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Original Article

Early prediction of iron deficiency in females in child bearing age in central Saudi Arabia

Mysara M. Mogahed*, Shereen Mohamed Abdelwahab

Faculty of Medicine, Benha University, Egypt

1. Introduction

Despite advances in healthcare, anaemia and iron deficiency (ID) remain the most common disorders in women.^{1–3} Globally, the prevalence of anaemia increased to 30% in non-pregnant women of reproductive age (15–49 yr).⁴

Prevalence of IDA varies widely by age, sex, race and geographical areas.^{5,6} A study in Saudi Arabia reported prevalence of IDA by 20.5%, among school students.⁷

IDA impairs physical activity and cognitive performance and may also cause irreversible intergenerational effects when it occurs in women of reproductive age⁸; and detrimental findings have even been reported for those with non-anaemic ID.⁹

Hemoglobin (Hb) concentration and complete blood count (CBC) are used for primary evaluation of anaemia. A CBC can be helpful in determining the mean corpuscular volume (MCV), which measures the average size of RBCs, and mean corpuscular Hemoglobin concentration, which measures the concentration of Hemoglobin in a given amount of packed RBCs. The common characteristics of IDA include hypochromic RBCs, microcytic, and low iron stores. The red cell distribution width (RDW) is a measure used in combination with the MCV to differentiate between mixed causes for anaemia from that of a single cause. An elevated RDW value signifies a variation in the size of the red blood cell. In addition, RDW may also be elevated at the early stages of IDA.¹⁰ Hemoglobin (Hb) concentration is the most commonly used test to screen for IDA which reflects the amount of functional iron in the body. Because changes in Hb concentration occur only at the late stages of iron deficiency, it is a late indicator of iron deficiency.¹¹

Hence, there is a need to have a screening test which is cheap and of high reliability and accuracy in identifying the iron deficiency. The definitive test for the diagnosis of iron deficiency is the bone marrow aspiration (to assess the iron stores). The procedure, however, is invasive, difficult and expensive for a very common medical problem especially in developing countries. Alternate to bone marrow aspiration test is serum ferritin, which is found to be the best test for distinguishing those with ID from those who are not iron deficient.^{12–18}

Unfortunately, serum ferritin estimation test is not available freely at many primary health care centers, especially in developing countries.

Therefore, this study was conducted to detect the prevalence of iron deficiency and iron deficiency anaemia among healthy women of child bearing age and to explore if it could be detected by simple parameters obtained on a complete blood count, using serum ferritin level as a standard of reference.

2. Patients and methods

This is a cross sectional study conducted between January and December 2016, in an outpatient clinic in Riyadh, Saudi Arabia.

We recruited 100 consecutive females of child bearing age (15–49 years, as defined by WHO),¹⁹ who visited the clinic and met the inclusion criteria during the study period.

The criteria for selecting the individuals in the sample included

1. Age of 15–49 years.
2. Not being pregnant, lactating or post-menopausal.
3. Lack of history of any pregnancy related conditions for the last three months (abortion and postpartum period) and post-hysterectomy.
4. Lack of history of chronic diseases including patients on renal dialysis and having any type of hemoglobinopathy or acute and chronic infection or inflammation.
5. The lack of recent consumption of iron medicine at any time during the last 6 months.

Individuals of the studied group were subjected to the following

1. Full history taking, which include information on Socio demographic data, age, symptoms, menstrual history, dietary, medical history, and nutritional habits. Family history of anaemia and if so, it's type as well as other chronic diseases (such as bronchial asthma, diabetes mellitus, renal, cardiac diseases etc).
2. Thorough clinical examination.

After informed consent, laboratory investigations carried out on each subject were complete blood count (CBC), Hemoglobin electrophoresis (to exclude hemoglobinopathy), serum pregnancy test

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* Corresponding author.

E-mail address: mysara757@gmail.com (M.M. Mogahed).

(to exclude pregnancy) and serum ferritin. One hematologist was assigned to follow, analyze and complete the hematological data.

The measured RBCs' parameters were total RBC count, mean corpuscular volume (MCV), mean corpuscular Hemoglobin (MCH), mean corpuscular Hemoglobin concentration (MCHC), red cell distribution width coefficient of variation (RDW-CV%).

Anemia was defined as Hemoglobin < 12 g/dl (cut off point according to WHO criteria).¹⁷ IDA was defined as anaemia with ferritin level \leq 15 ng/ml.^{16,17,20}

Serum ferritin was measured fasting using a microparticle enzyme immunoassay on the BIOMRIEUX MINI Vidas (France) analyzer. Red cell distribution width (RDW) was calculated as (standard deviation of MCV/mean MCV) x100 and was reported as a percentage (Normal value is 11–14.5%).¹⁷

The collected data were statistically analyzed using statistical package for social sciences

(SPSS) program for windows version 20. Results were summarized in terms of mean \pm SD. Pearsons Corr coeff (r) were done between serum ferritin and RDW-CV%, RBC count, Hb, MCV, MCH and MCHC and between MCV and Hb. The diagnostic performances of different red cell indices were plotted on Receiver operator characteristic (ROC) curves to explore their significant correlation to ferritin and to look for which one gave maximum area under curve (AUC).

3. Results

Taking a cut-off of Hb of 12 g/dL for anaemia, and 15 ng/mL for ferritin for diagnosis of iron deficiency, we found 62(62%) of studied women had iron deficiency (ferritin \leq 15 ng/mL), while 38 (38%) of the study participants were non-iron deficient [Table 1](#).

[Table 2](#) shows the socio-demographic characteristics of the study participants. 72.6% of iron deficient women were in the age group of 26–49 years. About 70% of iron deficient population were married and live in urban areas. More than 30% of the studied women (iron deficient and non-iron deficient) were educated at university level.

Among our studied group, the mean age was 30.2 ± 8.84 years. General characteristics of the studied group are shown in [Table 3](#).

Using (Pearsons Corr coeff (r)) to study the performance of Hb and different red cell indices in relation to ferritin among the studied groups; in the (26) IDA patients we found that there were significant correlation between serum ferritin and (Hb, HCT, MCV, MCH and MCHC), ($p = .004, .04, .03, .02, .02$, respectively); while in the (36) non-anaemic with iron deficiency group RBCs count, Hb, HCT and all other red cell indices had no significant correlation with serum ferritin. In the (34) non-anaemic with normal ferritin all parameters except RDW were significantly related serum ferritin [Table 4](#).

By drawing ROC curves for RBCs count, Hb, HCT and other iron related parameters i.e. MCV, MCH, RDW and MCHC, to screen cases with iron deficiency anaemia from non-anaemic with normal ferritin group; we found that among iron related parameters ROC for MCH was found to have area under its curve (0.89) and had

Table 1
Description of study participants as per anaemic status.

Iron deficient group (62)	Iron deficiency anaemia(Hb < 12 g/dL; ferritin \leq 15ng/mL)	26
	Non-anaemic with iron deficiency(Hb \geq 12 g/dL; ferritin \leq 15ng/mL)	36
Non-iron deficient group (38)	Non-anaemic with normal ferritin(Hb \geq 12 g/dL; ferritin > 15ng/mL)	34
	Anemia not due to iron deficiency(Hb < 12 g/dL; ferritin > 15ng/mL)	4

Table 2
Socio-demographic characteristics of the studied women:

	Iron deficient group ferritin \leq 15 ng/ml (62) NO. (%)	Non-iron deficient group ferritin > 15 ng/ml (38) NO. (%)
<i>Age group (in years)</i>		
15–25	17(27.4)	20(52.6)
26–49	45(72.6)	18(47.4)
<i>Marital status</i>		
Married	43(69.3)	22(57.9)
Single	19(30.7)	16(42.1)
<i>Education</i>		
Illiterate	3(5)	0(0)
Primary	9(14.5)	4(10.5)
Intermediate	14(22.5)	8(21)
High school	16(25.8)	14(37)
University	20(32.2)	12(31.5)
<i>Geographical location</i>		
Urban	45(72.6)	31(81.6)
Suburban	17(27.4)	7(18.4)
<i>Occupation</i>		
Housewife	19(30.6)	13(34.2)
Employed	17(27.4)	15(39.5)
Student	26(42)	10(26.3)

Table 3
Characteristics of the studied group.

	Mean \pm SD	Range
Age (year)	30.2 \pm 8.84	15–49
RBCs count in millions	4.42 \pm 0.54	3–5
Hb (g/dl)	12.02 \pm 2.01	8–14
HCT (%)	36.76 \pm 4.07	27–44
MCV (fl)	81.9 \pm 8.57	61–94
MCH (pg)	25.98 \pm 3.24	18–30
MCHC (g/dl)	31.5 \pm 1.38	28–37
RDW (%)	15.5 \pm 2.04	13–21
Ferritin (ng/mL)	14.88 \pm 13.69	1–58

RBCs = Red blood cells; Hb = hemoglobin; Hct = hematocrit; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW = red blood cells distribution width; SD = standard deviation.

the maximum accuracy (81.3) and sensitivity (71.4) and it was seen that MCH < 26.5 fl can predict iron deficiency anaemia in females in child bearing age. Followed by RDW which show AUC: 0.92, accuracy of 78.2 and sensitivity 66.7. And finally, MCV and MCHC had nearly the similar AUC: 0.85 and 0.84, sensitivity: 71.4 and 61.9 respectively while accuracy was 75 for both parameters ([Table 5](#) and [Figs. 1 and 2](#)).

As for ROC curves for RBCs count, Hb, HCT and other iron related parameters to screen the non-anaemic with iron deficiency patients from non-anaemic with normal ferritin group; we found that among iron related parameters ROC for RDW was found to have the maximum area under its curve (0.69) and had the maximum accuracy (62.9) and its sensitivity was (71.4) and it was seen that RDW < 14.5 can predict iron deficiency without anaemia in females in child bearing age. Followed by MCH which show AUC: 0.63, accuracy of 60 and sensitivity 61.1. And finally, MCHC and MCV which had AUC: 0.64 and 0.59, sensitivity: 88.9 and 66.7 respectively while accuracy was 54.3 for both parameters ([Table 6](#) and [Figs. 3 and 4](#)).

4. Discussion

Iron deficiency is caused by negative iron balance in the body and is the most common scenario in the female population in the

Table 4

Correlation of red cell indices and Hb with serum ferritin among different studied groups.

Ferritin	Iron deficiency anaemia (Hb < 12 g/dL; ferritin ≤ 15ng/ mL)		Non-anaemic with iron deficiency (Hb ≥ 12 g/dL; ferritin ≤ 15ng/ mL)		Non-anaemic with normal ferritin (Hb ≥ 12 g/dL; ferritin > 15ng/ mL)	
	r	P value	r	P value	r	P value
RBCs	−0.23	.26	0.292	.084	0.634	.001**
Hb	0.54	.004**	−0.217	.203	0.469	.005**
HCT	0.41	.04 [†]	−0.085	.624	0.474	.005**
MCV	0.43	.03 [†]	−0.276	.104	−0.343	.047**
MCH	0.44	.02 [†]	−0.007	.968	−0.432	.011 [†]
MCHC	0.44	.02 [†]	0.246	.149	−0.522	.002**
RDW	−0.23	.26	0.064	.712	0.102	.566

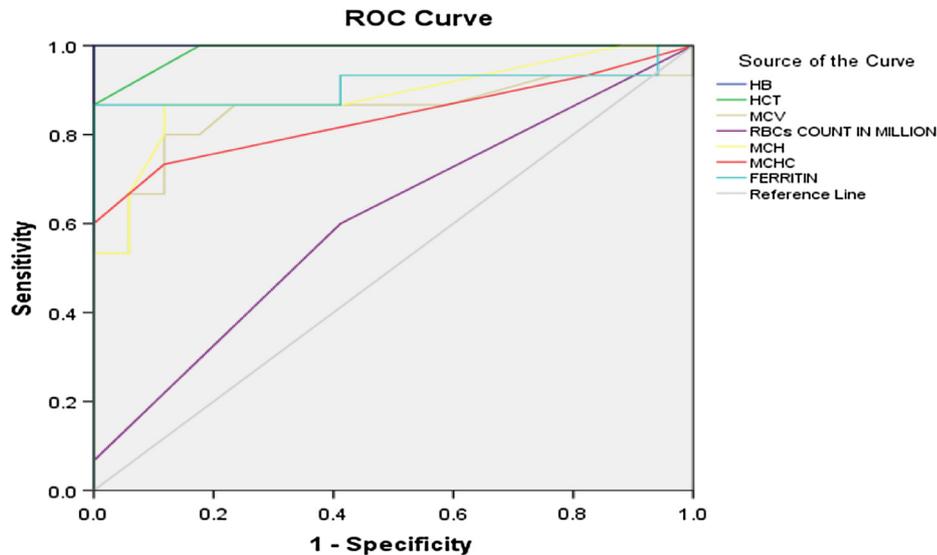
Table 5

Roc curve results that screen cases with IDA from non anaemic with normal ferritin.

Index	AUC	Best cut-off	Sensitivity (%)	Specificity (%)	Accuracy (%)
RBC count in millions	0.61	4.5	47.6	45.5	46.9
Hb (g/dl)	1.0	11.5	66.7	90.9	75.0
HCT (%)	0.988	36.5	71.4	83.3	71.9
MCV (fl)	0.85	84.5	71.4	81.8	75.0
MCH (pg)	0.89	26.5	71.4	100	81.3
MCHC (g/dl)	0.837	31.5	61.9	100	75.0
RDW-CV (%)	0.924	15.5	66.7	100	78.2

AUC = area under the curve.

RBCs = Red blood cells; Hb = hemoglobin; Hct = hematocrit; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW = red blood cells distribution width.

**Fig. 1.** Roc curve for Hb, HCT, MCV, RBCs count, MCH & MCHC that screen cases with IDA.

reproductive age group. Among these individuals, iron deficiency is landed up either due to dietary deficiency by inadequate intake/absorption or excess loss of blood.

Therefore, identification of iron deficiency and differentiation from other causes of anaemia is essential for proper management of this entity. The roots of the present study started from the idea of believing on a single, simple, cost-effective test, which can be used as a diagnostic test give clues for the identification of iron deficiency in developing countries especially at primary care level. So, in this study, the effectiveness of the Hemoglobin and red cell indices which can be derived from a simple haemogram done in recent automated cell counters is compared with serum ferritin in the diagnosis of iron deficiency was explored.

In this study, the prevalence of iron-deficiency anaemia in non-pregnant women aged 15–49 in Riyadh city was obtained as equal to 26%, based on two parameters of Hb less than 12 g/dl and Ferritin of less than 15 ng/mL. The prevalence of iron-deficiency anaemia has been reported differently in different studies. For example, Al-Sayes et al.²¹; who study the prevalence of IDA among females at university stage in Saudi Arabia and it was equal to 23.5%, Mousa et al.²²; explored iron-deficiency anaemia in adolescent girls in Rural Upper Egypt using the same parameters and reported the prevalence as equal to 30.2%, Suh et al.²³; reported that the prevalence of IDA among Korean women in age group 19–49 was 11.3%. In the study by Jangjoo and Hosseini²⁴, the prevalence of iron-deficiency anaemia in Marvdasht city (Iran) in non-pregnant women of

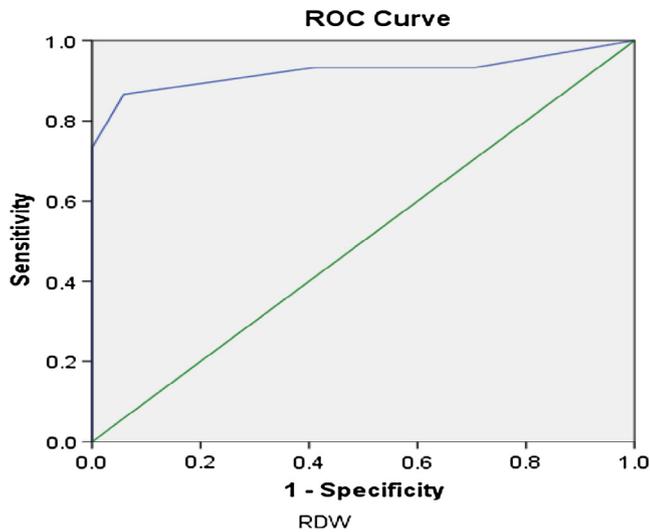


Fig. 2. Roc curve for RDW that screen cases with IDA.

reproductive age [14–45] based on three parameters of iron level of less than 30 mcg/dl, TIBC of over 360 mcg/dl and Ferritin of less than 15 ng/mL, was 6.5% and in the study of Tiwari et al.²⁵; who study IDA in pregnant Indian women reported prevalence of IDA was 34%.

One of the big challenges in this study was iron deficiency without anaemia which was present in 51.4% of the non-anaemic women of child bearing age, which was higher than the results of Al-Sayes et al.²¹; who reported iron deficiency without anaemia in 33.3% and the results of Mousa et al.²²; who had ID percentage of 11.4 and Suh et al.²³; whom study concluded that the overall prevalence of iron deficiency in Korean women of the same age group was 32.7%. While our results were in accord with the results of Tiwari et al.²⁵; who reported that the percentage of subclinical iron deficiency was 58 in their study.

In this study the overall prevalence of iron deficiency anaemia and iron deficiency without anaemia is relatively high in Saudi Arabian women of child bearing age (i.e. developing countries) as compared to the developed countries in a way that in the studies conducted in France, using the criteria of a hemoglobin level of lower than 12.1 g/dl, only 2.6% of the premenopausal women had iron-deficiency anaemia.²⁴ It seems that this difference can be due to the cultural, social and economic differences as well as differences in nutritional habits (consumption of high amounts of vegetable products that contain non-heme iron in developing countries while in developed countries the source of iron is animal products that contain heme iron), common diseases, the health status, enough education, the attention of the physicians and the medical system regarding this disease.

Table 6

Roc curve results that screen cases with ID from non anaemic with normal ferritin.

Index	AUC	Best cut-off	Sensitivity (%)	Specificity (%)	Accuracy (%)
RBC count in millions	0.63	4.5	66.7	58.8	62.9
Hb (g/dl)	0.55	12.5	50.0	58.8	54.3
HCT (%)	0.65	39.5	77.8	52.9	65.7
MCV (fl)	0.59	87.5	66.7	41.2	54.3
MCH (pg)	0.63	27.5	61.1	58.8	60.0
MCHC (g/dl)	0.64	32.5	88.9	17.6	54.3
RDW-CV (%)	0.69	14.5	66.7	58.8	62.9

AUC = area under the curve.

RBCs = Red blood cells; Hb = hemoglobin; Hct = hematocrit; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; RDW = red blood cells distribution width.

The present study showed that in females in child bearing age with IDA; apart from RDW and RBCs count; all red cell indices with Hb and HCT were significantly related to ferritin levels and can be used for detection of iron deficiency anaemia. And this was similar to the finding of Tiwari et al.²⁵; who also found that most of red cell indices except MCHC and RBCs count correlate with serum ferritin level. And AlQuaiz et al.²⁶; who also reported that MCV & MCH correlate with ferritin.

As for detection of iron deficiency without anaemia in premenopausal women, to decide which one should start iron supplementation before the development of overt anaemia, our study found that in (36) non-anaemic with iron deficiency non of the red cell indices correlate with ferritin. This means that it was difficult to pick up iron deficiency from a simple haemogram and raise the need to apply more accurate tests like serum ferritin or any other newer marker as a screening test for iron deficiency in primary care units. Our results were in accord with the results of Tiwari et al.²⁵; who also did not find any correlation between red cell indices and serum ferritin. However, we still could not decide that the simple haemogram available in primary care centers is a poor test for picking up iron deficiency due to small sample size in both studies.

By drawing ROC curves for iron parameters i.e. MCV, MCH, MCHC and RDW to screen IDA cases, we found that MCH was the most important parameter for screening and detecting IDA, with area under the curve of 0.89 and it had the maximum accuracy (81.3) and sensitivity (71.4) with a cut-off: 26.5 pg, followed by RDW which show AUC: 0.92, accuracy of 78.2, sensitivity 66.7 and cut-off 15.5. And finally, MCV and MCHC had nearly the similar AUC: 0.85 and 0.84, sensitivity: 71.4 and 61.9, cut-off: 87.5 fl and 32.5 (g/dl) respectively while accuracy was 75 for both parameters. This was nearly similar to the study of AlQuaiz et al.²⁶; who also found that MCH (24 pg) & MCV (76 fl) followed by RDW (16.1%) are the best markers in comparison with serum ferritin in predicting IDA in their studied group. The same was also found by Sunkara and Kotta²⁷ but with the highest sensitivity was for RDW (89%) followed by MCH and MCV (84%).

While on drawing ROC curves for iron parameters i.e. MCV, MCH, MCHC and RDW to detect ID without anaemia in the studied group we found that ROC for RDW had the maximum area under its curve (0.69) and had the maximum accuracy (62.9) and its sensitivity was (71.4) with cut off: 14.5. Followed by MCH which show AUC: 0.63, accuracy of 60, sensitivity 61.1 and cut off: 27.5 pg. And finally, MCHC and MCV which had AUC: 0.64 and 0.59, sensitivity: 88.9 and 66.7 and cut off: 32.5 (g/dl) and 87.5 fl respectively while accuracy was 54.3 for both parameters.

As per our study we found that individuals with Hb < 11.5 g/dL, a combination of MCV < 84.5 fl, MCH < 26.5 pg, MCHC < 31.5 (g/dl), RDW-CV% > 15.5% and RBC count < 4.5 million/cumm can detect patients with iron deficiency anaemia, while with Hb < 12.5 g/dL, a combination of MCV < 87.5 fl, MCH < 27.5 pg, MCHC < 32.5 (g/dl), RDW-CV% > 14.5% and RBC count < 4.5 million/cumm

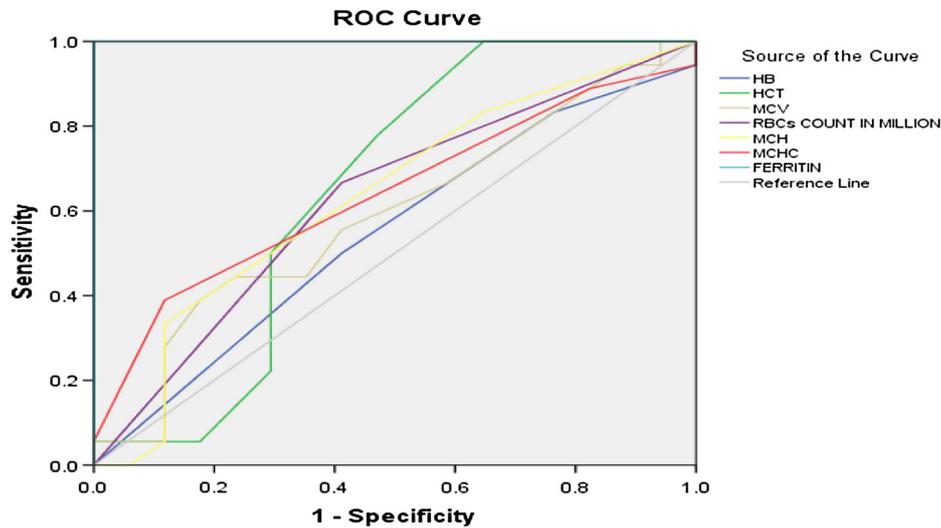


Fig. 3. Roc curve for Hb, HCT, MCV, RBCs count, MCH & MCHC that screen cases with ID.

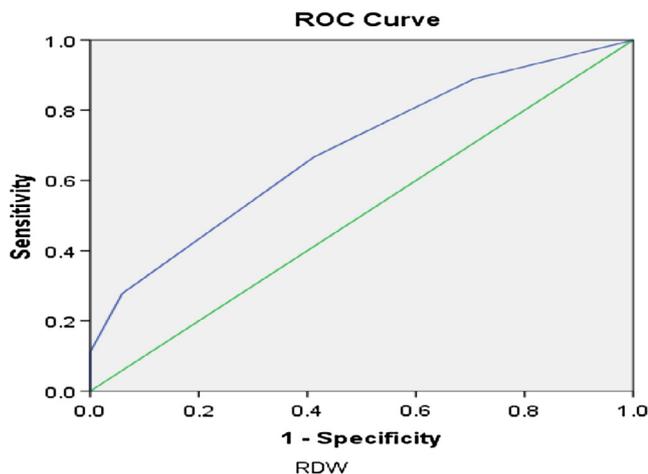


Fig. 4. Roc curve for RDW that screen cases with ID.

can be used for early prediction of iron deficiency without anaemia in women of child bearing age.

5. Conclusion

From this study we can conclude that females of reproductive age in Riyadh city have high prevalence of ID and IDA. Our data showed that CBC indices may be poor indicators for early prediction of iron deficiency and there is a need to look for other more accurate test to be applied freely in primary care centers for screening of iron deficiency in women of child bearing age. We can decide that iron deficiency anaemia could be diagnosed from simple CBC test at levels Hb < 11.5 g/dL, a combination of MCV < 84.5 fL, MCH < 26.5 pg, MCHC < 31.5%, RDW-CV% >15.5% and RBC count < 4.5 million/cumm in women of child bearing age.

Although we didn't find any significant correlation between different red cell indices and ferritin in patients with iron deficiency without anaemia; we could suppose that with Hb < 12.5 g/dL, a combination of MCV < 87.5 fL, MCH < 27.5 pg, MCHC < 32.5 (g/dl), RDW-CV% >14.5% and RBC count < 4.5 million/cumm could be used for early prediction of iron deficiency without anaemia in women of child bearing age. We still cannot conclude that CBC is a poor test for early prediction of iron deficiency due to small sample size

in our study. So large scale studies on both sexes all over the world should be done to explore the role of CBC in early prediction of iron deficiency before development of anaemia and if so, international guide lines should be planned to determine at which level we can diagnose iron deficiency from CBC and to start iron supplementation as early as possible.

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