Comparison Between Celiac Patients and Healthy Control Group Regarding Vitamin-Mineral Levels and Complete Blood Count Parameters

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ABSTRACT

Objective: *We aimed to compare the mean platelet volume (MPV) and plateletcrit (PCT) and vitamin-mineral levels in pediatric celiac disease patients with the healthy control group and to compare the results with the literature.*
Methods: *In this study, clinical and laboratory data of 80 pediatric patients diagnosed with celiac disease (CD) between July 2017 and December 2018 and 42 healthy children in the same age group were retrospectively analyzed.*
Results: *There was no significant difference between the groups in terms of age and gender (p=0.383, and p=0.462, respectively). The frequency of anemia, folate, iron and vitamin D deficiencies was higher in celiac patients compared to the control group (p=0.001, p=0.027, p<0.001, and p<0.001, respectively). When the patients were evaluated according to their complete blood count and vitamin-mineral levels; hemoglobin (Hb), mean corpuscular volume (MCV), ferritin and vitamin D levels were found to be significantly lower in the CD group compared to the control group (p<0.001, p=0.026, p<0.00, and p=0.001, respectively). Platelet (PLT), PCT, MPV levels were found to be significantly higher in the CD group compared to the control group (p=0.010, p<0.001, and p<0.001, respectively). We found a weakly negative correlation between the vitamin D levels and the degree of the Marsh classification (r: -0.273, and p=0.023).*
Conclusion: *Our study have shown that MPV, PCT values are higher and Hb, folate, iron and vitamin D levels are lower in patients with CD compared to healthy controls. We recommend investigating other nutrient deficiencies besides iron deficiency, especially in treatment-resistant anemias. We think that the correlation between vitamin D levels and the degree of histological damage should be elucidated with larger-scale and more comprehensive studies.*

INTRODUCTION

Celiac disease (CD) is an autoimmune disease that develops against gluten found in foods such as barley, wheat and rye in genetically susceptible individuals. The main underlying pathology of this disease is inflammation in the small intestine. Mean platelet volume (MPV) was investigated as an inflammatory marker in diseases such as inflammatory bowel disease and acute pancreatitis.[1,2] Some studies have stated that there is a negative correlation between MPV and inflammatory activity, while others have suggested a positive relationship between increased MPV and disease severity.[3] Purnak et al.[3] emphasized that high MPV values in CD patients may be an indicator of intestinal inflammation, and also, it can be a useful marker to follow diet compliance of patients at a lower cost. It has been shown that the major inflammatory cytokine that is increased in celiac patients is IL-6.[4] It is thought that IL-6 may stimulate megakaryocyte ploidy, leading to more reactive, increased platelet

production and increase in MPV values.[5] There is currently no study showing the change in the plateletcrit (PCT) value in the case of this reagent triggered by IL-6 and increased platelet production in celiac patients. For this reason, we aimed to compare MPV and PCT and vitamin-mineral levels in the pediatric CD patients at the time of diagnosis with a healthy control group and to compare our results with the literature.

MATERIAL and METHOD

In this study, clinical and laboratory data of 80 pediatric patients diagnosed with CD and 42 healthy children of the same age group between July 2017 and December 2018 were retrospectively analyzed.

The study was conducted in accordance with the Principles of Declaration of Helsinki. Before starting the study, approval was obtained from the ethics committee of an education and research hospital and a tertiary university-affiliated hospital (date: 10.24.2018; session: 2018/19; protocol No: 418.

The diagnosis of celiac disease was made in line with the recommendations contained in the guideline of European Association of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) published in 2012.[6]

Exclusion criteria

Patients with hypertension, hypercholesterolemia, hypertriglyceridemia, obesity, acute coronary syndrome, heart failure, cancer, hematological diseases, diabetes, liver failure, renal failure, acute or chronic infection were not included in the study.

Evaluation of nutritional status

In children less than 2 years of age, height was measured with the aid of an infantometer with the children placed in a supine position on a flat surface. Their head and knees were fixed by a second person. Children older than two years of age were measured with socks and shoes removed and using a vertical portable stadiometer calibrated to the nearest millimeter. Participants' weights were measured with a digital electronic scale calibrated to the nearest decimal fraction of one kilogram. Weight Z score, height Z score, body mass index (BMI) Z score for age and gender were calculated using World Health Organization (WHO) data. Patients with any of the parameters of body weight, height and BMI Z score below -2 were considered undernourished.

Evaluation of laboratory data

Iron deficiency: ferritin <30 ng/mL[7]
Folate deficiency: folate <4 ng/mL[8]
Vitamin B12 deficiency: vitamin B12: <200 pg/mL[9]
Vitamin D deficiency: vitamin D: <20 ng/mL[10]
Anemia: A lower than normal level of hemoglobin for age and gender.

Statistical analyses

Statistical Package for the Social Sciences for Windows (SPSS Inc., Chicago) 22 software package was used for statistical analysis. Study variables were presented as number (n) - percentage (%), mean ± standard deviation. The normal distribution of variables was tested using the Kolmogrov- Smirnov test. Normally distributed parameters were evaluated by one-way analysis of variance (ANOVA) or Student's t test; Kruskal- Wallis or Mann- Whitney U test was used for numerical variables that did not show normal distribution. Student's t test, Mann-Whitney U test or chi-square test were used to evaluate statistical significance.

Correlation analysis was performed to determine whether there was a linear relationship between the two numerical measurements and to show the direction and severity of this relationship. For data with normal and non-normal distribution, use of Pearson correlation coefficient, and Spearman Rank correlation coefficient was preferred, respectively. A p value of less than 0.05 was considered statistically significant.

RESULTS

The mean age of the patients was 8.68±5.16 years in the control group and 9.51±4.76 years in the CD group. There was no statistically significant difference between the groups in terms of age and gender (p=0.383, and p=0.462, respectively) (Table 1).

When the patients were evaluated according to their anthropometric measurements, weight, height and BMI z scores in CD were found to be significantly

lower than the control group (p <0.001). Malnutrition was not observed in the control group, while it was detected in 29 patients (36.3%) in the CD group. This intergroup difference was statistically significant (p<0.001) (Table 1).

We detected anemia in 2 patients (4.8%) in the control and 24 patients (30%) in the CD group. Vitamin B12 deficiency was seen in 8 patients (12.7%) in the CD group and 1 patient (2.4%) in the control group. While folate deficiency was seen in 7 patients (11.1%) in the CD group, there was no folate deficiency in the control group. Iron deficiency was seen in 53 patients (66.3%) in the CD and in 20 patients (47.6%) in the control group. Vitamin D deficiency was seen in 41 patients (59.4%) in the CD and in 9 patients (21.4%) in the control group. The frequency of anemia, folate, iron and vitamin D deficiency was higher in the CD group compared to the control group (p=0.001, p=0.027, p<0.001, and p <0.001, respectively). Although frequency of vitamin B12 deficiency was higher in the CD group, this increase was not statistically significant (p=0.064) (Table 1).

When the patients were evaluated according to their complete blood counts and vitamin-mineral levels; hemoglobin (Hb), mean corpuscular volume (MCV), ferritin and vitamin D levels were found to be significantly lower in the CD group compared to the control group (p<0.001, p=0.026, p<0.00, and p=0.001, respectively). Platelet (PLT), plateletcrit (PCT), and mean platelet volume (MPV) levels were significantly higher in the CD group compared to the control group (p=0.010, p<0.001, and p<0.001, respectively). There was no significant difference between the two groups in terms of white blood cell (WBC) counts, mean corpuscular hemoglobin (MCH), Mentzer Index, vitamin B12 and folate levels (p=0.399, p=0.705, p=0.647, respectively, p=0.833, and p=0.131) (Table 2).

When the correlation between the degree of pathological Marsh classification and hematological parameters and vitamin-mineral levels in celiac patients was evaluated, there was no significant correlation between Hb, MPV, PCT, vitamin B12 and folate levels and the degree of Marsh classification. However, we found a weakly negative correlation between vitamin D level and the degree of the Marsh classification (r: -0.273, p=0.023).

DISCUSSION

This study is one of the rare studies evaluating

Table 1. Comparison of the groups based on anthropometric measurements, demographic characteristics and vitamin-mineral deficiencies

	Control (n=42) Mean±SD	CD (n=80) Mean±SD	p*
Age	8.68±5.16	9.51±4.76	0.383
Weight Z score	0.13±0.84	-1.09±1.57	<0.001
Height Z score	0.23±1.08	-0.83±1.51	<0.001
BMI Z skor	-0.05±0.86	-0.89±1.23	<0.001
	n (%)	**n (%)**	**p****
Gender			
Female	25 (59.5%)	53 (66.3%)	0.462
Male	17 (40.5%)	27 (33.8%)	
Malnutrition	0 (0%)	29 (36.3%)	<0.001
Anemia	2 (4.8%)	24 (30%)	0.001
Vitamin B12 deficiency	1 (2.4%)	8 (12.7%)	0.064
Folate deficiency	0 (0%)	7 (11.1%)	0.027
İron deficiency	20 (47.6%)	54 (80.6%)	<0.001
Vitamin D deficiency	9 (21.4%)	41 (59.4%)	<0.001

*Statistics: *Independent Student T test, **Crosstabs-chi-square*
BMI: body mass index; CD: celiac disease; SD: standard deviation

Tablo 2. Comparison of complete blood count parameters according to groups, mean±SD

	Control (n=42) Mean±SD	CD (n=80) Mean±SD	p*
WBC (x10^3 cells/uL)	7.93±2.18	8.44±3.51	0.399
Hb (g/dL)	13.26±1.67	11.74±1.65	<0.001
PLT (x10^3 cells/uL)	303.59±93.84	361.56±125.81	0.010
PCT (%)	0.28±0.08	0.35±0.08	<0.001
MPV (fL)	9.72±0.69	10.30±0.89	<0.001
MCH (pg)	25.15±4.61	24.52±3.05	0.705
MCV (fL)	77.90±5.07	75.25±7.75	0.026
Mentzer Index	15.95±1.82	15.77±1.97	0.647
B12 (pg/mL)	362.14±185.87	371.06±228.27	0.833
Folate (ng/mL)	9.80±4.09	8.43±4.68	0.131
Ferritin (ng/mL)	34.49±20.89	17.89±24.34	<0.001
Vitamin D (ng/mL)	25.22±9.16	18.73±10.08	0.001

*Statistics: *Independent Student T test*
SD: standard deviation; CD: celiac disease; WBC: white blood cell; Hb: hemoglobin; PLT: platelet; PCT: plateletcrit; MPV: mean platelet volume; MCH: mean corpuscular volume

hematological parameters and vitamin-mineral levels in detail between CD and healthy children. Wierdsma et al.[11] reported folate deficiency in 20%, vitamin B12 deficiency in 19%, and ferritin deficiency in 46% of their CD patients. Other studies have found folate deficiency approximately in 11-12%, vitamin B12 deficiency in 8-41%, iron deficiency in 8-93% of their CD patients.[12-14] In our study, we found that the rates of folate, B12 and iron deficiencies were compatible with the literature data.

The prevalence of iron deficiency anemia (IDA) in CD is quite variable in different geographical regions and different age groups. It is lower in developed countries (5-40%) than in developing countries (>80%).[15,16] The prevalence rates of anemia in CD have been reported as (93.2%) in an Indian study, 21.6% in a European study, 8-40% in the American cohorts, and 50% in the Middle East and North Africa population.[12,17-20]

In our study, we found the prevalence of anemia similar to the rates of developed countries. This rate (30%) was significantly higher than the control group patients. The main mechanism of IDA in celiac disease is malabsorption. Iron deficiency is not the only factor that causes anemia in CD. Vitamin B12 and folic acid deficiencies can also cause megaloblastic anemia, which can increase the severity of anemia. In the study of Berry et al.[12], it was emphasized that mixed nutrient deficiencies (vitamin B12, folate, iron, vitamin B6, zinc, and vitamin A) can increase the frequency of anemia. In our study, zinc, vitamin A, and vitamin B6 were not measured in any patient. However, indicated number of patients had iron (n=2: 2.5%), folate and vitamin B12 deficiency (n=6: 7.5%), folate and iron deficiency (n=6: 7.5%), vitamin B12 and iron deficiency (n=7: 8.75%). For this reason, we recommend investigating other nutrient deficiencies in the presence of anemia that does not improve despite iron supplementation, as mentioned in the literature.

Recent studies have emphasized that as the severity of villous atrophy and anti-tissue transglutaminase (DTG) levels increase, the frequency of anemia and resistance to treatment are higher.[12,21,22] In our study, we did not find a significant correlation between the degree of villous atrophy and DTG levels and ferritin, vitamin B12 and folate levels. However, unlike the literature, we found a weakly negative correlation between vitamin D levels and the degree of villous atrophy (r: -0.273, p=0.023). We did not have any information about the diet and its nutrient content of these patients before the diagnosis of CD. Therefore, the data we found different from the literature may be due to differences in dietary intake and duration of exposure to sunlight.

As far as we know, a weakly significant negative correlation between the vitamin D level we found in our study and the severity of villous atrophy has not been emphasized in any previous study. Tanpowpong and Camargo[23] (suggested that vitamin D deficiency

at an early age may play an important role in childhood-onset (<15 years) celiac disease. Vitamin D deficiency may cause an irregular intestinal immune response in genetically susceptible individuals with increased disruption of the intestinal epithelial barrier as a result of the immune response to gluten and microorganisms. This impaired immune response can result in increased susceptibility to acute gastrointestinal infection. It has been emphasized that these mechanisms may pave the way for the development of celiac disease that begins in childhood.[24] Vitamin D is known to play an important role in bone health and regulation of the immune system. Low levels of bone mineral density (BMD) have been reported in children with CD.[24] Additionally, ACG, BSG and NASPGHAN, Italian Pediatric Societies also recommend evaluation of vitamin D status in CD.[25-28] Vitamin D supplementation during an intake of a gluten-free diet has been shown to prevent further bone loss, improve symptoms associated with osteomalacia, and normalize calcium levels.[29] In their study Ahlawat et al.[30] emphasized that vitamin D levels were higher in CD patients compared to the control group, but it was observed that the vitamin D ratios that CD patients took from milk, milk products and multivitamin preparations were similarly high. They associated this condiiton with the excess of estimated vitamin D intake rates. In our study, as in many other studies,[31-34] we found that vitamin D levels were significantly lower in patients with CD compared with the control group (p=0.001) (Table 2).

Another important finding of our study is that we detected higher MPV and PCT values in the CD group compared to the control group. Although the relationship between MPV and CD has been emphasized in several studies in the literature, ours is the only study that evaluates the PCT and MPV values in combination in CD and compares them with the control group. In the literature, MPV levels have been the subject of research in diseases such as myocardial infarction, stroke, diabetes, ulcerative colitis, chronic hepatitis B and acute pancreatitis. It has been emphasized that there may be a relationship between disease severity and MPV. In the first study about the relationship between CD and MPV, higher MPV values were reported in patients with CD.[35] In another study, it was reported that MPV increased in newly diagnosed CD patients compared to healthy controls, and these mean MPV values became normal over time in patients who followed the diet. Even MPV has been suggested to be used as a biomarker in the assessment of dietary compliance.[3] Although we could investigate the relationship between MPV,PCT and dietary compliance in CD in our study, high levels of PCT and MPV in CD patients seem to be compatible with other studies. Golwala et al.[36] stated that MPV and PCT levels could be predictors of mortality and accurately predicted 65% - 67% of related deaths. In another study, it was reported that PCT values were significantly higher in severe preeclampsia cases compared to mild preeclampsia cases. Ours is the only study comparing the relationship between CD and PCT relative to healthy controls. We found that PCT and PLT values were significantly higher in CD patients compared to the healthy control group. However, there was no significant correlation between PLT and PCT levels and serological findings and severity of histological damage in CD. Prospective randomized controlled large series are needed for a more reliable and detailed analysis of this relationship.

One limitation of our study is that our study was a retrospective study, so the retrospective nutritional history of the patients and the rate of exposure to sunlight were not known. Besides, the data were not re-evaluated after intake of a gluten-free diet, and the data concerning the presence of diseases such as megaloblastic anemia and chronic disease anemia that may accompany iron deficiency were not available. In addition, the fact that ours is a rare study comparing MPV, PCT values detected in CD patients and healthy controls and it is the only study showing a negative correlation between vitamin D levels and the degree of Marsh classification makes this article valuable.

In conclusion, our study shows that MPV, PCT values are higher and Hb, folate, iron and vitamin D levels are lower in CD patients compared to healthy children. In addition, we think that mixed vitamin-mineral deficiencies may coexist in CD patients, therefore, other nutrient deficiencies should be investigated in addition to iron deficiency in treatment-resistant anemias. We have found a negative correlation between vitamin D levels and

the degree of histological damage which requires conduction of more comprehensive studies.

Ethics Committee Approval: Approval was obtained from Kahramanmaras Sutcu Imam University Faculty of Medicine Clinical Research Ethics Committee (24.10.2018/10).

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REFERENCES

1. Yuksel O, Helvaci K, Basar O, et al. An overlooked indicator of disease activity in ulcerative colitis: mean platelet volume. Platelets. 2009;20:277-81 https://doi.org/10.1080/09537100902856781
2. Mimidis K, Papadopoulos V, Kotsianidis J, et al. Alterations of platelet function, number and indexes during acute pancreatitis. Pancreatology. 2004;4:22-7. https://doi.org/10.1159/000077024
3. Purnak T, Beyazit Y, Efe C, Ozaslan E, Yuksel O, Altiparmak E. Authors' reply: 'Mean platelet volume could be a promising biomarker to monitor dietary compliance in celiac disease'. Ups J Med Sci. 2013 Aug;118(3):208. https://doi.org/10.3109/03009734.2013.806617
4. Kapoor A, Patwari AK, Kumar P, Jain A, Narayan S. Serum soluble interleukin-2 receptor, interleukin-6 and tumor necrosis factor alpha as markers of celiac disease activity. Indian J Pediatr. 2013;80:108-13. https://doi.org/10.1007/s12098-012-0830-9
5. Debili N, Masse JM, Katz A, Guichard J, Breton-Gorius J, Vainchenker W. Effects of the recombinant hematopoietic growth factors interleukin-3, interleukin-6, stem cell factor, and leukemia inhibitory factor on the megakaryocytic differentiation of CD34s cells. Blood. 1993;82:84-95. https://doi.org/10.1182/blood.V82.1.84.bloodjournal82184
6. Husby S, Koletzko S, Korponay-Szabó IR, et al. ESPGHAN Working Group on Coeliac Disease Diagnosis; ESPGHAN Gastroenterology Committee. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. J Pediatr Gastroenterol Nutr. 2012;54:136-60. https://doi.org/10.1097/MPG.0b013e31821a23d0
7. Theurl I. Dysregulated monocyte iron homeostasis and erythropoietin formation in patients with anemia of chronic disease. Blood. 2006;107:4142-8. https://doi.org/10.1182/blood-2005-08-3364
8. Kang SS, Wong PW, Norusis M. Homocysteinemia due to folate deficiency. Metabolism. 1987;36:458-62. https://doi.org/10.1016/0026-0495(87)90043-6
9. Stabler SP, Allen RH, Savage DG, Lindenbaum J. Clinical spectrum and diagnosis of cobalamin deficiency. Blood. 1990;76:871-81. https://doi.org/10.1182/blood.V76.5.871.bloodjournal765871
10. Yao Y, Fu S, Zhang H, et al. The prevalence of depressive symptoms in Chinese longevous persons and its correlation with vitamin D status. BMC Geriatr. 2018;18(1):198. https://doi.org/10.1186/s12877-018-0886-0
11. Wierdsma N, van Bokhorst-de van der Schueren MA, Berkenpas M, Mulder CJ, van Bodegraven A. Vitamin and mineral deficiencies are highly prevalent in newly diagnosed celiac disease patients. Nutrients. 2013;5:3975-92. https://doi.org/10.3390/nu5103975
12. Berry N, Basha J, Varma N, et al. Anemia in celiac disease is multifactorial in etiology: A prospective study from India. JGH Open. 2018 Aug 2;2(5):196-200. https://doi.org/10.1002/jgh3.12073
13. Dahele A, Ghosh S. Vitamin B12 deficiency in untreated celiac disease. Am. J. Gastroenterol. 2001;96:745-50. https://doi.org/10.1111/j.1572-0241.2001.03616.x
14. Dickey W. Low serum vitamin B12 is common in coeliac disease and is not due to autoimmune gastritis. Eur. J. Gastroenterol. Hepatol. 2002;14:425-7. https://doi.org/10.1097/00042737-200204000-00016
15. Kochhar R, Jain K, Thapa BR, et al. Clinical presentation of celiac disease among pediatric compared to adolescent and adult patients. Indian J. Gastroenterol. 2012;31:116-20. https://doi.org/10.1007/s12664-012-0198-9
16. Harper JW, Holleran SF, Ramakrishnan R, Bhagat G, Green PH. Anemia in celiac disease is multifactorial in etiology. Am. J. Hematol. 2007;82:996-1000. https://doi.org/10.1002/ajh.20996
17. Sanseviero MT, Mazza GA, Pullano MN, et al. Iron deficiency anemia in newly diagnosed celiac disease in children. Minerva Pediatr. 2016;68:1-4.
18. Lo W, Sano K, Lebwohl B, Diamond B, Green PH. Changing presentation of adult celiac disease. Dig. Dis. Sci. 2003;48:395-8. https://doi.org/10.1023/A:1021956200382
19. Masjedizadeh R, Hajiani E, Hashemi J, Shayesteh AA, Moula K, Rajabi T. Celiac disease in South-West of Iran. World J. Gastroenterol. 2006;12:4416-9. https://doi.org/10.3748/wjg.v12.i27.4416
20. Demir H, Yuce A, Kocak N, Ozen H, Gurakan F. Celiac disease in Turkish children: presentation of 104 cases. Pediatr. Int. 2000;42:483-7. https://doi.org/10.1046/j.1442-200x.2000.01286.x
21. Abu Daya H, Lebwohl B, Lewis SK, Green PH. Celiac disease patients presenting with anemia have more severe disease than those presenting with diarrhea. Clin. Gastroenterol. Hepatol. 2013;11:1472-7. https://doi.org/10.1016/j.cgh.2013.05.030
22. Singh P, Arora S, Makharia GK. Presence of anemia in patients with celiac disease suggests more severe disease. Indian J. Gastroenterol. 2014;33:161-4. https://doi.org/10.1007/s12664-013-0423-1
23. Tanpowpong P, Camargo CA. Early-life vitamin D deficiency and childhoodonset coeliac disease. Public Health Nutr 2014;17:823-6.

https://doi.org/10.1017/S1368980013003510
24. Ahlawat R, Weinstein T, Pettei MJ. Vitamin D in pediatric gastrointestinal disease. Curr Opin Pediatr. 2017 Feb;29(1):122-7. https://doi.org/10.1097/MOP.0000000000000451
25. Hill I, Fasano A, Guandalini S, et al. NASPGHAN clinical report on the diagnosis and treatment of gluten-related disorders. J Pediatr Gastroenterol Nutr. 2016;66:156-65. https://doi.org/10.1097/MPG.0000000000001216
26. Rubio-Tapia A, Hill ID, Kelly CP, et al. American College of Gastroenterology clinical guideline: diagnosis and management of celiac disease. Am J Gastroenterol. 2013;108:656-77. https://doi.org/10.1038/ajg.2013.79
27. Ludvigsson JF, Bai JC, Biagi F, et al. BSG Coeliac Disease Guidelines Development Group; British Society of Gastroenterology. Diagnosis and management of adult coeliac disease guidelines from the British Society of Gastroenterology. Gut 2014;63:1210-8. https://doi.org/10.1136/gutjnl-2013-306578
28. Saggese G, Vierucci F, Prodam F, et al. Vitamin D in pediatric age: consensus of the Italian Pediatric Society and the Italian Society of Preventive and Social Pediatrics, jointly with the Italian Federation of Pediatricians. Ital J Pediatr. 2018;44:51. https://doi.org/10.1186/s13052-018-0488-7
29. Di Nardo G, Villa MP, Conti L, et al. Nutritional Deficiencies in children with celiac disease resulting from a gluten-free diet: A systematic review. Nutrients. 2019 Jul 13;11(7):1588. https://doi.org/10.3390/nu11071588
30. Ahlawat R, Weinstein T, Markowitz J, Kohn N, Pettei MJ. Should we assess vitamin D status in pediatric patients with celiac disease? J Pediatr Gastroenterol Nutr. 2019 Oct;69(4):449-54. https://doi.org/10.1097/MPG.0000000000002417
31. Wierdsma NJ, van Bokhorst-de van der Schueren MA, Berkenpas M, et al. Vitamin and mineral deficiencies are highly prevalent in newly diagnosed celiac disease patients. Nutrients 2013;5:3975-92. https://doi.org/10.3390/nu5103975
32. Caruso R, Pallone F, Stasi E, et al. Appropriate nutrient supplementation in celiac disease. Ann Med. 2013;45:522-31. https://doi.org/10.3109/07853890.2013.849383
33. Erdem T, Ferat C¸ Nurdan YA, et al. Vitamin and mineral deficiency in children newly diagnosed with celiac disease. Turk J Med Sci. 2015;45:833-6. https://doi.org/10.3906/sag-1408-94
34. Haapalahti M, Kulmala P, Karttunen TJ, et al. Nutritional status in adolescents and young adults with screen-detected celiac disease. J Pediatr Gastroenterol Nutr. 2005;40:566-70. https://doi.org/10.1097/01.MPG.0000154658.16618.F9
35. O'Grady JG, Harding B, Stevens FM, Egan EL, McCarthy CF. Influence of splenectomy and the functional hyposplenism of coeliac disease on platelet count and volume. Scand J Haematol. 1985;34:425-8. https://doi.org/10.1111/j.1600-0609.1985.tb00772.x
36. Golwala ZM, Shah H, Gupta N, Sreenivas V, Puliyel JM. Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Platelet Count and Plateletcrit (PCT) as predictors of in-hospital paediatric mortality: a case-control Study. Afr Health Sci. 2016 Jun;16(2):356-62. https://doi.org/10.4314/ahs.v16i2.3