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Original Research Article

The Frequency of Gastroesophageal Reflux Symptoms in Patients with Type 2 Diabetic Neuropathic Pain

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Abstract: In our country, the prevalence of Type 2 diabetes mellitus (T2DM) is increasing. In some studies, gastrointestinal symptoms are reported to be higher in patients with T2DM. In our study, we planned to examine the relationship between diabetic neuropathy and Gastroesophageal reflux (GER) in T2DM. 106 patients with T2DM whose electromyography had been already performed and who were admitted to our hospital between January 2014 – April 2014 were included in the study. Patients were divided into two groups – those with diabetic peripheral neuropathy and those without peripheral neuropathy. The Belafsky reflux questionnaire which had been adapted to the Turkish language was performed face-to-face. The mean age of patients was found to be 55.4±11.4 (31-85) years. In all, 55.7% of patients (n=59) were female. 36.8% of the patients had neuropathy. In cases those patients with and without neuropathy the frequency of pyrosis [20.5% (n=8/39) and 10.4% (n=7/67), respectively p=0.162) and regurgitation (23.1% (n=9/39) and 10.4% (n=7/67), respectively p=0.096] were not statistically significant difference. The data of present study shows that there is no relationship between the development of peripheral neuropathy and GER symptoms in this diabetic patients cohort.

Keywords:diabetes, Gastroesophageal reflux disease, neuropathy

INTRODUCTION

The incidence of Type 2 DM is on the increase in our country which is ranked first in terms of diabetic prevalence among all European countries, according to the International Diabetes Federation Sixth Atlas. It is also anticipated as likely be one of the top ten countries relating the incidence of Type 2 DM in 2035[1]. Studies in our country support this data as well. The prevalence of Type 2 DM was found to be 7.2% in the TURDEP-1 study carried out between 1997 and 1998, while it was 13.2% in the TURDEP-2 study, using the same method[2, 3].

The symptoms of gastrointestinal system (GIS) are known to be common in patients with diabetes. Studies report that GIS symptoms are more common than in controls and have a wide range of severity, depending on the population selected and methodology[4, 5]. This leads to a reduced quality of life, as well labor loss. In gastroesophageal reflux (GER), it is also known that the major pathophysiological mechanisms include the delayed discharge of stomach contents and reduced pressure at the gastroesophageal junction. Although not fully elucidated, it is believed that the underlying cause of GIS symptoms may originate from motor dysfunction in patients with Type 2 DM. It may be a reasonable suggestion that diabetic neuropathy, a complication in prolonged diabetes, could lead to motor dysfunction. However, some researchers indicate that increased GIS symptoms in diabetic patients are not associated with diabetic neuropathy, but with psychiatric diseases already present in these patients[6, 7]. In the present study, we aimed to examine the frequency of GER symptoms in diabetic neuropathy

and its association with peripheral neuropathy in Type 2 DM.

MATERIAL AND METHODS

In this prospective cross-sectional questionnaire study, 106 patients with Type 2 DM were enrolled, all of which had already undergone EGM and been seen at the General Internal Medicine Outpatient Clinic in the Department of Internal Diseases, Fırat University Hospital, between January 2014 and April 2014. Patients who had previous angina attacks, any known coronary artery disease, chronic obstructive respiratory disease, asthma and sinusitis, as well as those who currently used any nitrate, calcium channel blocker, β-blocker, anticholinergic drugs, proton-pump inhibitor, histamine-2 receptor antagonists and non-steroid anti-inflammatory drugs were excluded from the study. All the patients were divided into groups with and without any diabetic peripheral neuropathy as proven by EMG. Voluntary consent forms were obtained from all the patients. Information about age, gender, and body mass index (BMI) was recorded. The Reflux Disease Questionnaire was applied to each patient in person and this was prepared by Belafsky *et al.;* and translated into the Turkish language[8]. Prevalence of pyrosis and regurgitation was compared between the groups with and without neuropathy. Any association between pyrosis and regurgitation frequencies and diabetic neuropathy was examined.

STATISTICAL ANALYSES

All data entries and statistical analyses were performed using SPSS for Windows 20.0 (SPSS Inc., Chicago, Illinois, USA) software. Numerical variables were presented via the mean ± standard deviation. In order to make a comparison between the two groups in terms of mean values, independent two-sample t-tests were used. Categorical variables were analyzed by using a chi-square test. Any p values under 0.05 were considered statistically significant.

FINDINGS

The mean age of 106 patients with Type 2 diabetes mellitus was found to be 55.56 ± 11.35 years (range 31 to 85 years). Fifty-nine of the patients were female (55.6%), whereas 47 were male (44.3%). Thirty-nine of the patients had diabetic neuropathy detected by EMG (36.79%), while 67 patients did not have any neuropathy (63.21%). When comparing both the patient groups, with and without diabetic neuropathy, there were significant differences in their characteristics, such as age (60 ± 11 vs. 53 ± 10 years and p=0.002) and disease duration (15.9 ± 6.7 vs. 11.9 ± 4.6 years and p=0.001). But the other demographic characteristics, such as height, weight and BMI, made no significant difference between the two groups (Table 1).

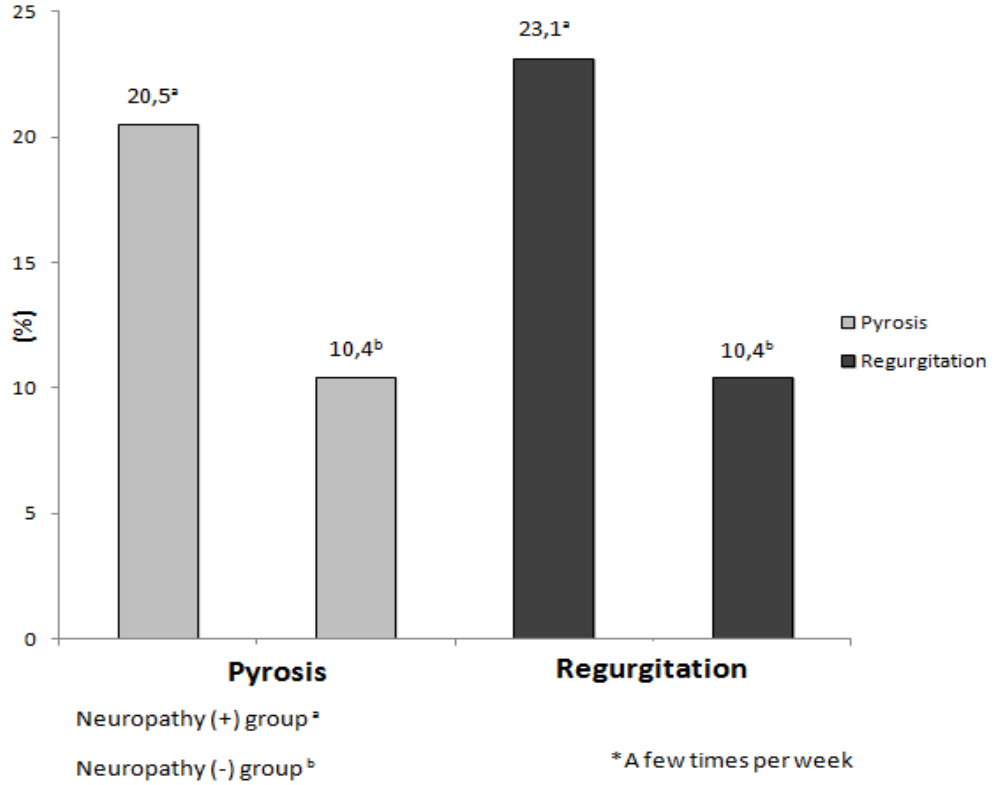

Fig 1: Patients with and without neuropathy and frequency of pyrosis and regurgitation

Table 1: Demographic characteristics

	NEUROPATHY (+) (n=39)	NEUROPATHY (-) (n=67)	P value
Age	60±11	53±10	0.002
DM duration	15.9±6.7	11.9±4.6	0.001
Height(cm)	163±10.5	162±9.8	0.58
Weight (kg)	86.1±17.3	82.8±15.6	0.32
BMI(kg/m^2)	32.5±6.9	31.6±5.8	0.49

Regarding the evaluation of the incidences per week of pyrosis and regurgitation which are the dominant symptoms of GER, we found 20.5% (n=8/39) and 23.1% (n=9/39), respectively, in patients with diabetic neuropathy. However, in patients without diabetic neuropathy, pyrosis and regurgitation were 10.4% (n=7/67) and 10.4% (n=7/67), respectively (Figure 1). There was no statistically significant difference between the frequencies of pyrosis and regurgitation (p=0.53).

DISCUSSION

The prevalence of Type 2 diabetes mellitus is increasing both in our country and all over the world. According to projections, it has been estimated that the number of patients with Type 2 diabetes mellitus between the ages of 20 and 79 will reach 439 million from the current number of 285 million by the year 2030 all over the world[9]. In our country and across the world, the number of patients with Type 2 DM is rapidly increasing, and the TURDEP-2 study carried out in 2010 revealed that 13.2% of the population had Type 2 DM[2, 3]. The direct annual cost of a diabetic without any complications was calculated as approximately 400 U.S. dollars, according to a multicentre Diab Cost study which was performed in 1993 in Turkey. As for diabetics with complications, the cost was calculated as being four times higher than of those without complications[10], suggesting that the treatment of Type 2 DM constitutes a considerable percentage of health expenditures within our country.

Complaints about GIS are more common in patients with Type 2 DM as compared to the normal population and these complaints adversely affect quality of life. About 75% of patients with Type 2 DM attend hospitals with GIS complaints[11]. Changes in dietary habits and increased obesity also increase the frequency of GER. However, in our study, we did not find any significant difference in terms of BMI between the groups with and without GER. The frequency for GER was estimated as ranging from between 8.7% and 33.1% in the Middle East where our country is located[12]. In a study of the disease's prevalence, it was found to be 20% in Turkey[13]. There are limited data on the frequency of laryngo esophageal reflux (LER) which is considered as a variant of GER disease in patients with Type 2 DM. In another study, LER frequency was found to be increased in patients with Type 2 DM, but this was not considered to be statistically significant[14].

Some of our observations suggest that the autonomic neuropathy developed during diabetes has a close association with peripheral neuropathy[15]. In patients with diabetes, demyelization and axonal degeneration were found in both the myenteric and submucosal plexus on the nerves of vagal system[16]. In light of this information, it is suggested that the onset of GIS symptoms is associated with autonomic neuropathy in patients with diabetes. The primary factor to prevent the development of GER is Sub esophageal sphincter (SES) pressure. Contemporary relaxation at SES is the most important factor in GER development. A complex association between the contemporary relaxation of SES, gastric distension, vagal tonus and hyperglycemia appears. Zhang *et al.;* referred to a relationship between hyperglycemia and relaxation at SES in their study which compared hyperglycemic and euglycemic patients. However, the mechanism has not been elucidated yet[17]. Nishda *et al.;* indicated that the frequency of GER symptoms in patients with less than five years of Type 2 DM were increased 2.4 fold over the normal population and it was much more higher in those who had each of the three complications (retinopathy, neuropathy, and nephropathy)[18]. Another factor that increases the frequency of GER symptoms in patients with Type 2 DM is esophageal dysmotility with a development rate of 63%[19, 20]. The reported components of esophageal dysmotility included decreased peristalsis, especially in the velocity and duration of peristaltic motions of the esophagus, decreased SES pressure, and increased contradictions with multi-peaks[21, 22]. In the presence of prolonged diabetes, the myenteric plexus that innerves the distal esophagus and SES are affected which, in turn, leads to esophageal dysmotility. Such a condition is likely to develop, regardless of diabetic neuropathy[19, 23-25].

Gastro paresis is a GIS condition induced by diabetes. Delayed gastric emptying leads to increased gastric content and increased volume of reflux[26]. All this information indicates that diabetes-related GIS pathologies are relatively high as compared to the normal population and that they also have a close correlation with diabetic neuropathy.

Our study has some limitations due to its cross-sectional design and the small sample size. However, in our study examining the relationship of GER in the

diabetic population with and without neuropathy, pyrosis and regurgitation – the main symptoms of GER- were found to be relatively higher in the group with neuropathy, as compared to the other group, suggesting no significant difference between these groups. We believe that this could be due to the low number of patients.

REFERENCES

1. International Diabetes Federation. Diabetes Atlas. 6th edition, 2013. http://www.idf.org/diabetesatlas.
2. Satman I, Yilmaz T, Sengül A, Salman S, Salman F, Uygur S, *et al.;* Population-based study of diabetes and risk characteristics in Turkey: results of the Turkish diabetes epidemiology study (TURDEP). Diabetes Care.2002; 25:1551-1556.
3. Satman I, Omer B, Tutuncu Y, Kalaca S, Gedik S, Dinccag N, *et al.;* TURDEP-II Study Group. Twelve-year trends in the prevalence and risk factors of diabetes and prediabetes in Turkish adults. Eur J Epidemiol. 2013; 28: 169-180.
4. Bytzer P, Talley NJ, Leemon M, Young LJ, Jones MP, Horowitz M; Prevalence of gastrointestinal symptoms associated with diabetes mellitus. A population-based survey of 15,000 adults. Arch Intern Med. 2001; 161:1989-1996.
5. Ko GT, Chan WB, Chan JC, Tsang LW, Cockram CS; Gastrointestinal symptoms in Chinese patients with type 2 diabetes mellitus. Diabet Med. 1999; 16: 670-674.
6. Clouse RE, Lustman PJ; Gastrointestinal symptoms in diabetic patients: lack of association with neuropathy. Am J Gastroenterol 1989; 84: 868-872.
7. Talley SJ, Bytzer P, Hammer J, Young L, Jones M, Horowitz M; Psychological distress is linked to gastrointestinal symptoms in diabetes mellitus. Am J Gastroenterol 2001; 96: 1033-1038.
8. Belafsky PC, Postma GN, Koufman KA; Validity and reliability of the reflux symptom index (RSI). J Voice 2002; 16: 274-277.
9. Shaw JE, Sicree RA, Zimmet PZ; Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes research and clinical practice.2010; 87: 4-14.
10. Akalın E, Hayran M, Özdemir O, Açbay Ö, Aydın N, Ayvaz G *et al.;* Direct medical cost analysis in patients with diabetes mellitus in Turkey: Diab Cost Turkey. Turkish J Edocrinol Metab 1998; 1(2): 9-14.
11. Chandran M, Chu NV, Edelman SV; Gastrointestinal disturbances in diabetes. Curr Diab Rep 2003; 3: 43-48.
12. El-Serag HB, Sweet S, Winchester CC, Dent J; Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut.2013; 63: 871–880.
13. Kitapcioglu G, Mandiracioglu A, Bor CC, Gilbert RJ; Overlap of symptoms of dyspepsia and gastroesophageal reflux in the community. Turk J Gastroenterol. 2007; 18: 14–19.
14. Hamdan AL, Jabbour J, Barazi R, Korban Z, Azar ST; Prevalence of laryngo pharyngeal reflux disease in patients with diabetes mellitus. J Voice. 2013; 27: 495-459.
15. Young RJ, Zhou YQ, Rodriguez E, Prescott RJ, Ewing DJ, Clarke BF; Variable relationship between peripheral somatic and autonomic neuropathy in patients with different syndromes of diabetic polyneuropathy. Diabetes 1986; 35: 192-197.
16. Guy RJ, Dawson JL, Garrett JR, Laws JW, Thomas PK, Sharma AK, *et al.;* Diabetic gastro paresis from autonomic neuropathy: surgical considerations and changes in vagus nerve morphology. J NeurolNeurosurg Psychiatry 1984; 47: 686–691.
17. Zhang Q, Horowitz M, Rigda R, Rayner C, Worynski A, Holloway RH; Effect of hyperglycemia on triggering of transient lower esophageal sphincter relaxations. American journal of physiology Gastrointestinal and liver physiology.2004; 286:797-803.
18. Nishida T, Tsuji S, Tsujii M, Arimitsu S, Sato T, Haruna Y, *et al.;* Gastroesophageal reflux disease related to diabetes: analysis of 241 cases with type 2 diabetes mellitus. Journal of gastroenterology and hepatology. 2004; 19:258-265.
19. Ahmed W, Vohra EA; Esophageal motility disorders in diabetics with and without neuropathy. J Pak Med Assoc. 2006; 56: 54-58.
20. Annese V, Bassotti G, Caruso N, De Cosmo S, Gabbrielli A, Modoni S; Gastrointestinal motor dysfunction, symptoms, and neuropathy in non-insulin-dependent (type 2) diabetes mellitus. J Clin Gastroenterol [Internet]. 1999; 29:171-177.
21. Jorge JX, Panão EA, Simões MA, Borges CI, Delgado FJ, Coelho AC, *et al.;* Esophageal body motility in people with diabetes: comparison with non-diabetic healthy individuals. Diabetes research and clinical practice. 2012; 97: 77-81.
22. Ahmed W, Vohra EA; Esophageal motility disorders in diabetics. J Pak Med Assoc. 2004; 54: 597-601.
23. Kinekawa F, Kubo F, Matsuda K, Kobayashi M, Furuta Y, Fujita Y, *et al.;* Esophageal function worsens with long duration of diabetes. J Gastroenterol. 2008; 43: 338-344.
24. Kinekawa F, Kubo F, Matsuda K, Fujita Y, Tomita T, Uchida Y, *et al.;* Relationship between esophageal dysfunction and neuropathy in diabetic patients. Am J Gastroenterol. 2001; 96:2026-2032.
25. Annese V, Bassotti G, Caruso N, De Cosmo S, Gabbrielli A, Modoni S; Gastrointestinal motor dysfunction, symptoms, and neuropathy in non-

insulin-dependent (type 2) diabetes mellitus. J Clin Gastroenterol.1999; 29: 171-177.

26. Sellin JH, Chang EB; Therapy Insight: gastrointestinal complications of diabetes--pathophysiology and management. Nature clinical practice Gastroenterology &hepatology 2008; 5:162-171.