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Egyptian Pediatric Association Gazette (2023) 71:11
https://doi.org/10.1186/s43054-022-00148-5

Egyptian Pediatric Association Gazette

RESEARCH

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Assessment of subclinical myocardial dysfunctions in Egyptian children with celiac disease, a cross-sectional study

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Abstract

Background Celiac disease (CD) is a chronic immune-mediated disorder with multiple extraintestinal manifestations. The increased incidence of cardiac morbidities in celiac patients highlights the importance of early detection of subclinical myocardial dysfunctions. In this study, we aimed to assess the cardiac functions and explore early subclinical myocardial dysfunctions in celiac patients by tissue Doppler imaging.

Results A cross-sectional analytical study which included 42 celiac patients with CD and 36 age- and sex-matched controls. They were subjected to full medical history and examination and complete transthoracic echocardiography including tissue Doppler imaging to assess cardiac functions. Evidences of early subclinical systolic and diastolic dysfunctions were found in our patients; they had significantly lower tricuspid E/A ratio; lower S, E′, a′ in both ventricles; reduced mitral E′/a′ (2.13 ± 0.87, 2.94 ± 0.061 respectively, $p < 0.001$); and increased tricuspid E/e′ (6.09 ± 0.8, 4.15 ± 1.33 respectively, $p < 0.001$) compared to the controls. Biventricular MPI were within normal limits, yet with a significant difference from the control ($p = 0.001$). lower E′/a′ in the RV is significantly related to the extraintestinal manifestations (1.5 ± 0.48, 2.16 ± 0.71 respectively, $p = 0.009$).

Conclusion Children with CD had subclinical myocardial dysfunction especially in RV which is better detected by tissue Doppler imaging (TDI). These dysfunctions are increased with the presence of extraintestinal manifestations.

Keywords Celiac disease, Myocardial dysfunction, Tissue Doppler echo, Children

Background

Celiac disease (CD) is an autoimmune disorder that occurs in individuals who are genetically predisposed [1]. It is characterized by inflammation caused by an immune response to ingested wheat gluten and related proteins of rye and barley [2]. The clinical presentations of CD include severe diarrhea, malabsorption, weight loss, and nutritional deficiencies, and extraintestinal manifestations as anemia, osteopenia, short stature, or neurological disorders [3]. Celiac patients have a higher chance of developing cardiovascular diseases (CVD) than the general population such as cardiomyopathy, ischemic heart disease, and arrhythmia [4]. These hazardous effects on the heart are perhaps due to an immunological response, or the presence of autoantibodies [5]. Identification of cardiovascular risk through early evaluation of cardiac functions benefits CD patients [6]. In this study, we aimed to detect subclinical myocardial dysfunctions before the first clinical manifestations are obvious and explore its association to the extraintestinal manifestations in children with CD.

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Methods

This is a cross-sectional study in which 78 children aged between 6 months and 18 years were included. They were enrolled over a period of 6 months from December 2021 to May 2022 at Cairo University Children Hospital. They were divided into two groups; group 1 included 42 patients with celiac disease (24 females and 18 males), following up in the gastroenterology outpatient clinic of Cairo University Children Hospital. Diagnosis was confirmed by clinical data, serology, and esophagogastroduodenoscopy with biopsy, after exclusion of patients with other gastrointestinal illnesses, congenital or acquired heart diseases, and additional systemic illnesses, e.g., diabetes mellitus and autoimmune thyroiditis. And group 2 included 36 healthy, age- and sex-matched children (18 males and 18 females) without gastrointestinal or cardiac problems as a control group. The study was approved by Higher studies Research Committee of Faculty of Medicine Cairo University. Oral informed consent was obtained from the legal guardians. For all patients who met the inclusion criteria, full medical history was taken with special emphasis on gastrointestinal manifestations, extraintestinal findings, cardiac symptoms, and dietary compliance that was evaluated 6 months after adequate diet control (strict gluten-free diet). Comprehensive physical examination was done including anthropometric measurements, vital signs including HR, RR, and BP; full abdominal examination; and cardiac examination. The patients' files were revised for the results of antibody titers: anti-tissue transglutaminase immunoglobulin A (anti-tTG IgA) and immunoglobulin G (IgG), total IgA, anti-endomysial (EMA) antibody IgA, anti-gliadin (DGP) antibody IgA and IgG, CBC and iron profile, upper endoscopy, and biopsy.

For each participant, full transthoracic echocardiography (TTE), with experienced pediatric cardiologist, was carried out using a General Electric Vingmed Ultrasound System (Vivid E95) with 6S and M5Sc probes, according to the recommendations of the American Society of Echocardiography [7]. The following were measured by conventional echocardiography:

1. M-mode measurements including fractional shortening (FS), ejection fraction (EF)
2. Pulsed Doppler echocardiography to measure: Peak early diastolic filling velocity (E wave), peak late diastolic velocity (A wave), early to late diastolic flow ratio (E/A), deceleration time (DT) for both mitral (MV) and tricuspid valves (TV)

By tissue Doppler imaging, we assessed the following: systolic myocardial velocities at the basal segments of the lateral, septal, and anterior walls (S) as well as early and late diastolic myocardial velocities and their ratios (E′, a′, and E′/a′, E/e′ respectively). Myocardial performance index (MPI) of both ventricles was calculated as follows: MPI = (a − b)/b, the normal MPI index for LV and RV are 0.32 ± 0.07 and 0.27 ± 0.09, respectively [8] (Fig. 1). For all measures, the mean of three cardiac cycles was taken.

Statistical analysis

Data were coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative

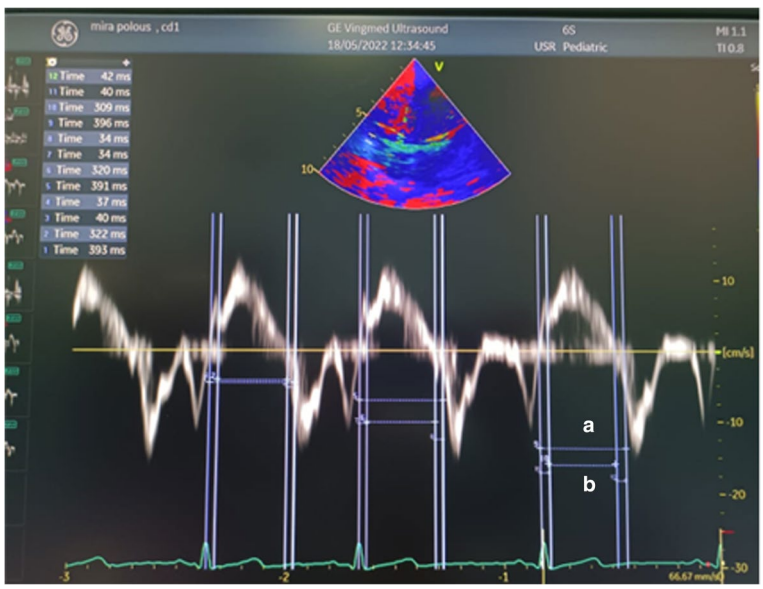

Fig. 1 Calculation of MPI by tissue Doppler imaging. MPI, myocardial performance index

data were presented as mean, standard deviations, and ranges when parametric and median, inter-quartile range (IQR) when data found non-parametric. The comparison between groups regarding qualitative data was done by using chi-square test and/or Fisher's exact test when the expected count in any cell found less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done by using independent *t*-test while with non-parametric distribution was done by using Mann–Whitney test. The comparison between two paired groups regarding quantitative data and parametric distribution was done by using paired *t*-test while with non-parametric distribution was done by using Wilcoxon rank test. The comparison between more than two groups regarding quantitative data and parametric distribution was done by using one-way ANOVA test while with non-parametric distribution was done by using Kruskal–Wallis. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *p*-value was considered significant as the following: *P*-value > 0.05: nonsignificant (NS), *P*-value < 0.05: significant (S), *P*-value < 0.01: highly significant (HS).

Results

This is a cross-sectional analytic study that was conducted on 78 children, at Cairo University Children Hospital, over a period of 6 months. They were divided into two groups: 42 patients who were diagnosed with celiac disease before enrollment in the current study, and 36 age- and sex-matched controls. The patients were evaluated 6 months after strict diet control (gluten-free diet). The demographic data of included cases and controls regarding age, sex, and family history and BP are shown in Table 1.

Our patients had significantly lower weight, height, and BMI in relation to the controls. They had significantly higher SPB and significantly lower DBP than the controls.

The most prominent abdominal complaints in our patients were abdominal distention (65.9%) followed by chronic diarrhea (63.4%). The most prominent extraintestinal manifestations were failure to thrive (50%), iron deficiency anemia (42.9%0), short stature (30.9%), and behavioral changes/insomnia/fatigue (14.3%). Twenty six (61.9%) patients had positive serology. All our patients had done endoscopy and biopsy to confirm the diagnosis. Forty (95.2%) children were strict to gluten-free diet (GFD) while 2 (4.8%) children were incompliant as registered in their files. As regards M mode measurements of our patients, they are shown in Table 2.

As enlisted in Table 2, our patients had dilated aortic root and dilated RV in relation to controls. LV was dilated but not to a significant level.

Results of conventional pulsed Doppler are shown in Table 3.

As seen in Table 3, the patients had significantly lower E/A ratio of tricuspid valve and higher E/A ratio of mitral valve in relation to controls.

Table 1 Clinico-demographic data of studied groups

Demographic data	Cases ($n=42$) Mean ± SD	Controls ($n=36$) Mean ± SD	*P* value
Age (years)	8.8 ± 3.8	8.2 ± 3.8	0.183
Males	18 (42.9%)	18 (50.0%)	0.528
Females	24 (57.1%)	18 (50.0%)	
Family history (+ve)	4 (9.5%)	0 (0.0)	0.057
Weight (kg)	26.0 ± 12.6	27.88 ± 8.74	0.001
Height (cm)	121.6 ± 17.2	123.96 ± 10.24	0.049
BMI (km/m$^{2)}$	16.7 ± 3.8	17.12 ± 2.3	0.001
SBP (mmHg)	107.5 ± 14.5	102.5 ± 4.6	0.035
DBP (mmHg)	66.3 ± 13.6	73.8 ± 3.3	0.001

BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure

Table 2 M-mode measurements of patients and controls

Conventional echocardiographic measurements	Cases ($n=42$)	Controls ($n=36$)	*P* value
M-mode parameters (mm)	**Mean ± SD**	**Mean ± SD**	
AO	25.9 ± 3.24	17.62 ± 2.91	**0.027**
LA	21.69 ± 3.62	18.6 ± 2.99	0.286
RV	20.13 ± 5.57	12.74 ± 3.44	**< 0.001**
IVST	5.55 ± 2.4	5.7 ± 1.98	0.234
LVPWT	5.38 ± 1.29	5.4 ± 2.22	0.186
LVEDd	39.5 ± 4.87	34.8 ± 3.67	0.143
LVESd	24.95 ± 3.73	20.7 ± 2.54	0.314
FS %	36.81 ± 5.15	37.52 ± 4.25	0.915
EF	67.07 ± 6.26	70.48 ± 3.33	0.362

Table 3 Pulsed wave Doppler imaging measurements in celiac disease patients and healthy controls

Conventional pulsed Doppler parameters (cm/s)	Cases ($n=42$)	Controls ($n=36$)	*P* value
	Mean ± SD	**Mean ± SD**	
Tricuspid valve			
E wave velocity	62.45 ± 17.79	82.83 ± 6.39	**< 0.001**
A wave velocity	43.95 ± 16.05	44.08 ± 3.24	0.968
E/A ratio	1.45 ± 0.31	1.89 ± 0.19	**< 0.001**
DT	93.48 ± 25.4	93.17 ± 3.29	0.896
Mitral valve			
E wave velocity	94.66 ± 14.71	97 ± 6	0.324
A wave velocity	55.43 ± 25.44	69.03 ± 3.21	**0.001**
E/A ratio	1.86 ± 0.56	1.41 ± 0.11	**< 0.001**
DT	91.63 ± 27.35	97.22 ± 8.7	0.261

SD standard deviation, *P > 0.05* nonsignificant (NS), *P < 0.05* significant (S), *P < 0.01* highly significant (HS)

Table 4 Tissue Doppler imaging measurements in celiac patients and healthy controls

Tissue Doppler parameters (cm/s)	Cases ($n=42$)	Controls ($n=36$)	*P* value
	Mean ± SD	Mean ± SD	
Septal wall			
S wave velocity	7.97 ± 1.44	11.33 ± 1.57	**< 0.001**
E′ wave velocity	13.4 ± 2.72	14.44 ± 1.16	**0.036**
a′ wave velocity	7.22 ± 1.33	7.83 ± 1.13	**0.033**
E′/a′ ratio	2 ± 0.64	1.87 ± 0.25	0.283
Lateral wall (mitral valve)			
S wave velocity	8.1 ± 2.3	10.81 ± 1.62	**< 0.001**
E′ wave velocity	16.38 ± 3.64	15.25 ± 1.25	0.080
a′ wave velocity	8.45 ± 3.45	5.39 ± 1.13	**< 0.001**
E′/a′ ratio	2.13 ± 0.87	2.94 ± 0.61	**< 0.001**
E/e′ ratio	6 ± 1.39	6.41 ± 0.7	0.104
MPI (Tie index)	0.33 ± 0.10	0.35 ± 0.03	**0.04**
Anterior wall (tricuspid valve)			
S wave velocity	12 ± 2.66	14.53 ± 2.05	**< 0.001**
E′ wave velocity	15.62 ± 2.85	13.75 ± 1.48	**< 0.001**
a′ wave velocity	10.42 ± 3.46	8.61 ± 1.1	**0.003**
E′/a′ ratio	1.58 ± 0.55	1.62 ± 0.27	0.676
E/e′ ratio	6.09 ± 0.8	4.15 ± 1.33	**< 0.001**
MPI (Tie index)	0.33 ± 0.08	0.28 ± 0.02	**0.001**

SD standard deviation, *P > 0.05* nonsignificant (NS), *P* < 0.05 significant (S), *P < 0.01* highly significant (HS), *MPI* myocardial performance index

As shown in Table 4, our patients had significantly lower mitral E′/a′ and higher tricuspid E′/e′ when compared to controls. There was statistically significant longer MPI of RV in patients than controls. Yet biventricular MPI were within normal limits.

As shown in Table 5, there are statistically significant lower E′/a′ ratio of the tricuspid and mitral valves in patients with extra intestinal manifestations ($p=0.041$, $p=0.009$ respectively).

Discussion

Celiac disease is an autoimmune disorder affecting young children with wide range of manifestations ranging from asymptomatic to severely affected. The classic presentation is failure to thrive, malnutrition, diarrhea, abdominal pain, and distension [9]. Although the development of cardiac morbidity in CD patients has been established in many studies, the exact mechanisms are not exactly known. An increased incidences of dilated cardiomyopathy, ischemic heart disease had been reported in CD patients [9, 10].

The aim of the present study was to assess the effect of CD on cardiac functions to detect any subclinical myocardial affection. This cross-sectional study included 78 children who were divided into two groups: group 1 included 42 patients (24 females and 18 males), with ages ranging from 2 to 18 years; group 2 included 36 age- and sex-matched healthy children (18 males &18 females) with ages ranging from 5 to 18 years. There was no significant sex predominance in celiac patients which was confirmed by previous studies [3, 9]. Our celiac patients had higher systolic blood pressures and lower diastolic blood pressures when compared to the controls, this may be due to hyperdynamic circulation caused by anemia in those patients [4]. It was different from Bayar et al. who found that patients with CD had increased systolic and diastolic blood pressure than the controls; however, his patients were adults with additional risk factors like smoking [11].

In our study, there was no statistically significant difference between patients and controls as regards the FS and EF of the LV ($p=0.915$, 0.362 respectively); the same was confirmed by several studies [9, 10].

In the current study, we found notably lower TV E/A ratio and higher MV E/A ratio in CD patients than controls ($p=0.001$). Lower E/A ratio measured by conventional pulsed Doppler indicates diastolic dysfunction of the related ventricle. These results were different from the results of Saylan et al. who found a significantly lower E/A ratio of MV and TV in the patients than the control group [9] and also different from Alkan et al. who found no statistically significant difference between the two groups in MV E, MV A, and MV E/A parameters [10]. This incomparability may be because conventional echocardiography assesses the global systolic and diastolic functions and can miss modest myocardial dysfunction. Tissue Doppler can overcome these limitations and detect preclinical myocardial injury [3]. With TDI of left ventricle, our data revealed systolic dysfunction detected by significantly lower S wave in patients in comparison to controls (8.1 ± 2.3, 10.81 ± 2.61 respectively, $p<0.001$), and modest LV diastolic dysfunction as evidenced by significantly lower mitral E′/a′, with mean (2.13 ± 0.87) in cases compared to (2.94 ± 0.61) in controls $p<0.001$. In addition, there were systolic dysfunction of RV as proved by significantly reduced S wave in relation to control (12 ± 2.66, 14.53 ± 2.05, $p<0.001$) and diastolic dysfunction as detected by increased E/e′ ratio when compared to the control group (6.09 ± 0.8, 4.15 ± 1.33 respectively, $p<0.001$). These abnormalities were compatible with Fathy et al., who found systolic and diastolic dysfunctions of both ventricles [3], while incompatible with other studies which reported no evidence of substantial systolic or diastolic dysfunctions measured by these waves [9]. The proposed mechanisms for the development of cardiomyopathy in celiac patients include the nutritional deficiencies which result from chronic malabsorption,

Table 5 Relation between the presence of extraintestinal manifestations and tissue Doppler results in Celiac patients

Tissue Doppler (TVI) cm/s		Extraintestinal manifestations		Test value	*P* value
		No ($n=5$)	Yes ($n=37$)		
Septal wall					
S	Mean ± SD	7.40 ± 0.89	8.05 ± 1.49	− 0.943	0.351
	Range	6–8	5–10		
E′	Mean ± SD	13.67 ± 2.50	13.37 ± 2.78	0.227	0.821
	Range	10.33–17	8.3–18		
a′	Mean ± SD	7.10 ± 0.74	7.24 ± 1.40	− 0.210	0.835
	Range	6.3–8	4.3–10		
E′/a′	Mean ± SD	2.54 ± 1.11	1.92 ± 0.52	2.110	**0.041**
Lateral wall					
S	Mean ± SD	7.20 ± 0.45	8.22 ± 2.43	− 0.924	0.361
	Range	7–8	5–16		
E′	Mean ± SD	17.00 ± 3.08	16.30 ± 3.74	0.401	0.691
	Range	12–20	9–24		
a′	Mean ± SD	6.00 ± 1.41	8.78 ± 3.52	− 1.732	0.091
	Range	4–7	4–21		
E′/a′	Median (IQR)	2(1.7–2.6)	2.2(1.42–2.75)	− 0.058 ≠	0.954
	Range	1.7–3	0.14–4		
E/e′	Mean ± SD	5.73 ± 0.63	6.04 ± 1.47	− 0.467	0.643
	Range	4.8–6.3	4.29–11		
MPI (Tie index)	Mean ± SD	0.40 ± 0.21	0.32 ± 0.08	1.629	0.111
	Range	0.23–0.75	0.21–0.53		
Anterior wall					
S	Mean ± SD	11.40 ± 1.52	12.08 ± 2.78	− 0.533	0.597
	Range	9–13	6–17		
E′	Mean ± SD	16.40 ± 3.36	15.51 ± 2.81	0.647	0.521
	Range	11–20	10–23		
a′	Mean ± SD	7.94 ± 2.28	10.77 ± 3.47	− 1.758	0.087
	Range	5–10	5–21		
E′/a′	Mean ± SD	2.16 ± 0.71	1.50 ± 0.48	2.734	**0.009**
	Range	1.65–3.4	0.4–2.4		
E/e′	Mean ± SD	4.16 ± 2.00	4.15 ± 1.25	0.013	0.989
	Range	2.59–7.09	2.4–7.4		
MPI (Tie index)	Mean ± SD	0.29 ± 0.06	0.33 ± 0.08	− 1.136	0.263
	Range	0.21–0.36	0.18–0.49		

the myocardial damage caused by the absorption of variable infectious agents or luminal antigens due to changes in the permeability of the intestine, and the autoimmune process which is the most acceptable theory [12–14].

Myocardial performance index (MPI) is a sensitive index of systolic and diastolic functions of the ventricles; we found a statistically significant difference in MPI of RV between patients and controls, yet it was within normal limits. This relation was not established for the LV. The longer RV MPI in our patients may indicate early dysfunction as proved by the previously described lower waves and ratios. Our results were partially compatible with the results of several studies [3, 9, 10]; they found a significant lengthening of the MPI values for RV and LV in their patients. This difference may be attributed to the variable degree of ongoing inflammation related to the duration and severity of the CD and the strictness of diet control.

Patients with extraintestinal manifestations had significantly lower RV E′/a′ ratio than controls (1.5 ± 0.48, 2.16 ± 0.71 respectively, $p=0.009$) and lower E′/a′ ratio of the septal wall of LV (1.92 ± 0.52, 2.54 ± 1.11 respectively, $p=0.04$) pointing to more cardiac affection in the presence of extraintestinal manifestations in CD patients,

possibly due to the increased severity of the inflammatory process, or the addition of more etiological factors to the cardiac dysfunction.

Our study was limited by the relatively small number of patients and lack of multiple echo measurements to allow for better comparison.

Conclusion and recommendations

Children with CD had early subclinical myocardial dysfunctions especially in the RV (dilated RV, lower E/a ratio, higher E/e′, longer MPI). These early dysfunctions may be exacerbated by the presence of extraintestinal manifestations in our patients. We recommend close collaboration between gastroenterologists and cardiologists by large multicenter studies for screening CD patients for myocardial dysfunctions. Regular tissue Doppler echocardiography for CD patients especially those with extraintestinal manifestations is advised, to detect modest myocardial dysfunctions and lessen CVD-related morbidity and mortality.

Abbreviations

CD	Celiac disease
CVD	Cardiovascular disease
DT	Deceleration time
DBP	Diastolic blood pressure
EF	Ejection fraction
FS	Fractional shorting
MPI	Myocardial performance index
MV	Mitral valve
SBP	Systolic blood pressure
TDI	Tissue Doppler imaging
TV	Tricuspid valve

Acknowledgements

Not applicable.

Authors' contributions

LAI: analysis, interpretation of data, did the echocardiography, manuscript preparation, and drafting of the article. AMF: concept, design of the study, did echocardiography, and final approval of the version to be published. YAA: collection of cases, analysis, and interpretation of data. HHM shared in design of the study, interpretation, analysis of data, and review the literature. All authors had full access to the data (including statistical results and tables), approved the final manuscript as submitted, and agreed to be accountable for all aspects of the work.

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Funding

Not applicable.

Availability of data and materials

Data will be made available by the corresponding author to the editor after a request email from the editor. The reason for sharing the data should be justified, and it will be shared after all the authors approve the same.

Declarations

Ethics approval and consent to participate

The study was approved from the ethical committee of Cairo University Children Hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 4 November 2022 Accepted: 19 November 2022
Published online: 27 February 2023

References

1. Sapone A, Bai JC, Ciacci C et al (2012) Spectrum of gluten-related disorders: consensus on new nomenclature and classification. BMC med 10(1):1–12. https://doi.org/10.1186/1741-7015-10-13
2. Ludvigsson JF, Leffler DA, Bai JC et al (2013) The Oslo definitions for coeliac disease and related terms. Gut 62(1):43–52
3. Fathy A, Abo-Haded HM, Al-Ahmadi N, El-Sonbaty MM (2016) Cardiac functions assessment in children with celiac disease and its correlation with the degree of mucosal injury: Doppler tissue imaging study. Saudi J Gastroenterol 22(6):441. https://doi.org/10.1186/1741-7015-10-13
4. Noori N, Shahraki T, Teimouri A, Shahramian I (2018) Cardiac involvements in patients with celiac disease by doppler tissue echocardiography compared to conventional echocardiography. Int Cardiovasc Res J 12(1):13-21
5. Mogyorósy G, Felszeghy E, Kovács T et al (2014) Pediatric myocarditis: A sentinel of non-cardiac chronic diseases. Interv Med Appl Sci 6(4):154–159
6. De Marchi S, Chiarioni G, Prior M, Arosio E (2013) Young adults with coeliac disease may be at increased risk of early atherosclerosis. Aliment Pharmacol Ther 38(2):162–169
7. Lai WW, Geva T, Shirali GS et al (2006) Guidelines and standards for performance of a pediatric echocardiogram: a report from the Task Force of the Pediatric Council of the American Society of Echocardiography. J Am Soc Echocardiogr 19(12):1413–1430. https://doi.org/10.1016/j.echo.2006.09.001
8. JrA J, Jurko A, Minarik M (2011) Doppler-derived myocardial performance index in healthy children. Bratisl Lek Listy 112(2):77–79
9. Saylan B, Cevik A, Kirsaclioglu CT, Ekici F, Tosun O, Ustundag G (2012) Subclinical cardiac dysfunction in children with coeliac disease: is the gluten-free diet effective? Int Sch Res Network ISRN Gastroenterology 2012:706937. https://doi.org/10.5402/2012/706937. Epub 2012 Nov 14
10. Alkan F, Dogan G, Kasırga E, Coskun S (2021) The effect of Celiac disease on cardiac functions and aortic elasticity parameters in children. Cardiol Young 31(4):627–630. https://doi.org/10.1017/S1047951120004461
11. Bayar N, Çekin AH, Arslan Ş et al (2016) Assessment of aortic elasticity in patients with celiac disease. Korean Circ J 46(2):239–245
12. DeMeo MT, Mutlu EA, Keshavarzian A, Tobin MC (2002) Intestinal permeation and gastrointestinal disease. J Clin Gastroenterol 34(4):385–396
13. Van Elburg RM, Uil JJ, Mulder CJ, Heymans HS (1993) Intestinal permeability in patients with coeliac disease and relatives of patients with coeliac disease. Gut 34(3):354–357. https://doi.org/10.1136/gut.34.3.354
14. Curione M, Barbato M, Viola F, Francia P, De Biase L, Cucchiara S (2002) Idiopathic dilated cardiomyopathy associated with coeliac disease: the effect of a gluten-free diet on cardiac performance. Dig Liver Dis 34(12):866–869. https://doi.org/10.1016/S1590-8658(02)80258-4

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