

Megaloblastic Anaemia: Prevalence and Causative Factors

Dr Versha Prasad

Asst. Professor

University Institute of Health Sciences, C.S.J.M. University Kanpur

Abstract

Megaloblastic anaemia has been recognized as a clinical entity forever a century. The first clinical description of pernicious anaemia, which is one of the known causes of megaloblastic anaemia, has been attributed to Thomas Addison in 1849. Anaemia is the most common problems encountered by clinicians in INDIA. The affected population includes male, female as well as children. Over the last two decades, it has been found that incidence of megaloblastic anaemia is increasing. Folic Acid and Vitamin B12 deficiency are the most common cause of megaloblastic anemia. Of these two micronutrients, Vitamin B12 deficiency is more common now, due to vegetarian life style of people. At present, Anemia control or prophylaxis program give only Iron and Folic acid. This study has been chosen to focus on this issue. The cases for increasing incidences of Folate / Vit. B12 deficiency needs to be elucidated. For a number of years, the disease was known as Addisoniananaemia⁶. Megaloblastic anaemia is a heterogeneous group of disorders that have common blood abnormalities and symptoms.

All patients presenting to hospital over a period of 2 months with a haemoglobin <10 g/dl and peripheral smear findings consistent with megaloblastic anaemia will be included in the study. Diet, drug intake, previous blood transfusion, presenting symptoms and other relevant history will be taken into consideration. Complete blood counts, peripheral film examination, reticulocyte count and cobalamin and folate assays will be recorded. Patients with chronic disease like renal disease, cancer, tuberculosis, liver disease etc. will be excluded from the study. All data will be collected and evaluated statistically. Total 100 patients were diagnosed as macrocytic anaemia. The sex distribution were-70(male), 30(female) All the patients were vegetarian and from middle class and low socio economic group Most of the patients were found to be vegetarian. Even those who consider themselves as non-vegetarians usually consume meat only occasionally. Megaloblastic anaemia seen in infants and young children may be attributed to maternal deficiency which results in poor body stores at the time of birth. Cobalamin content of breast milk is lower in vegetarian mothers and is directly proportional to serum cobalamin levels. Cobalamin deficiency was responsible for megaloblastic anaemia in the majority of our patients. The supplementation program for Anemia control and prophylaxis should vary according to the regional requirements. Vitamin B12 should be included in the nutritional programme along with iron and folic acid. Awareness camp and Education program about megaloblastic anemia can be implemented for the prevention.

Keywords:

Megaloblastic Anemia, Vitamin B12, Nutritional Deficiency.

Introduction

Megaloblastic anaemia has been recognized as a clinical entity forever a century. The first clinical description of pernicious anaemia, which is one of the known causes of megaloblastic anaemia, has been attributed to Thomas Addison in 1849. Anaemia is the most common problems encountered by clinicians in India. The affected population includes male, female as well as children. According to World Health Organization (WHO), the global prevalence of anaemia is 24.8%, which means about 1.62 billion people worldwide¹. Overall health status of a person is judged on level of haemoglobin of a person. Much of the early work on megaloblastic/pernicious anaemia was done on western subjects. Megaloblastic anaemia results from abnormal maturation of haematopoietic cells due to faulty DNA synthesis. Two vitamins, cobalamin (vitamin B12 and folic acid are essential for DNA biosynthesis. Deficiency of either vitamin results in asynchrony in the maturation of the nucleus and cytoplasm of rapid regenerating cells. In the haematopoietic system this asynchrony results in abnormal nuclear maturation with normal cytoplasmic maturation, apoptosis, ineffective erythropoiesis, intramedullary haemolysis, pancytopenia and typical morphological abnormalities in the blood and marrow cells.² Megaloblastic anaemia leads to substantial morbidity if unrecognized or

misdiagnosed. Its aetiology is multifactorial and may result from dietary deficiency, impaired absorption and transport or impaired utilization of these vitamins in DNA synthesis. In India with diverse ethnic populations, different dietary and social customs, the incidence of megaloblastic anaemia and its associated problems have not been adequately documented.

The high prevalence of anaemia is a serious health hazards for the economic development and productivity of the country. Over the last two decades, it has been found that incidence of megaloblastic anaemia is increasing. Folic Acid and Vitamin B12 deficiency are the most common cause of megaloblastic anaemia. Of these two micronutrients, Vitamin B12 deficiency is more common now, due to vegetarian life style of people. Cobalamin is synthesized by bacteria and is found in soil and in contaminated water. Foods of animal origin (e.g. meat, eggs, and milk) are the primary dietary sources. The amount of cobalamin in the average Western diet (5 to 15 mg/day) is more than sufficient to meet normal requirements. The body can store large amounts of cobalamin. Because of this, it can take 2 to 5 years of deficiency to develop even in the presence of severe malabsorption.³ As the totally vegetarians do not consume any animal products, they are at high risk of developing vitamin B12 deficiency. It is generally agreed that in some communities the only source of vitamin B12 is from contamination of food by microorganisms. When vegetarians move to countries where there are high standards of hygiene and the rules of sanitation are stringent, there is good evidence that risk of vitamin B12 deficiency increases in adults and particularly in children born to and breastfed by women who are strict vegans.³ In India with diverse ethnic populations, different dietary and social customs, the incidence of megaloblastic anaemia and its associated problems have not been adequately documented. Unfortunately, from public health view point, deficiency of B12 / folate has been regarded to contribute little to nutritional anemia⁴.

Material and Methods

It is a prospective and retrospective study. All patients presenting to our hospital over a period of 2 months from March 2017 to 30th April 2017 with a haemoglobin <10 g/dl and peripheral smear findings consistent with anaemia were included in the study. Diet, drug intake, previous blood transfusion, presenting symptoms and other relevant history were taken into consideration. Complete blood counts, peripheral film examination, reticulocyte count and cobalamin and folate assays were recorded.

Results

In this study, total 100 patients were evaluated. All these patients met the inclusion criteria. Depending on the MCV value, serum assay and peripheral smear finding, they were categorised into 3 Groups- *Macrocytic, normocytic and microcytic* anaemia. The normal MCV value but with megaloblastic blood film or low serum markers were considered into macrocytic anaemia. Total 100 patients were diagnosed as macrocytic anaemia.⁵ The sex distribution were- 70(male), 30(female). Fifty-five per cent of patients with cobalamin deficiency and 08% of patients with folate deficiency were found. All the patients were vegetarian and from middle class and low socio economic group. Presentation: The predominant symptoms were

- Neurological symptoms (50%),
- Fatigue (38%)
- Anorexia,
- Low grade fever,
- Palpitation.

Laboratory findings: The MCV ranged from 70fL to 128fL.

Peripheral smear revealed Macro-ovalocytes, Tear drop cells, Basophilic stippling, Polychromatic, Hyper segmented neutrophils or Pancytopenia. 15 patients had received blood transfusions for anaemia.

Discussion

Megaloblastic anemia is a result of vitamin B12 or folic acid deficiency. This leads to failure of the normal process of the rbc maturation and immature RBCs circulates in the blood. Megaloblastic anaemia most commonly results from folate or cobalamin (vitamin B12) deficiency. Paul Ehrlich in 1880 first used the term megaloblast to describe the abnormal cells in the bone marrow of a patient with pernicious anaemia.^{6,7} Thomas Addison first described pernicious

anaemia, the best known of the megaloblastic anaemia, in 1855. For a number of years the disease was known as Addisonian anaemia⁶. Megaloblastic anaemias are a heterogeneous group of disorders that have common blood abnormalities and symptoms. It is a macrocytic anaemia that is usually accompanied by leukopenia and thrombocytopenia and specific bone marrow morphology affecting erythroid, myeloid and platelet precursors. Anton Biermer in 1872 first used the term, pernicious anaemia. Vitamin B12 was first identified in the 1920's by Minot and Murphy as being the extrinsic factor present in the liver which reverses the symptoms of pernicious anaemia, as reviewed by Markle and Okuda. The incidence of megaloblastic anaemias is increasing, although evidence for this may not be forthcoming easily. The diagnosis of vitamin B12 deficiency is not straightforward. There are no uniform diagnostic criteria and no single laboratory test constitutes a gold standard. Various criteria have been used in the literature for the diagnosis of this anaemia which includes macrocytosis of red cells, presence of megaloblastic changes in the bone marrow and subnormal micronutrient levels. Gomber S et al in 1998 conducted a study on Prevalence & aetiology of nutritional anaemia's in early childhood in an urban slum. Randomly selected 300 children aged 3 months-3 year were analysed over a period of one year for estimating prevalence of nutritional anaemia. Pure iron deficiency anaemia (IDA) was detected in 41.4% of anaemic children.⁸ Cobalamin deficiency was responsible for megaloblastic anaemia in the majority of our patients (55% pure cobalamin deficiency and 10% combined deficiency) and pure folate deficiency in 8%. The MCV was found to be >90fl in 80% of the cases. In the rest of the cases, though MCV was normal, peripheral smear findings were characteristic. It includes Macro-ovalocytes, hyper segmented neutrophils, basophilic stippling. This could be because of concomitant iron deficiency. Pancytopenia was found in a few patients. Complete blood count, peripheral smear and the serum assay of vitamins are the diagnostic tests of megaloblastic anaemia.^{9,10} Bone marrow can also be done for the diagnosis. Since megaloblastic anaemia is a chronic disorder, most of the patients are well compensated. Most of the patients were found to be vegetarian. Even those who consider themselves as non-vegetarians usually consume meat only occasionally. Megaloblastic anaemia seen in infants and young children may be attributed to maternal deficiency which results in poor body stores at the time of birth. Cobalamin content of breast milk is lower in vegetarian mothers and is directly proportional to serum cobalamin levels.¹¹ The above findings suggest that most cases of megaloblastic anaemia are caused by nutritional deficiency of vitamin B12, folate or both. The other causes of deficiency account for minority of cases. Irrespective of the cause, vitamin B12 deficiency now appears to be more common than folate deficiency in causing nutritional macrocytic anaemia. In India, the national nutritional program for anaemia control or prophylaxis gives only Iron and Folic acid. The various studies done earlier and the present study highlight the rise in incidences of vitamin B12 deficiency which needs to be elucidated. But, in India inadequate diet is the main cause rather than absorption.¹²

Conclusion The incidences of megaloblastic anaemia come next to iron deficiency anaemia. Data regarding the magnitude of the problem. Vitamin B12 deficiency causing megaloblastic anaemia is associated with other systemic manifestation and the morbidity is more.¹³ Our anaemia control programme only takes care of iron and folic acid deficiency. Vitamin B12 should be included in the national nutritional programme especially in the region where majority of the people are vegetarian. The Physician must keep in mind vitamin B12 deficiency in their differential diagnosis of anaemia.

References

1. Sachdev HPS, Chandhary P. Nutrition in children: Developing country concerns Reprint. 1995; 1
2. Baker SJ, DeMaeyer EM. Nutritional anemia; its understanding and control with special reference to work of World Health Organization. *Amer J Clin Nutr* 1979; 32: 368-417
3. S.N. Wickramasinghe SN. Morphology, biology and biochemistry of cobalamin- and folate-deficient bone marrow cells. *Baillieres Clin Haematol*. 1995; 8(3):441- 59.
4. A. Shah. Megaloblastic anemia - Part II. *Indian J. Med. Sci.* 2004;58:309-11.
5. M.S. Harakati MS. Pernicious anemia in Arabs. *Blood Cells Mol Dis*. 1996;22(2):98-103. 6. R. Green, L.J. Kinsella. Current concepts in the diagnosis of cobalamin deficiency. *Neurology*. 1995;45(8):1435-40.
6. Addison T. Anaemia—disease of the suprarenal capsules. *London Med Gazette* 1849;43:517–18.
7. G Richard Lee, John Foerster, John Lukens, Frixos Paraskevas, John P Greer, George M Rodgers, *Wintrobe's Clinical Hematology* 10th edition 1998, Williams & Wilkins A Waverly company volume 1 page 942.
8. Gera R, Singh ZN, Chaudhury P. Profile of nutritional anemia in hospitalized children over a decade. *Conference Abstracts, 38th National conference of Indian academy of Pediatrics Patna 2001; HO-09, pp 60*
9. Allen LH, Rosado JL, Casterline JE et al. Vitamin B12 deficiency and malabsorption are highly prevalent in Mexican communities. *Amer J Clin Nutr* 1995; 65: 1013-1019.
10. Casterline JE, Allen LH, Ruel MT. Vitamin B12 deficiency is very prevalent in lactating Guatemalan women and their infants at three months postpartum. *J Nutr* 1997; 127: 1966-1970
11. Madood-ul-Mannan, Anwar M, Saleem M et al. Study of serum vitamin B12 and folate levels in patients of megaloblastic anemia in northern Pakistan. *J Pak Med Assoc* 1995; 45: 187-188.
12. Sarode R, Garewal G, Marwaha N, Marwaha RK, Varma S, Ghosh K, Pancytopenia in nutritional megaloblastic anemia: A study from north-west India. *Trop Geogr Med* 1989; 41:331–6.
13. Mukibi JM, Makumbi FA, Gwanzura C. Megaloblastic anemia in Zimbabwe: Spectrum of clinical and haematological manifestations. *East Afr Med J* 1992; 9: 83-87.