



UTILITY OF AUTOMATED HEMATOLOGICAL INDICES IN EARLY DIAGNOSIS OF IRON DEFICIENCY ANEMIA IN RESOURCE LIMITED SET UP

Haematology

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ABSTRACT

Introduction: The study aimed at exploring the utility of automated hematological indices in early diagnosis of iron deficiency anemia, especially in small set ups.

Material And Methods: This was a retrospective case and control study where 104 cases were registered at our centre in the year 2020, out of those 104 cases, 64 were diagnosed cases of iron deficiency anemia with low serum ferritin and remaining 40 with normal iron profile taken as controls. Laboratory evaluation of 104 such cases done where sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of these hematological parameters were extracted taken serum ferritin as gold standard.

Results: The difference between values of MCV, MCH, MCHC and RDW in diagnosed anemic cases found statistically significant when compared with normal controls and all hematological indices shown statistically significant correlation with serum ferritin.

Conclusion: Present study signifies the importance and need of evaluating automated hematological parameters in diagnosing early iron deficiency anemia in the light of biochemical parameter like serum ferritin.

KEYWORDS

Iron deficiency anemia, automated hematology analyzer.

INTRODUCTION

Iron deficiency is one of the most prevalent forms of malnutrition. In India, more than half (51%) of all women of reproductive age have anemia as per WHO report in 2017. Iron deficiency anemia is the most common form of anemia observed in India⁽¹⁾. Given the multitude of clinical presentations and pathological investigations, evaluation of anemia is ever challenging. Use of automated hematology cell analyzer has improved the accuracy and precision, and has reduced the subjective error provided quality of analyzer is well maintained with time. RBCs parameters provides important guidelines for diagnosing, classification and monitoring the treatment of anemia⁽²⁾. Analyzers have already established in routine laboratory practice even in such set ups where there is no quick facility of microscopy or patients can't afford for costly iron studies, there it might help clinicians to rule out anemia in the light of clinical presentations and automated hematological reports.

MATERIALS AND METHODS

The study data was taken from **Modern Diagnostic and Research centre** at Kurukshetra (Haryana) in the year 2020, 64 confirmed cases of iron deficiency anaemia with haemoglobin <12gm/dl in females and 13gm/dl in men, serum ferritin <15mcg/l with automated haematological indices like MCV <80fl/cell, MCH <27pg/cell, MCHC <30g/dl and RDW >14.5% and rest 40 with normal hematological indices and serum ferritin. Since it was a retrospective study, I had no clinical data and peripheral picture of these cases, complete blood counts measured by Sysmex and iron profile based on Ferrozone, Chromazurol B measured by Biosystem A-25.

Statistical Methods:

Continuous data were reported as mean and standard deviation. The association between the serum ferritin and other blood indices were analyzed using Pearson's correlation coefficient. Further, all the hematological indices were binary coded using their respective cut-off values. The diagnostic performance (sensitivity, specificity, PPV and NPV, diagnostic accuracy) of binary coded data of blood indices was calculated and ROC analysis was performed against serum ferritin (<15mcg/l and ≥15mcg/l) taken as gold standard. Logistic regression model was also performed to predict the iron deficiency anemia using blood indices as independent variable. All the statistical analysis was performed in R v4.0.0 for Windows.

OBSERVATIONS AND RESULTS:

Out of 64 confirmed cases of iron deficiency anemia, there were 48 females (75%), 16 males (25%) as compared to females 18 (45%) and 22 males (55%) in 40 controls.

The mean distribution of age and hematological parameters were described in case and control group in the Table 1. The analysis revealed that the study subjects among cases were younger than

control group however the difference was not found statistically significant (P>0.05). Further, analysis revealed that the mean of hematological parameters were significantly higher among control group than cases except RDW CV which was higher in cases than control (P<0.0001).

Table1 Depicts The Comparison Between The Baseline Characteristics Of Cases (64) And Control (40) Groups.

Variables	Group				t test	P value
	Control		Case			
	Mean	SD	Mean	SD		
AGE	41.93	19.16	34.64	18.05	1.96	0.05
S FERRITIN	90.76	59.13	7.56	3.64	11.26	<0.0001
MCV	87.70	4.47	72.47	7.65	11.42	<0.0001
MCH	28.97	1.39	21.71	3.76	11.71	<0.0001
MCHC	32.76	1.11	28.97	2.58	8.78	<0.0001
RDW CV	13.36	1.18	17.75	2.56	10.15	<0.0001
HB	14.05	1.55	9.26	2.13	12.32	<0.0001

Table2 Depicts: Diagnostic Performance Of Hematological Indices To Predict The Iron Deficiency Diagnosed By Serum Ferritin As Gold Standard.

Hematological Indices	Diagnostic parameters	
MCV	Sensitivity (95% CI)	82.8(71.3-91.1)
	Specificity (95% CI)	100(91.2-100)
	ROC area (95% CI)	0.91(0.87-0.96)
	PPV (95% CI)	100(93.3-100)
	NPV (95% CI)	78.4(64.7-88.7)
	Accuracy (95% CI)	89.4(81.9-94.6)
MCH	Sensitivity (95% CI)	95.3(86.9-99.0)
	Specificity (95% CI)	100(91.2-100)
	ROC area (95% CI)	0.98(0.95-1.0)
	PPV (95% CI)	100(94.1-100)
	NPV (95% CI)	93.0(80.9-98.5)
	Accuracy (95% CI)	97.1(91.8-99.4)
RDW CV	Sensitivity (95% CI)	96.9(89.2-99.6)
	Specificity (95% CI)	82.5(67.2-92.7)
	ROC area (95% CI)	0.90(0.83-0.96)
	PPV (95% CI)	89.9(80.2-95.8)
	NPV (95% CI)	94.3(80.8-99.3)
	Accuracy (95% CI)	91.3(84.2-96.0)
MCHC	Sensitivity (95% CI)	53.1(40.2-65.7)
	Specificity (95% CI)	100(91.2-100)
	ROC area (95% CI)	0.77(0.70-0.83)
	PPV (95% CI)	100(89.7-100)
	NPV (95% CI)	57.1(44.7-68.9)
	Accuracy (95% CI)	71.1(61.4-79.6)

Analysis of diagnostic performance showed that sensitivity was 95.3, 82.8, 96.9 and 53.1 in MCH, MCV, RDW CV and MCHC respectively. The specificity was 100, 100, 82.5 and 100 respectively in MCH, MCV, RDW CV and MCHC. The PPV was 100, 100, 89.9 and 100 and NPV was 93, 78.4, 94.3 and 57.1 in MCH, MCV, RDW CV and MCHC respectively. Furthermore, the diagnostic accuracy defined as concordance of the results was 97.1, 89.4, 91.3 and 71.1 respectively (Table 2).

Table 3 Depicts: Comparison Of Diagnostic Performance Of Haematological Indices.

Hematological indices	ROC area	SE	Chi square	P value
MCH	0.9766	0.0133	Reference	
MCV	0.9141	0.0238	7.0	0.0082
RDW CV	0.8969	0.0323	5.144	0.0233
MCHC	0.7656	0.0314	45.973	<0.0001

ROC analysis to predict the iron deficiency anemia revealed that the area under ROC (AUC) was highest in MCH (0.98) followed by MCV (0.91), RDW CV (0.90) and least in MCHC (0.77). The AUC of MCH was significantly higher than other indices (Table 3, Figure 1).

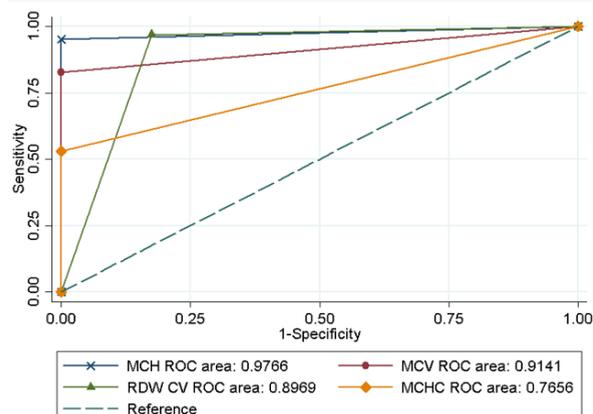


Figure 1: ROC Plot Showing The Sensitivity, 1-specificity And Comparison Of Area Under Curve Of Hematological Indices For Diagnosis Of IDA

Table 4 Depicts: Correlation Of Various Haematological Indices With Serum Ferritin.

Hematological Indices	Pearson's Correlation Coefficient	Pvalue
MCV	0.543	<0.0001
MCH	0.555	<0.0001
MCHC	0.488	<0.0001
RDW CV	-0.530	<0.0001

The correlation analysis revealed that Sr. ferritin was significantly associated with blood indices (P<0.0001).

Table 5 Depicts: Binary Logistic Regression Model To Predict The IDA With The Haematological Indices.

IDA	Beta Coefficient	SE	Z value	P value	95% CI	
					Lower	Upper
MCV	-1.97586	1.182753	-1.67	0.095	-4.29401	0.342293
MCH	-12.1351	8.616904	-1.41	0.159	-29.0239	4.753705
MCHC	2.699691	2.261117	1.19	0.232	-1.73202	7.131399
RDW CV	0.881639	1.42393	0.62	0.536	-1.90921	3.67249
Constant	392.407	251.3313	1.56	0.118	-100.193	885.0073

Logistic regression model was applied to predict the iron deficiency anemia (IDA) which revealed that the IDA may predict with the derived equation $IDA = 392.407 - 1.97586(MCV) - 12.13512(MCH) + 2.699691(MCHC) + 0.8816385(RDW CV)$ and this model explain about 94% ($R^2 = 0.944$) rest may contributed by other factors.

DISCUSSION:

Iron deficiency anemia is the most common form of anemia observed in India. Decreased serum ferritin is a good indicator of pre-latent iron deficiency while iron stores are depleted. Other iron parameters like serum iron, transferrin saturation and TIBC correspond well to circulating iron and may be used to recognize latent iron deficiency with diminished erythropoiesis⁽⁹⁾ and all hematological indices are

affected by change in levels of iron stores. Use of automated hematology cell analyzer has improved the accuracy and precision and has reduced the subjective error provided quality of analyzer is well maintained with time. With the advent of automated analyzers, RBC indices have emerged as low cost parameters for early detection of anemia, however in case of microcytic anemias, RBC parameters gives similar results that is low hemoglobin and low MCV⁽⁴⁾ that can be differentiated with the help of RDW CV as iron deficiency anemia shows raised RDW along with low MCV (microcytic heterogenous anemia) whereas other microcytic anemia like thalassemia trait shows low MCV with normal RDW (microcytic homogenous anemia)⁽⁵⁾. On evaluating utility of RBC indices, the highest diagnostic accuracy for prediction of iron deficiency anemia is given by MCH that is 97.1% which is supported by ROC area that is 97% with sensitivity (95.3%), specificity (100%), PPV(100%), NPV(93%)^(6,7) followed by MCV with sensitivity (82.8%), specificity(100%), PPV(100%), NPV(78.45), ROC area(91%), DA (89.4%), RDW CV with sensitivity(96.9%), specificity(82.5%),PPV(89.9%), NPV(94.3%), ROC area(90%),DA(91.3%)and MCHC with sensitivity(53.1%), specificity(100%), PPV(100%), NPV(57.1%), ROC area(77%), DA(71.1%). In present study, all RBC parameters shown statistically significant correlation with serum ferritin comparable with Rabindrakumar et al (except RDW CV shown statistically non significant correlation with serum ferritin).

CONCLUSION

Iron deficiency could be predicted using hematological indices, this is a cost effective test that could of great value in areas with limited resources besides serum ferritin, however further studies are warranted on a larger population across different socio economic strata to confirm our results.

Abbreviations:

Hb (Haemoglobin), MCV(Mean corpuscular volume), MCH(Mean Corpuscular Haemoglobin), MCHC(Mean Corpuscular Haemoglobin Concentration, RDW(Red Distribution Width), PPV(Positive Predictive Value),NPV(Negative Predictive Value), DA(Diagnostic Accuracy), CBC(Complete Blood Counts),ROC curve(Receiver Operating characteristics).

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