VOLUME-7, ISSUE-11, NOVEMBER-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Pediatrics

STUDY OF CLINICOHEMATOLOGICAL PROFILE AND NEUROLOGICAL MANIFESTATIONS OF VITAMIN B 12 DEFICIENCY IN CHILDREN

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ABSTRACT Vitamin B12 deficiency is an important and under recognised cause of anemia and neurological morbidity in children. As per previous studies from India iron deficiency was most common cause for anemia. But from the past two to three decades prevalence of cobalamin deficiency is increasing. This study aims to study the various clinical, neurological manifestations and hematologic profile of Vitamin B12 deficiency anemia in children aged 6 months to 12 years. A total of 58 children with Vitamin B12 deficiency were studied of which the most common age group affected were 1 to 4 years. Pallor, Anorexia, generalised weakness (100%), hyper pigmented knuckles (94%) and Hyper pigmented distal phalanges (90%), Glossitis (68%) were the most common presentations. The neurological features were seen in all the cases in 6 – 12 month age group. Leucopenia was seen in 74% and Thrombocytopenia in 49% cases. Early identification and treatment can prevent irreversible brain injury and its profound impact on neurological outcome of child.

KEYWORDS : Vitamin B12, Neurological features

INTRODUCTION

Vitamin B12 is classified as a water soluble vitamin and distinctive among all vitamins due to its large size, complexity and it contains the metal ion cobalt[1]. Vitamin B12 is essential for development of the central nervous system, synthesis of DNA and for the metabolism of carbohydrate, protein, and fat. Nutritional vitamin B12 deficiency occurs between 3 to 18 months of age, usually in children fed exclusively with breast milk, due to under nutrition of the mothers in underdeveloped or developing countries[2]. The reason for maternal vitamin B12 deficiency in these countries is low socioeconomic status, and infants presenting with severe hematological and neurological manifestations of vitamin B12 deficiency are more common than formerly appreciated [3]. Deficiencies in B12 can lead to inefficient erythropoiesis and megaloblastic anemia[4]. Neurological symptoms of vitamin B12 deficiency are heterogeneous and include muscular hypotonia, lethargy, apathy, regression of psychomotor development, tremor, ataxia, and seizures [5]. The recognition and treatment of vitamin B12 deficiency is critical since it is a reversible cause of bone marrow failure and demyelinating nervous system disease[6]. The present study is intended to observe the various clinical, neurological manifestations and hematologic profile of Vitamin B12 deficiency anemia in a tertiary health care centre.

MATERIALS AND METHODS

This was a retrospective observational study done at Department of Pediatrics, Government Medical College, Anantapuramu where all children aged between 6 months and 12 years, admitted with diagnosis of Vitamin B12 deficiency anemia during August 2016 to August 2018 were included in the study. The case records were accessed through admission and discharge database of the institute. The case records of all enrolled children were examined and details of age, sex, presenting complaints, nutritional history, clinical findings, mode of diagnosis, peripheral smear findings, bone marrow examination findings and Serum B12 levels were noted in a proforma. The cases with only clinical diagnosis, but without laboratory or pathological evidence of disease were excluded from the study. The mode of diagnosis considered was Vitamin B12 assay. Vitamin B12 was estimated by enzyme immunoassay, and a value of <200 pg/ml was considered low value. All the case records were analysed and tabulated the clinical features, hematological profile and neurological features and common modes of presentation in various age groups.

RESULTS

A total of 58 children were included in the study. Of the 58 patients 24 (57%) were male, 34 were female (43%). The most common age group affected were between 1 to 4 years followed by infants between 6 to 12 months. The age and sex wise distribution of cases is shown in table 1

TABLE 1: Distribution of cases according to sex

AGE	MALES	FEMALES
6-12 MONTHS	8	9
1-4 YEARS	10	9
5-8 YEARS	4	5
9-12 YEARS	2	11
TOTAL	24	34

Among the 17 cases of age group 6 - 12 months 80% of the children were exclusively breastfed without any weaning foods. Amongst the 9 – 12 years age group females are most commonly affected and 9 out of 13 children in this age group are vegetarians who do not consume any animal food except milk. Pallor, Anorexia, generalised weakness was observed in all the children (100%). Other common presentations included loss of appetite (98%), weight loss or decreased weight gain (85%), vomiting (46%), dyspnea (40%), tremors (17%) and developmental delay (41%). Among the examination findings, the most common were hyper pigmented knuckles (94%) and Hyper pigmented distal phalanges (90%). Glossitis was seen in 68% cases and recurrent aphthous stomatitis in 52% cases. Hepatomegaly was seen in 46% and splenomegaly was seen in 37 % cases. Four cases (6.8%) presented with CCF.

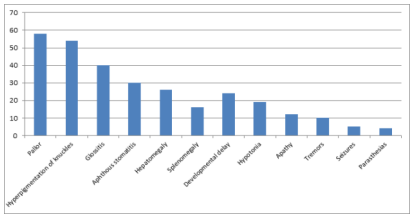
The neurological features were seen in all the cases (100%) in 6 – 12 month age group. The age wise distribution of neurological features is shown below in table 2.

TABLE 2: Age wise distribution of neurological features

AGE	NO. OF CASES	NEUROLOGICAL FEATURES
6-12 MONTHS	17	17 (100%)
1-4 YEARS	19	12 (63%)
5-8 YEARS	9	2 (22%)
9-12 YEARS	13	2 (15%)
TOTAL	58	33 (56.8%)

The most common neurological features were neurodevelopmental delay (41.4%), hypotonia (32.7%), apathy (20.6%). Tremors were present in 10 cases (17.2%). Five infants presented with seizures (8.6%). Parasthesias were seen in 5 cases (8%). The following figure 1 summarises the various clinical and neurological features.

FIGURE 1: Clinical manifestations



Macrocytic anemia was seen in all the cases (100%). Leucopenia was seen in 74% cases and Thrombocytopenia in 49% cases. Hypersegmentation of neutrophils is noted in 6 (10%) cases. Bone marrow examination was done in 3 cases which revealed hypercellular marrow with more immature cells like proerythroblasts, mature granulopoietic cells with hypersegmented nuclei large megakaryocytes. Neuroimaging was done in 14 cases which revealed cortical atrophy. The Serum B 12 levels are shown in table 3.

TABLE 3: Serum B 12 levels

VITAMIN B12 LEVEL	No. of cases	Percentage
Cautious low (150-200 pg/ml)	34	58.6%
Low (< 150 pg/ml)	24	41.4%

DISCUSSION

In the human body Vitamin B12 occurs in 3 different forms: the natural form hydroxocobalamin (OH-Cbl) and in its two active forms methylcobalamin (Me-Cbl) and adenosylcobalamin (Ado-Cbl). Cobalamin is synthesized by microorganisms present in the environment and in the intestines of animals. The main dietary sources of B12 are animal products including meat, fish, eggs, and dairy products[7], fortified plant products and B12-fortified yeast extract[8]. Nutritional deficiency had been the main culprit for widespread disease manifestations in a large population, especially among low income groups[9]. Early manifestations of cobalamin deficiency in infancy are nonspecific and thus can lead to a delayed diagnosis[10]. Reported infantile neurological manifestations of B12 deficiency include poor feeding, hypotonia, developmental delay, developmental regression, irritability, chorea, tremor and seizures[11]. A key observation is that infants with neurological manifestations of B12 deficiency can still have normal haematological parameters[12].

In our study there is higher incidence of B12 deficiency in females (58%) than males (42%) which is similar to that of study done by Chaturbhuj Singh et al[13]. In our study the most common age group affected were children between 6months to 4 years (62%) which is similar to that of a study done by S Yellinedi et al[14]. Amongst the 9 – 12 years age group females are most commonly affected which was in accordance with Khanduri et al[15]and Salma haq et al[16]. In this age group 80% are strict vegetarians which is similar to that of Khanduri et al.

In this study pallor, fatigue and anorexia were most common clinical symptoms which is similar as study by Ravi kumar et al[17]. In the present study knuckle pigmentation is seen in 94% cases which is in accordance with Chandra J et al[18]. In our study neurological manifestations are seen in all the cases in the age group of 6months to 1 year of which 80% of children are predominantly breastfed without proper weaning which is similar to that of a study done by Rahul jain et al[19]. In this study tremors are seen in 17% cases and parasthesias in 8% cases which is high compared to that of G. Scalabrino [20]. In our study Leucopenia was seen in 74% cases and Thrombocytopenia in 49% cases which was consistent with R.Sarode et al[21].

CONCLUSIONS

The importance of adequate vitamin B12 status particularly during pregnancy and early childhood should be emphasized in light of the role of vitamin b12 in neural myelination, brain development and child growth. Screening of all antenatal mothers and children upto 5 years may detect B12 deficiency at an early stage which can have significant impact in decreasing the neurological problems and anemia. Education about proper dietary habits is essential as it is more common in vegetarian people and infants with improper weaning. The addition of vitamin B12 along with iron and folate tablets in the antenatal period to mother and ongoing school health programs can have considerable benefits to prevent vitamin B12 deficiency thereby preventing developmental delay and improving cognitive performance and hematological manifestations.

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