CLINICO-HAEMATOLOGICAL AND BIOCHEMICAL PROFILE OF DIMORPHIC ANAEMIA WITH BONE MARROW STUDY

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ABSTRACT

BACKGROUND

Dimorphic anaemia is very common in India. Dimorphism indicates the presence of two distinct populations of red cells. The term is most often applied when there is one population of hypochromic, microcytic cells and another population of normochromic cells, either normocytic or macrocytic.

Aims and Objectives-

1. Dimorphic anaemia has been studied, because treatment may be ineffective if the dual deficiency is not diagnosed.
2. To correlate and compare the clinico-haematological, biochemical parameters with bone marrow study.
3. To find out the clinical and haematological features of severe anaemia with bone marrow study.

MATERIALS AND METHODS

This descriptive study included 51 cases of dimorphic anaemia to evaluate association of biochemical profile of dimorphic anaemia with bone marrow study. Data collected from case files, patient history, clinical profile, peripheral blood findings, haematological parameters, bone marrow aspiration and biochemical parameters.

RESULTS

In our study, dimorphic anaemia (DA) was mostly found in 15 - 30 years of age. The male-to-female ratio was 1.5: 1 in our study. The most common clinical presentation was pallor and generalised weakness (100%) followed by easy fatigability (72.5%), fever (54.90%), altered behaviour (19.6%) and tingling (8%) are found. Bleeding (13.7%), itching and red spots (13.7%) are found in patients having thrombocytopenia. DA was found mostly in vegetarians (62.7%). The mean haemoglobin was 6.6 gm/dL. Splenomegaly and hepatomegaly were present in 35.2% and 23.5% respectively. There was complete correlation between three parameters in 8/51 (15.68%) cases only.

CONCLUSION

Bone marrow examination provides rapid and cost-effective investigation for confirming the diagnosis of dimorphic anaemia by reliably assessing the iron stores. Serum ferritin is more specific in predicting the iron deficiency. Serum vitamin B12 and serum folate are also specific, but not sensitive.

KEY WORDS

Bone Marrow, Dimorphic Anaemia, Ferritin, Folate, Vitamin B-12.

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BACKGROUND

Anaemia is defined as a reduction in haemoglobin concentration below the level, which is expected for healthy person of same age and sex and in the same environment. Adequate oxygen cannot be delivered to various organs and tissues due to low oxygen carrying capacity of blood.(1)

In the United States the prevalence of anaemia in population studies of healthy, non-pregnant people depends on the Hb concentration chosen for the lower limit of normal values. The World Health Organisation (WHO) chose 12.5 g/dL for both adult males and females.

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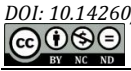

In the United States, limits of 13.5 g/dL for men and 12.5 g/dL for women are probably more realistic. In India, anaemia is considered below 11.0 g/dL in females and 13.0 g/dL in males.

Internationally, anaemia caused by iron deficiencies is the most common nutritional disorder.

In underprivileged countries, the prevalence of anaemia is found to be 2 - 5 times greater than that in the United States. Although, geographic diseases such as sickle cell anaemia, thalassemia, malaria, hookworm and chronic infections are responsible for a portion of the increase, nutritional factors with iron deficiency and folic acid deficiency play major roles in the increased prevalence of anaemia.

In developing countries, about 40% of preschool children and 50% of pregnant women are estimated to be anaemic. 20% of maternal deaths can be contributed to anaemia.(2) Anaemia affects approximately 17% in industrialised countries. Nutritional megaloblastic anaemia in children occurs commonly among undernourished or malnourished societies of tropical and subtropical countries.(3)

Dimorphic anaemia (DA) is defined by two distinct red cell populations- one is hypochromic, microcytic cells and another of normochromic cells, either normocytic or macrocytic.

DA is very common in India. It is estimated that 30% of the world's population is anaemic. In India, according to ICMR (district nutrition survey data report), prevalence of anaemia is 84.2% with severe anaemia in 13.1% population.[4]

Certain races and ethnic groups have an increased prevalence of genetic factors associated with certain anaemias. Race is a factor in nutritional anaemias and anaemia associated with untreated chronic illnesses, eg. malaria, tuberculosis, acquired immunodeficiency syndrome.

Severe genetically acquired anaemias (eg. sickle cell disease, thalassemia, Fanconi syndrome) were more commonly found in children, because they did not survive to adulthood.[5]

Overall, anaemia is twice as prevalent in females as in males. This difference is significantly greater during the childbearing age due to pregnancies and menses. In the younger age groups, males have a higher incidence of acute anaemia from traumatic causes.[5]

Acute anaemia has a bimodal frequency distribution, affecting mostly young adults and persons in their late fifties. Causes among young adults include trauma, gastrointestinal bleeding, menstrual and ectopic bleeding and problems of acute haemolysis.[5]

Neoplasia increases in prevalence with each decade of life and produce anaemia from bleeding, from the invasion of bone marrow with tumour or from the development of anaemia associated with chronic disorders.[5]

Dimorphic anaemia can occur when iron deficiency anaemia responds to iron therapy, after the transfusion of normal blood to a patient with hypochromic anaemia, sideroblastic anaemia, refractory anaemia, macrocytic anaemia, post transfusion, unmasking of iron deficiency following treatment of megaloblastic anaemia, delayed transfusion reactions and dual deficiency of iron and either vitamin B12 or folic acid,[4] which is the focus of our study.

A dimorphic picture on peripheral blood smear is not correlated with bone marrow iron level and S. ferritin level. Iron may be reduced, normal or increased on bone marrow examination. Biochemical parameters may be fluctuated.

This descriptive study was planned to correlate and compare the clinico-haematologic, biochemical parameters with bone marrow study in cases diagnosed as DA on peripheral smear finding.

MATERIALS AND METHODS

This descriptive study period was conducted in the Department of Pathology, Gandhi Medical College, Bhopal. 51 patients who were diagnosed as dimorphic anaemia on peripheral blood smear and who consented for bone marrow aspiration with relevant biochemical investigations were included in the study.

The study included all cases of anaemia having haemoglobin less than 11 gm/dL. Patients with recent blood transfusion, treatment with haematinics, pregnancy and with underlying haemoglobinopathies are excluded.

Ethical Clearance

The study was approved by Institutional Ethics Committee of Gandhi Medical College, Bhopal (MP) with letter no. 7625-27/MC/IEC/2016 dated 03/03/16.

Grading of Anaemia

The patients were then grouped as mild (10 - 10.9 gm%), moderate (7 - 9.9 gm%) and severe (< 7 gm%) anaemia based on their initial haemoglobin level. Patients were recorded in proforma including detailed history, clinical profile, haematological parameters, bone marrow aspiration and biochemical parameters.

Haematological Parameters

Blood sample was collected for complete blood counts using automated 3 and 5 part Mindray counter machine. Leishman stained smears of PBS and BMA were examined. Iron store were graded in Perls' stained bone marrow smear.

Estimation of Biochemical Parameters

Blood sample in a plain vial was collected. After centrifugation, the clear supernatant serum was collected. It was used for the estimation of serum vitamin B12, folate, ferritin by the chemiluminescence method.

Statistical Analysis

All analysis was done using Epi Info version 7.2.1.0. Qualitative data was expressed as number and percentage. Quantitative data was expressed as mean. Qualitative data was analysed using chi-square test. Correlation between ordinal variables was determined by calculating Spearman rank order correlation coefficient. P value < 0.05 was taken as statistically significant.

RESULTS

Age Group	Male		Female		Total	
	N	%	N	%	N	%
≤15 years	5	16.1%	4	20%	9	17.6%
16 –30 years	13	41.9%	7	35%	20	39.2%
31 –45 years	7	22.9%	6	30%	13	25.5%
46 –60 years	5	16.1%	1	5%	6	11.8%
>60 years	1	3.2%	2	10%	3	5.9%
Total	**31**	**100%**	**20**	**100%**	**51**	**100%**

Table 1. Age and Sex Distribution of Study Subjects

Chi-square= 2.743 with 4 degrees of freedom; P= 0.602 (NS). Maximum number of cases (64.7 %) were found in 16-45 years of age group (Age range: 5-70 years) with male predominance.

Dietary Habit	N	Percentage
Vegetarian	32	62.7%
Non-Vegetarian	19	37.3%
Total	**51**	**100%**

Table 2. Distribution of Study Subjects according to their Dietary Habit

Maximum number of cases were vegetarian- 62.7%

Religion	N	Percentage
Hindu	43	84.3%
Muslim	8	15.7%
Total	**51**	**100%**

Table 3. Distribution of Study Subjects according to their Religion

Maximum patients were Hindu.

Clinical Features	N	Percentage
Paleness of skin	51	100%
Generalised weakness	51	100%
Easy fatigability	37	72.5%
Fever	28	54.9%
Altered behaviour	10	19.6%
Tingling, numbness	8	16.9%
Bleeding from nose and rectum	7	13.7%
Itching, red spots	7	13.7%

Table 4. Distribution of Clinical Symptoms and Signs in Study Subjects

Maximum no. of cases present with symptoms of pallor and generalised weakness (100%) followed by easy fatigability (72.5%), fever (54.9%), altered behaviour (19.6%) and tingling sensation (8%) were found in vitamin B12 deficiency. Bleeding (13.7%), itching and red spots (13.7%) were attributed due to thrombocytopenia.

Radiological Findings	N	Percentage
Splenomegaly	18	35.3%
Hepatomegaly	12	23.5%

Table 5. Radiological Findings in Study Subjects

In our study, cases of splenomegaly were 35.3% and cases of hepatomegaly were 23.5%.

Haemoglobin Level	Male		Female		Total	
	N	%	N	%	N	%
< 7 gm%	20	64.5%	12	60%	32	62.7%
7 - 9.9 gm%	9	29%	7	35%	16	31.4%
10 – 10.9 gm%	2	6.5%	1	5%	3	5.9%
Total	**31**	**100%**	**21**	**100%**	**51**	**100%**

Table 6. Distribution of Study Subject according to Severity of Anaemia

Chi-square= 0.221 with 2 degrees of freedom; P= 0.895 (NS). Severe anaemia 62.7%, moderate anaemia 31.4% and mild anaemia 5.9% with male predominance. In males 64.5% and in females 60% of severe anaemia were found.

Bone Marrow		Serum Ferritin		Correlation between BM and S. Ferritin (%)
Status	Low	Normal	High	
Low (31)	22	4	5	70.90%
Normal (15)	0	13	2	86.6%
High (05)	0	4	1	20%

Table 7. Distribution of Bone Marrow Iron and S. Ferritin Level Study

Spearman rank order correlation coefficient r= 0.629; p<0.001 (S). Bone marrow iron decreased in 60.78% cases and serum ferritin decreased in 43.1% cases. The values of decreased BM iron and decreased S. ferritin are correlated to each other 70.9%.

Parameter	Low		Normal		High	
	N	%	N	%	N	%
BM Iron	31	60.8	15	29.4	5	9.8
S. ferritin	22	43.1	21	41.2	8	15.7
S. folate	15	29.4	29	56.9	7	13.7
S. B12	17	33.3	25	49.0	9	17.6

Table 8. Correlation of Biochemical Parameters

Correlation of S. ferritin with BMA and PBS are 43.1%. S. vitamin B-12 with BMA, PBS are 33.3% and S. folate with BMA, PBS are 29.4% which showed megaloblastosis in bone marrow pictures. All were found decreased in only 15.68% cases. 3.92% cases showed decreased S. ferritin value and increased Vit. B-12/ folate.

DISCUSSION

In our study period of 18 months, there were 52.4% cases of anaemia, of which dimorphic anaemia was found to be 8.3% of the total anaemic cases in all age groups. Riwan Ather et al[4] found DA in 12.5% of cases, which is similar to our study. In India dietary habits are influenced and affected by differences in religion, cultural and socioeconomic status. Majority of patients in our study belonged to low socio-economic status.

The mean age of our patients is 39 years (Age range: 5 - 70 years). 39.2% of patients in our study were in the age group of 16 - 30 years with male: female ratio of 1.5: 1. Saira Perwaiz et al[6] reported the mean age as 38.9 years (1 - 80 years) and peak age group was 35 - 50 years. The male-to-female ratio was 1: 1. Jagdish Chandra et al[5] reported peak age less than 2 years (6 months - 12 years), male-to-female ratio was 1.04: 1.

Male predominance could be due to social pattern in our society, as males get more attention in Indian families resulting in higher access to the hospital.

The most common clinical presentation besides pallor and generalised weakness, which were present in all cases where easy fatigability was (72.5%) and Fever was (54.9%).

In our study, DA was found mostly in vegetarians (62.7%). These findings are similar to Saira Perwaiz et al[6] and Pogura Nagarjuna et al[1] who reported anaemia in 85% and 60% vegetarians respectively. It may be due to religious and social issues.

The mean haemoglobin in our study was 6.6 g/dL. Saira et al[6] and Iqbal et al[2] reported the mean haemoglobin was 6.8 g/dL. In Sunil Gomber et al[3] and Jagdish Chandra et al[5] reported haemoglobin was 5.32 g/dL and 5.65 g/dL.

In our study, splenomegaly and hepatomegaly were present in 35.2% and 23.5%. Amieleena Chhabra et al[1] reported splenomegaly and hepatomegaly were 28.8% and 53.3%. Sunil Gomber et al[3] reported splenomegaly and hepatomegaly were 21% and 66% respectively. Splenomegaly was present in most of the moderate-to-severe anaemic and thrombocytopenic patients.

Eosinophilia was present in 21.5% cases with complaint of breathlessness. In our study, bone marrow iron stores revealed increase in 9.80%, normal in 29.41% and depleted in 60.78% of the patients. Only 5.88% patients found elevated serum ferritin level, which show decreased bone marrow iron. Ali et al[7] in his study of 27.82% patients found lack of iron stores. Of these, the serum ferritin was elevated in 20 patients (29%) despite lack of demonstrable iron in the marrow specimen. They concluded that a low serum ferritin value probably indicates iron depletion, while an elevated value does not exclude that possibility. In our study, they could attribute prior iron therapy and blood transfusion and chronic diseases as cause of increased ferritin.[8]

All 51 cases showed megaloblastosis in the bone marrow. But only 17 cases (33.33%) had either and low serum Vit-B12/Folate or both. The rest 34 cases (66.66%) had either normal or high Vitamin B12/Folate. So, there was a correlation between bone marrow findings and Vitamin B12/ Folate in

33.3% cases only. Serum Folate/ Vitamin-B12 levels are known to be highly labile to the extent that a low serum folate concentration can be rapidly normalised shortly after consumption of a single nutritious folate rich meal.

Our study showed isolated B12 deficiency in 29.4%, combined deficiency in 33.3% and isolated folate deficiency was not found. Rizwan Ather et al[4] showed isolated vitamin B-12 deficiency in 10.34%, isolated folate deficiency in 17.24% and combined deficiency in 15.5% of cases. The low percentage of isolated folate deficiency in our study could be due to exclusion of pregnant ladies from this study.[4] There was complete correlation between three parameters in 8/51 (15.68%) cases only. Clinically, it is important to know whether the anaemia is due to folate or vitamin B12 or combined deficiency, so that the appropriate treatment may be given.

CONCLUSION

1. Inadequate dietary intake, overcooking of our food and poor absorption contributing to high prevalence of dimorphic anaemia.
2. Besides medication, foods can alter the parameters, so bone marrow aspiration is better than biochemical profiles for estimation of megaloblastosis.
3. Bone marrow examination provides rapid and cost-effective investigation for confirming the diagnosis of dimorphic anaemia by reliably assessing the iron stores, as serum ferritin is more specific in predicting the iron deficiency.
4. Bone marrow aspiration though invasive, can be easily performed, which will give correct diagnosis.

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