

A clinicopathological study of severe non-haemolytic anemia in age group of 0-18 years

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Abstract

Introduction: Anaemia is typically defined as reduction in the haemoglobin concentration below certain value. The normal reference value of haemoglobin concentration defined by W.H.O. is 12.5gm/dl for men and women. Evaluation of the causes of severe non haemolytic anaemia seems to be important as the various causes would respond to different treatment modalities. **Methods:** This was a hospital based prospective study that was carried out in a tertiary referral centre for one year, from January to December 2014. A total of fifty cases were subjected for thorough clinical examination and various investigations in order to provide information to evaluate their causes. **Results:** The maximum numbers of cases were reported in the age group of 3-6 years with male predominance. The maximum number of cases were diagnosed as Iron Deficiency Anaemia (22%); followed by Acute Lymphoblastic Leukaemia (20%), Acute Myeloblastic Leukaemia (16%), Megaloblastic Anemia (16%), Aplastic Anemia (10%), Anemia of Chronic Disease (8%). **Conclusion:** Evaluation of the causes of non haemolytic anemia seems to be important because different causes would respond to different treatment modalities; thus enabling the physician to plan out a successful therapeutic outline.

Key words: Clinicopathological, Severe anaemia, Non-haemolytic, Paediatric age, Haematological malignancies.

Introduction

Anemia, by modern simple definition, is a condition characterised by an abnormal reduction in body's total red cell mass [1]. As routine measurement of red cell mass is not always easy, anemia is typically defined as reduction in the haemoglobin concentration below certain value. The normal reference value of haemoglobin concentration defined by W.H.O. is 12.5gm/dl for men and women [2]. Anemia is accordingly classified as-

10.0-11.9gm/dl—mild anemia

07.0-09.9gm/dl—moderate anemia

< 07.0gm/dl—severe anemia [3]

Anemia in the group 0-18 years occupies a numerically important group of diseases which is leading a high morbidity and mortality [4]. Therefore, rapid and accurate diagnosis of paediatric anemia, including haematological malignancies have an increasing importance because an early and accurate diagnosis and treatment can reduce morbidity and can save many lives.

If the easily diagnosable blood loss and hemolytic group of anemia are excluded, the nutritional deficiency is the leader of severe anemia. Thus, Iron Deficiency Anemia, Megaloblastic Anemia, Aplastic Anemia, the malignant diseases including leukaemia, lymphoma and anemia of chronic diseases are the distinct causes of non haemolytic anemia [5,6,7]. Keeping in mind all the facts delineated, the present study had been undertaken- to analyse the different causes of severe non haemolytic anemia among the children of 0-18 yrs with their relative incidence.

Materials and Methods

Study design: This is a hospital based prospective study. This study was conducted with 50 patients of age 0-18 years referred from the paediatric and medical units of a tertiary referral centre with clinical presentation of severe anemia.

Aim and Objectives

- To evaluate the different causes and incidence of severe non haemolytic anemia among the age group 0-18 years.

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b) To make an analytical study of important clinical presentation and the haematological findings in different pattern of anemia.

Exclusion criteria: Patients with obvious blood loss, haemolytic group of anemia and patients with haemoglobin concentration of 7 gm/dl and above were excluded from this study. A provisional diagnosis based on clinical findings was recorded. Complete haematological examination was done including bone

marrow and additional examinations (where necessary)- Serum iron estimation, vitamin B12 & folate estimation, serum bilirubin, Hb electrophoresis, Pearl's stain cytological stain and BM trephine biopsy were included. FNAC & histopathology for cervical and abdominal mass and radiological studies like Chest X-ray, USG, CT scan etc. were done in selected cases. MGG stain was done for PBS and BM examination. MPO, PAS were used as cytochemical stain in BM aspiration.

Results

A total of fifty cases were subjected for thorough investigations. The most common physical finding apart from pallor was hepatomegaly and fever. Majority of the patients in the study were male in the age group of 3-6 years (28%).

Table-1: Demographic distribution of cases

Age in years	Male	Female	No of cases	Percentage
0 to 3	7	0	7	14.00
3+ to 6	6	8	14	28.00
6+ to 9	2	3	5	10.00
9+ to 12	4	6	10	20.00
12+ to 15	3	2	5	10.00
15+ to 18	4	5	9	18.00
Total	26	24	50	100

The majority of the cases were between the age group of 3 to 6 years, followed by the group between 9 to 12 years. Between 0-3 years of age no female cases were found. In this study male slightly outnumbered the female.

Table-2: Haemoglobin level of the cases.

Hb level (gm/dl)	Number of cases	Percentage (%)
< 3	5	10
3 to < 5	16	32
5 to < 7	29	58
Total	50	100

Majority of the cases had haemoglobin level between 5 to < 7 gm/dl and 5 cases had haemoglobin level below 3gm/dl.

The causes of anemia under this study were found as –Iron deficiency anemia -22% cases, Acute lymphoblastic leukaemia-20%, Acute myeloblastic leukaemia-16%, Megaloblastic anemia-16%, Aplastic anemia-10%, Anemia of chronic diseases-8%, Juvenile CML-04% , Lymphoma-04% and Anemia of mixed deficiency -02%.

Table-3: Aetiological Pattern of Severe Non Hemolytic Anemia.

Aetiology	No of Cases	Percentage (%)
IDA	11	22.0
Megaloblastic Anemia	08	16.0
Mixed Deficiency Anemia	01	02.0
Aplastic Anemia	05	10.0
Anemia of chronic diseases	04	08.0
Acute LymphoblasticLeukemia	10	20.0
Acute Myeloblastic Leukemia	08	16.0
Juvenile Chronic Myelocytic Leukemia	02	04.0
Lymphoma–NHL	02	04.0
Total	50	100.0

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It was found that iron deficiency anemia was the most common cause of severe non haemolytic anemia followed by malignant causes (ALL).

Among the non malignant cases iron deficiency anemia was followed by megaloblastic anemia and aplastic anemia. And in malignant group acute lymphoblastic leukemia was the leader; followed by acute myeloblastic leukemia.

Discussion

In developed countries, a steady decline in prevalence of anemia in childhood age has been observed [8]. A study conducted in 2001-2002 in Nindura Block, Barabanki District, North India found severely anemic children in 3 subcentres as 2.73%; 2.25% and 5.29% [9].

In another study, done by Deeksha Kapur et al (2001) found severe anemia as 7.8% among children. In this study, the severely anemic patients were found 8.5% within the specified age group.

A peak incidence of age distribution was found to be similar as compared to other studies like Harbans Lal et al and Sharma D K et al which showed 3-6 years as the commonest and second commonest age group respectively [10, 11].

Studies conducted worldwide, sex incidence varied from place to place. Hasanbegovic E et al found 49.33% male and 50.67% female. Similarly Rahim Fazlur et al found 66.27% male and 33.73% female which corresponds well to our study [12, 13].

Amongst the non malignant haematological disorders, nutritional anemia constituted 44% of which IDA is the most common (22%), followed by megaloblastic anemia (16%) and 2% cases had mixed deficiency causes. Similar observations were found by other authors.

White K. C et al (2005) found IDA as the major cause. In Amritsar, Harbans Lal et al studied 210 cases and found IDA as the major cause (24.5%) [14,15].

Regarding Megaloblastic anemia, Gera et al found 7.8% and Choudhury et al found 27.1% and present study concordance with these two results (16%) [16,17].

Incidence of Aplastic anemia were 18.7% and 12.8% in two separate studies done by Fazlur et al (2005) and S.P. Shah et al (1999) which is slightly higher than the present study [18]. This may be due to higher sample number and better facilities of BM evaluation.

Among the 44% of malignant causes of anemia, ALL is the most common (20%) followed by AML (16%) JCML (4%) and NHL (4%).

Fazlur et al reported 23.6% ALL, and 08.4% AML [19]. In a separate study by Vandana Jain et al ALL cases found in 27.2% and AML in 04% cases [20]. The higher incidence of AML in our study may be due to the higher age range.

In a comparative study with Fazlur R et al found Megaloblastic anemia to be most common followed by Aplastic anemia. In our study IDA is found to be most common cause followed by Megaloblastic anemia among non malignant causes.

The difference of the incidence may be due to factor like geographic variation, bigger sample size and age variation. This study is conducted in an area with more BPL population where nutritional deficiency is more common.

More cases of Aplastic anemia could have been diagnosed had BM biopsy been undertaken.

Among the malignant causes slightly higher incidence in AML than the Fazlur R et al study is found. But similar findings with that of Dube et al is found.

And about JCML and NHL, the incidence is almost similar to the findings of the other workers.

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Table-3: Showing correlation between provisional clinical diagnosis and consistency with haematological diagnosis.

Hematological Diagnosis (No. of cases)	Provisional clinical Diagnosis (No of cases)	Number of consistent cases	Number of inconsistent cases
IDA(11)	Severe anemia with hepatosplenomegaly-(2) Nutritional anemia-(9)	9	2
Megaloblastic Anemia(7)	?Viral encephalitis with severe anemia-(1); Severe anemia with hepatosplenomegaly and bleeding manifestation-(1) Severe anemia with hepatosplenomegaly -(2); Nutritional anemia-(3)	3	4
Mixed Defi. Anemia (1)	Severe anemia. ? Nutritional with viral hepatitis-(1)	1	0
Anemia of Chronic Disease (4)	Anemia of chronic diseases-(3) TB intestine with nutritional anemia(1)	3	1
Aplastic Anemia(5)	Severe anemia for evaluation-(3) Anemia of nutritional origin-(2)	3	2
ALL (10)	Anemia with lymphadenopathy and hepatosplenomegaly -(9) Severe anemia with hepatomegaly -(1)	9	1
AML (8)	Anemia with hepatosplenomegaly and bleeding manifestation	8	0
NHL (2)	Anemia with generalized lymphadenopathy and hepatosplenomegaly-(2)	2	0
Juvenile CML (2)	Severe anemia with hepatosplenomegaly and lymphadenopathy-(2)	2	0

Percentage of accuracy of provisional clinical diagnosis in the diagnosis of severe on haemolytic anemia by haematological analysis:

Total Anemia Cases (studied)	:	50
Consistent Results	:	40
Inconsistent Results	:	10
Percentage of Accuracy	:	80%

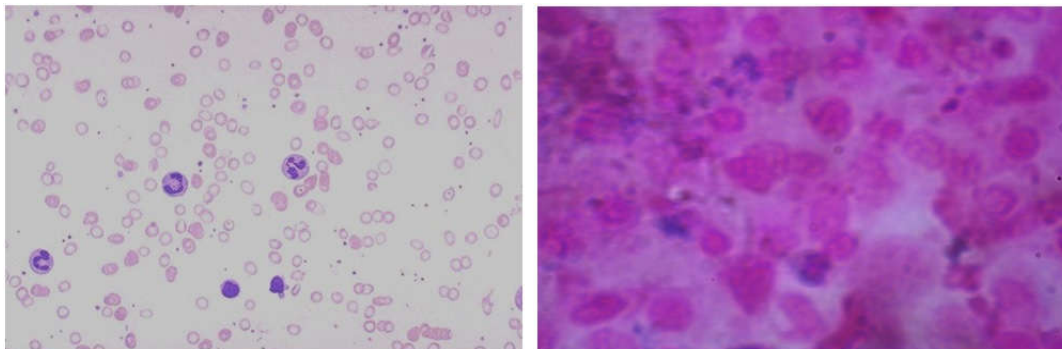


Fig-1A: IDA-PBS of a 6 Yrs Boy shows Severe Hypochromia with Poikilocytosis, Numerous Microcytic Cells with Adequate Platelets and White Blood Cells (Case 3). **Fig 1B-PERL'S STAIN-** Bone Marrow Smear of a 10 Yrs Boy showing Perl's Stain in a Diagnosed Case of Jcml with Score '2' (normal iron particles, Case 49)

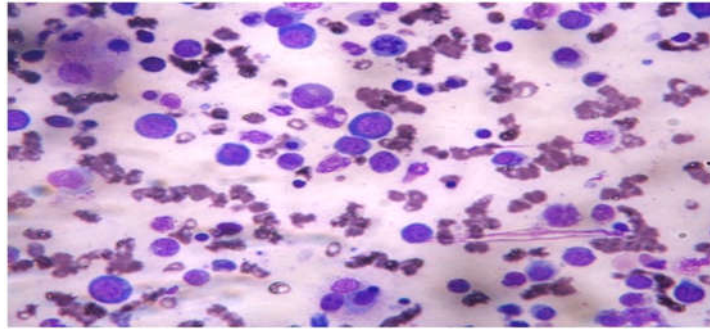


Fig-2: MA Bone Marrow Picture of a 14 Yrs Boy Shows Numerous Basophilic and Orthochromatic Megaloblasts with Open Lacy Chromatin (Case 30)

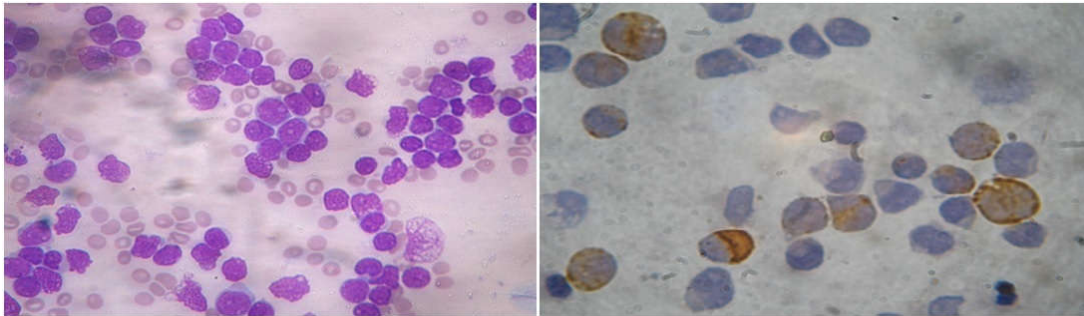


Fig-3A: AML M1 BM smear of an 11 Yrs Girl Shows Blast Cells with Large, Somewhat Irregular Nuclei with 1 or more Nucleoli. Cytoplasm Is Eccentric and Mostly Agranular. Very Few Cells Showed MPO Positivity (Case27). Fig 3B- AML M2 Bone Marrow Smear of a Patient Showing MPO Positivity (Case X1)

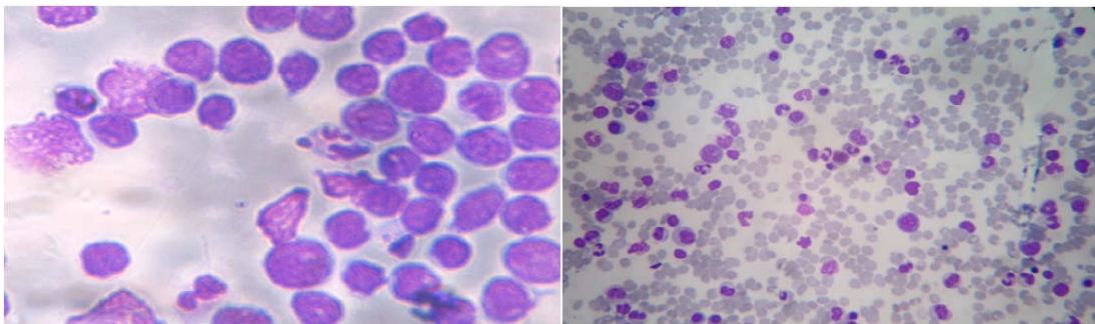


Fig-4A: ALL: (FAB-ALL L1) BM Picture of a 16 Yrs Male Shows Small, Uniform Blast Cells with Scanty Cytoplasm and Mostly Single Nucleolus. MPO was Negative (Case40). Fig 4B- JCML: Peripheral Blood Smear of a 10 Yrs Boy Shows Occasional Blast Forms, Atypical Agranular Bands And Segmented Neutrophils (Case49).

Conclusion

Evaluation of the causes of non-haemolytic anemia seems to be important as the various causes would respond to different treatment modalities; thus enabling the physician to plan out a successful therapeutic outline that increase the patient's longevity.

The investigation of a case of severe non haemolytic anemia should include thorough clinical, haematological and related specific investigations. The causes of anemia varies from place to place depending on geographical variation, ethnicity, economy, food habits etc.

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References

1. Ed. Uthman, MD, Understanding anemia: University press of Mississippi 1998: 1-11
2. Fredrick M. Abraham: Anemia, Chronic: eMedicine: 2005: eMedicine.medscape.com
3. Deeksha Kapur, Kailash N. Agrawal, Sushma Sharma, Kusum Kela and Iqbal Kaur. Detecting iron deficiency anemia among children by implementing a screening program in an urban slum: Indian Paediatrics: 2002 Aug; 39 (7): 136-144, 671-6
4. Hussain Imam Hj Muhammad Ismail, Ng Hoong Phak, Terrence Thomas: Malaysia Paediatric Association: Why paediatric age limit must be raised to 18 years in Malaysia: Current Issue 2005; 1st edition
5. Frank Firkin, C. Chesterman, D Penington, B Rush: de Gruchy's Clinical hematology in Medical practice: 5th edition: 24
6. Louis A Kazal, JR. Prevention of iron deficiency in infants and toddlers: Am Fam Physician, 2002 Oct 1;66 (7): 1217-1225
7. Dr. Saul Greenburg, MD, FRCP: Blood diseases and immune disorders. In: Caring for kids: Toronto; 2005
8. Margaret Lee. Anemia Acute: An article: American Academy of Paediatrics 2005
9. Awasthi S, et al. Anemia of under nutrition among preschool children in UP, India: Indian Paed: 2003;40 (10):985-990
10. Lal H, Manchanda SS, Khanna S, et al. Megaloblastic anaemia of infancy: a clinical and haematological study of 210 patients. Indian J Pediatr. 1972 Jul; 39 (294):217-26.
11. Sharma DK, Kalra K, Thapar RK, et al. Anemia in childhood. Indian Pediatr. 1970 Jul; 7 (7): 388-93.
12. Hasanbegović E, Bijedić V, Mehadzić S. Diagnostic value and cytomorphologic findings in bone marrow punctures in children with severe deficiency anemia. Med Arh. 2002;56 (3 Suppl 1) :33-5.
13. Fazlur Rahim et al: A spectrum of haematological disorders in children: Pak J Med Science :2005; Vol 21: 4: 433-436
14. White KC. Anemia is a poor predictor of iron deficiency among toddlers in the United States: for heme the bell tolls. Pediatrics. 2005 Feb;115(2):315-20. doi:10.1542/peds.2004-1488
15. Lal H, Manchanda SS, Khanna S, et al. Megaloblastic anaemia of infancy: a clinical and haematological study of 210 patients. Indian J Pediatrics: 1972 Jul;39(294):217-26.
16. Dr. Jagadish Chandra, MD: Vitamin B₁₂ and Folate deficiency: Megaloblastic anemia and Beyond: Indian Journal of Paediatrics: 2010 July;77: 795-799
17. Fazlur R et al: A spectrum of haematological disorders in children: Pak J Med Science: 2005, Vol 21: 4: 433-436
18. SM Lewis; GJ Bain; I Bates: Dacie and Lewis Practical hematology: Basic Hematology Techniques: 9th edition:20-21
19. John P Greer, MD; John Foerster, MD, FRCPC; John N Lukens, MD: Wintrobe's Clinical Hematology: Anemia: General Considerations: 11th edition (Volume-1): 960-961
20. Vandana J, Dubey A. P, Gupta S K: Nutritional parameter in children with malignancy: Indian paediatrics 2003;40:976-984

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