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Original Article

Metabolic Syndrome in Celiac Disease: What Does Following a One-Year Gluten-Free Diet Bring?

Nasrin Motazedian[1], Mehrab Sayadi[2], Amirali Mashhadiagha[1], Seyed Ali Moosavi[1], Fatemeh Khademian[1], Ramin Niknam[3]*

[1]Transplant Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Cardiovascular Research Centre, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Gastroenterohepatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Abstract

Background: Metabolic syndrome (MetS) is a set of conditions that occur together and increase the risk of cardiovascular disease. Previous studies have linked a gluten-free diet (GFD) to obesity and MetS in some populations. However, others have suggested that weight gain is usually regulated only in underweight individuals with celiac disease (CD). Owing to the lack of sufficient data and the importance of GFD in controlling cardiovascular disease, we surveyed the prevalence of MetS and its components before and after a year of GFD in patients referred to the main celiac clinic in southern Iran.

Methods: This was a repeated cross-sectional study conducted on 69 patients with a definite diagnosis of cardiovascular disease who were on follow-up and registered at the Shiraz Celiac Clinic. Demographic, anthropometric, and laboratory measurements at the time of diagnosis and one year after the GFD were extracted from their medical records.

Results: The participants' mean age was 35.53, and 68.1% were women. The prevalence of MetS increased from 5.8% to 11.6% after a year of the GFD; however, this increase was not statistically significant. Waist circumference (WC) and serum triglyceride levels were significantly elevated during the study period.

Conclusion: A GFD may contribute to the development of MetS in patients with cardiovascular disease; however, the rate of MetS is still lower than that in the general population. It is critical to educate patients about these potential risks and encourage them to have a healthy lifestyle that includes a balanced diet and physical activity.

Keywords: Metabolic syndrome, Gluten-free, Diet, Celiac disease

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Introduction

Metabolic syndrome (MetS) is a set of metabolic states that include at least three of the following five components: abdominal obesity, impaired glucose tolerance, hypertriglyceridemia, lower levels of high-density lipoprotein cholesterol, and hypertension. This is a common phenomenon, particularly in Asian countries.[1,2]

In recent years, MetS has become more prevalent, probably due to changes in lifestyle, social and economic status, and eating habits.[3] As mentioned, MetS is more widespread in the Asia-Pacific region, with the lowest and highest percentages among Filipinos (11.9%) and Pakistan (49.0%), respectively.[4] A meta-analysis showed that 34.8% of Iranian women and 25.7% of men fulfilled the MetS criteria, and this difference in sex was significant. Previous studies have reported an increase in MetS with age and higher rates in the female sex.[5,6] The prevalence of MetS in Shiraz is estimated to be 16.6% in men, which is significantly lower than that in women (36.8%).[7]

Celiac disease (CD) usually presents with symptoms of malabsorption, immune activation, and autoantibodies. It can be diagnosed through the presence of gastrointestinal and/or extra-gastrointestinal manifestations as well as paraclinical examinations. It is a unique autoimmune disease that is stimulated by dietary gluten, and the most effective way to control the symptoms and eliminate autoantibodies is by following a gluten-free diet (GFD).[8]

Numerous studies have indicated that weight changes are common in patients with CD after starting a GFD; however, the correlation between the establishment of MetS after initiating a GFD has not been well studied in different populations.[9] According to a prospective study, the prevalence of MetS increases from 2% at the time of diagnosis to 30% after a year on GFD.[9] In contrast, CD commonly leads to undernutrition and low weight in both children and adults.[10] At the same time, some other studies found that up to 44% of patients with CD were overweight or obese at the diagnosis.[11,12] Another study on underweight patients showed a tendency to gain weight on a GFD at the time of diagnosis; 22% to 82% of overweight and obese patients gain weight on a GFD.[13]

Given the importance of GFD in the control of CD and the considerable sequelae of MetS, as well as the high prevalence of these two diseases, well-designed studies on this issue are necessary.

Due to the lack of sufficient data and consensus, we

*Corresponding Author: Ramin Niknam, Email: niknamramin@yahoo.com

decided to investigate the prevalence of MetS and its components before and after a GFD treatment in patients referred to the main celiac clinic in southern Iran.

Materials and Methods

Study Population

This was a repeated cross-sectional study conducted on 69 patients with a definite diagnosis of CD who were on follow-up and registered at the Shiraz Celiac Clinic, Iran. Eligible patients were at least 18 years of age and were on a GFD for one year of follow-up between January 2018 and January 2019. The medical records of eligible patients were extracted from the Fars Celiac Registry database (Approval ID: IR.SUMS.REC.1397.557) using the census method. The data were recorded at the time of diagnosis of CD and one year after being fed a GFD. The exclusion criterion was incomplete data. Finally, 69 participants aged 18–71 years were included in the study.

Data Collection

All participants were on regular visits by a gastroenterologist and nutritional counseling every three or six months. Lipid profile, fasting blood sugar (FBS), blood pressure, and anthropometric measures, including waist circumference (WC), height, and weight, were recorded at the time of diagnosis and one year after diagnosis. Data regarding this study were extracted from medical records.

The CD was diagnosed based on positive anti-tTG results and small bowel biopsies.[14,15] The CD was defined as anti-tTG > 18 international units/mL or higher and Marsh type 2 or more on histology according to the Oberhuber-modified Marsh classification.[16]

At the time of diagnosis, all patients consumed gluten, and the interval between bowel biopsy and the anti-tTG test was less than one month. MetS was labeled based on the Adult Treatment Panel III (ATP III) criteria, in which a person must meet at least three of the following criteria to be considered as a patient with MetS: (WC > 102 cm in men or > 88 cm in women, blood pressure > 130/85 mm Hg, fasting triglyceride (TG) level > 150 mg/dL, fasting high-density lipoprotein (HDL), cholesterol level less than 40 mg/dL in men or 50 mg/dL in women, and FBS > 110 mg/dL.[17]

Statistical Analyses

Data are presented as the mean ± SD or number (%) for continuous and discrete variables. To compare the before and after means of the variables, we used a paired sample t-test. The McNemar test was used to compare the prevalence of MetS and its abnormalities, and data analysis was performed using the SPSS software for Windows, version 21.0. Chicago, SPSS Inc. A significance level of 5% was considered for all tests.

Results

A total of 69 individuals with a mean age of 31.13 ± 12.73 participated in this study, of which 68.1% were women. The demographic characteristics and primary data are listed in Table 1. Of the patients, 27.6%, 39.1%, and 33.3% had under high school diplomas, high school diplomas, and college education levels, respectively. Most of them lived in urban areas.

The mean (standard deviation) of each component of MetS, body mass index, and *P* value before and after the GFD and their changes are also shown in Table 2.

Based on the paired sample t-test, the mean changes in WC ($P=0.001$) and TG ($P=0.027$) were statistically significant. On the other hand, both variables increased after one year following the GFD.

There were no significant differences in the mean HDL ($P=0.852$), systolic blood pressure ($P=0.142$), diastolic blood pressure ($P=0.418$), and FBS ($P=0.210$) before and after the GFD. tTG IgA levels were dramatically reduced after starting the GFD ($P<0.001$). We obtained the percentage of relative change by dividing the change by the previous value multiplied by 100. The mean relative changes in MetS components are summarized in Figure 1. The most remarkable changes were attributed to TG levels, which showed an increasing trend. On the other hand, diastolic blood pressure changed the least and declined. The prevalence of MetS and its components before and one year after the GFD is shown in Table 3 and Figure 2. It should be mentioned that MetS prevalence did not change significantly after one year of GFD ($P=0.289$).

Discussion

A GFD consists of products with a high glycemic index and little dietary fiber. These foods contain several simple carbohydrates and fats. These elements contribute to the development of MetS.[18] This study investigated the prevalence and characteristics of MetS and its components after a course of a GFD in patients with CD in Southern Iran.

Table 1. Demographic characteristics of the patients with celiac disease on gluten-free diet

Variables		Mean ± SD or number (%)
Number		69 (100)
Current age (y)		35.53 ± 11.53
Age at diagnosis time (y)		31.13 ± 12.73
Gender (female)		47 (68.1)
Number of siblings (median, min–max)		4 (0 – 10)
Education	Under diploma	19 (27.6)
	Diploma	27 (39.1)
	University	23 (33.3)
Residency (n, %)	Urban	61 (88.4)
	Rural	8 (11.6)
Housing situation	Proprietary	48 (69.6)
	Leased	18 (8.7)
	Others	3 (4.3)
Monthly household Income, Rails (per million)	≤15	42 (60.9)
	>15	27 (39.1)

Table 2. Components of metabolic syndrome at diagnosis time of celiac disease and one year after being on a gluten-free diet (n=69)

Variables	Before Mean±SD	After Mean±SD	Change Mean±SD	*P* value*
WC (cm)	83.44±15.46	85.40±15.01	1.95±4.77	0.001
TG (mg/dL)	94.68±30.51	107.73±51.35	13.05±47.96	0.027
HDL (mg/dL)	50.28±21.61	49.70±13.49	-0.58±25.91	0.852
SBP (mmHg)	111.15±16.1	109.92±13.21	-2.39±13.3	0.142
DBP (mmHg)	68.55±11.15	67.97±11.45	-0.5±5.9	0.418
FBS (mg/dL)	94.68±13.76	98.69±30.08	4.01±26.35	0.210
BMI (kg/m²)	23.61±5.64	23.52±5.53	-0.09±1.86	0.684
TTG IgA (U/mL)	216.37±212.88	28.93±69.90	-174.39±199.68	<0.001

WC: waist circumference; TG: triglyceride; HDL: high density lipid; FBS: fasting blood sugar; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: Body mass index; TTG IgA: tissue transglutaminase IgA.
*The *P* value is calculated using paired-samples *t* test.

Table 3. Prevalence of metabolic syndrome and change of its components among patients with celiac disease before and after one year of a gluten-free diet (n=69)

Variables	Before Number (%)	After Number (%)	*P* value
WC	23 (33.3)	24 (34.8)	>0.999
TG	2 (2.9)	12 (17.4)	0.013
HDL	44 (63.8)	44 (63.8)	>0.999
HTN	6 (8.7)	6 (8.7)	>0.999
FBS	9 (13.0)	5 (7.2)	0.219
MetS	4 (5.8)	8 (11.6)	0.289

WC: waist circumference; TG: triglyceride; HDL: high density lipoprotein; FBS: fasting blood sugar; HTN: hypertension; MetS: metabolic syndrome.

Of the 69 patients with CD included in this study, 4 (5.8%) had MetS at baseline. There was a further increase in the prevalence of MetS, with 8 of 69 patients (11.6%) having features of MetS one year after the initiation of GFD. Additionally, a meta-analysis of the prevalence of MetS in Iran showed that the overall prevalence of MetS was 30.4%. They reported that MetS was more prevalent in women (34.8%) than in men (25.7%).[5] A comparison of our findings with the mentioned prevalence in the normal population showed that people with CD had a lower prevalence of MetS before and after starting a GFD in Iran. In a study of 840 patients with CD, the prevalence of MetS was significantly lower in patients with CD than

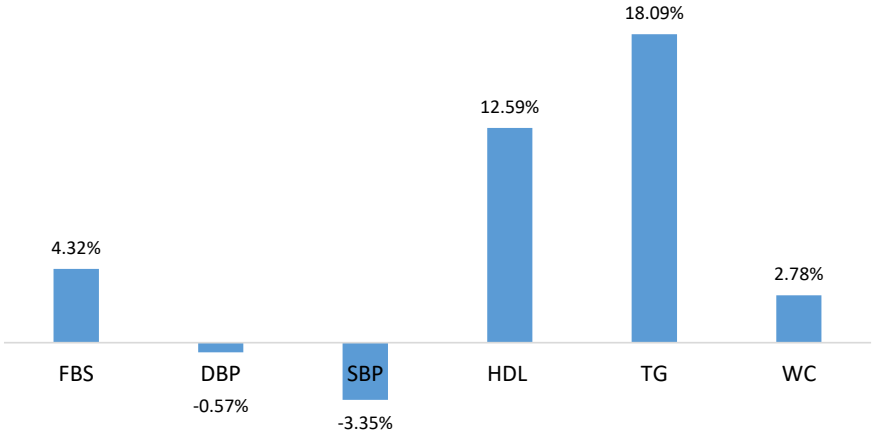

Figure 1. Mean percentage of relative changes in metabolic syndrome components after one year of following a gluten-free diet (n=69). WC: waist circumference; TG: triglyceride; HDL: high density lipid; FBS: fasting blood sugar; SBP: systolic blood pressure; DBP: diastolic blood pressure

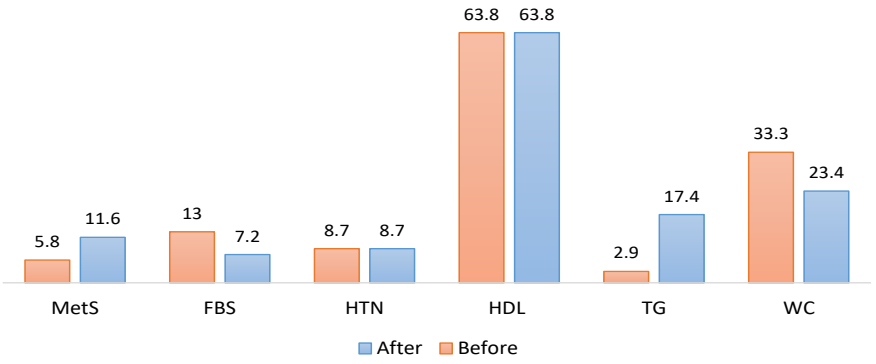

Figure 2. Prevalence (%) of metabolic syndrome and its components before and after one year of a gluten-free diet (n=69). WC: waist circumference; TG: triglyceride; HDL: high density lipoprotein; FBS: fasting blood sugar; HTN: hypertension; MetS: metabolic syndrome

in controls (3.5% vs. 12.7%).[19] Furthermore, in a study of 98 newly diagnosed patients conducted by Tortora et al,[9] the number of individuals diagnosed with MetS increased after one year of GFD. Moreover, similar findings were reported by Italian researchers who enrolled 185 patients in their study. MetS was diagnosed in 3.24% of participants at the time of diagnosis, and the number of patients with MetS increased to 14.59% after introducing a GFD.[20] These findings are consistent with our findings.

Our results showed that the baseline BMI of patients with CD was 23.61, which is lower than the average BMI in Iran (26.2).[21] This is in line with the study by Kabbani et al, which indicated that the mean BMI of patients with CD was significantly lower than that of the controls (24.7 vs. 27.5). This may be due to the malabsorptive nature of CD.[19] However, Cheng et al showed a bipartite effect of GFD, which helps underweight patients gain weight, and overweight/obese patients lose weight.[22]

In the current study, WC and TG were significantly higher one year following a GFD. However, there were no significant differences in other variables before and after the GFD, including BMI. A retrospective cohort study of 185 patients with CD from Italy found an increase in TG and WC after adherence to a GFD, which is consistent with our results. However, BMI > 25 was significantly higher after GFD than at baseline at CD diagnosis.[20] This inconsistency could be attributed to differences in lifestyle, such as food culture and physical activity. Furthermore, previous research has linked an inadequately balanced GFD to an increase in total cholesterol, LDL, and TG and a decreased concentration of HDL fraction, which is consistent with our findings.[20,23,24] In contrast, in a study by Kabbani et al, the incidence of dyslipidemia was significantly lower than that in the control group (18.3% vs. 34.9%).[19] Moreover, in a randomized control trial of 50 subjects diagnosed with MetS without CD, compared with short-term GFD and regular diet, the GFD group showed a significant reduction in FBS, WC, and TG compared with the control.[25] It is also worth noting that in a recent study of 155 GFD followers without CD in the United States, it was concluded that being on a GFD may be beneficial in weight management; however, there was no significant difference in the prevalence of MetS in GFD followers without CD.[26] In summary, in our research, one year after the onset of GFD, all five components of MetS changed in favor of this syndrome, although these changes were only significant in increasing WC and TG levels (Figure 1 and Table 2). Due to the gradual nature of MetS, a longer follow-up of participants may show more significant changes in other components.

These conflicting findings in different studies on the effect of GFD on MetS components in patients with CD should be further investigated. It is also crucial to note that the metabolic profile of patients with CD, and of each individual in general, is influenced by factors other than nutrition, such as heredity, lifestyle, and physical activity.

This study has some limitations. It was performed at a single center without a control group, and the follow-up of patients was only for one year. Therefore, multicenter studies with long-term follow-up are recommended, considering the control group.

Conclusion

A GFD may contribute to the development of MetS in patients with CD; however, the rate of MetS is still lower than that in the general population. It is critical to educate patients about these potential risks and encourage them to have a healthy lifestyle that includes a balanced diet and physical activity. Other studies with longer follow-up periods and more patients with CD are needed to investigate the effects of GFD on MetS.

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Authors' Contribution

Conceptualization: Nasrin Motazedian, Ramin Niknam, Fatemeh Khademian.
Data curation: Nasrin Motazedian, Ramin Niknam, Mehrab Saydai.
Formal analysis: Mehrab Sayadi.
Funding acquisition: Ramin Niknam.
Investigation: Nasrin Motazedian, Ramin Niknam, Mehrab Saydai, Mashhadiagha, Seyed Ali Mosavi, Fatemeh Khademian.
Methodology: Nasrin Nasrin Motazedian, Ramin Niknam, Mehrab Saydai, Fatemeh Khademian, Amirali Mashhadiagha, Seyed Ali Mosavi.
Project administration: Motazedian, Ramin Niknam.
Resources: Ramin Niknam.
Software: Mehrab Sayadi.
Supervision: Ramin Niknam, Nasrin Motazedian.
Validation: Nasrin Motazedian, Ramin Niknam, Mehrab Saydai, Amirali Mashhadiagha, Seyed Ali Mosavi, Fatemeh Khademian.
Visualization: Nasrin Motazedian, Ramin Niknam, Mehrab Saydai, Amirali Mashhadiagha, Seyed Ali Mosavi, Fatemeh Khademian.
Writing–original draft: Nasrin Motazedian, Amirali Mashhadiagha, Mehrab Sayadi, Seyed Ali Mosavi, Fatemeh Khademian.
Writing–review & editing: Nasrin Motazedian, Mehrab Saydai, Amirali Mashhadiagha, Seyed Ali Mosavi, Fatemeh Khademian.

Competing Interests

The authors declare no conflict of interest related to this work.

Ethical Approval

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (Approval ID: IR.SUMS.REC.1398.1164).

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