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Research Article

Clinico-hematologic profile of megaloblastic anemia in children

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ABSTRACT

Background: Megaloblastic Anemia is an important reversible cause of neurodevelopmental deterioration. The present study intended to describe the common presenting scenarios, clinical and haematological manifestations of the disease. The main objective of study is to describe the varied clinical and hematologic manifestations of Megaloblastic Anemia in children admitted to a tertiary care hospital, and to observe the mode of presentation of disease and its distribution among various age groups.
Methods: A Retrospective cross - sectional study was conducted in children between 6 months and 18 years, who were admitted with diagnosis of megaloblastic anemia from June 2010 to May 2015. Case records of eligible participants were analysed for primary outcome measures like presenting complaints, mode of diagnosis, peripheral smear findings, and clinical features and secondary outcome measures like age, sex, coexisting morbidities and nutritional status.
Results: Of a total of 129 cases, in 58% subjects, diagnosis was confirmed by Vitamin B12 assay, 42% were diagnosed by bone marrow examination. Macrocytic anemia was observed in peripheral smear examination in 100% subjects. Hyperpigmentation was noticed in 78% of subjects. Blood transfusion secondary to severe anemia was needed in 79% of subjects. Anorexia, generalised weakness, pallor was observed in 100% subjects, neurologic manifestations in 38% subjects.
Conclusions: The most common presenting complaint in megaloblastic anemia due to Vitamin B12 deficiency is anorexia, generalised weakness, irritability manifesting clinically as pallor, hyperpigmentation and haematologically as macrocytic anemia with bicytopenia. Regular report of common presentations of megaloblastic anemia in various age groups keeps the child care expert vigilant for its early detection.

Keywords: Hyperpigmentation, Macrocytic anemia, Pallor, Vitamin B_{12} deficiency

INTRODUCTION

Megaloblastic Anemia is classically defined as a macrocytic anemia that is characterized by a specific megaloblastic bone marrow morphology showing metamyelocytes and megaloblasts, accompanied by leukopenia and thrombocytopenia.[1,10] The spectrum of disease associated with vitamin B12 deficiency is wide, from asymptomatic to life-threatening pancytopenia or myelopathy. 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.[2] Nutritional deficiency had been the main culprit for widespread disease manifestations in a large population, especially among low income groups.[3]

The present study intended to observe the clinical and hematologic profile of megaloblastic anemia in a tertiary health care centre, and common modes of presentation and distribution among various age groups.

METHODS

This retrospective observational study was undertaken at Department of Pediatrics, JJM Medical College, Davangere, Karnataka, India where all children aged between 6 months and 18 years, admitted with a diagnosis of Megaloblastic Anemia bearing ICD-9 code of 281 during June 2010 to May 2015 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 primary outcome measures like presenting complaints, mode of diagnosis, peripheral smear findings, and clinical features were noted. The secondary outcome measures noted were age, sex, coexisting morbidities and nutritional status. 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 either Vitamin B12 assay or bone marrow examination. Vitamin B12 was estimated by enzyme immunoassay using Architect plus Ergotron Instrument, and a value of <187 pg/ml was considered low value.[11] Bone marrow examination was performed by using Jamshidi bone marrow biopsy needle, and the aspirate was examined for metamyelocytes, megaloblasts, and reported by the pathologist.[4] All the case records were analysed and tabulated clinical features and common modes of presentation in various age groups. Multivariate regression analysis was performed to identify the association of aforementioned outcome measures with the disease.

RESULTS

A total of 129 children (n =129) were included in the study out of 48511 admissions. They were distributed over the years as 30 (June 2010 to May 2011), 24 (June 2011 to May 2012), 22 (June 2012 to May 2013), 20 (June 2013 to May 2014) and 33(June 2014 to May 2015). In 58% (n = 75) subjects, diagnosis was made by Vitamin B12 assay, whereas, 42% (n=54) were diagnosed by bone marrow examination. 52% (n=67) were females, 48% (n=62) were males. Age wise distribution listed in Table 1.

Table 1: Age wise distribution of cases.

Age	Percentage (n)
Infants (>6 months, upto 1 year)	30 (n = 39)
1-5 years	25 (n = 32)
5-10 years	8 (n = 10)
10-18 years	37 (n = 48)

Anorexia, generalised weakness, pallor was observed in 100% (n=129) subjects, hyperpigmentation in 78% (n=100) subjects, neurologic manifestations like irritability, tremors/seizures in 38% (n=49) subjects.

Table 2: Clinico-hematologic profile of megaloblastic anemia.

Clinical profile	Total %	Number of cases (n)
Pallor	100%	129
Irritability / tremors / neurologic involvement	38%	49
Anorexia / generalised weakness	100%	129
Hyperpigmentation	78%	100
Haematological profile		
Bicytopenia	78%	100
Macrocytic anemia (MCV >100 µg/L)	100%	129
Severe Anemia (Hb <6 g/dl.) Need blood transfusion.	79%	101
Diagnosed by bone marrow findings of megaloblasts.	42%	54
Diagnosed by Vitamin B12 assay	58%	75

Macrocytic anemia, bicytopenia was observed in peripheral smear examination in 100% (n=129) and 78% (n = 100) subjects respectively. The median haemoglobin was 7g/dL with severe anemia noted to be in 79% (n=101) subjects who needed blood transfusion. Cases were equally distributed in both the extreme age groups as mentioned in Table 1. All the measured outcomes correlated with the disease outcome with a p value <0.005.

DISCUSSION

The present study revealed the most common presenting complaint in megaloblastic anemia due to Vitamin B12 assay to be generalized weakness and/or anorexia, irritability with the most common clinical finding of pallor, hyperpigmentation which is comparable to study by Zengin et al who also reported the mean hemoglobin as 6.4 g/dL and similar rate of presenting complaints.[5] Incecik F et al reported incidence of neurologic manifestations (irritability, tremors /seizures) to be 33% in their study which is comparable to present study (38%).[6]

Hyperpigmentation results from decreased glutathione which induces tyrosinase activity, which in turn mobilizes melanocytes to keratinocytes, causing increased melanin synthesis.[8]

55% of the cases needed blood transfusion secondary to severe anemia in a study conducted by Gomber et al, whose percentage is higher in the present study.[7] Given the fact that Vitamin B12 is necessary for red cell maturation, this correlation with severe anemia is no surprise.

Bicytopenia, was noted in the same study as well as in Meghann et al, study to be 44.8%, which is far less compared to present study (78%) which could be explained by the increased number of cases with severe anemia in the present study.[9] The increased incidence in two extreme age groups can be attributed to improper weaning practices and continued exclusive breastfeeding in infants group, and late medical consultation in 10–18 years age group. Megaloblastic anemia was predominantly diagnosed by bone marrow and Vitamin B12 assay, where emphasis has to be laid on Vitamin assay in order to standardise the diagnostic options among various hospital settings. It also adds the advantage of less expertise, easy to perform process and decreased risk of infection.

We are in an opinion that regular reporting of common diseases like megaloblastic anemia and its varied presentation in various age groups guides child care physicians in early detection of disease.

The merits of study being the description of varied clinical features and modes of presentation of Megaloblastic Anemia, along with the distribution among various age groups.

The drawbacks of our study are that we couldn't draw a causal relationship between nutritional deficiency and megaloblastic anemia.

CONCLUSION

The most common presenting complaint in megaloblastic anemia due to Vitamin B_{12} deficiency is anorexia, generalized weakness, irritability manifesting clinically as pallor, hyperpigmentation and hematologically as macrocytic anemia with bicytopenia. Regular report of common presentations of megaloblastic anemia in various age groups keeps the child care expert vigilant for its early detection.

Megaloblastic anemia is a preventive and treatable cause of progressive neurologic disease in children with poor reporting of wide range of clinical presentations and distribution among various age groups.

This study described the varied presentations of the disease in children, and degree of disease among various age groups.

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