Original Research Article

Assessment of Cardiac Functions in Children Suffering from Celiac Disease

Abstract

Background: Celiac disease (CD) is an autoimmune disorder that occurs in genetically predisposed individuals. Among the complications of celiac disease, idiopathic dilated cardiomyopathy and autoimmune myocarditis are popular causes of considerable mortality and morbidity. The objective of this study is to evaluate the heart functioning in CD children.

Methods: This cross-sectional study was conducted out on 40 children (twenty Patients diagnosed as having celiac disease and Twenty healthy, age and sex matched children send as control group). All participants underwent basic laboratory investigations. Every child had an echocardiogram, which comprised both traditional echocardiography and tissue Doppler imaging.

Results: The conventional echocardiographic assessment parameters (LVEED, LVESD, septal thickness, EF% FS%, E/A and TAPSE) were insignificantly different between both groups. There was no statistically substantial variation in mitral anulus velocity (S) and E/A among both groups. According to mean value of myocardial performance index (MPI) it was statistically significant greater in celiac disease of the affected group contrasted to the control group (P value 0.002).

Conclusions: The tissue doppler echocardiogram can identify subclinical early stage of cardiac involvement in CD patients.

Keywords: Celiac Disease, Cardiac Function, Tissue Doppler Echocardiography.

Introduction:

Celiac disease is an immune-triggered systemic disease initiated by gluten and its associated prolamins in people who are genetically predisposed to it. It is characterized by the existence of multiple forms of damage to the small intestine, celiac-specific immunoglobulins human leukocyte antigens HLA-DQ8 or HLA-DQ2, and gluten-dependent manifestations in the body [(1)]. It has been defined by an inflaming, villous atrophy, and hyperplasia of crypts in the gut due to an immunological reaction towards ingesting gluten from wheat and similar proteins of rye and barley [(2)]. In addition to asymptomatic variants, CD can present clinically with malabsorption, diarrhea, loss of weight, and deficiencies in nutrition [(3)]. Anemia, short stature, osteopenia, or neurological conditions are among the extra-intestinal symptoms of CD that are frequently present [(4)]. A growing concern is cardiac problems linked to CD [(5)]. Among other complications of celiac disease, idiopathic dilated cardiomyopathy and autoimmune myocarditis are recognized to cause substantial mortality and morbidity [(6)].

Several hypotheses have been put out to explain how cardiomyopathy develops in celiac disease. According to one notion, dietary deficiencies caused by intestinal malabsorption may be the cause of cardiomyopathy [(7)].

A different hypothesis contends that abnormalities in intestinal absorption result in a greater absorption of antigenic and infectious substances, which in turn activates the immune system and eventually damages the myocardium and small intestine directly through the immune response [(8)]. After celiac disease is correctly treated, it is debatable whether a diet without gluten can stop the advancement of cardiac affection [(9)].

It is commonly acknowledged that Tissue Doppler Echocardiography (TDE) is helpful in identifying subclinical ventricular malfunctions [(10)]. There is little information in the literature about TDE studies examining the impact of a diet without gluten on the subclinical heart

dysfunction that accompanies CD in children [11]. Therefore, the purpose of this research is to evaluate the heart functioning in kids with CD utilizing several echocardiography modalities

Patients and Methods:

From December 2021 to December 2022, forty kids at Tanta University Hospital's Paediatric Department participated in this cross-sectional study. They were divided into two categories as follows: Twenty children who have been identified to be suffering from celiac disease according to the standards of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) [(12)] are in Group 1 (the case group), and 20 well, age- and sex-matched kids participate in Group 2 (the control group).

All patient caregivers provided written authorization after being fully briefed. Tanta University's Faculty of Medicine Ethics Committee gave its approval to the project. No. of registration (34358).

Exclusion criteria were children with pre-existing cardiac conditions or those taking any substances that might impact heart function, Children have long-term illnesses that impact heart function, such as systemic lupus erythematosus (SLE), chronic renal disease, and diabetes mellitus (DM).

The following protocols were applied to all patients:

I. **Complete taking of history with a focus on:**

Demographic data (Sex, age and residence), Past history especially age of diagnosis as having celiac disease.

II. Comprehensive physical examination focusing in particular on:

A) Anthropometric Measurements of the studied groups such as: Weight: Measured using Granzia digital weighing scale (PSTG-80, Italy). **Height:** Assessed using (seca 216, Germany) anthropometer. **Body Mass Index (BMI)**: With divided the weight in kilogrammes by the height square in metres, the BMI was computed, calculated as (kg)/ (m^2).

All measurements were displayed on the corresponding growth charts of The National Center for Health Statistics to assess z-scores to determine degree of nutritional status [13].

B) Nutrition-focused physical examination: Assessment of any finding of specific micronutrients deficiency with evaluation of skin, hair and nails.

III. The following studies were carried out on all of the involved kids.:

A) Basic routine lab investigations.

B) Echocardiography

Different echocardiographic modalities were used to produce an echocardiogram (Vivid 9; GE Healthcare, Horten, Norway) employing 3.5 MHz, S7 and V3 matrix real-time 3-D probes to evaluate heart function. For offline evaluation, digital loops were copied from the echocardiography device's hard drive to a workstation (Echo PAC PC, 113; GE Healthcare). Various methods were used to examine the patients, including traditional transthoracic echocardiogram (TTE) and tissue doppler imaging (TDI) echocardiography.

Conventional echocardiography parameters were as follow: the measurements of the left ventricle's end diastolic and end systolic diameters (LVEDD) and (LVESD), Septal thickness, fractional shortening (FS%), ejection fraction (EF%), early to late diastolic trans-mitral flow velocity (E/A), and tricuspid annular plane systolic excursion (TAPSE) are all important parameters to consider.

Statistical analysis

SPSS v26 (IBM Inc., Armonk, NY, USA) was used for the statistical evaluation. The unpaired Student's t-test was used to compare quantitative data across both groups. The quantitative parameters were provided as mean and standard deviation (SD). When applicable, the qualitative parameters were examined using the Fisher's exact

test or Chi-square test and provided as frequency and percentage (%). Statistical significance was defined as a two-tailed P value < 0.05.

Results:

Table 1: Demographic information of the Groups under the Study, Distribution According to Dietetic History and Presenting Symptoms of Celiac Patients

Demographic Data		Patient group (n = 20)	Control group (n = 20)	P value
Age (years)	**Mean ± SD**	8.65 ± 3.65	9.24 ± 2.39	0.548
Sex	**Male**	7 (35%)	11 (55%)	0.480
	Female	13(65%)	9 (45%)	
Residence	**Rural**	16 (80%)	13 (65%)	0.480
	Urban	4 (20%)	7 (35%)	
Duration of illness (months)	**Mean ± SD**	14.40 ± 10.73	--	---
Dietetic History of Patient group (n = 20)				
Newly diagnosed		57.5%		
Non strict GFD		31.4%		
Strict GFD		11.1%		
Presenting symptoms of Patient group (n = 20)				
Abnormal bowel habit		**Diarrhea**	5 (25%)	
		Constipation	4 (20%)	
Abdominal distention		7 (35%)		
Short stature		13 (65%)		
Poor weight gain		16 (80%)		
Refractory iron deficiency anemia		14 (70 %)		
Sign of vitamin and mineral deficiency		**Pallor**	8 (57.1%)	
		Hair loss	3 (21.4%)	
		Nail white spots	2 (14.3%)	
		Angular stomatitis	(7.1%) **1**	

SD: standard deviation showed that demographic data (age, sex and residency) were insignificantly different between both groups. Also showed the 57.5 % were newly diagnosed, 31.4 % were on non-strict GFD and 11.1% were on strict GFD. The Present history and examination of patient group illustrated in Table 1 showed that there were 9 (45%) patients had abnormal bowel habit, as 5 (25%) patients had diarrhea and 4 (20%) had constipation. There were 7 (35%) patients had abdominal distension, 13 (65%) patients had short stature, 16 (80%) patients had poor weight gain and 14 (70 %) patients had refractory iron deficiency anemia. Also there were 14 patients had signs of vitamin and mineral deficiency, as 8 (57.1%) patients had pallor, 3 (21.4%) patients had hair loss, 2 (14.3%) patients had nail white spots and 1 (7.1%) had angular stomatitis.

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SD: standard deviation, GFD: Gluten free diet.

Error! Reference source not found. **showed:** Anthropometric measurement of the studied group including weight (Kg), weight Z-score, height (cm), height Z-score and BMI Z-score. They were substantially decreased in Celiac disease affected group compared to the control group (P value <0.05).

Also the laboratory investigations of the studied groups illustrated in Table 2 as the serum Hb, serum ferritin and serum 25 OH vitamin D were substantially decreased in the celiac disease affected group contrasted to the control group (P value < 0.001, <0.001 and 0.003 correspondingly). The platelets, TLC with differential leukocyte count (neutrophils % and lymphocytes %), CRP, renal functions (blood urea, serum creatinine), lipid profile (serum cholesterol, triglycerides) and calcium panel (serum phosphorus, serum ionized calcium, serum alkaline phosphatase) were insubstantially various between both groups. The liver function tests (AST, ALT) and serum albumin in the celiac disease affected group were insubstantially vary between both groups.

Table 2: Anthropometric Measurements and Laboratory Investigations of the Studied Groups

	Patient group (n = 20) **Mean ± SD**	Control group (n = 20) **Mean ± SD**	P value
Anthropometric Measurements			

Weight Z-score		-1.56 ± 1.2	0.23 ± 0.66	**<0.001***
Height Z-score		-2.08 ± 1.23	-0.04 ± 0.61	**<0.001***
BMI (Kg/m^2)		15.84 ± 3.57	17.55 ± 1.86	0.065
BMI Z-score		-0.68 ± 2.01	0.38 ± 0.77	**0.033***
Laboratory Investigations				
CBC	Hb (g/dl)	8.6 ± 0.52	11.42 ± 0.43	**< 0.001***
	Platelets ($*10^3$cells/μL)	239.95 ± 59.16	241.85 ± 57.03	0.918
	TLC ($*10^3$cells/μL)	6.79 ± 1.99	6.78 ± 2.11	0.988
	Neutrophils (%)	56.95 ± 7.34	55.3 ± 3.64	0.374
	Lymphocytes (%)	28.05 ± 6.29	27.45 ± 4.72	0.735
Serum ferritin (ng/mL)		14.8 ± 5.99	98.6 ± 27.7	**<0.001***
CRP		4.89 ± 1.65	4.88 ± 1.8	0.996
Renal function tests	Blood urea (mg/dL)	26.25 ± 5.65	25 ± 6.66	0.526
	Serum creatinine (mg/dL)	0.53 ± 0.08	0.56 ± 0.08	0.364
Lipid profile	Serum cholesterol (mg/dl)	162.95 ± 14.12	160.28 ± 17.5	0.598
	Serum triglycerides (mg/dl)	99.6 ± 14.81	99.75 ± 17.21	0.977
Liver function tests	AST(u/l)	30.25 ± 5.87	32.3 ± 4.23	0.213
	ALT(u/l)	30.26 ± 4.19	31.95 ± 7.2	0.380
	Serum bilirubin (mg/dL)	0.56 ± 0.27	0.66 ± 0.2	0.229
	Serum albumin (g/dL)	4.11 ± 0.21	4.15 ± 0.31	0.647
Calcium panel	Serum ionized calcium (mg/dl)	1.13 ± 0.06	1.16 ± 0.05	0.101
	Serum Phosphorus (mg/dl)	4.02 ± 0.53	4.21 ± 0.27	0.154
	Serum Alkaline phosphatase (IU/L)	138.79 ± 51.49	151 ± 21.96	0.335
	Serum Vit D (ng/ml)	22.98 ± 5.97	28.26 ± 3.22	**0.001***

Hb: hemoglobin. TLC: total leukocyte count. AST: aspartate aminotransferase. ALT: alanine transaminase. SD: standard deviation, CRP: C-reactive protein, *: Significantly different as P value ≤ 0.05. BMI: Body mass index.

Error! Not a valid bookmark self-reference. showed that the conventional echocardiographic assessment parameters including; LVEED, LVESD, Septal thickness, EF% FS%, E/A and TAPSE which were insubstantially various among the two groups.

Table 3: Conventional Echocardiography of the Studied Groups

Mean ± SD	**Patient group (n = 20)** Mean ± SD	**Control group (n = 20)** Mean ± SD	**P value**
LVEDD (cm)	3.31 ± 0.46	5.19 ± 7.02	0.251
LVESD (cm)	2.17 ± 0.23	2.3 ± 0.22	0.099
Septal thickness (cm)	0.68 ± 0.12	0.73 ± 0.07	0.117
EF%	66 ± 2.25	67.1 ± 2.13	0.120
FS%	33.05 ± 1.64	36.35 ± 7.27	0.055
E/A	1.28 ± 0.12	1.31 ± 0.23	0.610
TAPSE (mm)	16.05 ± 1	16.35 ± 3.59	0.721

LVEDD: left ventricular end diastolic diameter, LVESD: left ventricular end-systolic diameter. PW: Left ventricular posterior wall thickness, EF: ejection fraction, FS: fractional shortening, E/A: early to late diastolic transmitral flow velocity, TAPSE: tricuspid annular plane systolic excursion *: Significantly different as P value ≤ 0.05

Table 4 showed that: no statistically substantial variation was existed in mitral anulus velocity (S) and E/A among both groups. According to mean value of myocardial performance index (MPI) it was statistically significant increased in celiac disease of the affected group when contrasted to the control group (P value 0.002).

Table 4: Tissue Doppler Imaging Parameters of the Studied Groups

		Patient group (n = 20) **Mean ± SD**	Control group (n = 20) **Mean ± SD**	P value
TDI	S	5.95 ± 1.1	6.45 ± 0.6	0.083
	E'	12.8 ± 1.47	13.55 ± 1.23	0.089

	A'	6.55 ± 0.51	6.7 ± 0.47	0.340
	E' / A'	1.96 ± 0.2	2.02 ± 0.16	0.252
	MPI	0.61 ± 0.22	0.43 ± 0.1	0.002*

TDI: tissue doppler imaging, S: peak velocity during ventricular systole, A': peak velocity during atrial contraction, E': peak velocity during early ventricular diastole, MPI: myocardial performance index, *: Significantly different as P value ≤ 0.05

Discussion

Due to cardiac consequences like ischemic heart disease, a higher probability of arrhythmia, pericarditis, myocarditis, and pericardial effusion, CD has been linked to an elevated risk of cardiovascular mortality and morbidity. [(14)].

In our study as regard to extraintestinal manifestations there were 13 (65%) patients had short stature, 16 (80%) patients had poor weight gain, and 14 (70 %) patients had refractory iron deficiency anemia. Also, there were 14 patients had signs of vitamin and mineral deficiency, 8 (57.1%) patients had pallor, 3 (21.4%) patients had hair loss, 2 (14.3%) patients had nail white spots and 1 (7.1%) had angular stomatitis. Supporting our findings, **Samuli Nurminen et Al. (2018)** [(15)] they observed that Children with CD often had extraintestinal symptoms, which were also linked to a more serious clinical and histopathological presentation.

It is well established that iron deficiency is the cause of behind loss of hair, angular stomatitis, atrophic glossitis, and koilonychia. Also, deficiency of folic acid and vitamin B12 cause glossitis, angular stomatitis, and oral mucosa ulcers [(16)].

In the present study, the height Z-score, weight Z-score, and BMI Z-score were substantially decreased in Celiac disease affected group contrasted to the control group (P value <0.05). In agreement with our findings, **Setavand et al. (2021)** [(17)] sought to establish anthropometric measurements in CD children. Their Z-scores of weight, BMI and height were substantially decreased in children with CD group contrasted to the control group (P value <0.05). Our results came in the same line with

Dehbozorgi et al. (2022) [18] Their study demonstrated that height Z-score, weight Z-score, and BMI Z-score were substantially decreased in CD children contrasted to control ($p<0.05$). They also revealed that a reduced body weight along with reduced BMI for age, respectively, affected 31 and 29% of the CD children.

In our study, Hb, serum ferritin and serum vit D were substantially decreased in the celiac disease affected group contrasted to the control group (P value < 0.001, <0.001 and 0.003 respectively). Similarly, **Güngör et al. (2020)** [19] reported that In contrast to the control group, those with celiac disease were more likely to have anaemia, iron, and vitamin D deficiency. ($p=0.001$, $p<0.001$, and $p<0.001$, respectively). In the same context, **Rasha et al. (2022)** [20] they found that Individuals with refractory iron deficiency anaemia were more likely to have CD.

Signs of vitamin and mineral deficiency mostly included pallor (57.1%) followed by hair loss, nail white spots, and angular stomatitis (21.4%, 14.3%, 7.1%, respectively). Supporting our study, **Aseera Jivraj et al. (2022)** [21] found that the most prevalent micronutrient deficits in people with and without CD who followed a gluten-free diet (GFD) were ferritin, zinc, and vitamin D. Consistent with our results, **Jawed et al. (2016)** [22] their findings showed that serum ferritin and vit D were substantially decreased in CD patients contrasted to the control group ($P<0.05$).

The most prevalent form of cardiomyopathy, DCM may be 50% idiopathic because to its wide range of possible causes, including genetics, endocrine abnormalities, illness of the collagen tissue, medications, structural heart ailments, and myocarditis. According to reports, both secondary and idiopathic cardiomyopathies are associated with an increased risk of Celiac disease. [23].

In the current study, the conventional echocardiographic assessment parameters (LVEED, LVESD, septal thickness, EF% FS%, E/A and TAPSE) were insignificantly different between both groups.

Our findings agree with those of **Alkan et al. (2021)** [24] who looked at the impact of CD on variables relating to myocardial performances and aortic flexibility. They selected 30 CD children and 30 children who were healthy for their research. Both groups have a comparable age range and gender composition. Utilising traditional TTE and tissue Doppler imaging, the cardiac parameters of all the participants in the patient and control groups were assessed. They noted no statistical difference for conventional TTE including LVEDD, LVESD, Septal thickness, EF% FS%, and E/A between both groups.

Compatible to our findings, **Fathy et al. (2016)** [25] sought to use DTI to evaluate the subclinical effects of CD on the overall cardiac function in Saudi CD children. 20 Saudi youngsters with CD and 20 age- and sex-matched normal healthy controls underwent conventional two-dimensional echocardiography. RV and LV Tei indices were calculated using DTI. The Modified Marsh Classification of the histologic findings in CD and these results were associated. They also found insignificant differences between the two studied groups as regards LVEDD, LVESD, septal thickness, EF% FS%, E/A and TAPSE.

Similar results have been published by **Polat et al. (2008)** [26] who found no differences in the absolute values of the cardiac chamber dimensions among individuals with CD and healthy controls. They also found no differences in the parameters that are frequently used to evaluate LV function, such as shortening fractions and LV ejection.

In our study, TDI (S, E`, A`) were insubstantially variation among the two groups. TDI (MPI) was substantially greater in the celiac disease affected group contrasted to control group (P value 0.002).

Alkan et al. (2021) [24] reported comparable results as their study displayed insignificant variation among control and CD group as regards TDE (S, E, and A) yet MPI was substantially greater in the CD group contrasted to control group (P =0.002). In contrast, The DTI variables such as mitral valve late diastolic (Am) velocity, mitral valve early diastolic (Em) velocity, mitral Em/Am ratio, tricuspid valve early diastolic (Em) velocity, and LV myocardial index of performance were significantly different among individuals with CD and the control groups, according to **Saylan et al. (2012)** [27].

Consistent to our study, **Bolia, et al. (2018)** [28] examined the impact of a diet without gluten on heart function in individuals with CD and observed that untreated CD (n = 50) children had a greater (>0.6) myocardial performance index (MPI, 66% versus. 0%; $p \leq .01$) than controls. Following a one-year follow-up with excellent dietary compliance, improvements in isovolumic relaxation time (72.5 ± 4.2 vs. 50.62 ± 2.69; $p = .0001$) and deceleration time (121.05 ± 10.1 vs. 99.87 ± 8.5; $p = .02$) were seen, all of which indicated better cardiac diastolic function. Participants who followed the GFD had a reduced MPI than those who didn't ($0.60 \pm .03$ vs. $0.66 \pm .08$; $p = .04$), which was indicative of improvements in load-independent echocardiographic variables.

Conclusions:

We concluded that there is an correlation between celiac disease and subclinical cardiac affection. The tissue doppler echocardiogram is a promising technique to detect early-stage subclinical cardiac dysfunction in CD patients.

References:

1. Anania C, Pacifico L, Olivero F, Perla FM, Chiesa C. Cardiometabolic risk factors in children with celiac disease on a gluten-free diet. World J Clin Pediatr. 2017;6(3):143-8.

2. Fathy A, Abo-Haded HM, Al-Ahmadi N, El-Sonbaty MM. Cardiac functions assessment in children with celiac disease and its correlation with the degree of mucosal injury: Doppler tissue imaging study. Saudi J Gastroenterol. 2016;22(6):441-7.

3. Ciaccio EJ, Lewis SK, Biviano AB, Iyer V, Garan H, Green PH. Cardiovascular involvement in celiac disease. World J Cardiol. 2017;9(8):652-66.

4. Alzaben AS, Turner J, Shirton L, Samuel TM, Persad R, Mager D. Assessing Nutritional Quality and Adherence to the Gluten-free Diet in Children and Adolescents with Celiac Disease. Can J Diet Pract Res. 2015;76(2):56-63.

5. Nenna R, Mosca A, Mennini M, Papa RE, Petrarca L, Mercurio R, et al. Coeliac disease screening among a large cohort of overweight/obese children. J Pediatr Gastroenterol Nutr. 2015;60(3):405-7.

6. Emilsson L, Carlsson R, James S, Hambraeus K, Ludvigsson JF. Follow-up of ischaemic heart disease in patients with coeliac disease. Eur J Prev Cardiol. 2015;22(1):83-90.

7. Reilly NR, Lebwohl B, Hultcrantz R, Green PH, Ludvigsson JF. Increased risk of non-alcoholic fatty liver disease after diagnosis of celiac disease. J Hepatol. 2015;62(6):1405-11.

8. Tortora R, Capone P, De Stefano G, Imperatore N, Gerbino N, Donetto S, et al. Metabolic syndrome in patients with coeliac disease on a gluten-free diet. Aliment Pharmacol Ther. 2015;41(4):352-9.

9. Forchielli ML, Fernicola P, Diani L, Scrivo B, Salfi NC, Pessina AC, et al. Gluten-Free Diet and Lipid Profile in Children With Celiac Disease: Comparison With General Population Standards. J Pediatr Gastroenterol Nutr. 2015;61(2):224-9.

10. Demir AM, Kuloğlu Z, Yaman A, Fitöz S, Nergizoğlu G, Kansu A. Carotid intima-media thickness and arterial stiffness as early markers of atherosclerosis in pediatric celiac disease. Turk J Pediatr. 2016;58(2):172-9.

11. Korkmaz H, Sozen M, Kebapcilar L. Increased arterial stiffness and its relationship with inflammation, insulin, and insulin resistance in celiac disease. Eur J Gastroenterol Hepatol. 2015;27(10):1193-9.

12. Paul, S.P., Adams, H.L., Basude, D. and Collaborators Alison Rushforth Christopher Knight Camelia Vaina Girish Gowda James Hart Loh Ne-Ron Matthew Thorpe Rebecca Cordingley Samuel Broad, 2019. Interpretation and implementation of the revised European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) guidelines on pediatric celiac disease amongst consultant general pediatricians in Southwest of England. *Indian Journal of Gastroenterology*, *38*, pp.203-210.

13. Green Corkins K, Teague EE. Pediatric Nutrition Assessment: Anthropometrics to Zinc. Nutr Clin Pract. 2017;32(1):40-51.

14. Rashidinia A, Bozorgi A, Abdollahi A, Naserghandi A, Ataeinia B, Allameh F. Celiac Disease Seropositivity in Dilated Cardiomyopathy Patients and Correlation with Ejection Fraction. Journal of Iranian Medical Council. 2022;5(1):140-6.

15. Nurminen S, Kivelä L, Huhtala H, Kaukinen K, Kurppa K. Extraintestinal manifestations were common in children with coeliac disease and were more prevalent in patients with more severe clinical and histological presentation. Acta Paediatrica. 2019;108(4):681-7.

16. Caproni M, Bonciolini V, D'Errico A, Antiga E, Fabbri P. Celiac disease and dermatologic manifestations: many skin clue to unfold gluten-sensitive enteropathy. Gastroenterol Res Pract. 2012;2012:952753.

17. Setavand Z, Ekramzadeh M, Honar N. Evaluation of malnutrition status and clinical indications in children with celiac disease: a cross-sectional study. BMC Pediatr. 2021;21(1):147.

18. Dehbozorgi M, Honar N, Ekramzadeh M, Saki F. Clinical manifestations and associated disorders in children with celiac disease in southern Iran. BMC Pediatr. 2020;20(1):256.

19. Güngör Ş, Acıpayam C. Comparison Between Celiac Patients and Healthy Control Group Regarding Vitamin-Mineral Levels and Complete Blood Count Parameters. Trends Pediatr. 2020.

20. Ibrahim RI, Sulieman OB, Mansour MK, Abdelmotaleb MR, ALJarba NK. Prevalence of Celiac Disease Among Patients with Refractory Iron Deficiency Anemia in North-Western Saudi Arabia. The Egyptian Journal of Hospital Medicine. 2022;89(1):5717-20.

21. Jivraj A, Hutchinson JM, Ching E, Marwaha A, Verdu EF, Armstrong D, et al. Micronutrient deficiencies are frequent in adult patients with and without celiac disease on a gluten-free diet, regardless of duration and adherence to the diet. Nutrition. 2022;103-104:111809.

22. Jawed B. EVALUATION OF SERUM FERRITIN, CRP, VITAMIN D3, VITAMIN B12 AND IRON IN CELIAC DISEASE: A CROSS SECTIONAL STUDY. International Journal of Medical Laboratory Research. 2016.

23. Frustaci A, Cuoco L, Chimenti C, Pieroni M, Fioravanti G, Gentiloni N, et al. Celiac Disease Associated With Autoimmune Myocarditis. Circulation. 2002;105(22):2611-8.

24. Alkan F, Dogan G, Kasırga E, Coskun S. The effect of Celiac disease on cardiac functions and aortic elasticity parameters in children. Cardiol Young. 2021;31(4):627-30.

25. Fathy A, Abo-Haded HM, Al-Ahmadi N, El-Sonbaty MM. Cardiac functions assessment in children with celiac disease and its correlation with the degree of mucosal injury: Doppler tissue imaging study. Saudi J Gastroenterol. 2016;22(6):441-7.

26. Polat TB, Urganci N, Yalcin Y, Zeybek C, Akdeniz C, Erdem A, et al. Cardiac functions in children with coeliac disease during follow-up: insights from tissue Doppler imaging. Dig Liver Dis. 2008;40(3):182-7.

27. Saylan B, Cevik A, Kirsaclioglu CT, Ekici F, Tosun O, Ustundag G. Subclinical cardiac dysfunction in children with coeliac disease: is the gluten-free diet effective? ISRN Gastroenterol. 2012;2012:706937.

28. Bolia R, Srivastava A, Kapoor A, Yachha SK, Poddar U. Children with untreated coeliac disease have sub-clinical cardiac dysfunction: a longitudinal observational analysis. Scand J Gastroenterol. 2018;53(7):803-8.