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Haematological Profile in Microcytic Hypochromic Anaemia in Children

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Abstract: *Anaemia whether clinically overt or not is a common condition encountered by family physician. The most commonly encountered disorders with mild microcytic hypochromic anaemia are iron deficiency anemia (IDA) and Thalassemia Trait (TT). The establishment of an accurate diagnosis is of great importance in ensuring correct treatment. A total of forty four patients with hypochromic microcytic anaemia were screened for various hematological profiles in the age group of 1-12 years. Out of 44 patients studied 56.8% were girls, 43.2% were boys. Mild anaemia was observed in 59.1% of cases, moderate anaemia was observed in 29.5 % of cases and severe anaemia was observed in 11.4% of cases. Hb Electrophoresis, Serum Iron profile and Red cell indices are complementary to each other in the precise diagnosis of microcytic hypochromic anaemia of varied etiology, which would enable comprehensive wholesome treatment.*

Keywords: *Iron deficiency anaemia, Thalassemia, Red cell indices, Microcytic Hypochromic Aneamia.*

I. Introduction

Anaemia whether clinically overt or not is a common condition encountered by family physician. The most commonly encountered disorders with mild microcytic hypochromic anaemia are iron deficiency anemia (IDA) and Thalassemia Trait (TT).[1, 2] Hypochromic microcytic aneamia can also be due to anaemia of chronic disease or lead poisoning. The establishment of an accurate diagnosis is of great importance in ensuring correct treatment. Administration of iron to a patient with hypochromic aneamia due to a cause other than iron deficiency is not only useless but leads to undesirable effects of increase in body iron stores. Thalassemia Minor and Thalassemia Intermedia may pass off as iron deficiency anaemia, if only peripheral smear was the sole diagnostic modality.

β-Thalassemia is also an iron loading anemia, meaning that thalassemic patients have a dramatic increase in iron absorption from the gut due to their increased erythropoietic rate[3–6], and together with the iron influx from chronic transfusions contributes to the general setting of iron overload observed in thalassemic patients. Inadvertent iron therapy will prove detrimental in such situations.

Iron plays an essential role in many important biochemical processes.[7] As with all nutrients, the requirement for iron is greater during periods of rapid growth and differentiation such as in the late fetal and neonatal period. Consequently, poor iron homeostasis during this period can result in disordered development. Inadequate tissue iron levels can lead to reduced erythropoiesis and poor O_2-carrying capacity. The nervous system, which develops rapidly during the late fetal and early neonatal period, seems to be particularly susceptible to iron deficiency and excess.[8] Also, Iron excess can have severe effects on neuron development.[6–8] Thus, events occurring in early life can have long-lasting effects on neuronal function in the adult. Excessive iron in the circulation leads to abnormal accumulation in organs such as liver, spleen and heart, leading ultimately to liver disease, cardiac dysfunction, arthropathy, gonadal insufficiency and other endocrine disorders.[9]

Twenty percent of children in United States and eighty percent of children in developing countries will be anaemic at some point of time by the age of 18 years. Hence it is worthwhile to study the role of hematological profile including serum iron, serum iron binding capacity, haemoglobin electrophoresis and bone marrow iron which would delineate these disease entities and enable correct management. Proper care of anaemia in growing buds is very important especially for a developing country like India and is very helpful not only for the family but also for the nation.

II. Materials And Methods

Patients aged 1-12 years with microcytic hypochromic anaemia are selected for study. A total of forty four patients with hypochromic microcytic anaemia were screened for various hematological profiles. Since 1200 samples of hypochromic microcytic anaemia are received in our department per year, it represents about 3.67% of incidence in our department. The inclusion criteria were, age group 1-12 years, Patients with clinical symptoms of anaemia and Haemoglobin levels were, age 1-6 years <10.5 g/dl, 7-12 years <11 g/dl. The exclusion criteria were, age below one year and above twelve years, peripheral smear with dimorphic picture, H/O transfusion within past two months and children are on haematinics. The following reference value were used for our study.[Table – 1]

III. Observation And Results

Newly diagnosed cases of microcytic hypochromic anaemia admitted to our hospital with no prior blood transfusion or iron treatment were randomly enrolled. A total of 44 cases were enrolled as per inclusion and exclusion criteria.Patients with Microcytic Hypochromic Anaemia with age between 1-12 years were included in this study. Out of 44 cases, 27.3% were below 4 years, 36.4% were between 5-8 years and 36.4% were between 8-12 years. Among the randomly enrolled 44 patients, 25 were girls while the remaining 19 were boys. Girls constituted 56.82% and boys constituted 43.18%. Mild anaemia (Hb 10-12 g/dl) was present in 26 cases, moderate anaemia (Hb 8-9.9 g/dl) in 13 cases and severe anaemia (Hb <8 g/dl) in 5 cases. [Table-2]

97.7% of study population had Mean Corpuscular Volume (MCV) below 80 fl. 93.2% had Mean Corpuscular Heamoglobin (MCH) below 25pg. 95.5% had Mean Corpuscular Heamoglobin Concentration (MCHC) below 30 g/dl. Out of 44 cases, 52.3% had Serum (S) Ferritin below 12ng/dl, 20.5 % had Serum Ferritin between 12-50 ng/dl & 27.3% had Serum Ferritin above 50 ng/dl. Out of 44 cases, 6.8% had Total Iron Binding Capacity (TIBC) < 250 µg/dl, 45.5% had TIBC between 250-400 µg/dl & 47.7% had TIBC >400 µg/dl. Out of 25 girls in the study population, 80% had S. Iron < 60 µg/dl, 4% had S. Iron 60- 160 µg/dl & 16% had S. Iron >160 µg/dl. 89. 5% of boys in the study population had a S. Iron below 35µg/dl.

Mean haemoglobin level does not vary significantly with age. When ANOVA test was conducted (F=2.765; P>0.05) the mean haemoglobin was highest in the age group of 9- 12 years (7.76 g/dl) and lowest in the age group of 1-4 years (5.93 g/dl). Mean Red Blood Cell (RBC) counts varied significantly with age. When ANOVA test was conducted (F= 4.799; P<0.05*) the mean RBC count was highest in the age group of 9- 12 years (3.81million/ mm^3) and lowest in the age group of 5-8 years (2.73 million/mm^3). (*- significant at 5% level). Mean haematocrit does not vary significantly based on age. When ANOVA test was conducted (F= 3.098 ; P>0.05) the mean haematocrit was highest in the age group of 9- 12 years (22.33%) and lowest in the age group of 5-8 years (17.10%). Mean MCV varied significantly with age. When ANOVA test was conducted (F= 0.069; P < 0.05*) the MCV was highest in the age group of 5-8 years (62.25 fl) and lowest in the age group of 1-4 years (60.75 fl). Mean MCH does not vary significantly with age. When ANOVA test was conducted (F= 0.250; P>0.05) the mean MCH was highest in the age group of 5-8 years (19.27pg) and lowest in the age group of 1-4 years (17.99 pg).

Mean MCHC does not vary significantly based on age. When ANOVA test was conducted (F= 0.757; P >0.05) the mean MCHC was highest in the age group 9-12years (25.05g/dl) and lowest in the age group of 1-4 years (23.20g/dl). Mean RDW varied significantly based on age. When ANOVA test was conducted (F= 4.961; P<0.05*) the mean RDW was highest in the age group 1-4 years (53.01fl) and lowest in the age group of 9-12 years (44.15fl). Mean S. Iron does not vary significantly with age. When ANOVA test was conducted (F= 0.217; P>0.05) the mean Iron was highest in the age group of 1-4 years (66.40 gµ/dl) and lowest in the age group of 5-8 years (45.99µg/dl) [Table-4]. Mean TIBC does not vary significantly based on age. When ANOVA test was conducted (F= 0.569; P>0.05) the mean TIBC was highest in the age group 5-8 years (402.53µg/dl) and lowest in the age group of 9-12 years (372.40 µg/dl). Mean ferritin does not vary significantly based on age. When ANOVA test was conducted (F= 0.928; P>0.05) the mean ferritin was highest in the age group of 1-4 years (195.15ng/dl) and lowest in the age group of 5-8 years (43.30ng/dl).

Mean Haemoglobin level does not vary significantly between boys and girls. When t-test was applied (t= 0.087; P>0.05) the average haemoglobin in boys was 6.77g/dl & for girls 6.71g/dl. Mean RBC counts do not vary significantly between boys and girls. When t- test was applied (t=1.707; P>0.05) the average RBC count in girls was 3.40 million/mm^3 where as for boys it was 2.81 million/mm^3. Mean Haematocrit does not vary significantly between boys and girls. When t- test was applied (t= 0.559; P>0.05) the average HCT in girls was 19.63% where as for boys it was 18.47%. MCV does not vary significantly between boys and girls. When t- test was applied (t=1.985; P>0.05) the average MCV in boys was 65.07fl where as for girls it was 58.71fl.

Mean MCH does not vary significantly between men and women. When t- test was applied (t= 0.256; P>0.05) the average MCH in girls was 18.52pg whereas for boys it was 18.89 pg. Mean MCHC does not vary significantly between men and women. When t- test was applied (t=0.556; P>0.05) the average MCHC in girls was 24.39g/dL where as for boys it was 23. Mean Red Cell Distribution Width (RDW) does not vary significantly between girls and boys. When t- test was applied (t=1.067; P>0.05) the average RDW in girls was 47.74 fl whereas for boys it was 50.52 fl.

Mean serum Iron does not vary significantly between men and women. When t- test was applied (t=1.575; P>0.05) the average serum Iron in girls was 70.31µg/dl where as for boys it was 32.46 µg/dl. Mean TIBC does not vary significantly between men and women. When t- test was applied (F=1.079; P>0.05) the average serum Iron in girls was 373.79 µg/dl where as for boys it was 400.68 µg/dl. Mean ferritin does not vary significantly between boys and girls. When t- test was applied (t=0.796; P>0.05) the average ferritin in girls was 141.87 ng/dl where as for boys it was 70.81 ng/dl.

Statistical Analysis Between B **–Tt And Mild To Moderate (8-11.5 G/Dl) Ida**

Mean haemoglobin varied significantly between IDA, β-TT. When t-test was applied (t=3.239; P<0.01) the mean Haemoglobin in IDA patients was 8.99g/dl where as for β-TT 10.57g/dl [Table-3]. Mean MCV varied significantly between IDA, β-TT. When t-test was applied (t=5.402; P<0.01**) the mean MCV in IDA patients was 68.45 (fl) where as for β-TT 38.91(fl). (**- significant at 1% level)**.** Mean MCH do not vary significantly between IDA, β-TT. When t-test was applied (t=1.938; P>0.05) the mean MCH in IDA patients was 20.79 pg where as for β-TT 17.04 pg. Mean MCHC do not vary significantly between IDA, β-TT. When t-test was applied (t=1.382; P>0.05) the mean MCHC in IDA patients was 23.83g/dl where as for β-TT 27.52 g/dl. Mean RDW varied significantly between IDA, β-TT. When t-test was applied (t=5.407; P<0.01) the mean RDW in IDA patients was 47.77 fl where as for β-TT 35.02 fl.

Mean serum Iron does not vary significantly between IDA, β-TT. When t-test was applied (t=1.248; P>0.05) the mean serum Iron in IDA patients were 50.11 µg/dl whereas for β-TT 131.03 µg/dl. Mean TIBC varied significantly between IDA, β-TT. When t-test was applied (t=3.115; P<0.01) the mean TIBC in IDA patients were 424.87µg/dl whereas for β-TT 322.42 µg/dl. Mean serum ferritin varied significantly between IDA, β-TT. When t-test was applied (t= 22.800; P<0.01) the mean serum ferritin in IDA patients were 12.51 ng/dl whereas for β-TT 206.63 ng/dl.

IV. Discussion

The current study mainly focused on the utility of serum iron profile, hemoglobin electrophoresis and peripheral smear in microcytic hypochromic anaemia. This study also attempted to elucidate the diagnostic accuracy of seven indices to discriminate mild to moderate Iron deficiency from β - Thalassemia. The present study included patients between the age group of 1- 12 years. Two thirds of the study population was between the age of 5 & 12 years. This could be attributed to the increasing nutritional demands of growth spurt and puberty compounded by less attention to nutrition. In the present study girls with microcytic hypochromic anaemia out number the boys. This female preponderance could be due to less care of the girl child in Indian settings. Distribution of Hb, RBC, HCT, MCV, MCH, MCHC, RDW do not vary significantly in both sexes.

Mild anaemia (Hb10- 12 g /dl) was present in 26 cases (59.1%), moderate anaemia (Hb 8 -9.9g/dl) in 13 cases (29.5%) and severe anaemia (Hb <8 g/dl) in 5 cases (11.4%). A study conducted by Looker et al[10] in 1997, found that IDA is most prevalent in children. This finding correlates with the present study where 72.73% of microcytic hypocromic anaemia was found to be due to Iron deficiency. [β-Thalassemia trait; 6.82%, β-Thalassemia major; 6.882% & anaemia of chronic disease; 13.64%].

This is an expected observation as early childhood represents period of rapid growth and depletion of blood iron.**[10]** On the other hand, adolescent girls are also more susceptible to iron deficiency because of poor dietary intake in conjunction with high iron requirements related to rapid growth and menstrual blood loss. This study reflects similar findings probably due to the same factors. Mean haemoglobin varied significantly between IDA, β-TT. The mean Hemoglobin in IDA patient was 8.99g/dL whereas for β-TT 10.57g/dL. Mean MCV varied significantly between IDA, β-TT, mean MCV in IDA patient was 68.45 (fl) whereas for β-TT 38.91 (fl). MCV is known to be significantly low in β-Thalassemia as compared to Iron deficiency anaemia. Mean MCH does not vary significantly between IDA, β-TT, mean MCH in IDA patient was 20.79 pg whereas for β-TT 17.04 pg. Mean MCHC does not vary significantly between IDA, β-TT, mean MCHC in IDA patient was 23.83g/dl whereas for β-TT 27.52 g/dl.

A study conducted by M.A.Ehani et al[11] included 284 patients aged (range 10 – 38 years), this study utilized 4 indices including England and Fraser Index , Mentzer Index, Srivastava index & RBC count to discriminate 130 cases of IDA & 154 cases of β TT. Youden's index provides an appropriate measure of validity of a particular technique or question by taking into account both sensitivity and specificity[33,34], and was

first used by Demir et al.[12] Youdens index were calculated, showed MI (90.1) > Srivastava index (74.2) > England and fraser index(68.7).[Table-4]

According to another study conducted by Damir et al[12] sample size included was 63, best two indices were RBC count & RDWI. Youden's index calculated was 82 & 80 respectively. A study conducted by Ntaios et al[13] (2007), sample size included were 493, it was concluded that best two indices was Green and King, England and Fraser index, Youden's index calculated was 70.9 , 63.2 respectively. A study conducted in the year 2007 by Beyan et al[14] included a sample size of 111, it was concluded that best two indices were RBC count & Green and king indices, Youden's index calculated was 73.7& 65.5 respectively. A study conducted in the year 2008 by Sirdah et al[15] included a sample size of 2196; it was concluded that best two indices were Green and king indices, Red cell distribution width index, Youden's index calculated was 68.6 & 68.4 respectively. Another study conducted by Urrechaga et al [16], sample size included were 318, they come to a conclusion that best indices was Green and King, Youden's index calculated was 80.9. The S&L index was first defined by Shine and Lal in 1977 and was reported to have a sensitivity of 100%, a specificity of 11.8%and an efficiency value of 59.5% for differentiating between β-TT and IDA patients.

Yeo et al[17] found the S&L index and mean cell volume (MCV) to be applicable when applied to pregnant women in Singapore. Lafferty et al[18] found the S&L index, MI and MCV to be valuable in distinguishing IDA and β-TT minor cases; the RDW and the E&F indices were not useful. In studies including schoolchildren in Jordan, MI, MCV ≤ 72 fl, and E&F and S&L indices correctly identified 91.6%, 82.4%, 81.3% and 62.6%, respectively, of microcytosis cases as having or not having the β-TT trait. AlFadhli et al[19] found the E&F index to be the most discriminatory and the S&L index the least when comparing patients with IDA to those with β-TT or TT minor.

A study conducted by Okan et al[20] found the S&L and G&K indices to be best at differentiating IDA from β-TT patients, and the RDW index to be the worst. In particular, the S&L index had the highest Youden index value in discriminating β-TT cases from those with moderate-to-severe IDA and also from those with mild IDA.

Table-44. Following table shows sensitivity, specificity, positive predictive value, negative predictive value & Youden's index calculated in Okans et al study. Compared to the previous study, present study showed 100 % sensitivity , specificity in 4 indices. This can be due to the small sample size in the present study. The present study found that to differentiate mild to moderate IDA (Hb 8.5 – 11 g/dl) from β-TT Mentzer index, England and Fraser index, Srivastava index & Green and king index had highest specificity as well as per Youdens index. However RBC distribution width index was found to have reasonable specificity and sensitivity when compared to Shine and lal index & Ricerca index. A study conducted by Ehani et al[11] found that MCHC was low in Iron deficiency anaemia, whereas MCV, MCH were low in thalassemia & MCHC was normal. The present study showed similar results.

V. Conclusion

In the present study mild anaemia was observed in 11.4% of cases, moderate anaemia was observed in 29.5 % of cases and severe anaemia was observed in 59.1% of cases. Out of 44 cases, IDA constituted 72.73%, β-Thalassemia trait constituted 6.82%, β- Thalassemia major constituted 6.882% and Anaemia of chronic disease constituted 13.64%. MCV was found to be lower in β-Thalassemia Trait than in IDA, which could have a useful application in differentiating these two conditions. Hb Electrophoresis, Serum Iron profile & Red cell indices are complementary to each other in the precise diagnosis of microcytic hypochromic anaemia of varied etiology, which would enable comprehensive wholesome treatment.

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