Efficacy of Red cell distribution width (RDW) as a screening test for diagnosing children with Iron Deficiency anaemia

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Abstract: The Objective of present study is to evaluate the efficacy of Red Cell Distribution Width as a screening test for diagnosing children with Iron Deficiency anaemia. Prospective study method and Statistical methods were used. Sensitivity, specificity, positive predictive value, negative predictive value and Receiver Operating Characteristics (ROC) were studied. Out of 97 patients, Females were 32 (38%), Males 65 (62%). Maximum number of patients were in the age group of 1–6 years (40.2%). Out of 97 cases, 67 (68%) were found to have iron deficiency anaemia and 31 (32%) were non iron deficient anaemia. In this study, severe anaemia was found in 3 cases (3.1%), moderate anaemia in 26 cases (26.5%) and mild anaemia in 68 cases (70.4%). The mean standard deviation for RDW in iron deficient cases was 13.68±2.88. Sensitivity, specificity, positive predictive and negative predictive value were obtained using Receiver Operating Characteristics (ROC) curves with a cut off RDW of 14 and 13. With cut off 14, sensitivity was 47%, specificity 75%, positive predictive 60%, and negative predictive value 63%, False positive 25% and false negative 53%. With cut off 13, sensitivity was 64%, specificity 58%, positive predictive 56%, and negative predictive value 67%. False positive 42% and false negative 36%. RDW may not be useful as a screening test and other studies evaluating iron stores in the body like serum iron, serum ferritin, iron binding capacity and serum transferrin saturation may still be needed for appropriate diagnosis of iron deficiency anaemia.

Keywords: Iron Deficiency anaemia, RDW, ROC.

INTRODUCTION

Anaemia is a major public health problem all over the world especially in developing countries. Anaemia prevalence in young children continues to remain over 78% in most parts of India despite a policy being in place and a program that has been initiated for a long time. The irreparable damage that anaemia in childhood can cause particularly to the development of a young child on one hand and the knowledge and mechanism available for its control on the other, makes this silent morbidity completely unacceptable in modern times where we strive for millennium development Goal 4 [1].Out of all the causes, like nutritional anaemias, Hemolytic anaemias, Chronic infections, Lymphoreticular malignancy, etc., nutritional anaemias account for the major cause of anaemias.

Pregnant women, infants, young children and adolescents are at a higher risk of nutritional anaemia as they have a high demand of nutrients such as iron, folic acid, Vit B 12 and other nutrients. Nutritional anaemia is prevalent all over the world, with an estimated one billion people being iron deficient [2]. In India, anaemia is an important health problem, especially among children. Anaemia in children results in impaired cognitive performance, behavioural and language development and scholastic achievement. Anaemia is also associated with increased mortality and morbidity from infectious diseases[3]. The third National Family Health Survey ( NFHS – 3)(2005-06) found that the prevalence of anaemia among under 5 children approaches 78.9 % in children from 6 – 59 months [4] even though there is a national programme to control anaemia for many years.

Anemia is defined as an abnormally low hemoglobin level due to pathological condition(s). Iron deficiency is one of the most common, but not the only cause of anaemia. Other major causes of anaemia include chronic infections, particularly malaria, hereditary
hemoglobinopathies, and folic acid and vitamin B 12 deficiency. In public health terms, iron deficiency is by far the first cause of nutritional anemia worldwide.

One of the main differential diagnosis of iron deficiency anaemia is beta thalassemia trait because both have microcytosis in peripheral smear which creates confusion in diagnosis and hence treatment. Differentiation of these microcytic anemias is of clinical importance, particularly in a multi-ethnic Indian population, because each has entirely different cause, pathogenesis, prognosis and treatment. In order to diagnose these, a variety of investigations are done like serum ferritin, serum Iron, total iron binding capacity, serum transferrin saturation and serum electrophoresis which causes major financial burden to the patients. Hence it becomes important to diagnose these cases with cost effectiveness in mind. Various studies have shown that Red cell distribution width(RDW) will identify whether the anaemia is due to iron deficiency or thalassemia trait. The RDW represents the coefficient of variation of the red blood cell volume distribution and can be considered an index of heterogeneity, the equivalent of anisocytosis observed in the peripheral blood smear. Red cell distribution width (RDW) is an automated laboratory determination of red cell anisocytosis which is displayed by all modern automated blood analysers. Moreover studies from western countries have shown that RDW can be a good screening index especially for Iron Deficiency anaemia and the thalassaemia trait[5-8]. Some studies in adults found that RDW may not be useful for differentiating IDA and thalassemia trait [9]. In order to diagnose the cause of anaemia these children in developing countries with cost effectiveness, this study was undertaken to find out whether RDW can be used as a screening test in our population.

**METHODOLOGY**

This prospective study was conducted in paediatric ward of a tertiary care hospital in southern India. All patients admitted in paediatric ward of this hospital were evaluated for anaemia. Those patients who are less than 6 months of age, sick patients, blood transfusion within one month, patients who are on drugs, other conditions causing bone marrow suppression were not included in the study. All other patients with Hemoglobin levels less than the WHO cut off levels for anaemia were included in the study. WHO Expert group proposed that anaemia should be considered to exist when Haemoglobin is below the following levels in venous blood. 6 months to 6 years 11 gm / dl, less than 12 g/dL for girls from 12 to 18yrs and boys less than 14 years and less than 13 g/dL for boys from 15 to 18 yrs of age[10].

In those patients with anaemia, the following laboratory investigations were done like MCV, MCH, MCHC, RDW, Serum Ferritin, Serum Iron, TIBC, and Serum Transferrin (TRF) [11]. 5 ml of blood was collected in a EDTA tube for the study.

Hb, RDW was estimated by automated impedance and flow cytometric analyzer, Serum Ferritin by chemiluminescent immunoassay, Serum Iron by Ferrozine-no deprotenization method, TIBC by Ion exchange resin- Ferrozine method and Serum Transferrin (TRF) by rate nephelometry from Beckman coulter , USA.

The patients were diagnosed to have iron deficiency anaemia based on Serum ferritin < 7 ng/ml or Serum Iron < 22 or TIBC > 389 microgm/dl [12].

**RESULTS**

A total of 97 patients were enrolled in the study. Out of those 97 patients, Females were 32 ( 38 % ), Males 65 (62 % ).Maximum number of patients were in the age group of 1 – 6 years 39 (40.2 % ).Less than 1 year constituted 9 patients ( 9.2 % ), 6 – 10 years 27 (27.8%) and more than 10 years 22 (22.6%). Less than 1 year constituted 9 patients (9.2 %), 6 – 10 years 27 (27.8%) and more than 10 years 22 (22.6%). Out of 97 cases, 67 (68%) were found to have iron deficiency anaemia and 31 (32%) were non iron deficient anaemia. This correlates with the general prevalence of iron deficiency anaemia. In this study, severe anaemia was found in 3 cases (3.1%), moderate anaemia in 26 cases (26.5%) and mild anaemia in 68 cases (70.4%).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Iron deficiency</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>10.31±1.67</td>
<td>10.15±1.45</td>
</tr>
<tr>
<td>PCV</td>
<td>31.36±5.13</td>
<td>30.82±3.86</td>
</tr>
<tr>
<td>RBC</td>
<td>4.21±0.87</td>
<td>4.60±0.71</td>
</tr>
<tr>
<td>Platelet</td>
<td>count 2.93±1.51</td>
<td>3.77±1.95</td>
</tr>
<tr>
<td>MCV</td>
<td>75.72±8.29</td>
<td>68.33±14.7</td>
</tr>
<tr>
<td>MCH</td>
<td>24.39±2.93</td>
<td>22.61±4.79</td>
</tr>
<tr>
<td>MCHC</td>
<td>32.34±1.69</td>
<td>32.49±2.46</td>
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</tbody>
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RDW values were noted and compared with iron deficient and non iron deficient patients. The mean standard deviation for RDW in iron deficient cases was 13.68±2.88. RDW was more in iron deficient cases than in non iron deficient cases. With this in mind, sensitivity, specificity, positive predictive and negative
predictive value was obtained using Receiver Operating Characteristics (ROC) curves with a cut off RDW of 14 and 13. With cut off 14, sensitivity was 47%, specificity 75%, positive predictive 60%, and negative predictive

**ROC Curve**

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>1 - Specificity</th>
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<tbody>
<tr>
<td>0.47</td>
<td>0.60</td>
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Cut off 14

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>1 - Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.64</td>
<td>0.58</td>
</tr>
</tbody>
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With cut off 13, sensitivity was 64%, specificity 58%, positive predictive 56%, and negative predictive value 67%, False positive 42% and false negative 36%.

**Figure1: ROC curves with RDW cutoff of 14 and 13.**

DISCUSSION

As seen from the results, mean RDW was more in iron deficient cases. With the above statistical analysis RDW with cut off 14, sensitivity was 47%, specificity 75%, positive predictive 60%, and negative predictive value 63%. In a study by Sunil Sazawal et al in India in 2014 [13], the authors concluded that with RDW >15% as cutoff and with hemoglobin ≤10.0 g/dL identifies iron deficient anemic children without need for iron status markers which could help reduce cost of management. In another study done by Van Zeben D et al [14], it was found that RDW value within the reference interval can be used to exclude iron deficiency in those cases in which the serum ferritin concentration does not accurately reflect the iron stores as well as in inflammation or malignancy. Microcytic anaemias due to iron deficiency and beta thalassemia has to be differentiated because of different treatment protocols. D. Aslan et al [15] found no difference between the means of RDW in δβ-TT and IDA (18.00 ± 1.94) (P > 0.05). But they noted a significant rise in RDW in IDA 5–7 days after initiation of iron therapy (P = 0.00) which was continued to rise up to the 4th week of therapy as suggested as an important tool in differentiation of IDA from δβ-TT. Vishwanath et al [16], evaluated 100 anemic children, showed a sensitivity of 92.1% and specificity of 90.9% for RDW in detecting iron deficiency when RDW cutoff was 18.31 and for diagnosing mild and moderate iron deficiency anemia, RDW had a higher sensitivity than PS. There are various studies done before like Flynn MM [17] which concluded that RDW only may not be a major parameter for detecting iron deficient anemias and that a sequential evaluation including iron and hemoglobin studies should be done in all of cases of microcytosis to detect iron deficiency anemias. Thompson WG [18] studied 247 anemic hospitalized patients which showed limited sensitivity and specificity for detecting iron deficiency anemia using RDW. A red cell distribution width greater than 15% had a sensitivity of 71% and a specificity of 54% for iron deficiency. They concluded that since the sensitivity and specificity is less than reported in studies of healthier populations, they cannot be relied on for screening for iron deficiency in hospitalized patients. Another Indian study by Roosy Aulakh et al also concluded with the findings that RDW has got a limited specificity for iron deficiency anemias[14].

The main limitations of our study is that the sample size is small comparing the prevalence of anaemia in our community. Since this is a hospital based study, the findings may not be a true reflection as in the community.

CONCLUSIONS

In view of high prevalence of iron deficient anaemia in our community, it is important to diagnose them early to give adequate treatment with iron supplements and dietary modifications. We should develop low cost measures to diagnose them without stretching the financial resources. RDW, which all recent automated cell counters display in the reports could of great help in diagnosis of iron deficiency anaemia. The sensitivity and specificity for only RDW is limited for the diagnosis of iron deficient anaemia. Hence, mere RDW may not be useful as a screening test and other studies evaluating iron stores in the body like serum iron, serum ferritin, iron binding capacity and serum transferrin saturation may be still needed for appropriate diagnosis of iron deficiency anaemia.
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REFERENCES