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CLINICOHEMATOLOGICAL PROFILE OF MEGALOBLASTIC ANEMIA IN CHILDREN

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ABSTRACT **Background:** Children with B12 deficiency present with nonspecific manifestation like weakness, lethargy, failure to thrive, irritability. If left undiagnosed for long term, can result in neurological consequences. Megaloblastic anemia is underreported with prevalence varying between 21-45%. **Objective:** To study the clinical and hematological profile of children with megaloblastic anemia. **Method:** This is a cross sectional study conducted on 40 children for a period of 2 years. The study subjects were evaluated clinically and laboratory investigations were done for Vit B12, Hb, MCV and Folic acid. **Result:** In the present study, megaloblastic anemia was common in infants (60%). The most common presenting symptom was fever (70%), followed by hyperpigmentation (37.5%), cough (37.5%) and generalized weakness (32.5%). The most common underlying disease for admission in them was respiratory infection (32.5%) followed by viral episode (27.5%). Pallor (80%) and hyperpigmentation (62.5%) were the most common signs observed in the study subjects. Paired t test showed significant mean difference between the mean values of haemoglobin and MCV at 1 month period (p – 0.001). **Conclusion:** Megaloblastic anaemia was more common in infants and adolescents consuming vegetarian type of diet, with common symptom being fever, generalized weakness. Lab findings replicate low Hb, high MCV with bicytopenia and/or pancytopenia. The most common cause being deficient in vit B 12 which is a preventable and treatable cause.

KEYWORDS : Folic acid, Hemoglobin, Hyperpigmentation, Megaloblastic anemia, MCV, Pallor, Vitamin B12.

INTRODUCTION

Vitamin B12 (Vit B12) and folic acid (FA) deficiency results in asynchrony of nuclear and cytoplasmic maturation in hematopoietic stem cells, thus causing megaloblastic anemia (MA)[1]. Megaloblastic anaemia is defined as a macrocytic anaemia i.e characterised by a specific megaloblastic bone marrow morphology showing metamyelocytes and megaloblasts, accompanied by leucopenia and thrombocytopenia. Children with B12 deficiency present with nonspecific manifestation like weakness, lethargy, failure to thrive, and irritability[2]. If left undiagnosed for long term, can result in neurological consequences like paresthesia, sensory deficit, hypotonia, seizures, developmental delay, developmental regression, neuropsychiatric changes and life threatening pancytopenia[2,3,4]. It is often underreported in children from developing countries with a varying prevalence of 21-45%. Vegetarianism, minimal intake of animal products, poverty and malnutrition can lead to vitamin B12 deficiency [5,6,7]. Since it is a reversible cause of bone marrow failure and demyelinating nervous system disease, the recognition and treatment of vitamin B12 deficiency is critical. With this background, this study was done to evaluate the clinico-haematological profile of megaloblastic anaemia in a tertiary care teaching hospital.

OBJECTIVES

1. To study the clinical profile of children with megaloblastic anemia.
2. To study the hematological profile of children with megaloblastic anemia.

METHODOLOGY

This is a cross sectional study conducted over a period of 2 years (April 2018 – Mar 2020) at a tertiary care hospital, Karnataka. All the study subjects (n – 40) who were diagnosed as megablastic anaemia and/or children who were admitted for other underlying disease and later diagnosed to have megaloblastic anaemia were included as study subjects**.** A written informed consent was taken from parents of these children. Children who were already on Vit B12/ Folic acid replacement or who had received blood transfusion were excluded. Hemogram was measured using 2ml ethylene diamine tetraacetic acid anticoagulanted blood by Electrical Impedance and peripheral blood smear was examined. Children whose MCV (mean corpuscular volume) was high for age, peripheral smear showing hypersegmented polymorphs or macro ovalocytes and clinical features suggestive of megaloblastic anemia were subjected to B12 and folic acid levels by Immuno assay method. Serum B12 level <189 pg/mL, folic acid <1.8 ng/mL were considered as diagnostic marker for megaloblastic anemia. Demographic details, presenting complaints, clinical findings, developmental and diet history of the children were noted.

Statistical Analysis

Data was entered in the excel spread sheet. SPSS version 20 was used to perform the statistical analysis. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation for quantitative variables, frequency and proportions for qualitative variables. Paired t test was used to test the mean difference for Hb and MCV at baseline and 1 month period. The level of significance was set at 5%.

RESULTS

Table 1: Demographic data of the study subjects

Variables	n	%
Gender		
Female	18	45
Male	22	55
Age (years)		
<1	24	60
1-10	2	5
10-16	14	35
Birth weight (kg)		
< 2.5	4	10
2.5-3.5	34	85
>3.5	2	5
Diet		
Vegeterian	35	87.5
Mixed	5	12.5
Presenting symptoms		

Generalized weakness	13	32.5
Hyperpigmentation	15	37.5
Cough	15	37.5
Tremors	2	5
Hurried breathing	6	15
Fever	28	70

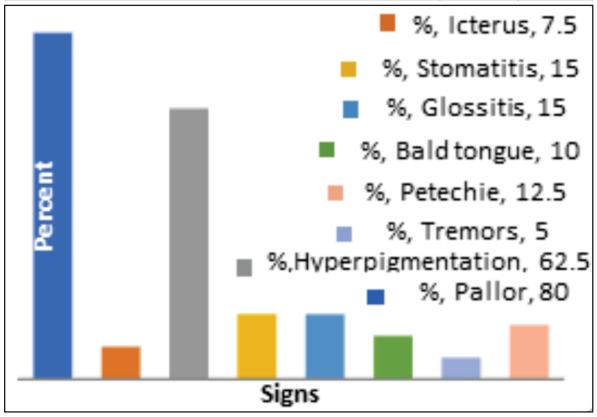

Table 2: Laboratory findings of the study subjects

Parameter	Min	Max	Mean	SD	p value
Hb - Baseline	2.5	14.3	8.48	2.85	0.01
Hb - 1 m	7	14.2	10.24	1.93	
MCV - Baseline	70	121	98.9	11.16	0.01
MCV - 1 m	72	107	89.98	7.89	
TC	1,600	24,400	7,856	5,298	
Platelet count	0.13	8.4	2.09	1.82	
Vit B12	28	265	113.08	47.07	
Folic acid	0.5	24	12.11	6.29	

In the present study, a total of 40 children who were reported to a tertiary hospital were included as study subjects. The demographic details are mentioned in table 1. The most common presenting symptom was fever (70%), followed by hyperpigmentation (37.5%), cough (37.5%), generalized weakness (32.5%), hurried breathing (15%) and tremors (5%). The most common underlying disease for admission in them was the respiratory infection (32.5%) followed by viral episode (27.5%). There was delayed developmental history noted in 7 children (17.5%) and 2 (5%) among them also had tremors. One child was admitted with intracranial bleed secondary to thrombocytopenia.

Pallor (80%) and hyperpigmentation (62.5%) were the most common signs observed in the study subjects (Chart 1).

The mean haemoglobin on day 1 and after 1 month was 8.48 ± 2.85 gms/dl and 10.24 ± 1.93 gms/dl respectively. The mean MCV at baseline and at 1 month was 98.9 ± 11.16 and 89.98 ± 7.89 respectively. Paired t test showed significant mean difference between the mean values (p – 0.001).

Lab findings showed 50% of the study subjects had bicytopenia and among them, 22.5% had pancytopenia. Vit B 12 deficiency was the main cause for megaloblastic anemia in 95% of the cases, rest of them had folate deficiency. One child presented with both nutrient deficiency.

DISCUSSION

In the present study, common age groups affected were infant (60%), followed by adolescent (35%). The reason for this in infants could be attributed to improper weaning practices and low cobalamine level in the breast milk of B12 deficient mother [2] and; in adolescents, it may be attributed to increased nutritional requirement in pre-pubertal and pubertal ages. Similar findings of high prevalence in adolescent groups was found by studies done by Khanduri et al[8] and Mukesh et al[9]. In the present study, 87.5% of cases were on vegetarian diet; this is in line with the studies done by Khanduri et al (87%)[8] and Mukesh et al (80%)[9]. 32.5% of children in the present study had generalised weakness which was similar to study by i.e. Mukesh et al [9]. The neurological findings such as tremors were low and were found only in 2(5%) patients in the present study, this was consistent with Mukesh et al [9] and Chandra et al [11] who showed it as 7.5% and 11.4% respectively.

Pallor (80%) and hyperpigmentation (62.5%) were the common clinical findings seen in the present study which is in comparable to Mukesh et al [9] where it was 100% and 55% respectively. Hyperpigmentation would be due to decreased glutathione which induces tyrosinase activity, in turn mobilizes melanocytes to keratinocytes, causing increased melanin synthesis [9].

In the present study, a total of 15% of children had bleeding manifestations like petechie, intracranial bleed which was similar to result observed in Gomber et al.,[12] (17.5%). Bleeding manifestations in these children was due to the underlying thrombocytopenia.

In a study by Gomber et al., bicytopenia was noted in 44.8% children, which was comparable with 50% in the present study[12]. Gomber et al., study also noted 17.2% children having pancytopenia, which was also comparable with the current study results i.e 22.5%[12]. But in a study by Sarode R et al, results showed that both bicytopenia and pancytopenia were very high i.e 80.5% and 43.8% respectively, this could be due to duration of anemia which is proportional to development of cytopenia[14]. It is generally believed that as severity of anemia increases, thrombocytopenia develops followed by neutropenia[15].

Predominance of B12 deficiency (95%) as a cause is observed in the present study, which was similar to Gomber et al., study findings[7]. This could be due to poor nutritional status of children, mothers and vegetarian habits.

All these children were treated with parenteral vit B12 for 5 days and then weekly for 4 weeks followed by monthly for 4 months, all children showed good improvement both clinically and haematologically except infants with tremors.

The drawback of the current study was that further work up of the causes other than nutritional deficiency was not able to be carried out.

CONCLUSIONS

The present study findings show that megaloblastic anaemia was more common in infants and adolescents consuming vegetarian type of diet, with common symptom being fever, generalized weakness, hyperpigmentation, developmental delay. Lab findings replicate low Hb, high MCV with bicytopenia and/or pancytopenia. The most common cause being deficient in vit B 12, which is a preventable and a treatable cause; when intervened at the right time, development of neurological disease in children can be prevented.

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