction of anemia in pregnancy or depletion of iron stores [17].

The study by Breyman *et al.* showed an increase in Hb concentration at 28 days from 1.3 to 2.5 g/dL in the iron sucrose injection group compared with 0.6 to 1.3 g/dL in the oral iron-treated group [21]. This shows that it is not much different from this study, which was re-examined 14 days after the intervention in increasing Hb levels after administration of iron sucrose injection. Another study in India by Kriplani *et al.* on 100 pregnant women with initial Hb between 5 and 9 g/dL with a diagnosis of iron deficiency who was given a regimen of intravenous iron sucrose injection at a dose of 200 mg twice a week, showed an increase in the mean Hb of 7.63 ± 0.61 to 11.20 ± 0.73 g% ($p < 0.001$) after 8 weeks of therapy [22].

A study of 1458 pregnant women with iron deficiency anemia given oral iron sucrose and iron injections found that at 6 weeks post-randomization, there were minor adverse events in 117 (16%) of the 737 women in the intravenous iron sucrose injection group compared to 155 (21%) of 721 women in the standard therapy group. No serious side effects were found associated with the study and intervention procedures [20]. A systematic review by Valdes *et al.* also supported the positive regarding the use of iron supplementation in pregnant women with iron sucrose injection where this injection is considered an effective method for treating IDA in pregnant women with minimal side effects. In addition, antenatal infusion of parenteral iron sucrose is universally associated with increased Hb and ferritin concentrations [23].

Another study in India showed a total of 990 women who received iron sucrose injection had a mean increase in Hb from 7.85 g/dL (0.80) at the start of the study to 9.62 g/dL (1.30) at the end of the study, with a mean increase of 1.76 g/dL (95% CI, 1.67, 1.85). The mean increase in Hb levels of pregnant women with severe and moderate anemia at baseline was 2.54 g/dL and 1.65 g/dL, respectively. Overall 15.33% of the women achieved normal Hb levels at the time of final measurement [24]. A study of giving 300 mg IV iron sucrose to pregnant women in India showed a mean change in Hb and serum ferritin levels 4 weeks after the last dose of iron sucrose injection of 2, 5 (2.1–3.0) g/dL ($p < 0.001$) and 63.0 (44.7–81.3) ng/mL ($p < 0.001$, 95% CI), respectively, and none life-threatening side effects encountered during the study [25].

The mean increase in ferritin and Hb levels after administration of iron sucrose injection to pregnant women at Araskabu Public Health Center, Deli Serdang

In this study, injection of iron sucrose 200 mg diluted in 100 mL of normal saline for 30 min given for

14 days resulted in an mean increase in ferritin levels of 79.97 ± 19.77 g/L and an mean increase in Hb levels of 1.88 ± 0.68 g/dL. The results of this study showed that the increase in Hb levels was lower than previous studies, while the increase in ferritin levels was higher than the results of previous studies. This is as reported in a study of 100 pregnant women with a diagnosis of iron deficiency who came to the antenatal clinic given an intravenous iron sucrose complex at a dose of 200 mg twice a week with the result that the mean Hb increased by 3.57g% while ferritin increased by 58.8 g/L [19]. In a study in pregnant women who received intravenous iron sucrose 300 mg per dose diluted in 300 mL normal saline for 20–45 min and followed up for 4 weeks after the last dose, there was a significant increase in Hb levels of 2.5 g/dL and serum ferritin levels of 63 ng/mL after 4 weeks [25]. Another study reported that an intravenous iron sucrose complex at a dose of 400 mg increased Hb levels by 2.5 g/dL [24].

The difference in these results was due to differences in the dose of iron sucrose injection given to pregnant women. This is as reported by Haldar *et al.* that the effect of dose on the mean increase in Hb levels depends on the total dose of iron prescribed, the rate of absorption of the prescribed dose, and the time lag between the infusion of the last dose of iron sucrose injection and the measurement of Hb levels. Guidelines issued by the Government of India stipulate a uniform total dose of 400 mg of iron for all pregnant women with moderate anemia, regardless of the Hb level in a particular woman [24]. Total iron requirements during pregnancy are approximately 1000 mg (500 mg for the fetus and placenta) that is developing, and the same amount for the increase in red blood cells [19]. An additional amount of 500 mg of iron is added to the calculated iron deficit to replenish the body's iron stores [26]. The maximum increase in Hb level (3.6 g/dL) was seen in a study that added 1000 mg of iron to replenish iron stores. The recommended dose of 400 mg of iron was not sufficient to achieve the desired non-anemic status [24]. In this study, intravenous infusion of 200 mg iron sucrose for 14 days had achieved the desired non-anemic status where all pregnant women have achieved Hb levels of more than 11 g/dL and serum ferritin levels of more than 30 g/L.

Research on 50 pregnant women with an mean gestational age of 28, 26 weeks with Hb < 7.0 – 9.0 g/dL there was an increase in Hb and serum ferritin more in the IV iron sucrose group than the oral group [21]. Meanwhile, the study In 271 anemic pregnant women with Hb levels below 110 g/L, the results showed that administration of 400 mg of intravenous iron sucrose significantly increased ferritin levels compared to the oral iron treatment group at 2 weeks after delivery, while the Hb value did not differ between group [27]. In this study, serum ferritin and Hb levels were both increased after intravenous infusion of iron sucrose but the increase in ferritin levels was much greater than Hb

levels. This is also in line with what was found in this study.

The main purpose of parenteral iron administration is basically to replenish iron stores in pregnant women with anemia. Serum ferritin levels are a good marker of body iron stores [25]. The increase in serum ferritin levels in this study reached 79.97 g/L after intravenous infusion of iron sucrose. Iron supplementation by any route of administration improves hematological indicators [28]. Hb and ferritin levels can be used to monitor the response of the hemopoietic system to iron sucrose complexes because of their relative effect on hemodynamics in pregnant women [29]. Iron sucrose had shown the best tolerance and lowest allergic effect (0.002%) due to the slow release of elementary iron from the polynuclear iron(III)-hydroxide in the sucrose complex [28].

Mean ferritin levels after iron sucrose injection based on ferritin levels

In this study, the mean increased in ferritin levels after administration of iron sucrose injection in pregnant women with ferritin levels of 16–30 g/L was 76.83 ± 19.63 g/L, whereas in pregnant women with ferritin levels 12–15 g/L gave the lowest increase in ferritin levels, which was 63.37 ± 8.51 g/L and in pregnant women with ferritin levels <12 g/L gave the highest increase in ferritin levels, which was 98.88 ± 8.59 g/L. And there was a significant difference in the mean increase in ferritin levels after administration of iron sucrose injection to pregnant women based on the level of ferritin levels before injection with a $p < 0.05$. In a previous study it was reported that 36 pregnant women with serum ferritin levels <13 g/L receiving two doses of intravenous iron sucrose (200 mg) showed a significant increase in serum ferritin levels at 14 days and 28 days of treatment [29]. A study in antenatal patients with moderate anemia with a gestation period of 32–35 weeks with a serum ferritin level of <12 g/L receiving intravenous iron sucrose at a dose of 200 mg showed that after 28 days of treatment, there was a statistically significant increase in serum ferritin levels from 10.33 ± 3.8 ug/L to 36.89 ± 5.7 ug/L [30].

Mean Hb level after administration of iron sucrose injection based on Hb level

In this study, the mean increase in Hb levels after administration of iron sucrose injection in pregnant women with Hb levels of 10–10.9 g/dL was 1.82 ± 0.66 g/dL, whereas in pregnant women with Hb levels of 7–9, 9 g/dL resulted in a higher increase in Hb levels, namely 2.07 ± 0.77 g/dL. And there was no significant difference in the mean increase in Hb levels after administration of iron sucrose injection to pregnant women based on the level of Hb levels before injection with $p > 0.050$. Another study in 36 pregnant women

with Hb <10 g/dL receiving two doses of intravenous iron sucrose (200 mg) showed that there was a significant increase in serum Hb levels at 14 days and 28 days of treatment [29]. Studies in pregnant women with moderate or severe anemia (Hb <10 g/dL) in the second or third trimester during routine antenatal care prescribed intravenous iron sucrose with a standard dose of 400 mg given as 100 mg on alternate days after 4 weeks [24]. In a study of 14 pregnant women with severe anemia who were given intravenous iron sucrose at a dose of 300 mg diluted in 300 mL of normal saline over a one hour period up to a maximum of 600 mg/week, it was found that the mean overall Hb level increased from 8.5 ± 0.88 g/dL at baseline to 10.3 ± 1.24 g/dL at the end of the 4th week. Changes from moderate and severe anemia to normal Hb levels were observed in pregnant women, respectively [31]. In this study, an intravenous infusion of 200 mg iron sucrose diluted in 100 mL of normal saline for 30 min was administered twice a week to pregnant women in the second and third trimesters. The third with mild and moderate anemia based on Hb levels has been able to increase serum Hb levels to reach normal levels in all pregnant women.

Mean ferritin level before and after and the difference based on the characteristics of pregnant women at the Araskabu Public Health Center, Deli Serdang

In this study, the results showed that the highest mean increase in ferritin levels was found in pregnant women >30 years of 82.86 ± 23.87 g/L, the mean increase in ferritin levels after iron sucrose injection was greater with the higher parity of primigravida. Secondigravida to multigravida, and the highest can be found in multigravida, namely, 90.43 ± 15.83 , but this was different in grand multigravida where the mean increase in ferritin levels is lower than in secondary gravida, the mean increase in ferritin levels after administration of iron sucrose injection based on gestational age was greater in the second trimester (85.02 ± 23.24) than in the third trimester (76.00 ± 16.35), and the mean increase in ferritin levels after administration of iron sucrose injection on nutritional status as measured by the value of upper arm circumference (UAC) which is greater than the nutritional status of underweight, normal to overweight, and found the highest UAC was in overweight nutritional status, namely 82.90 ± 22.73 , but in obesity nutritional status, the lowest mean increase in ferritin levels was found. However, the results of the comparison test showed that there was no significant difference in the mean difference in ferritin levels between before and after intravenous iron sucrose injection based on age, parity, gestational age, and UAC.

The previous research on 36 pregnant women where 6 of them were primigravida and the

rest were multigravida with as many as 72.22% aged 21–30 years, the mean serum ferritin level was 24.7 g/L and after 14 days receiving intravenous iron therapy the mean serum ferritin level was 128, 9 g/L. After 28 days of treatment, the mean serum ferritin level increased to 167 µg/L. There was a statistically significant increase in serum ferritin levels at 14 and 28 days after treatment with iron sucrose injection [28]. Therefore, further research is needed to re-examine ferritin and Hb levels according to the time specified based on other studies to see variations in outcome desired variable according to each dose.

Based on gestational age, it was reported that in another study 80 single pregnant women with iron deficiency anemia at 33 weeks of gestation were randomized to receive either oral iron fumarate 200 mg elemental iron daily until delivery or 200 mg intravenous iron sucrose complex weekly up to 500 mg. The results obtained that serum ferritin levels in the intravenous iron sucrose group were 4.7 times that of the oral iron fumarate group at 36 weeks gestation [32]. Research on primiparous and multiparous third trimester pregnant women, at the age of <20 and more than 30 years there was an increase in ferritin levels after 6 weeks at term from 26.7 ug/L to 65.34 ug/L [33]. Research at various ages, gestational age, parity and BMI were not significantly different in the 200 mg iron tablet group and the 200 mg iron sucrose group on alternate days with slow intravenous infusion, on day 30 there was a significant increase in ferritin levels between the two groups [29].

Mean Hb level before and after and the difference based on the characteristics of pregnant women at the Araskabu Public Health Center, Deli Serdang

In this study, it was found that the highest mean increase in Hb levels according to the difference was at the age of pregnant women 21–30 years, namely 1.96 ± 0.77 , the mean increase in Hb levels after iron sucrose injection was greater with the higher parity of primigravida, secondary to multigravida. Where the highest was found in multigravida, namely 2.08 ± 0.78 but this was different in grand multigravida where the lowest mean increase in Hb levels was found, the mean increase in Hb levels after administration of iron sucrose injection based on gestational age was found to be greater in the third trimester (1.94 ± 0.59) compared to the second trimester (1.81 ± 0.80) and the mean increase in Hb levels after administration of iron sucrose injection on nutritional status as measured by the UAC, namely the greater the nutritional status of underweight, normal to overweight, the highest was in overweight nutritional status (2.41 ± 1.00) but in obesity the mean increase in Hb levels was lower than overweight. However, the results of the comparison test showed that there was no significant difference in the

mean difference in the increase in Hb levels based on age, parity, gestational age, and UAC.

Multiparity is an important etiologic factor in iron deficiency anemia. Repeated short interval pregnancy predisposes pregnant women to suffer from iron deficiency anemia because the increased demand in pregnancy is not met with supply due to wrong dietary habits. A study in Gravida 1 (26%), Gravida 2 (46%), Gravida 3 (24%), and Gravida 4 (4%) found that intravenous infusion of iron sucrose can treat iron deficiency anemia during pregnancy because it is well tolerated and restores iron stores quickly which is safe and effective [20]. Research on 36 pregnant women where 6 of them are primigravida and the rest are multigravida with as many as 72.22% aged 21–30 years, the mean Hb in the pretreatment group was 6.38 g/dL. After 14 days of receiving intravenous iron therapy, the mean Hb level was 7.61 g/dL. After 28 days of treatment, the mean Hb level increased to 9.41 g/dL. There was a statistically significant increase in blood Hb levels at 14 and 28 days after iron sucrose injection treatment [28].

Intravenous iron sucrose can be an alternative to overcome the problems associated with oral iron therapy in the third trimester where it only takes a short time before delivery. Weekly injection of iron sucrose with a total dose of 500 mg in pregnant women with mild iron deficiency anemia is effective for increasing Hb concentration in late pregnancy. The current parenteral administration protocol has also been shown to rapidly replenish maternal iron stores and is beneficial for patients at risk for preterm delivery [32]. In a study in primiparous and multiparous third trimester pregnant women, at the age of <20 and over 30 years there was an increase in Hb and ferritin after 6 weeks and at term from 9.689 g/dL to 10.906 g/dL for Hb levels [34]. Hb levels in pregnant women before undergoing parenteral iron treatment were found to be significantly different between pregnant women aged 30 years and those aged >30 years. In pregnant women aged 20–39 years, with BMI from underweight to obesity, in the second and third trimesters and in primigravida to multigravida, the results showed that iron sucrose injection increased Hb levels by 1.91 ± 1.10 g/dL [35].

These results are in line with studies in a group of patients who were given oral iron tablets containing 100 mg of iron and 500 micrograms of folic acid daily during pregnancy. The group that was given a total of 1000 mg of iron sucrose intravenously was divided into five doses of 200 mg each at weekly intervals, in pregnant women aged 20–24 weeks, the Hb levels were not significantly different in the group of pregnant women aged 28–32 weeks and gestational age 35–36 weeks. The study in pregnant women with different ages, gestational ages, parity, and body mass index did not differ significantly in the group receiving 200 mg iron sulfate tablets, and the group receiving 200 mg iron sucrose on alternate days by slow intravenous infusion,

there was significant increase in Hb levels between the two groups [36].

Conclusions

It was found that there was a significant improvement in the condition of iron deficiency anemia in pregnancy after administration of iron sucrose injection based on the results of Hb and ferritin levels. There is a significant difference in the mean levels of ferritin and Hb between before and after administration of iron sucrose injection to pregnant women in the second or third trimester at Araskabu Public Health Center, Deli Serdang.

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