



Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Prediabetes and gastrointestinal (GI) symptoms; a cross-sectional study

Akram Ghadiri-Anari ^a, Somaye Gholami ^a, Fariba Zolfaghari ^b, Nasim Namirani ^{a,*}^a Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran^b Medical Student, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

ARTICLE INFO

Article history:

Received 19 November 2018

Accepted 7 December 2018

Keywords:

Abdominal symptoms
Gastrointestinal
Prediabetes
Diarrhea
Constipation
Impaired fasting glucose

ABSTRACT

Aims: Prediabetes associate with known micro and macrovascular complications of diabetes. Also gastrointestinal symptoms are present in diabetics higher than general population. The aim of this study was evaluation of gastrointestinal symptoms in subjects with prediabetes.

Methods: This analytical cross-sectional study was conducted on 130 persons 30–65 years old, 65 pre-diabetic patients and 65 persons without glucose disorders from 2014 to 2015 in YAZD province. FBS and HbA1c used for diagnosis prediabetes. Demographic and medical history were collected. A questionnaire according to Rome III Criteria was used to collect digestive information (diarrhea, abdominal pain, constipation, abdominal bloating, heartburn, increased gas passing, nausea, intermittent diarrhea and constipation in the last 6 months ago). Frequency of GI symptoms in subjects with and without glucose disorders were compared. Data were analyzed by SPSS software Version 20. Data were reported as mean \pm standard deviation or frequency and T-test, Chi Square and Spearman correlation coefficient tests were used. P-value less than 0.05 were considered statistically significant.

Results: Higher frequency of bloating, early satiety, nausea, heartburn, gas passing and constipation are seen in the pre-diabetes group than in the control group; (p-value 0.0001, 0.0001, 0.0001, 0.0001, 0.001 and 0.0001 respectively). 96.9% in prediabetics had at least one gastrointestinal symptom, while in the normal groups 50% had at least one GI symptom (p-value: 0.0001).

Conclusions: Gastrointestinal symptoms were seen in prediabetics higher than healthy persons. So, prediabetes can not be considered an entirely benign and asymptomatic condition. Lifestyle interventions maybe necessary at this state.

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1. Introduction

Prediabetes is a state between normal glucose tolerance and diabetes. It is a risk for developing diabetes. Prediabetes is more prevalent than diabetes, also is associated with cardiovascular mortality and morbidity [1]. The incidence of prediabetes in a cohort study in Isfahan was 32.3 per 1000 person-years [2].

Gastrointestinal (GI) symptoms are reported more common in people with diabetes than in the general population. The prevalence of GI symptoms is more than 70% in outpatient studies on diabetic patients [3–7].

GI symptoms are an important cause of morbidity in diabetic patients, although the relationships of GI symptoms with glycemic status remain unclear. Rare studies focus on GI system as a therapeutic target for glucose lowering [8]. So knowledge of GI presentation of diabetes seems necessary. GI symptoms decrease quality of life in diabetic patients [9,10].

Probable pathogenesis of GI symptoms in diabetes includes; autonomic and peripheral neuropathy [11], structural and functional central nervous system changes [12,13], acute and chronic hyperglycemia [14], psychological distress [15], and medical therapy.

Prediabetes is commonly an asymptomatic condition before the onset of diabetes. Also association between prediabetes and chronic complications of diabetes such as nephropathy, neuropathy, retinopathy and risk of macrovascular disease are reported [16]. The elevation of blood sugar is a range and prediabetes is not an entirely benign condition. So some GI complaints maybe present

* Corresponding author. Yazd Diabetes Research Center, Shahid Sadoughi University of medical sciences, Yazd, Iran.

E-mail addresses: namirani.nasim@gmail.com, N_namirani@ssu.ac.ir (N. Namirani).

in prediabetes state.

Therefore due to high prevalence of prediabetes (11.9%) in Yazd province [17] and high prevalence of GI symptoms in diabetic patients and no data in prediabetes state, this study performed. The aim of this study was to compare the frequency of GI symptoms in prediabetes patients and healthy subjects.

2. Methods and materials

2.1. Study population and data collection

This analytical cross-sectional study was conducted from 2014 to 2015 on 130 subjects. The studied sample contains; 65 normal people without glucose disorders as control group and 65 prediabetic patients. All of subjects were between 30 and 65 years old. They were selected from Yazd diabetes research center patients. The sampling method was convenient. Pre-diabetes was defined accordance with the American Diabetes Association (ADA2018); fasting plasma glucose between 100 and 125 mg/dl and HbA1c between 5.7 and 6.4% [18]. The exclusion criteria in control group were diabetes mellitus, pre-diabetes, presence of hypertension or hyperlipidemia, history of ischemic heart disease or stroke, renal failure, mental disorders, treatment with antihypertensive or anti-hyperlipidemia medications.

After selecting samples, demographic data and medical history were collected by researcher. A questionnaire according to Rome III Criteria was used to collect GI symptom information related to diabetes [19]. This GI symptoms include diarrhea, abdominal pain, constipation, abdominal bloating, heartburn, increased gas passing, nausea, intermittent diarrhea and constipation in the last 6 months ago based on a pre-determined checklist completed.

All tests were conducted at the Diabetes Center Laboratory. Blood chemistry tests such as Fasting Plasma Glucose (FPG), was analyzed using an auto analyser BA-400(Bio systems, European), and commercially available kits were used according to the manufacturer's instructions. HbA1C was measured by high-performance liquid chromatography on a Diamat Analyser (Bio-Rad, München, Germany).

Finally frequencies of GI symptoms in subjects with and without glucose disorders were compared.

2.2. Research ethics

This research was presented to the ethics committee of Shahid Sadoughi University of Medical Sciences and approved by the internal medicine department. The ethics committee approved the study with the number IR.SSU.MEDICINE.REC.1394.234. The patients were informed about the objective and nature of the study, and each participant provided written consent prior to the study.

3. Statistical analyses

The sample size was calculated according $\alpha = 0.05$ and $\beta = 0.2$ and comparison of two proportion formula. Data analysis was performed using SPSS software Version 20. Data were reported as mean \pm standard deviation or frequency and T-test, Chi Square and Spearman correlation coefficient tests were used. P-value less than 0.05 were considered statistically significant.

4. Results

In this study, 130 participants were included. The mean (\pm SD) age of subjects was 41.54 (\pm 8.6) years old. Most of them 95 (73.1%) were female. The baseline characteristics of studied groups are presented in Table 1. Also distribution and comparison of GI

Table 1

Baseline characteristics of participants with prediabetes and control groups

Variable	Prediabetes	Normal	p- value
Age (Mean \pm SD)	41.88 \pm 10.06	38.73 \pm 7.55	0.063
Sex (female) N%	50 (76.9%)	45 (69.23%)	0.429
BMI(kg/m ²)	29.71 (\pm 3.78)	28.62 (\pm 3.89)	0.106

symptoms in prediabetes and normal groups are presented in Table 2.

GI symptoms such as: bloating, early satiety, nausea, heartburn, gas passing and constipation are significantly higher in the prediabetes group than in the control group; (p-value 0.0001, 0.0001, 0.0001, 0.0001, 0.001 and 0.0001 respectively).

Among the 65 prediabetes patients, 96.9% (n = 63) had at least one GI symptom, while in the normal groups was 50% (n = 33) (p-value: 0.0001).

5. Discussion

In this study, bloating, early satiety, nausea, heartburn, gas passing and constipation were more prevalent in prediabetes patients than healthy persons.

In some studies, nausea, abdominal pain, vomiting, early satiety, bloating, dysphagia, regurgitation, heartburn, epigastric or abdominal pain, abdominal distension, constipation, diarrhea, and fecal incontinence were commonly reported symptoms in diabetic patients [20–23].

The rationale for treatment of prediabetes includes prevention of progression to diabetes, prevention of diabetes and prediabetes complications [16]. Association between prediabetes and other complications of diabetes were seen previously [16], but there are few studies in prediabetes patients regarding GI symptoms.

Delay in gastric emptying was seen in prediabetes patients [24] but no differences in gastric emptying or esophageal motility were seen between individuals with and without diabetes that is surprising finding in this article [24]. Explanation of authors for this finding is relatively good HbA1c control in diabetic groups, mean diabetes duration of 10 years with minor signs of peripheral neuropathy. So it is likely that they were also unaffected by autonomic neuropathy. However in prediabetes, delay of gastric emptying cannot be explained by autonomic neuropathy itself. More likely, hyperglycemic excursions reported important cause for this phenomenon by authors [24].

In another study, gastric *Helicobacter pylori* infection was not associated with prediabetes in a Taiwanese population [25]. Positive association between diabetes mellitus and *Helicobacter pylori* infection was seen in this study [25]. In our study, we did not assess this infection.

This study had several limitations. First, it was cross-sectional

Table 2

Comparison of GI symptoms in participants with prediabetes and control groups

GI symptoms	Prediabetes	Normal	p-value
Bloating	37 (56.9%)	6 (9.2%)	0.0001
Early satiety	25 (38.5%)	7 (10.8%)	0.0001
Nausea	24 (36.9%)	7 (10.8%)	0.0001
Heartburn	42 (64.6%)	20 (30.8%)	0.0001
Upper Abdominal Pain	4 (6.2%)	2 (3.1%)	0.341
Gas Passing	20 (30.8%)	5 (7.7%)	0.001
Diarrhea	4 (6.2%)	4 (6.2%)	0.641
Constipation	45 (69.2%)	11 (16.9%)	0.0001
Intermittent Diarrhea and Constipation	4 (6.2%)	9 (13.8)	0.121
At least one of the GI symptom	63 (96.9%)	33 (50%)	0.0001

and the nature of study did not allow for finding causal relationship. Also using oral glucose challenge test with FBS and HbA1c may be helpful for definite diagnosis of prediabetes. But the sample size was calculated according formula and the power of study is acceptable.

In conclusion, it seems that some GI symptoms were seen in prediabetes higher than healthy people. Although, the elevation of blood sugar in prediabetes state is mild but it is a continuum and hence prediabetes could not be considered an entirely silent and benign condition. So some GI complaints maybe present in prediabetes. It is necessary to advise prediabetes patients to lifestyle intervention programs for slowing or reversing this state.

Conflicts of interest

None of the authors have any potential conflict of interests associated with this research.

Acknowledgments

Great thanks to the Yazd Diabetes Research Center, Shahid Sadoughi University of Medical Science for the support and providing the facilities for this work. The authors declare that there is no conflict of interest.

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