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PATRA'S INDEX - A SIMPLE AND BETTER TOOL TO DIFFERENTIATE BETA THALASSAEMIA TRAIT FROM IRON DEFICIENCY ANAEMIA

Pathology

Dr. Satyabrata Patra MD, DEPT. OF PATHOLOGY, RIMS, RANCHI,

Dr. Camellia Patra* MBBS, PGDMCH, Dept. Of Anatomy, Rims, Ranchi *Corresponding Author

ABSTRACT

Most frequent types of microcytic anaemia in Indian patients are Beta Thalassemia Trait (BTT) and Iron Deficiency Anaemia (IDA).We retrospectively judged the reliability of Mentzer index for differential diagnosis of microcytosis with a new index, a ratio of MCV/RDW (PATRA'S INDEX) in the same patient group.

Methods. A total of 406 randomly selected patients with different age group were evaluated. We calculated 6 discrimination RBC indices in all with consideration of RBC histogram. All the samples were also tested for HbA2,serum iron, TIBC and Iron saturation.

Results: PATRA'S INDEX showed better sensitivity than Mentzer index.

KEYWORDS

MCV, RDW, BTT, IDA, POSITIVE CUT OFF VALUE, PATRA'S INDEX.

INTRODUCTION :

Iron deficiency anaemia (IDA) and Beta Thalassaemia Trait (BTT) are two different types of anaemias, where both show microcytic morphology of RBC. BTT is a haemoglobinopathy, a congenital disease whereas IDA is an acquired disease, which is mainly due to dietary deficiency of iron. BTT can't be prevented or cured but iron deficiency anaemia can be prevented and cured by supplementing iron. Both the disease have different diagnostic, prognostic and treatment protocol. Confirmatory test for BTT is HbA2 level more than 3.5% and for IDA is low Iron, high TIBC and low Iron saturation. But these tests are expensive in Indian context. So, in order to differentiate IDA from BTT, different Red Cell indices are taken into account.

TABLE 1 : Table Showing Relation Of Mcv With Rdw In Different Types Of Anaemia

Low MCV RDW Normal	Low MCV RDW High	Normal MCV RDW Nomal	Normal MCV RDW High	High MCV RDW Nomal	High MCV RDW High
Thalassemia Minor	Iron Deficiency	Normal	Regeneration	Refractory Anemia	B12, Folate Deficiency
Anaemia Chronic Disease	HbS/Thal HbH	Renal Chemotherapy	Early Iron Def.	Prelukemia	AIHA
Normal Children (1-8 yrs	Fragment Anaemias (MHA)	Aplasia Heterozygote Hemoglobinopathy (AS, AC)	Sideroblastic	Liver Disease	
		Acute Blood Loss	Hemolysis - G6PD		

Their treatment protocol is also totally different. So, it is important to differentiate BTT from IDA by a simple routine test. Confirmatory test in cases of BTT is done by Haemoglobin electrophoresis and HPLC; in cases of IDA by serum iron, TIBC, serum Ferritin estimation. Over the years, many scientists have come out with different indices to differentiate BTT from IDA.

Basic critreria of difference between BTT and IDA, as given by the earlier scientists, was that in BTT, MCV is never less than 70fl, RBC count is normal and Hb% is around 10 gm% whereas in IDA, MCV is much lower, RBC count is low and Hb% is also low. Later on, with the introduction of CBC, RDW was also incorporated.

TABLE 2: TABLE SHOWING COMMON INDICES THAT ARE IN USE -

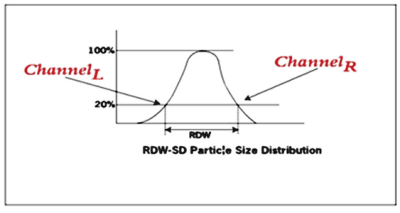
NAME OF INDEX	FORMULA	CUT OFF VALUE
1. MENTZER INDEX	MCV/RBC	<13
2. SRIVASTAVA	MCH/RBC	<3.8
3. ENGLAND AND FRASER	MCV-(5xHb)-RBC-3.4	<0
4. SHINE AND LAL	MCVxMCVxMCH /100	<1530
5. GREEN AND KING	MCVxMCVxRDW /Hbx100	<72
6. RICERCA	RDW/RBC	<3.3
7. RDWI	MCVxRDW/RBC	<220

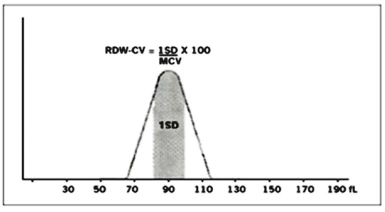
In Indian scenario, the value of these above indices cannot be used to arrive at a correct diagnosis as to the type of anaemia. The reasons being-

1. Here, many of the BTT patients also simultaneously suffer from iron deficiency or nutritional deficiency.
2. In many cases of BTT, we get a decrease in RBC count. So, indices which work with RBC count as a factor may give variable results.

In our study, we found MCV and RDW- CV to be better indicators for calculating an index which has higher specificity and sensitivity for diagnosing BTT.

DIAGRAM SHOWING RDW-SD AND RDW-CV





The index that we created for our study was :-
PATRA'S INDEX = MCV/RDW with a cut off value > 5.3
This index gives the correct cut off value to differentiate the two. In BTT, RDW is normal while in IDA, RDW is always increased. So, in BTT, we found MCV/RDW >/= 5.3 and in IDA to be < 5.3.

MATERIAL AND METHODS :

The investigations were conducted at the Haematology Laboratory, RIMS, Ranchi where patient's consent was taken for each patient. Approval by the local ethics committee was taken. There was no conflict of interest. 406 whole blood samples were used. The samples, collected in vials containing (EDTA-K3), were analysed within two hours of collection, using Haematology Analysers, Sysmex Corporation, Japan. Only the RBC parameters were noted. Histograms were taken into consideration. For each sample, a blood smear was prepared and stained manually, using Leishman stain. Every sample was tested for serum iron and TIBC, colorimetrically.

Each and every sample was rendered for HbA_2 estimation using Agarose gel electrophoresis and Elution method at alkaline pH.

We calculated PATRA'S index for every sample and compared it with the Mentzer index.

OBSERVATIONS :

SAMPLE	RBC $X10^6$?	Hb% g/dL	MCV fL	MCH Pg	MCHC g/dl	RDW %	MENTZER INDEX	MCV/RDW PATRA'S INDEX
1.	4.33	9.9	70.9	22.9	32.2	12.9	16.3	5.49#
2.	4.11	9.5	74	23.1	31.3	13.9	18.00	5.32#
3.	4.5	11.0	72.4	24.4	33.7	13.9	16.08	5.2
4.	4.43	10.9	73.6	24.6	33.4	14.2	16.61	5.18
5.	4.87	11.2	71	23	32.4	13.8	14.58	5.14
6.	4.84	12	73.6	24.8	33.7	14.4	15.20	5.11
7.	5.12	12.4	74.8	24.2	32.4	14.7	14.60	5.08
8.	4.33	11	75.1	25.4	33.8	14.9	17.34	5.04
9.	4.64	10	70.3	21.6	30.7	14.2	15.15	5.02
10.	5.38	11.3	66.5	21	31.6	15.1	12.36*	4.4
11.	4.32	10.3	72.7	23.8	32.8	14.8	16.82	4.9
12.	4.77	10.2	70	21.4	30.5	15.7	14.67	4.46
13.	3.38	7.2	73.4	21.3	29	20.7	21.71	3.54
14.	4.8	9.5	64.6	19.8	30.6	17.1	13.46	3.74
15.	4.93	9.6	65.1	19.5	29.9	17.2	13.20	3.78
16.	4.07	9.3	74.4	22.9	30.7	16.4	18.28	4.53
17.	5.05	10	71.7	19.8	27.6	16.8	14.19	4.26
18.	4.91	9.8	64.8	20	30.8	17.2	13.19	3.76
19.	4.31	9.6	69.8	22.3	31.9	14	16.19	4.98
20.	5.49	10.9	64.3	19.9	30.9	16.7	11.71*	3.85
21.	4.61	9	65.1	19.5	30	17.7	14.12	3.67
22.	5.2	10.2	64.6	19.6	30.4	16.5	12.42*	3.9
23.	4.04	6.9	64.4	17.1	26.5	17.6	15.94	3.66
24.	5.18	9	59.5	17.4	29.2	17	11.48*	3.5
25.	5.43	9.5	57.8	17.5	30.3	18.1	10.64*	3.19
26.	4.95	10.4	67.9	21	31	15.9	13.71	4.27
27.	5.1	10.6	66.9	20.8	31.1	16.7	13.11	4.0
28.	4.81	10.2	71.5	21.2	29.7	15.5	14.86	4.61
29.	4.92	10.8	69.5	22	31.6	22.7	14.12	3.06
30.	5.05	9.6	64.4	19	29.5	16.4	12.75*	3.93
31.	6.37	11.2	65.5	17.6	26.9	25.6	10.28*	2.56
32.	4.74	9	64.1	19	29.6	18	13.52	3.56
33.	3.98	8.4	68.8	21.1	30.7	16.8	17.28	4.09
34.	5.62	11.1	65.3	19.8	30.2	16.8	11.61*	3.88
35.	5.4	9.8	58.7	18.1	30.9	17.9	10.87*	3.39
36.	4.89	11.3	72.2	23.1	32	15.1	14.76	4.78
37.	3.72	8.8	72.3	23.7	32.7	14.5	19.43	4.98
38.	4.8	9.7	67.7	20.2	29.8	17	14.10	3.98
39.	5.5	10.7	63.1	19.5	30.8	16.1	11.47*	3.92
40.	4.71	11.2	73.5	23.8	32.4	18.3	15.60	4.01
41.	5.41	8.3	57.3	15.3	26.8	22.6	10.59*	2.53
42.	4.82	11.7	72.6	24.3	33.4	15.1	15.06	4.8
43.	4.7	8.6	64.3	18.3	28.5	16	13.68	4.01
44.	4.22	8.8	69.2	20.9	30.1	14.4	16.39	4.8
45.	5.74	8.4	54.9	14.6	26.7	20.6	9.56*	2.66
46.	5.78	10.7	61.2	18.5	30.2	20.8	10.58*	2.94
47.	2.37	4.4	52.3	18.6	35.5	41.7	22.06	1.25
48.	4.76	10.5	67.9	22.1	32.5	14.5	14.26	4.68
49.	4.87	8.1	57.7	16.6	28.8	22.3	11.84*	2.59
50.	5.82	10.5	59.3	18	30.4	17	10.18*	3.49

(*Marked patients are MENTZER INDEX positive, # marked patients are PATRA'S INDEX positive)

Randomly selected data of 50 patients were taken out of 406 total data in tabular form for comparision of Mentzer index with PATRA'S index. It was found that 15 pts were Mentzer positive of which only 1 pt. was of BTT.

But for PATRA'S index 2 positive patients were found of which 1 pt. was BTT. It proves better sensitivity of Patra's index.

RESULT :

We found 15 cases of True Positive BTT with PATRA'S index >/= 5.3
There were 388 True Negative cases (signifying cases of IDA) with PATRA'S index <5.3 (Value of 5.3 or more are considered as positive and value less than 5.3 are taken as negative.)

TABLE 3: TABLE SHOWING SENSITIVITY AND SPECIFICITY

SCREENING TEST RESULT	DIAGNOSIS	DIAGNOSIS
	INCREASED	DECREASED
POSITIVE	15 TRUE POSITIVE (A)	1 FALSE POSITIVE (B)
NEGATIVE	2 FALSE NEGATIVE (C)	388 TRUE NEGATIVE (D)

Sensitivity=A/ (A+C)*100=15/17*100=88.23%
Specificity=B/ (B+D)*100=388/389*100=99.7%

DISCUSSION :

Results found using the formula MCV/RDW had a sensitivity of 88%, whereas specificity was as high as 99%.

The main factors that are responsible for this high specificity and sensitivity are-

1. RDW correlated better than the RBC count in cases of BTT. In most of the cases of BTT, RDW was normal but in cases of IDA, it was invariably high.
2. Correlation of RBC count is not so rational in Indian cases.
3. It is the only index with a positive cut off value.

Normal persons also have PATRA'S index >5.3. So, only anaemic patients (haemoglobin </= 10 gm%) are to be considered as PATRA'S index positive, and have to be confirmed for BTT, by HbA2 estimation. PATRA'S index <5 correlated well with IDA and >5.5 with BTT, So 5 to 5.5 is a GREY ZONE. Anaemia of chronic disease (ACD) also shows microcytic anaemia with normal RDW, but incidence of ACD is very low as compared to IDA and therefore, has not been taken into consideration. We also get microcytic anaemia with normal RDW in children below the age of 8yrs.

At first 408 cases were taken for consideration but after Hb electrophoresis, 2 cases were taken out of the study, because one patient had HbA2 level as high as 45%, later on it was diagnosed as Hb E disease and another patient had Hb F 72%, who was suffering from (HPFH) hereditary persistence of foetal haemoglobin.

RDW within reference range indicates that erythrocytes follow a pattern of size distribution that approaches the normal of a population of individuals. Low RDW indicates the presence of a homogenous cell population, but it is not necessary that all cells have the same volume. So, it is important to make it clear that a normal RDW does not exclude the presence of a significant amount of cells that are much larger than the majority of cell population. Low RDW means the size of RBC's are

similar. In cases of high RDW, the variation in the size of RBC is more ie. Anisocytosis.

There is a natural desire to use the several possible combinations of MCV and RDW to arrive at possible diagnoses of anaemias, but this practice may produce errors and must never substitute more specific laboratory investigations, including the analysis of peripheral blood slides.

RDW reference intervals, calculated for healthy individuals, differ when obtained by analysers of different manufacturers, and sometimes, even on different models of the same manufacturer. This may be explained by the fact that analysers use different algorithms to analyse cell distribution. These algorithms are essential to eliminate extreme values, normally due to artifacts. Any consideration about the clinical use of RDW must be evaluated.

So it is to be kept in mind that the index can vary from instrument to instrument and may differ in different population. Hence, it's cut off needs to be adjusted accordingly.

Finally it is a better index for differentiation of BTT from IDA, since it can be easily calculated, correlates well, has a positive cut off value, can be automated, is cost effective and gives accurate results with high specificity and sensitivity.

It can be used for screening purpose in the society, as the sensitivity is high and the cost per test is low.

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