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EVALUATION OF SERUM FERRITIN, CRP, VITAMIN D3, VITAMIN B12 AND IRON IN CELIAC DISEASE: A CROSS SECTIONAL STUDY

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Abstract: Malabsorption associated with weight loss, growth retardation and vitamin/mineral deficiencies characterized classical Celiac disease(CD). The aim of this study was to assess the levels of serum Ferritin, Vitamin B 12, Vitamin D3, serum Iron in newly diagnosed untreated CD patients. Newly diagnosed CD patients (n=28) and same number of matched healthy individuals were compared. Serum Ferritin was below the lower limit of normal in 85%, serum Vitamin B12 in 86 %,serum Vitamin D3 in 92.86 % in CD patients. These values were statistically significant as compared to controls($p < 0.00001$),($p < 0.042479$) respectively. Levels of serum Iron were not statistically significant. Estimation of C-Reactive protein (CRP) was done to assess the inflammatory response which did not reveal any significant elevation. The study indicates that estimation of serum nutritional parameters should form an integral part of investigation in all clinically suspected or newly diagnosed CD patients.

Key words: Celiac disease, C-reactive protein, Endomysial antibodies, Deamidatedglidin peptide.

INTRODUCTION:

Celiac disease(CD) is an inflammatory autoimmune disorder traditionally known to involve the mucosa of the small intestine in genetically susceptible individuals.[1]However, in the past two decades, CD has been shown to be a multi-system disorder with non-classical presentation [2-3-4].These days, many individuals present with no or only minor extra-intestinal symptoms. Indeed, microcytic or macrocytic anemia may occasionally be the only clinical symptom to suggest CD.[5]

Several studies have demonstrated deficiency of micronutrients in CD with varying results.[6]The deficiencies of minerals and vitamins status of CD patients has not been widely reported in Indian literature. Therefore, we aim to measure essential serum nutritional variables in order to assess whether any significant difference exists among CD patients when compared with apparently healthy individuals. In the present study the levels of serum Ferritin, Vitamin D3, Vitamin B12 and Iron were evaluated. We also looked for changes in the serum C-reactive protein (CRP)levels to assess the inflammatory response.

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MATERIALS & METHODS:

A total of 77 subjects (both children and adults) with clinically suspected CD and elevated IgA tissue transglutaminase antibody (IgA tTG) were studied along with 75normal healthy subjectsas controls.The patients taken for study are from different age groups (01-60 years) irrespective of gender. CD associated antibodies i.e., IgA Endomysial antibodies (EMA), IgA and IgG class antibodies to deamidated gliadin peptides (DGP) and duodenal biopsies was performed and analyzed. Histopathological classification according to Marsh was used. Patients with Marsh 2b, 3a, 3b, 3c with elevated CD associated antibodies were selected for final statistical analysis. The determination of levels of ferritin, CRP, Vitamin B12 and Iron in human serum was performed on the dedicated Roche / Hitachi COBAS systems. Vitamin D3 was estimated on LIASION® XL (DiaSorin). Both groups were studied in the same period and measurements were performed at same clinical laboratory.

The statistical analysis was performed in T – Test calculator for 2 independent means. A p-value $\leq$ 0.05 was required for statistical significance.

RESULT:

A total of 28 patients (18 children, 10 adults M: F 1:1) fulfilled the clinical and serological criteria for the diagnosis of celiac disease. A statistical comparison using the paired t-test was carried out of the data for all the parameters between subjects which have been marked as true celiac during the study and matched controls for the same. The range and mean values of these parameters are shown in table 1.

Serum ferritin levels showed marked differences between CD patients and the control group. The CD patients and control group had different distribution of values for serum ferritin with the means and standard deviations of these two populations (9.85 ± 10.63 for the CD, and 39.52 ± 31.78for the controls).($p < 0.00001$).

Serum vitamin B12 levels was frequently observed to be significantly low in CD patients compared to the control group. 86% of the CD patients showed values less than the lower limit of normal reference range. The means and standard deviations of serum vitamin B12 in these two populations (170.6 ± 113.96 for the

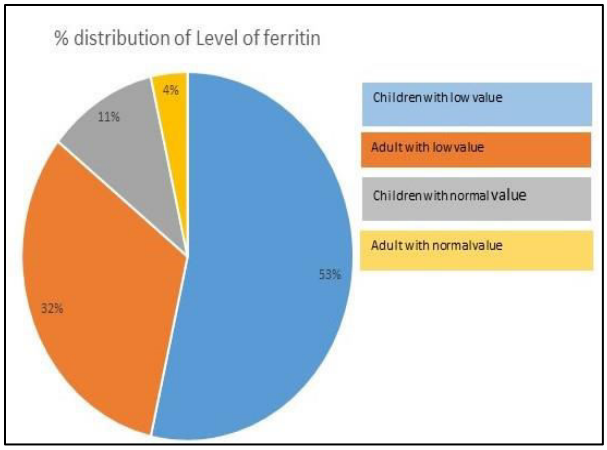
Table 1: Table shown the mean and range value of Ferritin, vitamin D3, vitamin B12, CRP and Iron in celiac and normal patients

Parameter	Celiac (Range)	Control (Range)	Celiac (Mean)	Control(Mean)
Ferritin (ng/mL)	1.77-57	15.1 – 169	9.85 ± 10.63	39.52 ± 31.78
Vitamin D3 (ng/mL)	4.2 – 55	6.8 – 104	12.6 ± 11.04	19.80 ± 18.86
Vitamin B12 (pg/mL)	45 – 676	146 – 999	170.6 ± 113.96	398.35 ± 224.92
CRP (mg/dL)	0.01 – 0.07	0.01 – 0.05	0.026 ± 0.016	0.025 ± 0.017
Iron (µg/dL)	12 – 38.7	39 – 137	32.88 ± 18.01	58.14 ± 23.88

CD, and 398.35 ± 224.92for the controls). (p <0.00001).

Serum vitamin D3 levels was low in 26 out of the 28 CD patients. 90 % of the adult CD patients were deficient in vitamin D3 (range 4.2 to 17.3 ng/mL). 94.4% of the CD patients in children were found to be deficient. The means and standard deviations of these two populations (12.6 ± 11.04 for the CD, and 19.80 ± 18.86 for the controls). (p < 0.042479)

There was no significant difference in the levels of iron (p < 0.40644) and CRP (p < 0.17945)levels



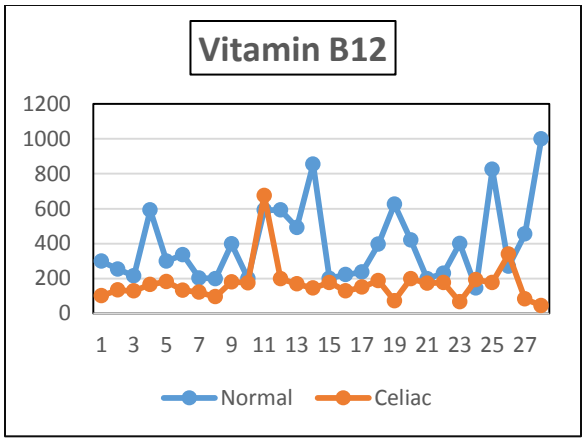
Pie diagram showing % distribution of ferritin in celiac subjects under study

amongst the two groups. The mean and standard deviations for the values of serum iron and CRP are given in table 1.

DISCUSSION:

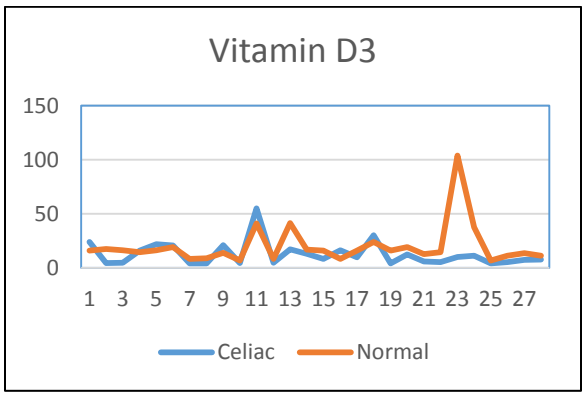
The main brunt of celiac disease is borne by the gastrointestinal system due to the damaging effects of ingested gliadin and therefore gluten sensitive enteropathy is currently a preferred term[7-8]. Most of these patients suffer from malabsorption of essential nutrients[9]. The current study reflects the deficiencies of some of the essential nutrients that are substantially low in patients suffering from celiac disease as compared to normal[10].Previous studies have shown decreased ferritin levels and vitamin B12 in celiac patients without significant iron deficient anemia which corroborates with the finding in the present study. The serum iron levels did not differ significantly as compared to normal healthy individuals indicating that serum ferritin levels reflect the iron-deficiency state (storage iron) better than serum iron. This is in accordance with literature quoting ferritin as the most reliable indicator of iron stores.

Vitamin B12 deficiency was frequently observed in our CD patients group (86%), in accordance with previous studies. Vitamin B12 is predominantly absorbed in the terminal ileum. Contrary to popular belief, the finding of low serum vitamin B12 indicates that the distal small intestine is functionally more affected. This has been shown to be true based on histopathological examination of distal small intestinal biopsy in previous studies[6].



Comparative plot between vitamin B12 levels in celiac and healthy patients

Although the levels of vitamin D3 were found to be low in CD patients, the difference from the control group was not so statistically significant ($p < 0.042479$). This can be explained by a high prevalence of vitamin D3 deficiency in our normal population[11].



Comparative plot between vitamin D3 levels in celiac and healthy patients

In clinical practice the estimation of high sensitive CRP is used as a sensitive marker for inflammatory response. Although, inflammation of the intestinal mucosa is an inherent finding in untreated CD the levels of CRP are not increased significantly as expected.

CONCLUSION:

Deficiencies of vitamins and minerals are frequently observed in untreated CD patients irrespective of age and gender. Almost 100% of newly diagnosed CD patients had one or more nutritional deficiency. This indicates that apart from the serological markers an integral part of the clinical work up of CD patients should include serum nutritional parameters like serum iron, vitamin B12 and vitamin D3.

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CONFLICT OF INTEREST: Authors declared no conflict of interest