

## Clinical utility of red blood cell count, red cell distribution width: will it provide more accurate differentiation of Beta thalassemia trait and iron deficiency anemia in pregnancy?

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**Objective:** To test clinical utility of red blood cell count, red cell distribution width (RDW), along with these previously used indices in differential diagnosis in Beta thalassemia trait (BTT) and iron deficiency anemia (IDA).

**Methodology:** This was cross sectional study, performed at Department Gynecology, Rawal Institute of Health Sciences, Islamabad, Pakistan for 18 months from January 2013 to July 2014 on 95 patients with microcytic anemia (MCV <82) in pregnancy. Eighteen patients were excluded due to incomplete data. Serum ferritin was checked for all patients. Patients with ferritin level <15mg/dl were labeled as IDA. Those with ferritin >15 were further evaluated by Hb electrophoresis to diagnose thalassemia trait. CBC parameters i.e.

Red blood cell count, Mean Corpuscular volume, Mean corpuscular hemoglobin, Mean corpuscular hemoglobin concentration, Red cell distribution Width were compared in both IDA and BTT groups.

**Results:** Out of total 77 patients, 50 were IDA and 27 patients BTT. Prominent erythrocytosis was feature of BTT group (P <0.05). While, RDW was not found significantly different in two groups.

**Conclusion:** Increased RBC count was found to increase the sensitivity of CBC in differentiating between IDA and BTT. (Rawal Med J 201;41:424-427)

**Key words:** Beta Thalassemia Trait, Iron Deficiency Anemia, Complete Blood Count, pregnancy.

### INTRODUCTION

Beta thalassemia trait (BTT) and Iron deficiency anemia (IDA) are two main reasons for microcytic anemia in Asian subcontinent. We encounter huge number of pregnant ladies with anemia in our clinics every day, where we need to differentiate between BTT and IDA. BTT is genetically transmitted disease with carrier rate of 8-10% in Pakistan. Mass screening of BTT with some convenient test is the only method to stop the birth of child with blood transfusion dependent beta thalassemia major disease. More over, management of IDA could be hazardous for patient especially with intra venous iron if BTT is not ruled out by iron studies and hemoglobin (Hb) electrophoresis. Thus, recognition of BTT is necessary on two grounds, one to differentiate from the microcytosis of IDA and second for genetic counseling.

Both iron studies and Hb electrophoresis are expensive tests and not easily available at all places in Pakistan. Complete blood count (CBC) is often

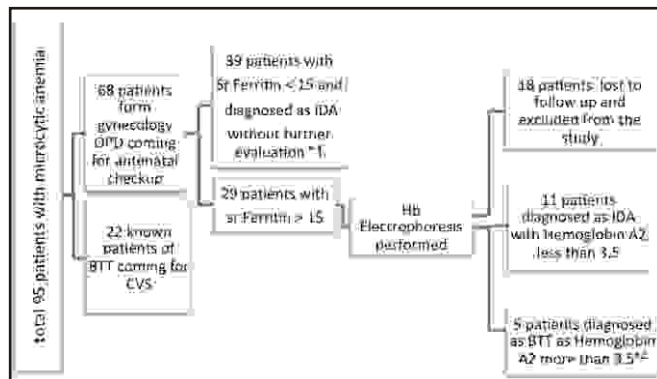
performed test on all pregnant ladies. Different component of complete blood count (CBC) i.e. Hb, red blood cell (RBC) count, hematocrit (HCT), mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC) are being used to discriminate between IDA and BTT. With the widespread use of cell counters, we have now acquired new RBC indices complementary of the old ones, i.e. Red Cell Distribution Width (RDW), which measures the heterogeneity of red cell size and anisocytosis in the blood smear.

RBC indices may show different efficiency in pregnancy but data on their use in pregnancy is scarce, especially role of RBC count and RDW is overlooked and unclear for this purpose. RBC indices had been primary test of preliminary diagnosis of microcytosis. Aim of this study was to compare the RBC indices between BTT and IDA in pregnant patients in order to determine any significant difference between the two groups.

## METHODOLOGY

This study was performed in Department of Gynecology, Rawal Institute of Health Sciences, Islamabad, Pakistan from January 2013 to July 2014.

**Fig. 1. Recruitment process.**



\* 1 Van Vranken M. Evaluation of microcytosis. *Am Fam Physician* 2010; 82(9):1117-22

\* 2 Rahman M, Kirtania K, Rahman M, Sultana N, Rahman S, Ahmed S. Iron Status In Beta Thalassemia Trait In Adult. *J Dhaka National Med Coll Hos* 2011;17:21-4.

The participants were 18-40 years of age with a low risk singleton pregnancy irrespective of gestational age. The inclusion criteria were Hb values  $>7.0$  and  $<10.9$  g/dl and  $MCV < 82$  fl.

The sample size 95 was calculated with the confidence level of 95%.

The recruitment procedure was a consecutive series of patients whose antenatal routine examination showed microcytic anemia ( $MCV < 82$ ) (Fig. 1). All data were analyzed using SPSS version 20. Paired-sample T test was applied on IDA and BTT group, separately for each hematological parameters i.e. RBC count, Hb, HCT, MCV, MCH, MCHC and RDW to find out any significant difference of these parameters in both groups.  $P < 0.05$  was taken as significant.

## RESULTS

Total 95 patients were enrolled in this study. 18 patients were excluded from study due to incomplete data. Out of remaining 77 patients, 27 were of BTT group, and 50 had IDA. Average age of patients was  $26.8 \pm 4.2$  years. Mean RBC count of BTT was  $4.98 \pm 0.74$  ( $\times 10^6$  mL) as compared to

$3.97 \pm 0.43$  ( $\times 10^6$  mL) in IDA ( $P = 0.00$ ).

**Table 1. Hematological parameters of patients (mean  $\pm$  SD + range).**

Parameter	IDA (N=50)	BTT (N=27)
RBC ( $\times 10^6$ mL)	$3.97 \pm 0.43$ (5.2-2.97)	$4.98 \pm 0.74$ (6.57-3.01)
HB (g/d L)	$9.09 \pm 1.02$ (10.9-7)	$9.84 \pm 0.96$ (10.9-7)
HCT (%)	$28.55 \pm 2.81$ (35-21.3)	$31.30 \pm 3.68$ (37.9-21.4)
MCV (f L)	$71.67 \pm 6.29$ (82- 54.4)	$61.60 \pm 7.18$ (70.3- 31.9)
MCH (pg cell)	$23.01 \pm 3.19$ (31.6-17.6)	$20.11 \pm 1.64$ (23.3-17.2)
MCHC (g/d L)	$31.73 \pm 2.71$ (37.6-19.4)	$31.97 \pm 1.90$ (34.6- 25.9)
RDW	$19.27 \pm 10.04$ (62.7-12.7)	$18.57 \pm 5.31$ (36.8-14.9)

Mean Hb as well as mean HCT were also found significantly high in BTT as compared to IDA. Mean MCV and mean MCH were low in BTT as compared to IDA. No statistically significant difference was observed between BTT and IDA for MCHC. Mean RDW was  $18.57 \pm 5.31$  in BTT which is not different significantly from RDW  $19.27 \pm 10.04$  in IDA ( $P = 0.965$ ) (Table 1).

## DISCUSSION

Anemia has become a challenging health problem for women in developing countries. In our society, pregnancy is the best window period in woman's life when she comes in contact with doctor or some medically trained person. We can avail this period for many screening programs for ladies. Although pregnancy is not the best time for screening of BTT but still in first trimester of pregnancy, thalassemia screening is very useful because we can diagnose fetal thalassemia major with the help of prenatal diagnosis and termination of pregnancy can be offered to the affected couple. In pregnant patients, missing thalassemia trait can prevent access to prenatal diagnostic services for major thalassemia.

Pregnancy causes significant changes in RBC indices. MCV increases up to average 4fl in iron depleted woman. MCH also show increase in 2<sup>nd</sup> trimester while MCHC does not show any

significant change during pregnancy. Looking at these mentioned changes different values of RBC indices are expected in pregnancy.

Erythrocytosis was a prominent feature of BTT in our study in comparison to IDA, as RBC count  $4.98 \pm 0.74$  in BTT patients as compared to  $3.97 \pm 0.43$  SD in IDA. Urrechaga et al had suggested that erythrocytosis with severe microcytosis is a hallmark of BTT. Functional availability of iron for erythropoiesis in BTT could be possible reason for increased RBC count in BTT as compared to IDA.

BTT group showed increased microcytosis also in our study with MCV of  $61.60 \pm 7.18$  with as compared to IDA group showing MCV of  $71.67 \pm 6.29$ . Same result were shown by Baxi et al. Amna et al used MCV to screen BTT and found it 79.9% sensitive and 30% specific with positive and negative predictive value of 56% in detection of BTT.

Sirichotiyakul et al concluded that MCV was useful tool for screening for alpha-thalassemia-1 and beta-thalassemia traits during pregnancy because of its simplicity, low cost and high sensitivity of 92.9%. In their another work, they compared the accuracy of the osmotic fragility test (OFT) and MCV when screening for the BTT and showed that MCV may be the first choice for screening wherever an automated hematology analyzer calculating MCV is available.

MCH was also found low in BTT as compared to IDA. Difference of values of MCH in both groups is not statistically significant. It means MCH has poor differentiation power. In contrast, Karimi et al found MCH 98.5% sensitive in premarital screening for BTT. While MCHC found normal in both group and statistically not significant for detecting BTT and IDA.

Mean RDW in our work was raised in IDA as compared to BTT. But this difference was not statistically significant. Similar results were reported by Sirdah et al that RDW was poor in differentiating between BTT and IDA in Palestinian population. Alwar et al showed that IDA was suspected in patients with microcytic hypochromic red blood cells associated with anisopoikilocytosis (resulting in raised RDW) and low RBC counts.

Significant microcytosis and erythrocytosis could both be helpful for differentiation between BTT and

IDA, according to this study. Barnhart-Magen et al in their recently published work devised method to diagnose BTT and presented that three parameter scheme based on MCV, RBC count, and RDW has specificity of 0.968 and sensitivity of 0.9 in differentiating BTT from IDA and suggested that CBC can be used initially for the diagnosis of BTT before high costs tests.

## CONCLUSION

CBC can be used as preliminary test for differential diagnosis for BTT and IDA while Iron studies and Hb electrophoresis are the gold standard for diagnosis. In CBC, when there is microcytic anemia, increased RBC count can be helpful hunt for BTT.

### Author contributions:

Conception and design: Shahida Tasneem  
 Collection and assembly of data: Shahida Tasneem  
 Analysis and interpretation of the data: Shahida Tasneem  
 Drafting of the article: Shahida Tasneem  
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## REFERENCES

1. Nisa Q, Habibullah, Rizwan F, Memon F, Memon A. Frequency of thalassemia trait in pregnant women. Med Channel 2011;17:56-9.
2. Khattack ID, Khattack ST, Khan J. Heterozygous beta thalassemia in parents of children with beta thalassemia major. Gomal J Med Sci 2006;4:2.
3. Bryant BJ, Hopkins JA, Arceo SM, Leitman SF. Evaluation of low red blood cell mean corpuscular volume in anapheresis donor population. Transfusion 2009;49:1971-6.
4. Ntaios G, Chatzinikolaou A, Saouli Z, Girtovitis F, Tsapanidou M, Kaiafa G, et al. Discrimination indices as screening tests for beta-thalassemic trait. Ann Hematol 2007;86:487-91.
5. Nazir G, Naz S, Ali S, Aziz S, Malik SA, Qari IH, Irum S. Anaemia: the neglected female health problem in developing countries. J Ayub Med Coll Abbottabad 2011;23:08-11.
6. Kiss TL, Ali MA, Levine M, Lafferty JD. An Algorithm to Aid in the Investigation of Thalassemia Trait in Multicultural Populations. Arch Pathol Lab Med

- 2000;124:1320-3.
7. Chandra S, Tripathi AK, Mishra S, Amzarul M, Vaish AK. Physiological changes in hematological parameters during pregnancy. *Indian J Hematol Blood Transf* 2012;28:144-6.
  8. James TR, Reid HL, Mullings AM. Are published standards for haematological indices in pregnancy applicable across populations: an evaluation in healthy pregnant Jamaican women. *BMC Pregnancy Childbirth* 2008;28(8):8.
  9. Urrechaga E, Borque L, Escanero JF. Erythrocyte and reticulocyte parameters in iron deficiency and thalassemia. *J Clin Lab Anal* 2011;25:223-8.
  10. Noronha JF, Grotto HZ. Measurement of reticulocyte and red blood cell indices in patients with iron deficiency anemia and beta-thalassemia minor. *Clin Chem Lab Med* 2005;43:195-7.
  11. Baxi A, Manila K, Kadhi P, Heena B. Carrier Screening for Beta Thalassemia in Pregnant Indian Women: Experience at a Single Center in Madhya Pradesh. *Indian J Hematol Blood Trans* 2013;29:71-4.
  12. Amna A, Zehra N, Haider G, Anjum F, Rani S, Munir AA. Role of mean corpuscular volume as screening test for thalassaemia in pregnant women at Isra University Hospital Hyderabad. *Pak J Med Sci* 2010;26:390-3.
  13. Sirichotiyakul S, Maneerat J, Sa-nguansermisri T, Dhananjayanonda P, Tongsong T. Sensitivity and specificity of mean corpuscular volume testing for screening for alpha-thalassemia-1 and beta-thalassemia traits. *J ObstetGynaecol Res* 2005;31:198-201.
  14. Sirichotiyakul S, Wanapirak C, Srisupundit K, Luewan S, Tongsong T. A comparison of the accuracy of the corpuscular fragility and mean corpuscular volume tests for the alpha-thalassemia 1 and beta-thalassemia traits. *Int J Gynaecol Obstet* 2009;107:26-9.
  15. M. Karimi, A. R. Rasekhi .Efficiency of premarital screening of beta-thalassemia trait using MCH rather than MCV in the population of Fars Province, Iran. *Haematologia* 2002;32:129-133.
  16. Sirdah M, Tarazi I, Al Najjar E, Al Haddad R. Evaluation of the diagnostic reliability of different RBC indices and formulas in the differentiation of the beta-thalassaemia minor from iron deficiency in Palestinian population. *Int J Lab Hematol* 2008;30:324-330.
  17. Alwar V, Kavdia R, Singh N, Rameshkumar K. Hunt for the Hidden Trait. *J Lab Physicians* 2009;1:158.
  18. Barnhart-Magen G, Gotlib V, Marilus R, Einav Y. Differential Diagnostics of Thalassemia Minor by Artificial Neural Networks Model. *J Clin Lab Anal* 2013;27:4816.