ejpmr, 2017,4(9), 357-360

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

SERUM VITAMIN B12, FOLIC ACID, FERRITIN AND VITAMIN D LEVEL IN CELIAC DISEASE

[1]Dr. Usha, [2]*Anju Bharti, [3]Shailza Singh, [4]N. K. Agarwal, [5]O. P. Mishra and [6]Mohd. Frayez

[1]Professor, Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
[2]Assistant Professor, Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
[3]Phd Scholar, Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
[4]Professor, Department of Endocrinology and Metabolism, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
[5]Professor, Department of Paediatrics, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
[6]Ex. Jr. Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

***Corresponding Author: Prof. Anju Bharti**

Assistant Professor, Department of Pathology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

Article Received on 11/07/2017 **Article Revised on 31/07/2017** **Article Accepted on 21/08/2017**

ABSTRACT

Background: Celiac disease (CD) is very common in India. Recurrent diarrhoea and anaemia are most common manifestation. Main aim of present study was to find out prevalence of vitamin B12, Folic acid, Ferritin and Vitamin D3 so that their diet can be supplemented. **Material & Methods:** Study included 100 cases of CD and 22 healthy controls. Serum ferritin, vitamin B12, Folic acid and vitamin D were done by auto analyser (based on chemiluminiscent technique) of Artichet plus Abbott USA, Anti Tissue Transglutaminase Antibody(Anti Ttg) antibody was done by ELISA technique. **Result**: Our 60% patients were children between 2 to 16 years of age, 25% were adults and 21% were above 50 years. Failure to thrive and weight loss was more common manifestations (79%) followed by diarrhoea (71%), anaemia (66%) and pain abdomen (56%).Serum ferritin was significantly reduced in 50% patients and 21.4% controls. Majority of patients of CD had vitamin B12 level of 450- 550 pg/ml hence mean value was significantly reduced in CD patients (P. 000). Serum folic acid was reduced in 75% patients and 64.28% healthy controls. Mean value of Folic acid was not significantly reduced. Vitamin D levels were not affected in CD patients. Thus our study concludes that, serum ferritin and vitamin B12 are reduced in CD, while vitamin D is not affected. Hence CD diet must be supplemented with iron and vitamin B12.

KEYWORDS: Celiac disease, serum ferritin, serum vitamin B12, serum folic acid, Nutritional deficiency in CD.

1. INTRODUCTION

Celiac disease (CD) is a chronic immune mediated disorder seen in genetically susceptible person after ingestion of gluten. Gluten is found in wheat, barley and rye.[1] Gluten proteins are rich in proline & glutamine. High proline content makes them resistant to digestion. There is strong association of CD with HLA DQ antigen. Majority of patients of CD are DQ2 and/or DQ8 positive whereas only 30-40% normal Caucasians have these haplotype.[2] Only 3% of population having DQ haplotype develops CD.[3,4] The prevalence of CD is 0.5-1% in different parts of the world.[5] Classical feature of celiac disease is in the form of malabsorption syndrome, which is characterized by Diarrhoea, Steatorrhoea, Weight loss, Growth failure, constipation, pain abdomen, vomiting & bloating.[4,6,7] These manifestations are more common in children.

Besides gastrointestinal tract & its related manifestations, CD also presents with extraintestinal manifestations e.g. Delayed puberty, short stature, fatigue, type 1 Diabetes Mellitus, hypothyroidism, anaemia, neuropathy, arthritis, stomatitis, dental enamel hypoplasia, low bone mineral density.[6,7,8,9,10] Neurological and psychiatric manifestations can also be found in CD. These are common in adult patient characterized by anxiety, peripheral neuropathy, cerebellar ataxia, impaired cognitive functions. Depression, personality changes are seen 50% cases.[2] Neurological manifestations do not respond to gluten free diet(GFD) whereas GIT manifestations may improve with GFD.[11] It leads to deficiency of iron, vitamin D, vitamin B12, folic acid, vitamin B6 and zinc(Zn), selenium, copper and manganese.[11,12,13] Iron deficiency causes iron deficiency anemia which is seen in 50% cases.[13] Vitamin B12 deficiency produces megaloblastic anaemia and neurological symptoms. Folate deficiency and ferritin deficiency is found in patients with total villous trophy.[14] Zn deficiency correlates with villous atrophy. Zn deficiency is found in 92% patients with total villous

atrophy, 80% with subtotal atrophy & 60% with partial villous atrophy.[12]

AIMS AND OBJECTIVES

Aim of the present study was to diagnose CD in patients who presented with chronic recurrent diarrhoea and to find out serum vitaminD, serum vitamin B12, serum folic acid and ferritin levels in CD patients so that these patients can be treated with gluten free diet and supplements.

MATERIAL AND METHODS

Total 100 cases of CD and 31 healthy controls were taken for this study from Pediatric OPD and Endocrine OPD of SS Hospital, BHU. Diagnosis of CD was done by clinician by recent criteria of ESPGHAN (European Society for Paediatric gastroenterology hepatology and nutrient) as described by Husby et al 2012.[15] ESPGHAN included CD specific antibody, genetic background and enteropathy changes. All our patients had elevated anti Ttg antibody and Marsh III grade mucosal changes. About 5ml blood was taken in plain vial for serological test (Anti tTG Ab) and serum vitamin B12, folic acid, vitamin D3 and ferritin after written consent of the patients were done only on 24patients and 14 controls. DQ typing was done by SSO PCR method by Histospot instrument of BAG company supplied by Shiva Scientific, New Delhi. Anti Ttg was done by ELISA kit of AESCU Company by M/S Immunoshop. serum vitamin B12, folic acid, ferritin and vitamin D3 were done by Architect plus Abott USA serum B12 was done in 64 patients and 22 healthy controls whereas serum ferritin, folic acid and vitamin D was done in only 24 patients and 14 controls because sample amount was less and patients were not willing to give blood again.

RESULTS

(a). Female predominance was noted (60%) over males(40%). Age distribution showed that 60% patients were children between 2 to 16 years of age, 25% were adults between 21 to 40% and only 21 cases were above 50 years of age(Table I &II).

(b). Failure to thrive and weight loss was the most common manifestation in 79% cases followed by chronic recurrent diarrhoea (71%) anaemia (66%) and pain in abdomen in (56%)(Table III). Reduction in serum ferritin was found in 50% 0f CD cases against 21.4% in controls. this reduction was stastiscally significant (Table IV).

Serum vitamin B12 below 200ng/ ml was found in only 4.8% patients while majority patients of CD had B12 level on lower side of normal range between 450-550 Pg/ml. Hence mean value in CD patients was stastically significant (p.000)(Table V).

Contrary to serum ferritin and vitamin B12 level vitamin D was not found to be reduced either in patients or controls (Table VI). Interestingly serum folic acid was reduced in 75% CD patients but at the same time it was also reduced in healthy controls in 64.28% cases (Table VII).

Table I showing Sex wise distribution of CD patients.

Sex of patients	CD patients(n=100)	
	No.	%
Male	40	40
Female	60	60

Table II showing Age wise distribution of CD patients.

Age in years		CD patients	
		No.	%
A	0-10	52	52
B	11-20	18	18
C	21-30	17	17
D	31-40	8	8
E	41-50	3	3
F	≥51	2	2

Table III showing Clinical features of CD patients.

Clinical Features	CD patients (n=100)	
	No.	%
Chronic recurrent diarrhoea	71	71
Pain abdomen and bloating	56	56
Failure to thrive and weight loss	79	79
Anaemia	66	66

Table IV showing Serum Ferritin in CD patients and controls.

Serum ferritin in ng /ml									
Groups (No of cases)	<15		15-250		>250		Range(ng/ml)	Mean±SD	P
	No.	%	No.	%	No.	%			
Patients(24)	12	50.0	11	45.8	1	4.2	0.8-193.7	54.37±75.83	
Controls(14)	3	21.4	11	78.6	0	0	8.4-219.5	56.35±56.66	0.035

Table V showing vitamin B12 level in CD and control cases.

Serum vitamin B12 in pg/ml										
Groups (No of cases)	<200		250-840		>840		Range(pg/ml)	i	T AVSB	p AVSB
	No.	%	No.	%	No.	%		mean±SD		
(A) Patients(64)	2	4.8	59	92.2	3	4.7	20-1450	500.78±211.36	3.866	0.000
(B) Controls(22)	0	0	16	72.7	6	27.3	450-1450	731.82±316.06		

Table VI showing vitamin D status in CD and control cases.

Serum vitamin D level in ng/ml									
Groups(no of cases)	<30ng/ml		30-300ng/ml		>100ng/ml		Range (ng/ml)	x^2 AVSB	p AVSB
(A)Patients (24)	0	0	22	91.7	2	8.3	40.4-127.2	1.231	0.267
(B)Controls (14)	0	0	14	100	0	0	41.8-73.4		

Table VII showing Folic acid level in CD and control cases.

Serum folic acid in ng/ml								
Groups(no of cases)	<3ng/ml		3-17ng/ml		>17ng/ml		x^2 AVSB	p AVSB
(A) Patients(24)	18	75	5	20.8	1	4.2	0.562	0.755
(B) Controls(14)	9	64.28	4	28.57	1	7.14		

DISCUSSION

In our series 60% patients were children & main clinical manifestations were failure to thrive, diarrhoea, anaemia & pain in abdomen and bloating similar to our study other workers also found CD in mostly children with features of diarrhoea, weight loss, pain abdomen.[7,16,17,18] Serum ferritin deficiency was seen in 50% patients which is more or less close to observation of Wierdsma et al 2013 who also found ferritin deficiency in 46.2% cases but in their series none of the controls were found to serum ferritin deficiency. This may be because most of Indians are vegetarians. Iron in vegetarian food is present in very small quantity. Serum vitaminB12 was not found in healthy control but in patient it was found in 4.8% cases. some of workers from India found B12 deficiency in 41% patients of CD while western literature noted B12 deficiency in only 19% cases.[13,19] In present study mean value of B12 was significantly low because most of the patients had value on lower side of normal range. Vitamin D levels were not found to be reduced in CD patients. In fact 8.3% patient had high D3 above 100mg/ml. Similar to us Wierdsma et al also found low prevalence of vitamin D deficiency in only 4.5% cases whereas Tavakkoli et al 2013 found Vitamin D3 deficiency in 25% cases. As such vitamin D deficiency is uncommon in CD patients. Few cases reports regarding vitamin D deficiency in CD are available.[20,21] This may be because of most patients of CD were taking vitamin D3 supplements because they had stunted growth.

Interestingly serum folic acid deficiency was found in 75% CD patients and & 64% healthy controls hence statistically deficiency in patients was not significant. Contrary to our study Wierdsma et al 2013 found folic acid deficiency in 20% and reported in 31% CD patients.[19]

CONCLUSION

It concludes that healthy population in our area have diet deficient in folic acid. In CD patients both serum B12 and serum ferritin levels are reduced. study also

concludes that in every case of chronic diarrhoea and failure to thrive test for CD to be performed so that they can be treated by diet modification and vitamin & mineral supplements.

REFERENCES

1. Piccini B, Vascotto M, Serracca L et al. HLA-DQ typing in the diagnostic algorithm of celiac disease. Rev Esp Enferm DIG(Madrid), 2012; 104(5): 248-254.
2. Barker J M and Liu E:Celiac Disease: Pathophysiology, Clinical Manifestations and Associated Autoimmune Conditions Adv. pediatr, 2008; 55: 349-365.
3. Hoffenberg EJ, McKenzie TL, Barriga KJ, et al. A prospective study of the Incidence of Childhood Celiac Disease. J Pediatr. 2003; 143: 308-314.
4. Kelly CP, Bai J C, Liu Edwin, et al. DA: Advances in Diagnosis and Management of Celiac Disease. Gastroenterology, 2015; 148: 1175-1186.
5. Gujral N, Freeman HJ, Thomsan AB Celiac disease: prevalence, diagnosis, pathogenesis and treatment. World J. Gastroenterol, 2012; 18: 6036-6059.
6. Green P.H.R, Krishnareddy S, Lebwohl B: Clinical manifestations of celiac disease. Dig Dis. 2015; 33: 137-140.
7. Dr. Usha, Dr Deepa Rani, Dr. Neha Chaurasia, et al. Antithyroid peroxidase antibody and extractable nuclear antigen antibody in celiac disease-A preliminary communication. International Journal of Current Research. 2017; 9(06): 52938-52941.
8. Lubrano E, Ciacci C, Ames PR et al: The arthritis of coeliac disease: prevalence and pattern in 200 adult patients Br J. Rheumatol, 1996; 35: 1314-1318.
9. Aguiree JM, Rodriguez R, Oribe D, et al. Dental enamel defect in celiac disease. Oral Surg Oral med Oral Pathology Radiol Endod. 1997; 84: 646-650.
10. Bucci P, Carile F, Sangianantoni A, et al Oral aphthous ulcers and dental enamel defects in children with coeliac disease. Acta Paediatr, 2006; 95: 203-207.
11. Zelnik N, Pacht A, Obeid R, et al: Range of neurologic disorders in patients with celiac disease. Pediatrics. 2004; 113(6): 1672-1676.
12. Jameson S et al Villous atrophy and nutritional status in celiac disease. Am J Clini. Nutrition, 1999; 69: 3573-3574.
13. Wierdsma N J, Van Bokhorst-De Van der schueren MAE, Berkenpas M, Mulder C J J, et al. Vitamin and mineral deficiencies are highly prevalent in newly diagnosed celiac disease patients. Nutrients, 2013; 5(10): 3975-3992.
14. Kemppainen TA, Kosma VM, Janatuinen EK, et al. Nutritional status of newly diagnosed celiac disease patients before and after the institution of a celiac disease diet--association with the grade of mucosal villous atrophy. Am J Clin Nutr. 1998; 67(3): 482-7.
15. Husby S, Kaletzko S, Korponay S Zabo IR et al: European society for pediatric gastroenterology, hepatology and Nutrition Guidelines for the Diagnosis of coeliac disease J. pediatric gastroenterology and nutrition, 2012; 54(1): 136-160.
16. Sachdeva A, Srinivasan V, Maheswary S, et al. Adult onset celiac disease in North India Trop gastroentral, 2002; 23: 117-119.
17. Sachdev A. Coeliac disease –An overview Journal of medical college chandigarh, 2011; 1(1): 1-9.
18. Barton SH, Murray JA. Celiac disease and autoimmunity in the gut and elsewhere. Gastroenterol Clin North Am. 2008; 37(2): 411-428.
19. Dahele Anna and Ghosh Subrata.ViatminB12 deficiency in untreated celiac disease. Amer. J. Gastroenteral, 2001; 93(3): 745-750.
20. Tavakkoli A, Digacana D, Green peter H et al. Vitamin D status and concomittant autoimmunity in celiac disease patients. J. Clin Gastroenteral, 2013; 47(6): 515-519.
21. Rabelink NM, Westgest HM, Bravenboer N, et al. Bone pain and extremely low density due to severe vitamin D deficiency in celiac disease. Arch. Osteoporosis, 2011; 6: 209-203.
22. Kozanglu E, Basaran S, Goncu MK: Proximal myopathy as an unusual presenting feature of celiac disease. Clin. Rheumatolal, 2005; 24: 76-78.