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Prevalence and clinic hematological profile of vitamin B12 deficiency associated megaloblastic anemia in children of Jammu region - A hospital based observational study

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ABSTRACT

Introduction: Vitamin B12 deficiency (VBD) Megaloblastic Anemia (MA) is a relatively common disease encountered by pediatricians in Jammu region of north India, yet the data on prevalence of VBD in this age group remains scarce. Hence this study was conducted to study the prevalence and clinic hematological profile of VBD associated MA in children between 6 months to 18 years of age.

Aim: To estimate the prevalence and clinico hematological profile of vitamin B12 deficiency associated MA in children between 6 months to 18 years, who were admitted in SMGS Hospital, Government Medical College Jammu.

Materials and Methods: A Retrospective cross sectional study was conducted in children between 6 months to 18 years, who were admitted in SMGS Hospital, Government Medical College Jammu with diagnosis of Nutritional Anemia from April 2020 - March 2021.Case records of patients were reviewed for vitamin B12 deficiency as a cause of MA who were included in study. Vitamin B12 deficiency was diagnosed by measuring B12 levels in blood and by bone marrow examination if required. Clinic hematological profile of the participants was observed by reviewing their records for age, sex, socioeconomic status, food habits, presenting complaints, clinical signs and symptoms, peripheral smear findings and need for transfusion. All descriptive data collected was represented by tables and evaluated for statistical outcomes.

Results : The prevalence of vit. B12 deficiency associated MA in our study is 16.66 %. Among them 60% were females and 40% males. Age wise distribution was 6months -1 year 20 %, 1-5 years 22%, 6-10years 16% and 11-18 years was 42%. Vitamin B12 deficiency was more prevalent in lower socioeconomic group 80% and in those who were vegetarians 60%. Anorexia, generalised weakness, pallor was observed in 100% subjects. Neurologic involvement in the form of irritability, tremors was present in 30%. Icterus was seen in 10% while hepatomegaly and splenomegaly was present in 20 % and 22% respectively. Edema was seen in 2% of the subjects. Hyperpigmentation of knuckles was observed in 86% of the patients. Macrocytic anemia (MCV >100 ug/L) was observed in 100%. Bicytopenia was seen in 80% while Pancytopenia was present in 20%. Among 150 cases of Megaloblastic Anemia 80% of the patients were diagnosed by Vitamin B12 essay, 20% were diagnosed by Bone marrow examination. Blood transfusion secondary to severe anemia was required in about 10%.

Conclusion: Vitamin B12 deficiency is not that uncommon in our population with prevalence of 16.66% in hospitalized children. However true prevalence can only be estimated by population based surveys in pediatric age group. The most common presenting complaint in Megaloblastic Anemia is anorexia, generalised weakness, irritability manifesting clinically as pallor, hyperpigmentation of knuckles and hematologically as macrocytic anemia with 80% bicytopenia and 20% pancytopenia. Thus vitamin B12 addition in anaemia control and prophylaxis programmes may be considered.

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1. Introduction

Megaloblastic Anemia describes a group of disorders that are caused by impaired DNA synthesis. Red blood cells (RBC) are larger than normal at every developmental stage and are characterised as macrocytic anemia. Myeloid and platelet precursors are also affected and giant metamyelocytes and neutrophil bands are often present in the bone marrow. There is often an associated thrombocytopenia and leukopenia. The spectrum of disease associated with Vitamin B12 deficiency is wide ranging from asymptomatic cases to life threatening pancytopenia. Early diagnosis and prompt treatment of Vitamin B12 deficiency helps in reversibility of various manifestations like bone marrow changes and demyelinating nervous system disorders. Vitamin B12 is synthesized exclusively by microorganisms and humans depend on dietary sources like animal products including meat, eggs, fish and milk for their needs. In young infants born to mothers with low vitamin B12 stores, clinical signs of vitamin B12 deficiency can become apparent in the first 6-18 months of life, the time which is crucial for CNS deveopmnent. Vitamin B12 deficiency is commonly encountered in strict vegetarians and in low socioeconomic strata.[1–3] Anaemia prophylaxis and control programs in India focus on iron and folic acid supplementation excluding vitamin B12.

This study has been chosen to estimate the burden of vitamin B12 deficiency and to observe the various clinical manifestations and hematological profiles of patients with megaloblastic anemia in a tertiary care hospital which can help in future strategy to combat VBD associated MA in children.

2. Materials and Methods

This Retrospective Observational hospital Study was conducted at the Department of Pediatrics, SMGS Hospital, Government Medical College Jammu in children aged 6 months to 18 year from April 2020–March 2021 with diagnosis of Nutritional Anemia.

2.1. Inclusion criteria

Children aged 6 months to 18 years, who were admitted in SMGS Hospital, Government Medical College Jammu with diagnosis of Megaloblastic Anemia. The VBD was considered to be present if vitamin B12 levels were below 187pg/ml and /or Bone marrow examination was suggestive of megaloblastic anaemia.

2.2. Exclusion criteria

The cases with only clinical diagnosis but without any laboratory or pathological evidence were excluded from the study. Patients with chronic diseases like renal disease, cancer, tuberculosis, liver disease and those who had already received vit.B12 or blood outside as treatment were also excluded.

2.3. Sample size

Considering confidence interval=95%, or z=1.96 and absolute precision=0.05, margin of error 10% minimal sample size would be 97, we have included 150 children for the study.

2.4. Method of estimation

Vitamin B12 levels were assessed by Enzyme Immunoassay using the Architect plus Ergotron instrument and a value less than 187 pg /ml was considered low value. Bone marrow examination was done by bone marrow aspiration needle and the aspirate was examined for metamyelocytes, myeloblasts and was reported by the pathologist.

The case records of 150 patients diagnosed with Megaloblastic anemia among 900 patients having nutritional anemia was assessed through the admission and discharge database of the institute.

The basic demographic and clinical profile (age, gender, socioeconomic, dietary pattern and clinical presentation) were noted and various hematological manifestations of Vitamin B12 deficiency (peripheral blood smear findings and bone marrow findings) in Paediatric patients admitted in the hospital were also studied. All the case records were analysed and tabulated.

3. Results

A total of 150 children (n=150) among 900 patients with nutritional anemia were included in the study. The prevalence of MA in our study is 16.66%. Age wise distribution was 6months -1 year 20% (n= 30), 1-5 years 22%(n= 33), 6-10 years 16% (n= 24) and 11-18 years was 42% (n= 63)[Table 1].

Table 1: Age wise distribution of cases.

Age	Percentage (n)
6 months -1 year	20 (n=30)
1-5 years	22 (n=33)
6-10 years	16 (n=24)
11-18 years	42 (n=63)

Among them 60% (n= 90) were females and 40% (n= 60) males)[Table 2].

Vitamin B12 deficiency was more prevalent in lower socioeconomic group 8. 0% (n=120)[Table 3]

VBD associated MA was more common in those who were vegetarians 60%(n=90)[Table 4]

Anorexia, generalised weakness, pallor was observed in 100%(n=150) subjects. Neurologic involvement in the

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Table 2: Sex wise distribution of cases.

Sex	Percentage	No. of Cases
Females	60%	90
Males	40%	60
Total	100	150

Table 3: Socioeconomic status of the patients: (as per modified Kuppuswamy classification)

Socioeconomic status	Percentage	No .of cases
Upper	20%	30
Lower	80%	120
Total	100%	150

Table 4: Different Food habits of the patients

Diet	Percentage	No. of Cases
Vegetarian	60%	90
Mixed	40%	60

form of irritability, tremors was present in 30% (n=45). Icterus was seen in 10% (n=15) while hepatomegaly and splenomegaly was present in 20% (n=30) and 23% (33%) respectively. Edema was seen in 2%(n=1) of the subjects. Macrocytic anemia was observed in 100% (n=150). Bicytopenia was seen in 80%(n=120) while Pancytopenia was present in 20%(n=30). The median hemoglobin was 7.5gm% /dl. Patients having hemoglobin less than 5gms were labelled as severe anemia and were given blood transfusion that consisted of 10% (n=50).[table/fig 5]. The diagnosis of Megaloblastic anemia was made by Vitamin B12 assay and bone marrow examination in 80% (n=120) and 20% (n= 30) of the subjects respectively)[table/fig 5].

Table 5: Clinico-hematological profile of megaloblastic anemia

Clinical profile	Total (%)	Number of cases (n)
Pallor	100%	150
Irritability / tremors / neurologic involvement	30%	45
Anorexia / generalised weakness	100%	150
Hyperpigmentation of knuckles	86%	129
Hepatomegaly	20%	30
Splenomegaly	22%	33
Icterus	10%	15
edema	2%	1
Haematological profile		
Macrocytic anemia (MCV>100 ug/L)	100%	150
Pancytopenia	20%	30
Diagnosed by Vitamin B12 essay	80%	120
Diagnosed by bone marrow findings of megaloblastic	20%	30

4. Discussion

In the present study the prevalence of MA is 16.66%. Among them 60% are females and 40% males. The increased incidence of Vitamin B12 deficiency was seen initially upto 5 years of age and than in 11-18 years age group, the main cause being deficient Indian women accounting for lower vitamin B12 levels in breast milk, later inadequate complementary feeding given to children further pushing them to malnutrition during the crucial time of brain and central nervous system development. The adolescent age group becomes the other vulnerable group as they are in a state of constant growth, having high requirement of nutrients, deficient diets, junk food consumption, leads to Vitamin B12 deficiency in them. The incidence is more in vegetarians 60% and in lower socioeconomic groups 80%. The results of our study are comparable to Ashok kumar et al., and Khanduri et al who also observed similar results.[4,5] Clinico-hematological profile of the patients with Megaloblastic anemia showed pallor 100%, anorexia / generalised weakness 100%, irritability / neurological manifestations 30%, hyperpigmentation of knucles 86%, splenomegaly 22%, hepatomegaly 20%, icterus 10%, edema seen in 2% of the subjects. Macrocytic anemia was observed in 100%. Bicytopenia was seen in 80% while Pancytopenia was present in 20%. The median hemoglobin was 7.5 gm%/dl. Diagnosis was made by vitamin B12 assay in 80% subjects while diagnosis was made by bone marrow findings of megaloblasts in 20%. Similar results were observed by Zengin et al, Incecik F et al, Ashok kumar et al, Khanduri et al and Sankeerth Yellinedi et al.[4–8] Sankeerth et al had reported in their study pallor 100 %, irritability/ tremors /neurological involvement 38%, anorexia / generalised weakness 100%, hyperpigmentation 78%, bicytopenia 78%, macrocytic anemia 100%, severe anemia i.e Hb <6 gm /dl requiring blood transfusion 79%, diagnosis made by Vitamin B12 essay 58%, diagnosis made by Bone marrow aspiration 42%. This author has reported only bicytopenia whereas present study reported 80% bicytopenia and 20% pancytopenia. Mishra D et al, Bhatanagar et al and Sharif M et al have also reported pancytopenia in Megaloblastic anemia.,[9–11] Ineffective erythropoiesis, leukopoiesis and thrombopoiesis resulting due to enhanced programmed cell death in absence of Vitamin B12 decreases the survival of precursors in peripheral blood and results in pancytopenia. Hyperpigmentation results from decreased glutathione which induces tyrosinase activity which in turn mobilizes melanocytes to keratinocytes causing increased melanin synthesis.[12] In present study icterus was seen in 10% subjects of megaloblastic anemia , indirect hyperbilirubinemia and raised serum lactate dehydrogenase are more frequently seen due to ineffective erythropoiesis as reported by Emerson et al.[13]

The Indian series from 1960's documented Folate deficiency to be more common cause of MA.[14,15]

Subsequent studies done in 1980's and 1990's were in opinion that vitamin B12 deficiency is far more common than Folate deficiency.[16–20] Increased prevalence of Vitamin B12 deficiency as compared to Folic acid deficiency is reported from countries outside India as well.[21–24] Increased prevalence of MA due to Vitamin B12 deficiency is reported by various other authors in recent studies as well.

5. Conclusion

Prevalence of VBD associated with MA is very high in children, especially at younger age when the brain is developing and at adolescence when the brain is adapting. Henceforth under National programmes along with the supplementation of Iron, Folic acid, Vitamin B12 supplementation should also be reinforced.

They are wide spectrum of symptoms, signs and hematological manifestations seen in Megaloblastic Anemia caused by Vitamin B12 deficiency in children which should be kept in mind for early detection and treatment with vitamin B12, folic acid supplementation and dietary modification to prevent irreversible damage.

6. Limitation(s)

The percentage of vitamin B12 deficiency in pediatric population in general would be different than that reflected in study due to limited number of patients requiring hospital admission for treatment of MA. We recommend population based surveys that might provide us the true prevalence of VBD associated MA.

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None.

9. Conflict of Interest

None.

References

1. Michael W, David R, Cooper B. Nathan and Oski's Hematology of Infancy and Childhood. Saunders; 2014. p. 419–21.
2. Sally S. Clinical Practice:Vitamin B12 Deficiency. *N Engl J Med*. 2013;368(2):149–60. doi:10.1056/NEJMcp1113996.
3. Sachdeva A. Practical Pediatric Hematology. India: Jaypee Brothers Medical Publishers; 2012.
4. Kumar A, Singh N, Joshi S, Deopa B, Gupta A. Megaloblastic Anaemia: A Study of Clinico-Haematological Spectrum in Paediatric Population. *J Evid Based Med Healthc*. 2020;7(24):1130–4.
5. Khanduri U, Sharma A. Megaloblastic anaemia: prevalence and causative factors. *Natl Med J India*. 2007;20(4):172–5.
6. Zengin E, Sarper N, Kiliç SC. Clinical manifestations of infants with nutritional vitamin B12 deficiency due to maternal dietary deficiency. *Acta Pediatrica*. 2009;98(1):98–102. doi:10.1111/j.1651-2227.2008.01059.x.
7. Faruk I, Hergüner MO, Altunbaşak S, Leblebisatan G. Neurologic findings of nutritional vitamin B12 deficiency in children. *Turk J Pediatr*. 2010;52(1):17–21.
8. Yellinedi S, Karanam S, Gowdar G. Clinico-hematologic profile of megaloblastic anemia in children. *Int J Contemp Pediatr*. 2016;1(3):29–30.
9. Mishra D, Kohli A, Yadav RB, Nayak D. Megaloblastic anemia: a common cause of pancytopenia in children. *Indian J Pathol Microbiol*. 2007;50(2):447–8.
10. Bhatnagar SK, Chandra J, Narayan S, Sharma S, Singh V, Dutta AK, et al. Pancytopenia in children : etiological profile. *J Trop Pediatr*. 2005;51(4):236–9.
11. Sharif M, Masood N, Zahoor M, Dodhy MA, Asghar RM. Etiological spectrum of Pancytopenia /Bicytopenia in children 2 months to 12years of age. *J Rawalpindi Med Coll*. 2014;18(1):61–4.
12. Lee SH, Lee WS, Whang KC, Lee SJ, Chung JB. Hyperpigmentation in megaloblastic anemia. *Int J Dermatol*. 1988;27(8):571–5.
13. Emerson PN, Wilkinson JH. Lactate dehydrogenase in the diagnosis and assessment of response to treatment of megaloblastic anaemia. *Br J Haematol*. 1966;12(6):678–88.
14. Bhende YM. Some experience with nutritional megaloblastic anemia. *J Postgrad Med*. 1965;11(4):145–55.
15. Mittal VS, Agarwal KN. Observations on nutritional megaloblastic anemia in early childhood. *Ind J Med Res*. 1969;57:730–8.
16. Gomber S, Kumar S, Rusia U, Gupta P, Agarwal KN, Sharma S, et al. Prevalence and etiology of nutritional anemias in early childhood in an urban slum. *Indian J Med Res*. 1998;107:269–73.
17. Sarode R, Garewal G, Marwaha N, Marwaha RK, Varma S, Ghosh K, et al. Pancytopenia in nutritional megaloblastic anemia: a study from north-west India. *Trop Geogr Med*. 1989;41(4):331–6.
18. Gomber S, Kela K, Dhingra N. Clinico-hematological profile of megaloblastic anemia. *Indian Pediatr*. 1998;35(1):54–8.
19. Chandra J, Jain V, Narayan S, Sharma S, Singh V, Kapoor AK, et al. Folate and cobalamin deficiency in megaloblastic anemia in children. *Indian Pediatr*. 2002;39(5):453–7.
20. Khanduri U, Sharma A, Joshi A. Occult cobalamin and folate deficiency in Indians. *Natl Med J India*. 2005;18(4):182–3.
21. Mukibi JM, Makumbi FA, Gwanzura C. Megaloblastic anemia in Zimbabwe: spectrum of clinical and hematological manifestations. *East Afr Med J*. 1992;69(7):83–7.
22. Madood-Ul-Mannan, Anwar M, Saleem M, Wiqar A, Ahmad M. A study of serum vitamin B12 and folate levels in patients of megaloblastic anaemia in northern Pakistan. *J Pak Med Assoc*. 1995;45(7):187–8.
23. Allen LH, Rosado JL, Casterline JE. Vitamin B12 deficiency and malabsorption are highly prevalent in Mexican communities. *Am J Clin Nutr*. 1995;65(5):1013–9. doi:10.1093/ajcn/62.5.1013.
24. Casterline JE, Allen LH, Ruel MT. Vitamin B-12 deficiency is very prevalent in lactating Guatemalan women and their infants at three months postpartum. *J Nutr*. 1997;127(10):1966–72. doi:10.1093/jn/127.10.1966.

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