| Research Article |
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# Mentzer and RDW Index in the Establishment of Iron Deficiency Anemia Diagnosis in the First Trimester of Pregnant Woman

## Indeks Mentzer dan RDW dalam Diagnosis Anemia Defisiensi Besi pada Ibu Hamil Trimester Pertama

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## Abstract

**Objective:** To determine the sensitivity and specificity of the Mentzer and RDW index to assist in the diagnosis of iron deficiency anemia in first trimester pregnant women at RSIA Asih.

**Methods:** This research was conducted by a cross-sectional method using the medical records of 100 samples of first trimester pregnant women with iron deficiency anemia by consecutive sampling and 100 samples of controls, which is also first trimester pregnant women with anemia. The data is then analyzed using Kolmogorov-Smirnov test and the independent-T test.

**Result:** This study showed a significant relationship between the Mentzer index and the RDW index in iron deficiency anemia patients and control with p value = 0.000. Calculated by the ROC curve, the cut-off of Mentzer and RDW indices were 18.33 (sensitivity 37%, specificity 36%) and 249.2 (sensitivity 36%, spesificity 36%). Calculated by chi-square, the sensitivity and specificity values of the Mentzer index were 69% and 22% (literacy cut-off = 13), while the sensitivity and specificity values of the RDW index were 63% and 34% (literacy cut-off = 220).

**Conclusion:** Mentzer index and RDW index cannot be proposed as the main parameter to help the establishment of iron deficiency anemia diagnosis in first trimester pregnant women.

**Keywords:** anemia, iron deficiency, mentzer index, pregnant woman, RDW index.

## Abstrak

**Tujuan:** Untuk mengetahui sensitivitas dan spesifitas dari Indeks Mentzer dan RDW untuk membantu penegakan diagnosis anemia defisiensi besi pada ibu hamil trimester pertama di RSIA Asih.

**Metode:** Penelitian ini dilakukan secara potong lintang dengan menggunakan rekam medis 100 sampel pasien ibu hamil trimester pertama dengan anemia defisiensi besi secara consecutive sampling dan 100 sampel kontrol, yakni ibu hamil trimester pertama dengan anemia. Data kemudian dianalisis dengan uji Kolmogorov-Smirnov dan uji statistik t tidak berpasangan.

**Hasil:** Penelitian ini menunjukan adanya hubungan yang bermakna antara indeks Mentzer dan indeks RDWI pada pasien anemia defisiensi besi dan kontrol dengan nilai p=0,000. Dihitung dengan kurva ROC, cut-off indeks Mentzer dan RDW adalah 18,33 (sensitivitas 37%, spesifisitas 36%) dan 249,2 (sensitivitas 36%, spesifisitas 36%). Dihitung dengan chi-square, nilai sensitivitas dan spesifitas indeks Mentzer adalah 69% dan 22% (cut-off literasi =13), sedangkan nilai sensitivitas dan spesifitas indeks RDW adalah 63% dan 34% (cut-off literasi = 220).

**Kesimpulan:** Indeks Mentzer dan indeks RDW tidak dapat diusulkan sebagai parameter utama dalam membantu penegakkan diagnosis anemia defisiensi besi pada ibu hamil trimester pertama.

**Kata kunci:** anemia, defisiensi besi, ibu hamil, indeks mentzer, indeks RDW.

## INTRODUCTION

A total of 48.9% of pregnant women in Indonesia experience anemia (Riskesdas, 2018) and based on data from the National Health Work Meeting (RAKERKESNAS) in 2019, the incidence of anemia is estimated to reach 13.6% of maternal deaths during pregnancy and childbirth.[1,2]

The increasing needs of iron and lack of iron intake are the main causes of iron deficiency anemia in pregnancy. Anemia deficiency in pregnant women can increase maternal and perinatal mortality, as well as increasing the risk of low birth weight, premature birth, postpartum hemorrhage, and stunted psychomotor and neurocognitive development of infants. Early diagnosis of iron anemia deficiency is needed so that treatment can be given as early and as accurately as possible. Various erythrocyte indices are still being developed in order to obtain diagnostic parameters with the highest sensitivity and specificity values, the lowest cost, and the easiest calculation.[3-5]

Mentzer index and RDW index are screening tests to differentiate beta-thalassemia minor from hypochromic microcytic anemia, especially iron-deficiency anemia. Therefore, this study aimed to determine the sensitivity and specificity of the Mentzer Index and RDW to assist in the diagnosis of iron deficiency anemia in first trimester pregnant women at *RSIA Asih*.[6-8]

## METHODS

This study is a retrospective cross-sectional study with a descriptive analytic approach. The sample in this study was taken by non-probability consecutive sampling, namely collecting medical records of first-trimester pregnant women with iron deficiency anemia from March 2018 - March 2020 at the ASIH Mother and Child Hospital, South Jakarta who met the inclusion and exclusion criteria of the study. The total samples that met the inclusion and exclusion criteria were 200 samples.

The inclusion criteria of this study were first-trimester pregnant women who were patients at ASIH Jakarta Mother and Child Hospital who had been diagnosed with iron deficiency anemia from the results of blood tests and clinically by obstetricians at ASIH Mother and Child Hospital Jakarta and had medical record results of routine hematological tests and ferritin levels. Exclusion criteria from this study were pregnant women with chronic disease or infection and pregnant women who consumed drugs that could affect routine hematological values and ferritin.

The data in this study were statistically analyzed using the program Statistical Product and Service Solutions (SPSS) 26 with normality test Kolmogorov Smirnov. Then the parametric independent t test was carried out and the sensitivity and specificity test on both erythrocyte indices using chi-square and curve Receiver Operating Characteristics (ROC).

## RESULTS

**Table 1.** Characteristics of Subject

| Variable | Anemia | Control |
|---|---|---|
| | % (N) | % (N) |
| **Maternal age ( y o)** | | |
| ≤19 | 1 (2) | 0 (0) |
| 20-29 | 28 (56) | 28 (56) |
| 30-39 | 19 (38) | 20.5 (41) |
| ≥40 | 2 (4) | 1.5 (3) |
| **Gestation age ( weeks )** | | |
| ≤4 | 2 (4) | 0 (0) |
| 5-8 | 11 (22) | 18 (36) |
| 9-12 | 37 (74) | 32 (64) |
| **Parity** | | |
| 1 | 30 (60) | 31.5 (63) |
| 2 | 12.5 (25) | 13 (26) |
| 3 | 5.5 (11) | 3.5 (7) |
| >3 | 2 (4) | 2 (4) |
| **Formal education** | | |
| High school | 8.5 (17) | 6.5 (13) |
| S1 Graduation | 41.5 (83) | 43.5 (87) |
| **Occupation** | | |
| House wife | 21 (42) | 20.5 (41) |
| Civil service employee | 5.5 (11) | 9 (18) |
| Private employee | 17 (34) | 17.5 (35) |
| Enterpreneur | 6.5 (13) | 3 (6) |
| Total | 50 (100) | 50 (100) |

**Table 2.** Mean, Standard Deviation and P-value of Mentzer and RDW Index

| Indices | Mean | Std Deviation | *p-value** | *p-value*** |
|---|---|---|---|---|
| **Mentzer** | | | | |
| IDA | 18.9 | 1.8 | 0.16 | < 0.001 |
| Control | 17.7 | 1.8 | 0.2 | |
| **RDW** | | | | |
| IDA | 263.4 | 35.1 | 0.143 | < 0.001 |
| Control | 240.1 | 1.2 | 0.2 | |

*\* p-value of Kolmogorov-smirnov test; \*\* p-value of T Independent test.*

**Table 3.** Chi-square Results of Mentzer and RWD Index

| | According to Ferritin Level | |
|---|---|---|
| | IDA | Control |
| Mentzer index > 13 and Hb < 11 | 69 | 78 |
| Mentzer index < 13 and Hb > 11 | 31 | 22 |
| RWD index  > 220 and Hb < 11 | 63 | 66 |
| RWD index  > 220 and Hb > 11 | 37 | 34 |

**Table 4.** Sensitivity, Spesificity and cut-off Results of Mentzer and RDW Index

| | Mentzer index | | | | | |
|---|---|---|---|---|---|---|
| | Sensitivity (%) | Spesificity (%) | *Cut-off* | Sensitivity (%) | Spesificity (%) | *Cut-off* |
| ROC Curve | 37 | 36 | 18.33 | 36 | 36 | 249.2 |
| Chi-square | 69 | 22 | 13 | 63 | 34 | 220 |

## DISCUSSION

The American Society for Reproductive Medicine states that the peak of the fertile period and the best egg quality for women is at the age of 20-30 years old, then it will decline after entering the age of 35 years.[9] This is in accordance with the results of the study 200 samples studied which have an age range of 19-43 years, with the largest number of samples in the age range of 20-29 years (56%, N=56), both in the iron-deficiency anemia group and the control group. The prevalence of pregnant women with anemia during their reproductive years is still very high and women over 35 years of age have a twofold greater risk of developing iron-deficiency anemia and women under 20 years of age have a thirteen-fold greater risk of developing iron-deficiency anemia.[10,11]

The more mature the pregnancy, the greater the risk of iron deficiency due to the increased need for the fetus[12]. The first trimester of pregnancy iron requirements are reduced due to the cessation of menstruation, while iron requirements will increase dramatically in the second trimester due to expansion of blood volume and increased erythropoiesis. This is in accordance with the sample of this study where the gestational age of the most iron deficiency anemia is weeks 9-12 which is approaching the second trimester.[13]

### Parity

In the results of this study, it was found that pregnant women with iron-deficiency anemia were primigravida. This result is similar with the theory and research who reported that primigravida pregnant women are more prone to anemia because of the frequent occurrence of hyperemesis gravidarum so that the food intake of pregnant women is reduced and nutrition is not fulfilled.[14,15] However, this results seem to contradict to the results of who got a higher prevalence result in multigravida than primigravida.[16]

The results of this study indicate that pregnant women with S1 graduates are more likely to experience iron deficiency anemia during pregnancy. These results are where most pregnant women who experience iron deficiency anemia are S1 graduates, but this study states that there is no significant relationship between education level and the incidence of anemia in pregnancy.[11] In contrast to the results where the most pregnant women who experience iron deficiency anemia are high school graduates because the mother's education level affects the incidence of iron deficiency anemia. If a mother gets higher education and knowledge, she will be able to choose nutritious foods to prevent anemia during pregnancy.[12]

### Occupation

From this study, it was found that the majority of pregnant women with iron deficiency anemia were housewives. There is a significant relationship between maternal occupation and the incidence of anemia during pregnancy because mothers who do not work can be associated with a lower socioeconomic status which is known to be a risk factor for the incidence of anemia in pregnancy.[17]

### Relationship between Mentzer Index and Pregnant Women with Iron Deficiency Anemia and Control

The principle of Mentzer index is to differentiate the etiology of hypochromic microcytic anemia, that is, between iron deficiency anemia and beta-thalassemia minor. Mentzer's theory is based on the understanding that in iron deficiency anemia, the bone marrow cannot produce adequate erythrocytes and produce smaller erythrocytes, which will result in low erythrocyte and MCV counts, also the quotient between MCV and RBC will be >13. In contrast, in thalassemia where there is abnormality in globin synthesis, the number of erythrocytes produced is normal, but small in size and easily lysed. This results in a normal RBC but a low MCV, hence the MCV and RBC quotient will be <13. Cut-off of 13 in Mentzer index is the result of several previous studies and is quite often used in daily practice.[4,6]

The results of this study indicate that there is

a difference in the Mentzer index value between patients with iron deficiency anemia pregnant women and controls. The results of the statistical test with the independent T test also showed a significant relationship with the value of p = 0.000 ($\alpha$ = 0.05 ; p <). Using the Mentzer cut-off from previous research and calculated using the test Chi-Square, obtained the sensitivity and specificity of Mentzer index are 69% and 22%, On Chi-square calculation, the researchers also included additional requirements in the form of Hb values due to differences in cut-off Hb anemia in RSIA Asih and WHO. *RSIA Asih* uses cut-off Hb <12 while WHO uses cut-off <11.

In this study, the researcher also wants to find cut-off based on the sample obtained at RSIA Asih, therefore analysis was also carried out using the ROC curve, obtained the value of Area Under Curve (AUC) 31.5%, sensitivity 37% and specificity 36%. Score cut-off based on the Youden index is 18.33. These results are similar to the research conducted by Sari et al. which also got a sensitivity value of 60.5% and a specificity of 28.6% with a cut-off value of 10.7.[18] The sensitivity and specificity values of the Mentzer index obtained in this study were significantly different when compared to the study which achieved a sensitivity and specificity value of >85%7,[19]. This is because, in previous studies, the samples used were patients with iron deficiency anemia and beta-thalassemia minor. This becomes important and critical to test the Mentzer index, remembering the principle of the Mentzer index itself, which has a fairly narrow scope of diagnosis, which can only diagnose both diseases. The control group used in this study were hypochromic microcytic anemia patients, but not iron deficiency anemia and beta-thalassemia minor.

### Relationship between RDW Index and Pregnant Women with Iron Deficiency Anemia and Control

The principle of the RDW index is to distinguish the etiology of hypochromic microcytic anemia, namely between iron deficiency anemia and beta-thalassemia minor. Red Cell Distribution Width or RDW is a number that shows how varied the size and volume of human erythrocytes are. The RDW theory is based on the understanding that when there is iron deficiency, the erythropoiesis process will also be disrupted and the blood cells produced become smaller and paler so that in the circulation there are normal and small-sized erythrocytes. This will have an impact on increasing RDW value because the size of red blood cells in the body is more varied. An increased RDW value is not only associated with iron deficiency but also deficiencies of other substances such as folic acid or B12. Cut-off The number used to differentiate between iron deficiency anemia and thalassemia is 220.[7.8]

The results of this study indicate that there is a difference in the RDW index value between patients with iron deficiency anemia pregnant women and controls. The results of statistical tests with independent T-test also showed a significant relationship with p<0.001 ($\alpha$=0.05 ; p<$\alpha$). Using RDW index' cut-off from previous studies, and calculated using the test Chi-square, obtained sensitivity and specificity of 63% and 34%, respectively. On Chi-square calculation, the researchers also included additional requirements in the form of Hb values due to differences in cut-off Hb anemia in RSIA Asih and WHO. *RSIA Asih* uses cut-off Hb <12 while WHO uses cut-off <11.

In this study, the researcher also wants to find cut-off based on the sample obtained at RSIA Asih, therefore an analysis was also carried out using the ROC curve, obtained the value of Area Under Curve (AUC) 32.6%, sensitivity 36% and specificity 36%. The cut-off score based on the Youden index is 249.2. The sensitivity and specificity values of the RDW index obtained in the study were significantly different when compared to the finding of which achieved sensitivity and specificity values >80%.[20,21]

This is because, in previous studies, the samples used were patients with iron deficiency anemia and beta-thalassemia minor. This becomes important and critical to test the RDW index, remembering the principle of the RDW index itself, which has a fairly narrow scope of diagnosis, which can only diagnose both diseases. The control group used in this study were hypochromic microcytic anemia patients, but not iron deficiency anemia and beta-thalassemia minor. This is what causes confusion in the RDW index value in the control group.

### CONCLUSION

The general distribution of the population of first-trimester pregnant women who experience iron deficiency anemia at RSIA Asih is at most 20-29 years old, with a gestational age of 9-12 weeks, is in its first pregnancy, has the last bachelor's

education and is a housewife. According to the ROC curve analysis, the sensitivity of the Mentzer index was 1% higher than the RDW Index, while the specificity values for the two indexes were the same. According to chi-square analysis the sensitivity of the Mentzer index was higher but the specificity of the Mentzer index was lower than the RDW index.

From these results, it can be concluded that the Mentzer index and RDW index cannot be proposed as the main parameters in helping to diagnose iron-deficiency anemia in first-trimester pregnant women.

## ACKNOWLEDGEMENT

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