RESEARCH ARTICLE

Megaloblastic anemia in children from Eastern Odisha, India: A clinical and hematological profile analysis

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ABSTRACT

Background: Anemia can have severe implications on the health of children including motor development, behavioral and cognitive development. Furthermore, morbidity from infectious disease is higher in anemic children. Nutritional anemia is a major concern in rural India.

Aim and Objective: We aimed to observe the percentage of megaloblastic anemia among the anemic children and their clinical and hematological parameters.

Materials and Methods: After obtaining permission from the Institutional Ethics Committee, this cross-sectional study was conducted from September 2018 to August 2021. The setting was a tertiary care hospital in the eastern part of Odisha, India. Children of 1–14 years of age presenting with anemia were included in the study. Details clinical examination and blood tests namely mean corpuscular volume, red blood cell count, total leucocyte count, and platelet count were carried out from venous blood. Descriptive statistical analyses were conducted in STATA software version 15.1.

Results: Among the total 150 anemic patients, the majority (126 [84%]) were in the 11–14 years of age group followed by 24 (16%) in 6–10 years of age (P < 0.0001). Girls were more (94 [62.7%]) than boys (56 [37.3%]), P < 0.0001. Anorexia was the most frequently encountered clinical symptom (99.3%) followed by pallor (94%), weakness (86%), fatigue (62%), and hyperpigmentation (37.4%). According to hemoglobin level, 40% were suffering from severe anemia, 38.7% was having moderate, and 21.3% was having mild anemia. The majority (74%) were having both Vitamin B12 and folic acid deficiency followed by 16.7% Vitamin B12, and 9.3% folic acid deficiency.

Conclusion: Girls were presenting with megaloblastic anemia more than boys. Majority of them were suffering from both Vitamin B12 and folic acid deficiency. Children suffering from megaloblastic anemia present with anorexia, pallor, weakness, and fatigue. A proper health promotion program may be designed to aware the parents about the prevention of nutritional anemia.

KEY WORDS: Folic Acid Deficiency; Anorexia; Pallor; Anemia; Vitamin B12; Hemoglobins

INTRODUCTION

Children’s health can be severely impacted by anemia.\(^1\) There are several aspects that can be impaired including motor and behavioral development, an optimal level of cognitive function, motor coordination for locomotion and fine motor task, and language development.\(^2\) As a result, anemic children may perform below average children in schools and that may be continued even later in adulthood.\(^3\) Furthermore, morbidity by infectious illness is found to be higher than in a child without anemia.\(^4\)

Due to several underlying factors, nutritional anemia is highly prevalent in the Indian population.\(^5\) Two important nutritional factors that can lead to anemia are Vitamin B12 and folic acid. Cobalamin or Vitamin B12 is a water-soluble vitamin that acts...
as a cofactor in DNA synthesis. Both deficiencies of Vitamin B12 and folic acid may lead to defective DNA synthesis that may lead to arrested nuclear division. However, as there is no derangement in the maturation of the cytoplasmic cycle of the cell, the blast cells come as larger than normal size and are known as megaloblast.\[6\]

As macrocytosis precedes the development of anemia, the isolated presence of macrocytosis without anemia could indicate early folate or cobalamin deficiency. Such children may present with weakness, growth retardation of failure, frequent illness such as diarrhea, glossitis, or neurological symptoms.\[7\]

Megaloblastic anemia is rather frequent among children in developing and impoverished nations. It is most frequent in children who are exclusively breastfed and are between the ages of 3 and 18 months. It might be caused by moms who are malnourished and have low Vitamin B12 and folate levels in their breast milk. Megaloblastic anemia has been more common in the past two decades, probably as a result of a growing number of people adopting vegetarian eating patterns. Some instances may be caused by genetic or acquired abnormalities that disrupt vitamin metabolism.\[7\]

In this context, this study aimed to observe the sex-wise distribution, presenting symptoms or clinical features, and hematological parameters among megaloblastic anemic children of age 1–14 in a tertiary care hospital in the eastern part of Odisha, India. This knowledge would help to know the pattern of presentation of children with megaloblastic anemia in this region and help in early screening and taking appropriate measures to correct the nutritional deficiency.

**MATERIALS AND METHODS**

**Type and Settings**

This was a hospital-based, cross-sectional, and observational study. The study was conducted in a tertiary care Hospital of Bhubaneswar, Odisha. The study period was from September 2018 to August 2020.

**Ethics**

This study was approved by the Institutional Ethics Committee of Kalinga Institute of Medical Science, Bhubaneswar, Odisha, India. For the participation, only volunteer patients were recruited after briefing about the aims and procedure of the study. Verbal assent was taken from the children and written informed consent was taken from their parents. The participants and their parents were informed about their freedom to quit the study at any point in time without stating any reasons.

**Recruitment Process**

Patients as research participants were recruited from the outpatient department and inpatient department of the department of pediatrics. Any children from ages ranging 1–14 were initially included after getting consent. Any children with hemolytic anemia, anemia due to chronic diseases like renal diseases, chronic liver diseases, blood transfusions, or hematinsics usage in the past 6 months, anemia due to acute blood loss were excluded from the study.

**History and Examination**

A detailed history was taken from the patients and their parents about the symptoms they are having. In addition, food habit and factors determining the social status was also obtained. The findings were recorded in a predesigned pro forma with a patient identifier for further input of laboratory parameters. Venous blood samples were collected in commercial plain vacutainers and Ethylenediaminetetraacetic acid added vacutainers and immediately sent to the central laboratory for testing. The complete blood count was done using an automated Sysmex blood cell analyzer with the recording of mean corpuscular volume (MCV), total red blood cell count, total leukocyte count, platelet count, Vitamin B12, and folic acid. The presence of anemia was diagnosed and graded according to the World Health Organization (WHO) criteria—blood hemoglobin level <11 g% in 1–5 years, <11.5 g% in 6–11 years, <12 g% in 12–14 years children and macrocytic anemia is diagnosed when the MCV exceeds 95 fl.\[8,9\]

**Statistical Analysis**

The data were entered and stored in WPS Spreadsheet software (WPS Software Pte. Ltd., Singapore). Descriptive and Inferential analyses were carried out in STATA software version 15.1 (StataCorp LLC, Texas, USA). The categorical variables were presented as frequency and percentage. For comparing categorical data, the chi-square or Binomial test was performed. All statistical calculations were performed considering a $P < 0.05$ as an indicator of statistical significance.

**RESULTS**

A total of 150 cases (37.5%) were diagnosed with megaloblastic anemia among the total 400 children presented with anemia. According to age, no children were enrolled in the age group of 1–5 years. A total of 24 (16%) children were in the 6–10 years group and 126 (84%) were in the 11–14 years age group, Binomial test $P < 0.0001$. Sex-wise distribution showed that girls were more (94 [62.67%]) than boys (56 [37.33%]), Binomial test $P = 0.002$.

Among the children, 124 (82.67%) were having vegetarian food habits and 26 (17.33%) were having non-vegetarian...
food habits, Binomial $P < 0.0001$. The socioeconomic distribution is shown in Figure 1. The majority (86 [57.33%]) of their families belonged to upper lower socioeconomic status as per the Modified Kuppuswamy classification. This class was followed by lower middle class 30 (20%), upper middle class 20 (13.33%), lower lower class 10 (6.67%), and upper class 4 (2.67%), $\chi^2 = 143.7$, $P < 0.0001$.

The occurrence of clinical manifestations is shown in Table 1. The most common clinical manifestation observed in the study is anorexia (99.3%), followed by pallor, weakness. The neurological symptoms (26.0%) were seen in the form of tingling, numbness, paresthesia. Subacute combined degeneration was noted in two of our children, and fine tremors were noted in 10 patients. All most all the patients had pallor (94.0%). Skin pigmentation, hyperpigmented knuckles, and glossitis were prominent features seen in nearly half of the patients.

The deficiency in Vitamin B12 and folic acid is shown in Table 2. The majority (74%) were having both Vitamin B12 and folic acid deficiency followed by 16.7% Vitamin B12, and 9.3% folic acid deficiency.

According to hemoglobin level, 40% were suffering from severe anemia, 38.7% was having moderate, and 21.3% was having mild anemia. Severity-wise vitamin B12 level is shown in Figure 2. Vitamin B12 was seen to be in 50–100 pg/mL range in mild ($\chi^2 = 9.5$, $P = 0.023$), moderate ($\chi^2 = 19.38$, $P = 0.002$), and severe ($\chi^2 = 12$, $P = 0.007$) anemic patients.

### DISCUSSION

Our study included a total of 150 children suffering from megaloblastic anemia. The majorities of the patients were in the age group of 11–14 years and belong to the upper-lower socioeconomic status. Boys were outnumbered by the girls. This finding may be due to the fact that during pre-pubertal and pubertal ages requires more nutritional support than childhood and that may cause deficiency if the demand is not fulfilled by increased intake. The most common presenting complaint in megaloblastic anemia is anorexia, and the most common clinical finding is pallor. Megaloblastic anemia is a chronic condition that develops over time, and thus these patients tend to be well compensated. Moreover, urgent blood transfusion is usually not required. According to deficiency of Vitamin B12 and folic acid, we found that majority of the patients are suffering from dual deficiencies.

In our study, the majority of the patients were in the age group of 11–14 years. This is similar to a study by Ravikumar et al. who found the mean age of the children 13.3 years.[10] In contrast, Yellinedi et al. showed a bimodal distribution—one at 1–5 years and another at 10–18 years of age.[11] However, our

### Table 1: Clinical manifestations among the sample of 150 anemic patients diagnosed as cases of megaloblastic anemia

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia</td>
<td>149</td>
<td>99.3</td>
</tr>
<tr>
<td>Pallor</td>
<td>141</td>
<td>94.0</td>
</tr>
<tr>
<td>Weakness</td>
<td>129</td>
<td>86.0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>93</td>
<td>62.0</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>52</td>
<td>34.7</td>
</tr>
<tr>
<td>Neurological symptoms</td>
<td>39</td>
<td>26.0</td>
</tr>
<tr>
<td>Glossitis</td>
<td>39</td>
<td>26.0</td>
</tr>
<tr>
<td>Icterus</td>
<td>23</td>
<td>15.3</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>20</td>
<td>13.3</td>
</tr>
</tbody>
</table>

$\chi^2=287.9$, $P<0.0001$

### Table 2: Cause of megaloblastic anemia as detected from blood test parameters

<table>
<thead>
<tr>
<th>Deficiency</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>B12 and folic acid</td>
<td>111</td>
<td>74</td>
</tr>
<tr>
<td>Only B12</td>
<td>25</td>
<td>16.7</td>
</tr>
<tr>
<td>Only folic acid</td>
<td>14</td>
<td>9.3</td>
</tr>
</tbody>
</table>

$\chi^2=112.8$, $P<0.0001$
study result was different. The cause may be attributed to the different geographical areas where the study was conducted. In our study, female patients were higher in number. These results were in synchrony with previous study Zengin et al.\textsuperscript{12} Finding by Zengin et al., and Yellinedi et al. about the clinical manifestation of megaloblastic anemia is supported by our study.\textsuperscript{11,12} In addition, a study by Incecik et al. reported the incidence of neurological manifestation to be 33% in their study, which was close to the result in our study (26%).\textsuperscript{13} According to Kaur et al., about 40% of the cases of megaloblastic anemia shows Vitamin B12 deficiency in 40% of the cases, and 25% of cases shows folinic acid deficiency. Furthermore, 35% of the cases shows combined deficiency.\textsuperscript{14} In the present study, B12 deficiency was seen in 16.7% of cases, folinic acid deficiency in 9.3% of cases, and combined deficiency was seen in 74% of cases. Khanduri et al., and Chandra et al. showed that Vitamin B12 deficiency is more found than folate deficiency and our study also support this finding.\textsuperscript{15,16}

This study adds the finding to the existing literature from this region of the state Odisha. Although we have taken an adequate sample for statistical tests, a large sample size would be better for increasing the power of the study and increasing the credibility of the study as a generalized one. However, there were time, manpower, and laboratory resource constraints. Furthermore, this study is hospital-based. Patients seeking medical attention were included. Hence, the actual burden of the children suffering from megaloblastic anemia may be the hidden part of an iceberg that should be explored with a suitable screening test. In any future study, these facts should be taken into consideration.

CONCLUSION

Megaloblastic anemia has become an important health problem due to inadequate consumption of foods that contains Vitamin B12 and folic acid namely. Varied presentations are starting from anorexia, weakness, and various other neurological symptoms with a principal clinical sign as pallor in megaloblastic anemia patients. Early detection and timely intervention are highly required. The fortification of diet to prevent megaloblastic anemia needs to be considered.

REFERENCES