



CLINICAL AND HISTOLOGICAL CHANGES OF ORAL MUCOSA IN VITAMIN B₁₂ DEFICIENCY

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ABSTRACT

Vitamin B₁₂ occurs in various forms and has a variety of names. The common sources of vitamin B₁₂ are microorganisms like bacteria, yeasts, molds and algae. Megaloblastic anaemia is the most commonly found anaemia due to deficiency of vitamin B₁₂. The clinical symptoms are weakness, fatigue, shortness of breath and various neurological abnormalities. Due to deficiency of haematopoietic vitamins the patients suffers from glossitis, angular cheilitis and recurrent oral ulcers. Diffuse erythematous mucositis and pale oral mucosa. Such symptoms provides a great opportunity to participate in the diagnosis of megaloblastic anaemia. The aim of the present study was to describe clinical and histological changes in patients with megaloblastic anaemia.

KEYWORDS: Megaloblastic anaemia haematopoietic symptoms provides megaloblastic anaemia.

INTRODUCTION

Megaloblastic anaemias are the group of macrocytic anaemia. It is caused due to impairment in the synthesis of DNA.^[1] Due to this reason the RBCs become enlarged, platelets and leucocytes abnormalities and changes in epithelial cells takes place. Particularly the mouth cells and gastrointestinal track cells are mostly affected.^[3] The most prevalent cause of megaloblastic anaemias are cobalamin (vitamin B₁₂) and folate (vitamin B₉) deficiency.^[3]

Vitamin B₁₂ cannot be synthesized by the body. The main dietary sources of B₁₂ are dairy products, liver, fish, eggs etc. Microorganisms are mainly responsible for the synthesis of vitamin B₁₂.^[5]

Vitamin B₁₂ plays an important role in general cell metabolism. It is required for the normal hematopoiesis.^[1] Vitamin B₁₂ is actively involved in the maintenance of integrity of the nervous system and formation of nerve cells.^[1,2] Cobalamin is the factor for two enzymes, methionine synthase and L- methyl-malonyl-CoA mutase. The interaction between vitamin B₁₂ and folate deficiency mainly responsible for megaloblastic anaemia.^[4] Hematological changes in vitamin B₁₂ and pernicious anaemia (PA) can aid clinicians in making a correct diagnosis. It will also useful for prevention of serious neurological complications.^[2]

The most common cause of vitamin B₁₂ deficiency is pernicious anaemia. This is a condition in which the portion of gastric mucosa that contain the parietal cell is destroyed through an autoimmune mechanism.^[6] The cobalamin released from food gets attached to cobalamin- binding proteins, R- binders present in the saliva and gastric juice.^[5]

In the jejunum the dissociated cobalamin binds to intrinsic factor which is produced by the gastric parietal cell in duodenum. Further it is transported to ileum. In the ileum specific receptor binds with the B₁₂ intrinsic factor complex. This results in the enhanced B₁₂ absorption.^[1,2,5]

The megaloblastic anaemia is silent till the last phase. Since many years a wide spectrum of oral, gastrointestinal, haematological and neuropsychiatric manifestations can be predicted many years before anaemia development.^[7,8,9]

Many of the times dental practitioners and medical doctors always ignore the oral manifestations. The pathologist found drastic changes in red blood cell distribution width (RDW), red blood cell count (RBCc), mean corpuscular volume (MCV) until haemoglobin level is drastically reduced.

All the patients with vitamin B₁₂ deficiency have an increased RDW. This is the differentiating variable from macrocytic anaemia with aplastic anaemia. This will be

serves as sensitive index for early diagnosis of vitamin B¹² deficiency.

MATERIALS AND METHODS

The present work was carried out in the Department of general Pathology and in collaboration with Department of Biochemistry, Rangoonwala Dental College and Research Centre, Pune, (MS). Prior to start the study, local institutional ethical committee approved the study. The utmost care was taken during experimental procedure according to the Declaration of Helsinki 1964.

Study type: community based case-control study.

This study has been performed on total 68 subjects which includes 34 age and sex matched (20 males and 14 females) healthy controls and 34 (15 males and 19 females) from the age group 35-60 years. All the patients were from low socio-economical class and having poor sanitation.

Inclusion criteria

1. All the cases of suspected vitamin B¹² deficiency anaemia belonging to the age group of 35-60 years.
2. Long duration history of sore mouth.
3. The oral complaints and presence of stomatitis and angular cheilitis.
4. All the patients having haemoglobin less than 8gm/dl.

Exclusion criteria

1. Patients previously transfused with blood within 120 days.
2. Patients having other oral mucosal problems.
3. Patients already on iron therapy.

Controls

1. Having haemoglobin concentration within the normal range from the same age group.

After obtaining a written consent form from all the subjects who were included in the study and by giving detail information of study, blood samples were collected

from controls and patients. Total 3ml blood was withdrawn aseptically from the antecubital vein from each subject in a plain container and EDTA bulbs. The samples were centrifuged at 3000 rpm for 10 min to separate serum.

All haematological parameters were carried out by automatic methods. Adequate quality control measures were taken on each test procedure to ensure the reliability of the results. Haematological and biochemical investigations were done in haematology laboratory and biochemistry laboratory, respectively.

I. Biochemical Examination

1. *Serum folate Estimation*- It was done with the help of serum folate estimation kit manufactured by Randox Laboratories LTD, UK by using Biochemistry Analyser.
2. *serum cobalamin Estimation*- It was done with the help of determination of serum cobalamin kit manufactured by Randox Laboratories LTD, UK by using Biochemistry Analyser.

II. Hematological Examination

1. *Automated Blood Count (Complete Blood Count)*- A complete blood count (CBC) was analyzed by the ABX PENTRA 60 which is a fully automated (Microprocessor controlled) haematology analyser used for the in vitro diagnostic testing of whole blood specimens.

Statistical Analysis

The statistical analysis was carried out by using the SPSS (Statistical Package for Social Sciences) statistical software, version 17.0 for Windows. The student t test was applied for the statistical analysis. The ($P < 0.01$) considered as highly significant. One-way ANOVA test were used for comparison of hematological parameters. The results were expressed in mean.

RESULTS

All the patients predominantly complained of oral symptoms. Tongue soreness was most common complaint. The tongue become smooth and beefy red in color.

Table No. -1. Shows the mean biochemical parameters of controls and vitamin B₁₂ deficiency patients.

Serial No	Biochemical parameters	Controls (n=34)	Vitamin B ₁₂ deficiency patients (n=34)	P value <
1	Serum folate (ng/ml)	3-16	7.81*	0.01
2	Serum cobalamin (pmol/L)	118-709	75.3*	0.01

Values were expressed in mean range only.

*indicates statistically significant ($p < 0.01$)

n=number of patients.

Table No. -2. Investigations showing the mean of comparative haematological values in controls and vitamin B₁₂ deficiency patients.

Serial No	Haematological parameters	Control (n=34)	Vitamin B ₁₂ deficiency patients (n=34)	P value <
1	Hb (g/dL)	12-15.3	7.5*	0.01
2	RBC (million/cmm)	3.85-5.03	1.59*	0.01

3	RDW (%)	13-15.2	24*	0.01
4	MCV(fl)	79-100	149*	0.01
5	Haematocrit (%)	34-43	22*	0.01

Values were expressed in mean only.

*indicates statistically significant ($p < 0.01$)

n=number of patients.

DISCUSSION

The major clinical manifestations of megaloblastic anaemia are pancytopenia and megaloblastic changes in the haematopoietic system with large number of abnormalities of the digestive system. It results in oral and gastrointestinal track mucosa which results in defective DNA synthesis.^[10] The average daily requirement for cobalamin in adults is 1-2µg.

In our study total concentration of the RBCs become reduced and size become enlarged. Our study was supported by the Helder Antonio Rebelo Pontes et al.^[3] The macrocytosis was due to vitamin B₁₂ or folate deficiency. This leads to ineffective erythropoiesis. Vitamin B₁₂ is required for DNA synthesis. When either of these factors deficient, then RBCs become enlarged erythroblasts with nuclear or cytoplasmic asynchrony. This is the characteristic of megaloblastic anaemia.^[3] In the current study the RDW and MCV was an increased significantly when compared with controls. Our study has been supported by other researches also.^[2]

An enhanced MCV to 100-150 fl predict that the patient is having B₁₂ or folate deficiency by several years.^[1,2,3] Vitamin B₁₂ deficiency was found to exist in the absence of drastic RBCs changes. In such situation the change in the oral mucosa was a relatively important diagnostic marker. It also suggest to further checkup of serum cobalamin and iron levels.^[5,6,7]

The Dentist's involvement in the diagnosis of vitamin B₁₂ deficiency is based on the change in oral mucosal membrane. More than 79% of the patients are having megaloblastic anaemia.^[1,2,3,4]

In such condition external supplementation is the only way of choice to treat the patient. Cobalamin deficiency is usually treated by a parenteral administration of cynocobalamin as per the rate of 1000µg/week for one month and monthly thereafter.

CONCLUSION

Vitamin B₁₂ deficiency or folate deficiency is very serious problem in developing countries. Megaloblastic anaemia has complex pathogenesis. The oral mucosal changes and lesions are the most common initial symptoms. The dentist who is often consulted first, they has a prime opportunity. In addition to this they having prime responsibility to contribute to diagnosis of megaloblastic anaemia.

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REFERENCES

1. Meghana Gowda Sricharan, Anjali P Shetty, Ujwala S Shetty. Megaloblastic Anaemia. eJournal of Dentistry, 2004; 4(2): 608-620.
2. Shin-YU LU, Ming-Chung Wang. Initial diagnosis of vitamin B₁₂ deficiency by sore mouth and assessment of the red blood cell distribution width, mean corpuscular volume, and hemoglobin level a preliminary study. J Dent Sci., 2006; 1(1): 23-31.
3. Hélder Antônio Rebelo, Nicolau Conte Neto, Karen Bechara Ferreira, Felipe Paiva Fonseca, Gizelle Monteiro Vallinoto et al. Oral Manifestations of Vitamin B₁₂ Deficiency: A Case Report. Clinical Practice JCDA, 2009; 75(7): 533-537.
4. Sally P Stabler. Vitamin B₁₂ and Dentistry. The New England Journal of Medicine, 2013; 368: 149-160.
5. Manu Rathee and Amit Kumar Tamrakar. Oral Health and Vitamin B₁₂: A Review. Research and Reviews: Journal of Dental Sciences, 2013; 1(3): 38-41.
6. Hitoshi Osano, Toru Miyauchi, Masaki Toshima, Koichi Matsumoto et al. A rare case of a tongue mass in a patient with magaloblastic anemia. Jichi Medical University Journal, 2007; 30: 159-163.
7. Lindenbaum J, Healton EB, Savage DG. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. N Eng J Med, 1988; 318(26): 1720-1728.
8. Snow CF. Laboratory diagnosis of vitamin B₁₂ and folate deficiency. Arch Intern Med, 1999; 59: 1289-1298.
9. Dharmarajan TS, Norkus EP. Approaches to vitamin B₁₂ deficiency: early treatment may prevent devastating complications. Postgrad Med, 2001; 110(1): 99-105.
10. Jee SH, Dong KN, Eun JL, Sun JL et al. A case of vitamin B₁₂ deficiency megaloblastic anaemia following total gastrectomy. Yorsei Medical Journal, 1988; 29(3): 270-277.