



Effect of Gluten-Free Diet on Aortic Elasticity in Children with Celiac Disease

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Abstract

Background: Celiac disease is a hereditary digestive disease in children associated with an autoimmune disorder of the small intestine. This study aimed to study aortic stiffness in children with celiac disease compared with controls and assess the effects of a gluten-free diet on aortic stiffness parameters.

Methods: This case-control study was conducted on 114 children with celiac disease and 57 healthy volunteers. Children with celiac disease comprised three groups: Gluten-free diet (GFD)-responsive, GFD-nonresponsive, and newly diagnosed. Systolic and diastolic diameters of the ascending aorta were recorded by M-mode echocardiography. Data were analyzed using SPSS 20. Study data had free distribution and nonparametric tests were applied for the analysis. The tests were Mann-Whitney U and Kruskal-Wallis with P value < 0.05 as the significance level.

Results: Aortic strain (11.15 ± 7.47 vs. 13.78 ± 6.95 , $P = 0.002$) and aortic distensibility (6.98 ± 5.03 vs. 8.33 ± 5.13 , $P = 0.037$) were lower in celiac disease (CD) while pressure strain elastic modulus (410.60 ± 247.45 vs. 330.71 ± 216.94 , $P = 0.012$) and aortic strain β index (1.79 ± 0.62 vs. 1.44 ± 0.51 , $P < 0.001$) were higher. The aortic strain significantly differed between control and response to GFD ($P = 0.026$), control and new diagnosis ($P < 0.001$), response to GFD and new diagnosis ($P = 0.003$), and no response to GFD and new diagnosis ($P < 0.001$) groups. The aortic strain β index differed significantly between control and response to GFD ($P \leq 0.001$), control and new diagnosis ($P < 0.001$), response to GFD and no response to GFD ($P = 0.035$), response to GFD and new diagnosis ($P = 0.002$), and no response to GFD and new diagnosis ($P < 0.001$) groups. Aortic distensibility significantly differed between control and new diagnosis ($P < 0.001$), response to GFD and new diagnosis ($P = 0.037$), and no response to GFD and new diagnosis ($P = 0.021$) groups. Pressure strain elastic modulus significantly differed between control and new diagnosis ($P < 0.001$), response to GFD and new diagnosis ($P = 0.037$), and no response to GFD and new diagnosis ($P = 0.021$) groups.

Conclusions: The present study concluded that the elasticity parameters will change due to celiac disease. Gluten-free diet had no significant effect on aortic stiffing measures except the AS/β index.

Keywords: Gluten-Free Diet, Aortic Elasticity, Celiac Disease, Children

1. Background

Celiac disease (CD) is a hereditary digestive disease in children associated with an autoimmune disorder of the small intestine (1). When the small intestine's villi are damaged due to the disease, it will disturb the absorption of substances (2). The prevalence of CD has been reported as 1 - 2% in the European region and 0.6 - 1.0% worldwide, with a peak in Western countries (2). It has been reported as 0.3% in Germany and 2.4% in Finland (3). Sistan & Baluchestan province of Iran showed a high prevalence of 7.35% based on a serologic test (4), 1.5- to 2-fold higher in women (2).

Anti-tTG IgA titers are an initial screening test for CD due to high sensitivity and specificity (5), correlated with

intestinal mucosal damage (4), making duodenal mucosal viability the gold standard method, confirmed by laboratory studies (6). Anti-tTG IgA titers are also correlated with histological changes in the duodenum (7) and can be used to monitor response to a gluten-free diet (GFD) (8). The best and most successful treatment for CD is GFD with complete adherence (9). Mucous membrane healing is slow and more incomplete in adults than in children (10) with unclear natural history. A study assessing mucosal recovery found that about 35% improved two years and 66% five years after GFD (11). Furthermore, strong data are supporting the benefits of GFD in patients with CD or symptomatic CD, regardless of symptoms, whereas GFD outcomes in sub-groups of asymptomatic and latent CD are largely un-

known.

Response to GFD cannot be measured in terms of symptoms or mucosal relief (11, 12). Aortic elasticity parameters are early indicators of structural and functional changes in the vessel wall and are independent predictors of atherosclerosis and age-related cardiovascular disease (13). Arterial function is critical for CD and untreated patients, can be detrimental, and is predictive of future cardiovascular events (14, 15). The effects of GFD on tTG-IgA and aortic stiffness have been studied in CD patients and shown a significant improvement in aortic elasticity especially in patients who adhered to GFD completely (16). In the recent studies by Noori et al. (17, 18) on chronic diseases such as thalassemia and celiac, they showed that both diseases had a significant effect on heart stiffing. A study of CD observed a decrease in aortic strain (AS) and aortic distensibility (AD) and an increase in pressure strain elastic modulus (PSEM) and AS β index in children with CD compared with controls. The did not assess the effect of GFD on heart stiffing in CD children. In this regard, Bayer et al. (16) attempted to find an answer to this question. They indicated that although CD had a significant effect on elasticity parameters, in patients with CD, adhering to GFD did not show acceptable effects on these parameters.

2. Objectives

To get more knowledge in this regard and because people in the study area consume high wheat products and follow a specific lifestyle that affect the prevalence of non-communicable diseases such as CD, the present study aimed to compare aortic stiffing in children with CD and controls and evaluate the impact of gluten-free diet on aortic stiffing in these patients.

3. Methods

3.1. Study Design

This case-control study was performed on 114 children with CD and 57 healthy children aged between 3.5 and 18 years at the Children's Heart Center in collaboration with the Special Diseases Center at Ali Asghar hospital of Zahedan, Sistan & Baluchestan province in 2020. Children with CD were categorized into three groups: response to GFD whose tTG-IgA improved to the normal range after 18 months of adhering to GFD, no response to GFD who had no improvement in tTG-IgA levels within the diet duration (18 months, possibly due to not proper adherence), and newly diagnosis whose CD was diagnosed in the last six months. The control group was randomly selected from children who had visited the clinic for regular health

check-ups. Celiac disease was diagnosed using a combination of clinical findings and a threshold of 20 for tTG-IgA, confirmed by intestinal biopsy (1).

3.1.1. Sampling

The results from the study of Bayer et al. (16) were used to calculate the sample size. The formulae: $N = \frac{1}{2} \left(\frac{(\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)^2} \right) * f(\alpha, \beta)$ gave a sample of 60 controls and 120 children with CD, with a little manipulation while $f(\alpha, \beta) = 7.84$. For the data collection, first, we selected children who were diagnosed within the last six months that were 22 individuals. Then, we used medical records of CD children on a specific diet. We randomly selected 60 patients from those who had a positive response to GFD and 38 patients from those who had negative responses for at least 18 months. After entering the information into the SPSS, six patients had missing data and were omitted from the database, including three with positive responses and three with negative responses. We randomly deleted three records from the controls for equality and accuracy.

3.2. Criteria

The following exclusion criteria were used for children with CD and controls: Age \geq 18 years on admission, comorbidities such as diabetes mellitus, obesity, hypertension, dyslipidemia, systemic autoimmune disease, active infection, signs of liver or kidney disease or lung disease, exposure to smoking, antihypertensive drugs, concomitant treatment with lipid-lowering drugs, and a positive family history of dyslipidemia and early coronary artery disease.

3.3. Measurement of tTG IgA

Three milliliters of blood were taken from fasting participants at 8:00 a.m. The samples were centrifuged for serum separation and kept at -70°C until tTG IgA measurement. From the samples, 250 microns were separated for serological tests with an ELISA kit (AESKU, LOT:22100, Made in Germany). The normal limit of tTG IgA was 20 U/mL.

3.4. Blood Pressure Measurement

Blood pressure (BP) was measured with a sphygmomanometer from the brachial artery at the heart level after resting in the supine position for at least five minutes. At least two minutes apart, three measurements were taken, and the average was used for the study.

Using a pressure drop rate of approximately 2 mmHg per second, Korotkoff phases I and V were used to measure systolic and diastolic blood pressure, respectively. A cardiologist performed all blood pressure measurements. Pulse pressure (PP) was calculated as systolic pressure minus diastolic pressure.

3.5. Echocardiographic Measurement

After taking history, physical examination, and chest X-ray, the participants were referred to a cardiologist, and then echocardiography was performed using My lab 60 with transducers 3 and 8 (made in Italy). Measurements were repeated in three cycles to achieve high precision of echocardiographic findings, and the average value was considered for the final value. The M-mode results showed the aortic diastolic diameter (AoD) and the aortic systolic diameter (AoS).

3.6. Evaluation of Aortic Elasticity

The aortic diastolic and systolic diameters were recorded in M-mode from a parasternal long-axis view approximately 3 cm above the aortic valve. The aortic systolic diameter was measured at the point of maximal aortic advancement, and the diastolic diameter was measured at the onset of the QRS complex on the electrocardiogram (Figure 1).

Elasticity parameters of the aorta WERE measured as follows (17).

$$\text{Aortic strain (\%)} = (\text{AoS} - \text{AoD}) \times 100 / \text{AoD}$$

Aortic stiffness β index = Natural logarithm (systolic blood pressure (SBP)/diastolic blood pressure (DBP))/([AoS - AoD]/AoD)

$$\text{Aortic distensibility (cm}^2 \times \text{dyne}^{-1} \cdot 10^{-6}) = 2 \times ([\text{AoS} - \text{AoD}]/\text{AoD})/(\text{SBP} - \text{DBP})$$

$$\text{Pressure strain elastic modulus (Kpa)} = (\text{SBP} - \text{DBP})/([\text{AoS} - \text{AoD}]/\text{AoD})$$

3.7. Ethical Approval

This study was approved under the ethical approval code of IR.ZAUMS.REC.1400.095.

3.8. Statistical Analysis

SPSS 20.0 (SPSS Inc., Chicago, IL, USA) was used to analyze data. First, the Kolmogorov-Smirnov test was applied to assess the data normality. It revealed that all the variables had free distribution in the present study. Then, the nonparametric tests were used for the analysis. The Mann-Whitney U test was used to analyze the data between the two groups, and the Kruskal-Wallis test by ranks was applied to analyze the data between three or more groups. For all the tests, a P value < 0.05 was considered significant.

4. Results

There were 96 girl children in the sample. Of the girls, 27.1% were healthy, while 21.9%, 33.3%, and 17.7% had no response to GFD, response to GFD, and new diagnosis, respectively. The same trends were observed for boys, and the

gender distribution was the same ($X^2 = 6.767$, $P = 0.080$) (Table 1). The normality test showed that all quantitative variables had free distribution ($P < 0.05$).

Table 2 shows the mean age of participants as 9.36 ± 3.85 years; it was 9.7 ± 3.66 and 9.19 ± 3.95 years in the healthy and patient groups, respectively (MWU = 2938.500, $P = 0.308$). The same age trend was observed when the participants were classified into four groups. In children with CD, those with no response to GFD, response to GFD, and new diagnosis were on treatment with GFD for 8.53 ± 3.96 , 9.67 ± 3.82 , and 8.99 ± 4.28 years, respectively.

Table 3 compares the elasticity properties between CD and healthy children groups. A significant decrease was observed in AS (11.15 ± 7.47 vs. 13.78 ± 6.95 , $P = 0.002$) and AD (6.98 ± 5.03 vs. 8.33 ± 5.13 , $P = 0.012$), while a significant increase was observed in PSEM (410.60 ± 247.45 vs. 330.71 ± 216.94 , $P = 0.012$) and AS β index (1.79 ± 0.62 vs. 1.44 ± 0.51 , $P < 0.001$).

Blood pressure, aortic diameters, and aortic elasticity were compared between healthy and CD children (Table 4). All variables were significantly different among the four groups, except AoD and AoS, with a slight but insignificant difference. In this regard, AoS ($X^2 = 15.052$, $P = 0.003$), SBP ($X^2 = 85.554$, $P < 0.001$), DBP ($X^2 = 77.783$, $P < 0.001$), AS ($X^2 = 23.927$, $P = 0.001$), AS β index ($X^2 = 44.071$, $P < 0.001$), AD ($X^2 = 13.044$, $P = 0.004$), and PSEM ($X^2 = 13.66$, $P = 0.004$) differed significantly between the groups.

Table 5 details the analysis regarding four groups in pairwise comparisons. Aortic diameter in systole differed significantly between control and no response to GFD ($P = 0.018$), control and newly diagnosed ($P = 0.003$), response to GFD and no response to GFD ($P = 0.030$), and response to GFD and newly diagnosed ($P = 0.006$) groups.

Systolic blood pressure differed significantly between control and no response to GFD ($P < 0.001$), control and response to GFD ($P = 0.013$), control and newly diagnosed ($P < 0.001$), response to GFD and no response to GFD ($P < 0.001$), and response to GFD and newly diagnosed ($P < 0.001$) groups.

Diastolic blood pressure differed significantly between control and response to GFD ($P = 0.035$), control and no response to GFD ($P < 0.001$), control and newly diagnosed ($P < 0.001$), response to GFD and no response to GFD ($P < 0.001$), and response to GFD and newly diagnosed ($P < 0.001$) groups.

Aortic strain differed significantly between control and no response to GFD ($P = 0.026$), control and newly diagnosed ($P < 0.001$), no response to GFD and newly diagnosed ($P = 0.003$), and response to GFD and newly diagnosed ($P < 0.001$) groups.

Aortic strain β index differed significantly between control and no response to GFD ($P \leq 0.001$), control and

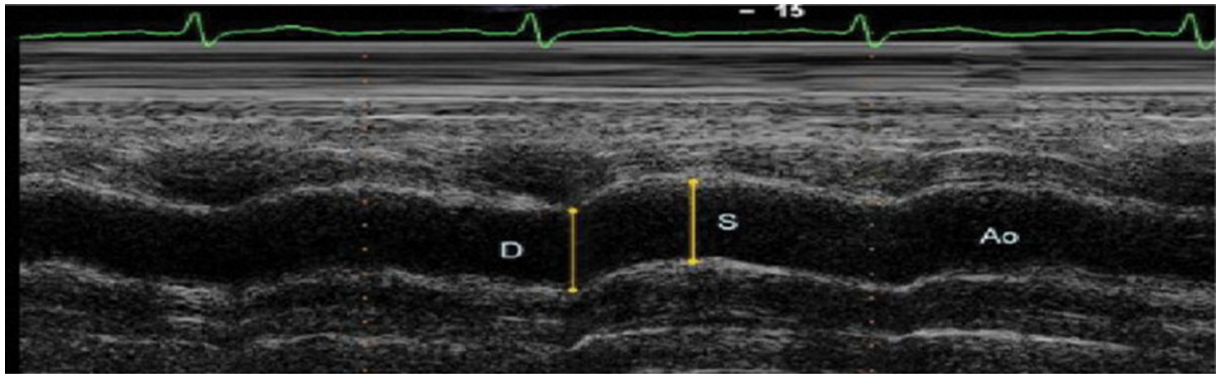


Figure 1. Measurements of systolic (AoS) and diastolic (AoD) diameters of the ascending aorta are shown on the M-mode tracing obtained at a level 3 cm above the aortic valve (17).

Table 1. Gender Distribution in Participants' Groups^a

Gender	Groups of Participants					P Value
	Control	No Response to GFD	Response to GFD	Newly Diagnosed	Total	
Girls	26 (27.1)	21 (21.9)	32 (33.3)	17 (17.7)	96 (100.0)	0.08
Boys	31 (41.3)	14 (18.7)	25 (33.3)	5 (6.7)	75 (100.0)	
Total	57 (33.3)	35 (20.5)	57 (33.3)	22 (12.9)	171 (100.0)	

^a Values are expressed as No. (%).

Table 2. Participants' Age Comparison Between Groups

Participants	N	Mean ± SD	Test Value	P Value
Control	57	9.7 ± 3.66	2.677 ^a	0.444
No response to GFD	35	8.53 ± 3.96		
Response to GFD	57	9.67 ± 3.82		
Newly diagnosed	22	8.99 ± 4.28		
Controls	57	9.7 ± 3.66	2938.50 ^b	0.308
Celiac	114	9.19 ± 3.95		
Total	171	9.36 ± 3.85		

^a Mann-Whitney test.

^b Kruskal-Wallis test.

newly diagnosed ($P < 0.001$), response to GFD and no response to GFD ($P = 0.035$), no response to GFD and newly diagnosed ($P = 0.002$), and response to GFD and newly diagnosed ($P < 0.001$) groups.

Aortic distensibility differed significantly between control and newly diagnosed ($P < 0.001$), no response to GFD and newly diagnosed ($P = 0.037$), and response to GFD and newly diagnosed ($P = 0.021$) groups.

Pressure strain elastic modulus differed significantly between control and newly diagnosed ($P < 0.001$), no response to GFD and newly diagnosed ($P = 0.037$), and re-

sponse to GFD and newly diagnosed ($P = 0.021$) groups.

5. Discussion

The present study revealed a significant decrease in AS and AD and a significant increase in PSEM and AS β index in children with CD. In pairwise comparisons, AS differed significantly between control and no response to GFD, control and newly diagnosed, no response to GFD and newly diagnosed, and response to GFD and newly diagnosed groups. Aortic stiffness β index (AS β I) differed significantly be-

Table 3. Comparison of Blood Pressure, Aortic Diameters, and Aortic Elasticity Parameters Between Children with Celiac Disease and Controls

Parameters and Groups	Mean \pm SD	P Value
AoD		0.468
Controls	1.75 \pm 0.33	
Celiac	1.69 \pm 0.29	
AoS		0.052
Controls	1.98 \pm 0.33	
Celiac	1.88 \pm 0.33	
SBP (mm Hg)		< 0.001
Controls	102.84 \pm 4.77	
Celiac	93.3 \pm 11.14	
DBP (mm Hg)		< 0.001
Controls	68.16 \pm 6.31	
Celiac	59.96 \pm 9.02	
AS (%)		0.002
Controls	13.78 \pm 6.95	
Celiac	11.15 \pm 7.47	
ASβI		< 0.001
Controls	1.44 \pm 0.51	
Celiac	1.79 \pm 0.62	
AD (cm² \times dyne\cdot1.10⁻⁶)		0.012
Controls	8.33 \pm 5.13	
Celiac	6.98 \pm 5.03	
PSEM (kPa)		0.012
Controls	330.71 \pm 216.94	
Celiac	410.6 \pm 247.45	

Abbreviations: AoD, aortic diameter in diastole; AoS, aortic diameter in systole; SBP, systolic blood pressure; DBP, diastolic blood pressure; AS, aortic strain; AS β I, aortic stiffness β index; AD, aortic distensibility; PSEM, pressure strain elastic modulus.

tween control and no response to GFD, control and newly diagnosed, response to GFD and no response to GFD, no response to GFD and newly diagnosed, and response to GFD and newly diagnosed groups. AD differed significantly between control and newly diagnosed, no response to GFD and newly diagnosed, and response to GFD and newly diagnosed groups. Pressure strain elastic modulus differed significantly between control and newly diagnosed, no response to GFD and newly diagnosed, and response to GFD and newly diagnosed groups.

In a similar study, Noori et al. (18) showed that all stiffening parameters, aortic strain, aortic stiffness β index, aortic distensibility, and pressure strain elastic modulus were significantly different between children with CD and controls. In their study, aging was one of the most significant

factors in stiffening damage. Sari et al. (19) found that AS and AD decreased and AS β I increased significantly in patients with CD. Bayar et al. (16) found an increase in AS β I and a decrease in PSEM and AD while AS retained similarities to controls. Karpuz et al. (20) concluded that AD did not change in celiac compared with healthy children, whereas AS and AS β I significantly increased in the patients. Our study showed a significant decrease in AS and AD and a significant increase in PSEM and AS β I in children with CD, inconsistent with some of the abovementioned results.

Gluten consumption causes tumult of the intestinal mucosa with hyperplasia of the crypts and atrophy of the small intestine (21). Anti-tTG titer antibodies are the primary tool to identify and rule out CD or susceptibility for further investigation with acceptable sensitivity and specificity (22). As high anti-tTG titers are significantly associated with histology changes in CD, Barker et al. (23) revealed that among symptomatic children with an anti-tTG titer of more than 100, at least one child had Marsh II enteropathies. A systematic review comparing endomysial antibodies with anti-tTG titers found that human recombinant tTG IgA antibodies screen asymptomatic individuals and rule out CD in symptomatic individuals (20). Donaldson et al. (24) revealed that children with anti-tTG titers of more than 100 were shown to have Marsh III histopathology of CD. Demir et al. (25) found many patients with CD in Marsh IIIC. It has been sought to determine the rate of mucosal recovery in CD children with GFD and found that about one-fifth of the children who received GFD did not respond to diet (26, 27). Leonard et al. (26), at the time of biopsy, found that tTG-IgA antibodies elevated in 43% of cases of persistent bowel disease and 32% of cases of mucosal recovery. They concluded that two out of 10 children with CD had persistent bowel disease despite adhering to GFD and that IgA-tTG was not an accurate marker of mucosal recovery.

Gidrewicz et al. (28) sought to determine whether the resolution of symptoms and the normalization of serology determine the response to GFD in CD. They assessed the normalization rate of tTG-IgA antibodies in children with CD who were adhering to GFD. They found that three-quarters of children adhering to GFD had tTG-IgA less than 20, which probably revealed that it would take about one year or more to normalize the celiac serology test. Alarida et al. (29) analyzed some children with CD who had a repeat small intestinal biopsy one year after GFD. They found that children in Marsh II had villous changes at diagnosis that normalized to Marsh 0 within the first year of diet, and about 86 children in Marsh III recovered within one year. In addition, about four-fifths of the CD patients recovered within two to three years, and more than 97% recovered after three years. Catal et al. (30) found that GFD signifi-

Table 4. Comparison of Blood Pressure, Aortic Diameters, and Aortic Elasticity Parameters Between Controls and Three Groups of Celiac Disease Children

Variables and Participants	N	Mean \pm SD	P Value
AoD			0.157
Control	57	1.75 \pm 0.33	
No response to GFD	35	1.63 \pm 0.25	
Response to GFD	57	1.75 \pm 0.3	
Newly diagnosed	22	1.64 \pm 0.3	
Total	171	1.71 \pm 0.3	
AoS			0.003
Control	57	1.98 \pm 0.33	
No response to GFD	35	1.8 \pm 0.26	
Response to GFD	57	1.97 \pm 0.36	
Newly diagnosed	22	1.74 \pm 0.29	
Total	171	1.91 \pm 0.33	
SBP (mm Hg)			< 0.001
Control	57	102.84 \pm 4.77	
No response to GFD	35	86.57 \pm 10.06	
Response to GFD	57	101.16 \pm 5.11	
Newly diagnosed	22	83.64 \pm 9.66	
Total	171	96.48 \pm 10.5	
DBP (mm Hg)			< 0.001
Control	57	68.16 \pm 6.31	
No response to GFD	35	54.57 \pm 8.43	
Response to GFD	57	65.81 \pm 5.16	
Newly diagnosed	22	53.41 \pm 8.08	
Total	171	62.7 \pm 9.07	
AS (%)			< 0.001
Control	57	13.78 \pm 6.95	
No response to GFD	35	11.05 \pm 6.35	
Response to GFD	57	12.96 \pm 8.55	
Newly diagnosed	22	6.65 \pm 3.1	
Total	171	12.03 \pm 7.38	
ASβI			< 0.001
Control	57	1.44 \pm 0.51	
No response to GFD	35	1.85 \pm 0.51	
Response to GFD	57	1.57 \pm 0.64	
Newly diagnosed	22	2.30 \pm 0.39	
Total	171	1.68 \pm 0.61	
AD (cm² \times dyne\cdot1.10⁻⁶)			0.004
Control	57	8.33 \pm 5.13	
No response to GFD	35	7.6 \pm 5.66	
Response to GFD	57	7.49 \pm 5.23	
Newly diagnosed	22	4.66 \pm 2.14	
Total	171	7.43 \pm 5.09	
PSEM (kpa)			0.004
Control	57	330.71 \pm 216.94	
No response to GFD	35	370.87 \pm 182.32	
Response to GFD	57	382.2 \pm 219.33	
Newly diagnosed	22	547.37 \pm 350.68	
Total	171	383.97 \pm 240.06	

Abbreviations: AoD, aortic diameter in diastole; AoS, aortic diameter in systole; SBP, systolic blood pressure; DBP, diastolic blood pressure; AS, aortic strain; AS β I, aortic stiffness β index; AD, aortic distensibility; PSEM, pressure strain elastic modulus.

cantly affected final tTG-IgA levels, which were significantly lower in patients who adhered to GFD than in those who did not comply with the diet. The tTG-IgA titers in patients exceeded 100 U/mL and decreased in patients with strict GFD. Bayar et al. (16) found significant differences in aortic elastic properties between those who adhered to GFD and those who did not.

The present study found that the AS β index and PSEM differed among the three groups. The pairwise comparisons showed that the AS β index differed significantly between control and response to GFD, control and newly diagnosed, response to GFD and no response to GFD, response to GFD and newly diagnosed, and no response to GFD and newly diagnosed groups. Aortic distensibility differed significantly between control and newly diagnosed, response to GFD and newly diagnosed, and no response to GFD and newly diagnosed groups. Pressure strain elastic modulus differed significantly between control and newly diagnosed, response to GFD and newly diagnosed, and no response to GFD and newly diagnosed groups. The difference between our results and Bayer's may be due to participants' age; as we already said, aging is the main cause of stiffening.

Based on studies, most symptoms and clinical findings improve early, and antibody titers are reduced with GFD adherence, but Bayer et al. (16) analysis showed that the aortic elastic properties were not associated with GFD. Nestel et al. (31) showed that elevated homocysteine caused a sharp increase in aortic stiffness due to increased methionine. To date, data regarding the effect of GFD on homocysteine levels in CD patients are conflicting (32). As Gefel et al. (33) show, GFD decreases homocysteine levels. On the other hand, De Marchi et al. (32) found no significant changes in homocysteine levels in patients with GFD. These results also suggest that chronic systemic inflammation decreases with GFD in CD patients and that persistent inflammation may be an essential factor in increasing CVD risk in patients who do not adhere to GFD. It would be concluded that there is no significant relationship between GFD and the elastic properties of the aorta. Therefore, impaired aortic elasticity in patients with CD is multifactorial and cannot be explained by inflammation alone. The study limitation was the small sample of newly diagnosed children with CD, which probably affected the results.

5.1. Conclusions

The present study concluded that the elasticity parameters changed due to celiac disease such that AD and AS decreased when AS β I and PSEM increased. The study also concluded that a gluten-free diet had no significant effect on all elasticity parameters except AS β I. A slight difference in the results of various studies is probably due to children's

age, as it is the most critical factor in stiffening. As a suggestion, assessing aortic elastic properties as a non-traditional cardiovascular risk factor can help identify cardiovascular risk in patients with celiac disease.

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Footnotes

Authors' Contribution: Main concept: Noor Mohammad Noori and Manijeh Khalili; data collection: Noor Mohammad Noori and Manijeh Khalili; analysis: Alireza Teimouri; drafting the manuscript: Alireza Teimouri; critical consideration: Noor Mohammad Noori.

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Data Reproducibility: The dataset presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to being part of a big database.

Ethical Approval: This study is approved under the ethical approval code of IR.ZAUMS.REC.1400.095. Link: ethics.research.ac.ir/IR.ZAUMS.REC.1400.095.

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Table 5. Mann-Whitney U Test Among the Groups for Significant Variables

Variables and Groups	P Value
AoS	
Control	
No response to GFD	0.018
Response to GFD	0.894
Newly diagnosed	0.003
No response to GFD	
Response to GFD	0.03
Newly diagnosed	0.283
Response to GFD	
Newly diagnosed	0.006
SBP (mm Hg)	
Control	
No response to GFD	< 0.001
Response to GFD	0.013
Newly diagnosed	< 0.001
No response to GFD	
Response to GFD	< 0.001
Newly diagnosed	0.26
Response to GFD	
Newly diagnosed	< 0.001
DBP (mm Hg)	
Control	
No response to GFD	< 0.001
Response to GFD	0.035
Newly diagnosed	< 0.001
No response to GFD	
Response to GFD	< 0.001
Newly diagnosed	0.579
Response to GFD	
Newly diagnosed	< 0.001
AS (%)	
Control	
No response to GFD	0.026
Response to GFD	0.206
Newly diagnosed	< 0.001
No response to GFD	
Response to GFD	0.401
Newly diagnosed	0.003
Response to GFD	

Newly diagnosed	< 0.001
ASβ1	
Control	
No response to GFD	< 0.001
Response to GFD	0.053
Newly diagnosed	< 0.001
No response to GFD	
Response to GFD	0.035
Newly diagnosed	0.02
Response to GFD	
Newly diagnosed	< 0.001
AD (cm² × dyne·1.10⁻⁶)	
Control	
No response to GFD	0.128
Response to GFD	0.19
Newly diagnosed	< 0.001
No response to GFD	
Response to GFD	0.936
Newly diagnosed	0.037
Response to GFD	
Newly diagnosed	0.021
PSEM (kpa)	
Control	
No response to GFD	0.128
Response to GFD	0.19
Newly diagnosed	< 0.001
No response to GFD	
Response to GFD	0.936
Newly diagnosed	0.037
Response to GFD	
Newly diagnosed	0.021

Abbreviations: AoS, aortic diameter in systole; SBP, systolic blood pressure; DBP, diastolic blood pressure; AS, aortic strain; AS β 1, aortic stiffness β index; AD, aortic distensibility; PSEM, pressure strain elastic modulus.