

**Original Articles**

## Clinico-haematological profile of children with vitamin B12 deficiency anaemia

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### Abstract

**Background:** In India, megaloblastic anaemia due to vitamin B12 deficiency is a major cause of nutritional anaemia in children.

**Objectives:** To assess the magnitude and study the clinical profile of megaloblastic anaemia due to vitamin B12 deficiency in the age group 3 months to 12 years.

**Setting and design:** This was an observational study carried out in Mahatma Gandhi Institute of Medical Sciences, Sewagram, Central India, from December 2015 to June 2017.

**Method:** All children visiting the hospital OPD or admitted in wards during the study period were screened for anaemia and those having haemoglobin <11g/dl (children <6 years) or <12g/dl (6-12 years) were included in the study. Total 110 children were included in study and their clinical and haematological profile was studied. Statistical analysis software used was SPSS 22.0 version and Graph Pad Prism 6.0 version.

**Results:** Out of 110 anaemic children, 22 had megaloblastic anaemia with vitamin B12 levels below 200ng/L and incidence was maximum in the age group of 6 to 12 months. Most common symptom was pallor followed by loss of appetite

and fatigue. On peripheral smear examination, 14 patients (63.6%) had macrocytosis and hypersegmented polymorphs and 4 patients (18.2%) had pancytopenia.

**Conclusions:** Out of 110 anaemic children 20% had megaloblastic anaemia with vitamin B12 levels below 200ng/L. More than 75% of megaloblastic anaemia due to B12 deficiency occurred in the 6 months to 6 years age group. On peripheral smear, 64% had macrocytosis and hypersegmented polymorphs and 18% had pancytopenia.

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(Key words: Megaloblastic anaemia, Vitamin B12 deficiency, nutritional anaemia, clinico-haematological profile, Central India)

### Introduction

In India, 60-70% of children under the age of 6 years have varying degrees of anaemia<sup>1</sup>. According to available studies in India, 65% infants, 60% 1-6 year olds, and 88% adolescent girls are anaemic<sup>2</sup>. In children, most anaemia is nutritional with megaloblastic anaemia a major contributory factor. Earlier, folate deficiency was a major cause of megaloblastic anaemia in comparison to vitamin B12 deficiency. However, during the past few years, prevalence of folic acid deficiency has decreased from 70-75% to 2-10%<sup>3-5</sup>. Today, vitamin B12 deficiency is a significant cause of megaloblastic anaemia.

### Objectives

Current study was undertaken to assess the magnitude and to study clinical profile of megaloblastic anaemia due to vitamin B12 deficiency in the age group 3 months to 12 years.

### Method

A single centre cross sectional observational study was conducted in the Department of Paediatrics of Mahatma Gandhi Institute of Medical Sciences (MGIMS), Sewagram, Central India. After approval from the institutional ethical committee (Ref no- MGIMS/IEC/MED/54/2016), the study was conducted from December 2015 to June 2017.

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All children in the age group of 3 months to 12 years, admitted as well as attending out-door facility, at Kasturba hospital were screened for anaemia by haemoglobin (Hb) concentration assessment. Those having Hb concentration less than 11g/dl (children less than 6 years) and 12g/dl (children between 6-12 years) were included in study after taking written informed consent from the parents. Their clinical and haematological features were observed and subjected to investigation (vitamin B 12 level). The normal reference range of serum vitamin B12 is above 300ng/L. The range between 200 to 300 ng/L is borderline. Hence the levels less than 200 were considered as low and as diagnostic of megaloblastic anaemia. Children who had received blood transfusion in the last 6 months and children whose peripheral smear showed the picture of thalassaemia, sickle cell anaemia, or some alternative diagnosis were excluded from the study.

Sample size was estimated using Open EPI software, by using formula of cross-sectional prevalence study for 95% confidence interval and a desired absolute precision of 6% with following assumptions: P=50% (assuming that 50% of women will have adequate health literacy so as to get the maximum possible sample size) Non-response rate of 20%. The sample size came out to be 110.

Statistical analysis used descriptive and inferential statistics using Chi square test, student's unpaired t-test and Pearson's correlation coefficient.

Software used in the analysis were SPSS 22.0 version and Graph Pad Prism 6.0 version. A p-value less than 0.05 was considered significant.

**Results**

The prevalence of megaloblastic anaemia is shown in Table 1.

**Table 1**  
*Features of megaloblastic anaemia (n=22)*

Feature	No. (%)
Vitamin B12 <200ng/L	22 (100)
MCV>100fL	19 (86.4)
Combined (B12<200+MCV>100)	19 (86.4)
Combined (B12<200+MCV≤100)	03 (13.6)

*MCV: Mean corpuscular volume*

Out of 110 anaemic children, 22 had megaloblastic anaemia with vitamin B12 levels below 200ng/L (prevalence 20%). In these megaloblastic children, 19 (86.4%) had mean corpuscular volume (MCV) >100fL and 3 (13.6%) had MCV≤100fL (Table 1).

Age wise prevalence of megaloblastic anaemia with mean Vitamin B12 levels is shown in Table 2. Prevalence of megaloblastic anaemia was maximum in the 6 to 12 month age group with mean vitamin B12 level 119.5ng/L. The relationship of age with megaloblastic anaemia was significant with a p value of 0.015.

**Table 2: Age wise prevalence of megaloblastic anaemia with mean Vitamin B12 levels**

Age group	Number (%)	Mean Vitamin B12	Standard Deviation	F-value
3-6 months	04 (18.2)	148.50 ng/L	48.09 ng/L	4.55 p=0.015
6-12 months	11 (50.0)	119.54 ng/L	12.09 ng/L	
1 -6 years	06 (27.3)	97.16 ng/L	14.07 ng/L	
6-12 years	01 (04.5)	90.00 ng/L	-	
Total	22 (100)	117.36 ng/L	28.04 ng/L	

The severity of anaemia in patients with megaloblastic anaemia is shown in Table 3. Out of

22 children with megaloblastic anaemia, 18 (81.8%) had severe anaemia with Hb < 7 g/dl.

**Table 3: Severity of anaemia in patients with megaloblastic anaemia**

Severity of anaemia	Number of patients	Percentage
Mild (Hb >10g/dl)	01	04.6
Moderate (Hb 7-10g/dl)	03	13.6
Severe (Hb <7g/dl)	18	81.8
Total	22	100
Mean ± SD	5.20±1.84 g/dl (3-10.2 g/dl)	

Mean corpuscular volume (MCV) of patients with megaloblastic anaemia is shown in Table 4. Mean MCV of megaloblastic children in age group 6 to 12 month was 116.9fL. The relationship of MCV

with megaloblastic anaemia was significant with a p value 0.047. The clinical profile of patients with megaloblastic anaemia is shown in Table 5.

**Table 4: Mean corpuscular volume (MCV) of patients with megaloblastic anaemia**

Age group	Number	Mean MCV	Standard Deviation	F-value
3-6 months	04	106.00fL	4.61fL	3.23 p=0.047
6-12 months	11	116.90fL	1.04fL	
1 -6 years	06	102.50fL	18.04fL	
6-12 years	01	112.00fL	.	
Total	22	110.77fL	11.16fL	

**Table 5: Clinical profile in megaloblastic anaemia**

Clinical profile	Number of patients	Percentage
Loss of Appetite	19	86.4
Fatigue	19	86.4
Yellowish discoloration of eyes and urine	14	63.6
Fever	6	27.3
Weight Loss	12	54.6
Bleeding Tendency	2	09.1
Pallor	22	100.0
Jaundice	15	68.2
Knuckle Pigmentation	17	77.3
Lymphadenopathy	6	27.3
Bony tenderness and sternal tenderness	2	09.1
Retinal haemorrhages and bleed	2	09.1
Developmental milestone delay	3	13.6
Tremors	4	18.2
Pigmentation of skin	6	27.3
Hepatomegaly	4	18.2
Splenomegaly	6	27.3

Out of 22 megaloblastic anaemia patients, 7 (31.8%) had leucopenia with a white blood cell (WBC) count less than 4500/ cu mm and 6 (27.3%) had thrombocytopenia with a platelet count less than 150,000/cu mm. On peripheral smear examination, 14 (63.6%) patients had macrocytosis and hypersegmented polymorphs and 4 (18.2%) had pancytopenia Bone marrow investigation revealed megaloblastic erythroid hyperplasia in 10 (45.5%) cases, 7 (31.8%) cases showed mild changes consistent with megaloblastic anaemia, 3 (13.6%) cases had dimorphic picture and normoblastic picture was present in 1 (4.5%) case.

### Discussion

The prevalence of megaloblastic anaemia varies widely according to different studies. Ghai OP<sup>6</sup>, and Dalal *et al*<sup>7</sup> reported the prevalence as 19% and 18% respectively, while Gomber *et al*<sup>3</sup>, Sharma *et al*<sup>8</sup>, and Chaudhary MW<sup>9</sup>, reported prevalence of megaloblastic anaemia as 24%, 42.1% and 27.1% respectively. Prevalence of megaloblastic anaemia due to vitamin 12 deficiency in our study was 20%. Out of 22 children, 19 had MCV more than 100fL and 3 children had MCV less than 100fL.

The age group 6 months to 1 year had 11(50%) cases with megaloblastic anaemia whilst the age

group 1 year to 6 years had 6 (27%) cases of megaloblastic anaemia. Thus the age group 6 months to 6 years is the most vulnerable age for the development of nutritional anaemia (megaloblastic anaemia).

Megaloblastic anaemia presents with varied clinical manifestations. Pallor was present among all 22 (100%) patients in our study which was in accordance with other studies. Ishtiaq O, *et al*<sup>10</sup> and Hamid GA *et al*<sup>11</sup>, found pallor in 100% of the cases and Niazi M, *et al*<sup>12</sup> found pallor in 98.8% of patients. Icterus was noted in 14 (63.6%) children in our study. This is probably due to decreased life span of red blood cells and to premature destruction of developing megaloblasts in marrow<sup>5,13,14</sup>. Bleeding is probably a result of thrombocytopenia which was noted in 9.1% of patients in our study. Previous studies by Gupta RK, *et al*<sup>15</sup>, Chandra J, *et al*<sup>16</sup>, and Gomber S, *et al*<sup>3</sup> documented bleeding in 17-20% of patients with megaloblastic anaemia. Impaired DNA synthesis resulting in ineffective thrombopoiesis is thought to be the aetiology of thrombocytopenia. Four (18.2%) children in our study presented with tremors, due to nutritional vitamin B12 deficiency. In a study by Chandra *et al*<sup>16</sup> on folate and cobalamin deficiency 11.4% children had tremors.

Hyperpigmentation of dorsa of hands and fingers, a diagnostic sign for the disease<sup>19,20</sup> was observed in 17 (77.3%) children. Khanduri *et al*<sup>21</sup>, reported hyperpigmentation in only 18% of cases. In our study, 3 (13.6%) patients presented with neurological involvement in the form of developmental delay while the study conducted by Hirachand S, *et al*<sup>22</sup> found neurological involvement to be 6.7%. Fever occurred in 27.3% of patients with megaloblastic anaemia, the most common aetiology being infection. In a study by Tahlan *et al*<sup>23</sup>, incidence of low-grade fever varied from 28% to 61% in patients with low iron stores and those with adequate iron stores respectively.

In our study, hepatomegaly was found in 4 (18.2%) patients and splenomegaly in 6 (27.3%). In a similar study by Hirachand S, *et al*<sup>22</sup>, hepatosplenomegaly was found in 23% of patients. In our study thrombocytopenia was reported in 27.3% of cases and leucopenia in 31.8%. Pancytopenia was observed in 18.2% of patients. In a study by Sarode R *et al*<sup>5</sup>, incidence of pancytopenia was 43.8% and bicytopenia was 80.5%. It is thought that as the anaemia becomes more severe, thrombocytopenia develops followed by neutropenia. Further, 27% patients had fever which resulted in leucocytosis which ultimately decreases the degree of pancytopenia. In our study hypersegmented polymorphs were observed in about 63.6% patients; however, another series reported the occurrence of hypersegmented polymorphs to be 43%. This disparity in clinico-haematological features of megaloblastic anaemia results because of difference in duration of onset of anaemia, socio-economical condition of patients, nutrition of patients, and coexisting illness.

### Conclusions

Out of 110 anaemic children 20% had megaloblastic anaemia with vitamin B12 levels below 200ng/L. More than 75% of megaloblastic anaemia due to B12 deficiency occurred in the 6 month to 6 year age group. On peripheral smear, 64% had macrocytosis and hypersegmented polymorphs and 18% had pancytopenia.

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