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PREVALENCE OF DIABETES MELLITUS-ASSOCIATED GASTROINTESTINAL SYMPTOMS

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Abstract

Gastrointestinal symptoms are reportedly prevalent in diabetes, but there is a controversial causal link and sufficient population control knowledge is missing. The goal of this study was to determine whether gastrointestinal symptoms, particularly those with poor glycemic control, are more frequent in people with diabetes. A questionnaire (response rate, 60.0%) containing validated questions on the occurrence of troubling gastrointestinal symptoms over the past 3 months, diabetic status, and self-reported glycemic control was sent to fifteen thousand adults. The incidence, reported to occur regularly or very frequently, of 16 symptoms and 5 symptom complexes was compared using logistic regression analysis, age and sex adjustment. As a consequence, 8657 qualifying subjects replied overall; 423 (4.9 percent) reported diabetes. Most had type 2 diabetes mellitus (94.8 percent). Both 16 symptoms and the 5 symptom complexes, modified for age and sex, were significantly more frequent in subjects with diabetes compared to controls. Lower levels of glycemic regulation, but not the length of diabetes or the type of diabetic treatment, were significantly correlated with an increased prevalence of symptoms. To conclude, an increased incidence of upper and lower gastrointestinal symptoms is associated with diabetes mellitus. This effect can be associated with impaired glycemic control, but not with the period or form of treatment for diabetes.

Keywords: Diabetes Mellitus, Gastrointestinal, glycemic.

Introduction

In diabetes mellitus, gastrointestinal (GI) symptoms are reportedly widespread and are commonly related to autonomic neuropathy. (1,2) While there is evidence that GI symptoms adversely affect the quality of life of patients with diabetes (3) and constitute a major cause of morbidity, (4) the epidemiological data available regarding the prevalence of GI symptoms in patients with diabetes are contradictory and can be questioned on methodological grounds. In a non-elected, population-based cohort of 110 young adult patients with long-standing type 1 diabetes mellitus, Schvarcz et al (5) recently assessed the prevalence of GI symptoms compared with age- and sex-matched control subjects. There was an increased incidence of upper GI symptoms in patients with diabetes, such as anorexia and vomiting, although there was no difference in the occurrence of symptoms related to the lower GI tract. As measured by glycated hemoglobin concentrations, the incidence of GI symptoms was substantially greater in women than in men and in those subjects with the poorest glycemic regulation. Janatuinen et a (l6) found, on the other hand, that the incidence of upper GI symptoms, abdominal pain, constipation and diarrhea in patients with diabetes and controls was comparable. In that report, only middle-aged patients with type 1 or type 2 diabetes mellitus treated with insulin or oral hypoglycemic drugs were examined,

and there was no established calculation of the questionnaire used to determine symptoms. A recent research from Hong Kong (7) recorded higher rates of all forms of GI symptoms relative to community controls in 149 patients with type 2 diabetes mellitus who were referred to a university clinic. The single factor separately correlated with GI symptoms was the length of diabetes in this case. A German study (8) of 333 diabetic patients referred to a research institute on diabetes found that only patients with type 2 diabetes mellitus had more symptoms of upper and lower GI than population controls, with constipation being the most frequent symptom. Finally, a recent U.S. community-based study (9) failed to identify discrepancies in prevalence rates for symptoms of the GI tract in people with or without diabetes.

Materials and Methods:

Survey Method

All adults aged 18 years and older in Australia are required to be enrolled on the electoral rolls by statute. Randomly chosen for the study were fifteen thousand subjects on the electoral rolls for Penrith and the Blue Mountains areas west of Sydney, Australia. According to the 1996 census results, this area has a population of 155000, which is demographically similar to the general Australian population, except that it is slightly younger and slightly higher in socioeconomic status. (11) The survey was carried out between 1 August 1999 and 15 September 1999 and closed at the end of November 1999. The list of selected subjects was divided into 5 batches of 3000 subjects each, and mailings were started approximately 1 week apart at intervals. All qualified participants were sent a letter detailing the research and requesting their participation. To increase the response rate, a $2.00 lottery ticket was included. (24) The option of refusing to participate was offered to the subjects. Two reminder letters were sent at intervals of 3 weeks. The Wentworth Area Health Service Study and Ethics Committee at Nepean Hospital, Penrith, has received ethical approval.

Assessment of Symptoms

The 2-page questionnaire was based on elements from previously validated questionnaires. (11,25,26) Individual questions were taken from the Bowel Disease Questionnaire, (25) and Agre'us et al. (27) adapted the duration from the validated questionnaire. (27) The questionnaire included 16 questions regarding the occurrence of GI symptoms that had been problematic in the previous 3 months. Each symptom frequency was calculated on a 5-point Likert scale and coded as not at all, seldom, occasionally, sometimes, or very often. A positive response was registered for the purposes of this study when the problematic symptoms were claimed to occur regularly or very frequently. A standard definition, consistent with the Rome II criteria, accompanied all symptoms that were not entirely self-explanatory (28): early satiety (feeling full soon after starting to eat, making the person unable to finish a normal meal); postprandial fullness (an uncomfortable feeling of food lingering in the stomach after a normal meal); bloating (a feeling as if the stomach or abdomen were wide); Based on their symptoms, participants were grouped into the following 5 symptom complexes reported to occur regularly or extremely frequently: esophageal symptoms (heartburn, dysphagia, or both); upper dysmotility symptoms (all of the early satiety symptoms, postprandial fullness, bloating, nausea , or vomiting); any bowel symptoms (any of the symptoms of self-reported diarrhea or constipation, loss or watery stools)

Subjects with Diabetes

"People with diabetes were identified as people who answered yes to the question," Have you ever been diagnosed by a doctor with diabetes? Diabetes participants were asked to provide details on their diabetic treatment (insulin-free, insulin-only and oral hypoglycemic tablets, oral hypoglycemic tablets only, or diet-only) and diabetes period (in years and months). Finally, on a 5-point Likert scale, they were asked to rate control over their blood glucose levels in general. The following choices were included in the scale: very good control, good control, average control, weak control or very bad control. The grades "very good control" and "good control" were combined into one grade ("good control") to examine the relationship between self-reported glycemic control and symptoms, and the grades "very poor control" and "poor control" were combined into one grade ("poor control"), since few subjects classified their glycemic control in the severe grades. Subjects were listed as having type 1 diabetes mellitus if they were older than 30 years of age at the time of diagnosis and were currently using insulin. (29,30) The other diabetic subjects were listed as having type 2 diabetes mellitus. Further research removed those who reported diabetes only during pregnancy.

Results:

429 of the 15,000 mailed questionnaires were returned because the address was either unclear or incorrect. A further 99 individuals did not obtain their questionnaires; this category consisted mainly of individuals who had recently died or who were abroad. Six hundred and twenty-three persons declined to participate and returned a blank questionnaire. Of the 14472 delivered, 8657 questionnaires were completed and returned, with a 60.0 percent response rate. The mean±SD age of the respondents was 45.3±15.8 years (range, 18-101 years) and the proportion of respondents aged 40 years and older was comparable (61.8 percent vs 61.0 percent) to that of the total Australian adult population. The proportion of

women in the responding sample was marginally higher (53.5 percent vs 51.4 percent) compared to that of the Australian population. Four hundred and seventy-two subjects reported having diabetes (5.4 percent). Of these, 49 women reported diabetes only during pregnancy, leaving 423 subjects with diabetes for further study (4.9 percent). Diabetes subjects were older than control subjects (59.5±14.1 years vs 44.6±15.6 years, P,.001) and more likely to be male subjects (229/423[54.1%] vs 3793/8185[46.3%], P,.002). Three hundred and sixty-two people (85.6%) with diabetes were 45 years of age and older. Therefore, these variations in the logistic regression analyses were accounted for. In Table 1, the characteristics of subjects with diabetes are summarized. The mean period (interquartile [IQ] range, 2.2-11.0 years) of documented diabetes was 5.0 years. Of the patients, most (94.8 percent) had type 2 diabetes mellitus and received oral hypoglycemic therapy. No sex difference was identified in the form of diabetes, self-reported glycemic control levels, or period of the disease. Compared with men, there was a tendency for more women to be treated with insulin (23.4 percent vs 15.7 percent, P=.08). Diabetes patients reported substantially more symptoms than control subjects per person (1.39, IQ range, 0-2 vs 0.96, IQ range, 0-1; P,.001). 59.6 percent and 9.7 percent of subjects with diabetes reported no symptoms and 6 or more symptoms, respectively; the equivalent control figures were 66.5 percent and 4.6 percent. There was a marked sex disparity between subjects with diabetes (1.77 vs 1.07, P,.002) and controls (1.17 vs 0.72, P,.001), with women showing more symptoms per person compared to men.

The crude prevalence rates and age- and sex-adjusted ORs for symptoms and classes of symptoms in subjects with diabetes and in controls are shown (Table 2). After adjusting for age and sex, all GI symptoms and each of the 5 symptom classes had a substantially higher prevalence among people with diabetes compared with control subjects. Fecal incontinence (OR, 2.74; 95 % CI, 1.40-5.37), dysphagia (OR, 2.71; 95 % CI, 1.69-4.36) and vomiting (OR, 2.51; 95 % CI, 1.12-5.66) have been found to be the strongest associations. 54 (12.8 percent) of 423 subjects with diabetes reported fecal incontinence at least sometimes, compared with just 3.8 percent of controls (P,.001). Most patients with fecal incontinence (61.1 percent) at least often did not report any signs of diarrhea, a rate close to that of control subjects (54.1 percent).

Glycemic Control

Overall, 37 subjects with diabetes rated their glycemic control as bad or very poor, compared with 229 subjects who rated their control as good or very good; on average, 143 subjects rated their glycemic control (Table 1).

Table 1. Characteristics of 423 Diabetic Subjects*

Mean age (SD), y	59.5 (14.1)
Male:female, No.	229:194
Type 1 diabetes mellitus	22 (5.2)
Diabetes treatment	
Insulin only	45 (10.6)
Insulin and tablets	32 (7.6)
Tablets only	198 (46.8)
Diet only	125 (29.6)
No data	23 (5.4)
Duration of known diabetes, y	
<5	183 (43.3)
5-10	85 (20.1)
>10	124 (29.3)
No data	31 (7.3)
Glycemic control	
Very good	88 (20.8)
Good	141 (33.3)
Average	143 (33.8)
Poor	32 (7.6)
Very poor	5 (1.2)
No data	14 (3.3)

*Data are given as number (percentage) unless otherwise indicated.

There was a dose-response relationship between the consistency of self-reported glycemic control and the prevalence rates of all symptoms, with higher prevalence rates associated with lower levels of glycemic control, with the exception of early satiety and fecal incontinence (Table 3). There was an association between weak glycemic regulation and the 5 symptom complexes after adjusting for age and sex, and a moderate to heavy association with 12 of the 16 symptoms (Table 3).

The correlation failed to achieve statistical significance for 4 of the symptoms (early satiety, vomiting, 3 bowel movements a week, and loose or watery stools), but there was a strong trend in the direction of self-reported impaired control (Table 3). The symptoms of lumpy or hard stools (OR, 3.75; 95 percent CI, 1.72-8.17) and urgency (OR, 3.12; 95 percent CI, 1.55-6.26) and the symptoms of complex upper dysmotility (OR, 1.97; 95 percent CI, 1.16-3.37) were separately associated with self-reported impaired glycemic control, adjusted for the confounding factors of age and sex. There were substantially more symptoms per person in patients with diabetes who registered poor glycemic control than in patients with mean glycemic control (3.49, IQ range, 0-6 vs 1.38, IQ range, 0-2; P,.001) or in patients with strong glycemic control (3.49, IQ range, 0-6 vs 0.89, IQ range, 0-1; P,.001). Eleven (29.7 percent) of 37 patients with inadequate control reported no symptoms and seven (18.9 percent) reported 6 or more symptoms. The corresponding figures were 77 (53.8 percent) and 13 (9.1 percent) for 143 patients with average glycemic control. 96 (68.1 percent) of 141 patients with good glycemic control reported no symptoms and only 6 (4.3 percent) reported 6 or more symptoms.

Table 3. Association Between Gastrointestinal Symptoms and Self-reported Glycemic Control*

	Prevalence Rates of Symptoms by Glycemic Control, %				
	Good (n = 228)	Average (n = 142)	Poor (n = 36)	Unadjusted Odds Ratio (95% CI)	Adjusted† Odds Ratio (95% CI)
Symptom					
Abdominal pain or discomfort	9.2	15.5	33.3	2.69 (1.56-4.64)	2.63 (1.52-4.55)
Early satiety	4.9	3.5	16.2	1.83 (0.81-4.13)	1.72 (0.76-3.90)
Postprandial fullness	6.2	7.8	29.7	3.09 (1.61-5.93)	2.86 (1.48-5.50)
Bloating	8.3	15.4	27.0	2.54 (1.45-4.45)	2.41 (1.37-4.25)
Heartburn	9.3	14.0	37.8	2.89 (1.68-4.99)	2.80 (1.61-4.84)
Nausea	2.2	5.6	21.6	6.02 (2.58-14.05)	5.69 (2.42-13.38)
Vomiting	1.3	1.4	5.4	2.37 (0.58-9.66)	2.03 (0.50-8.33)
Dysphagia	3.5	4.9	18.9	3.36 (1.49-7.59)	3.40 (1.50-7.70)
Diarrhea or constipation	12.3	16.1	32.4	2.13 (1.28-3.54)	2.12 (1.26-3.57)
Anal blockage	5.4	7.1	24.3	2.91 (1.45-5.83)	2.87 (1.42-5.80)
>3 Bowel movements per day	5.8	9.9	13.9	1.99 (1.00-3.94)	2.04 (1.03-4.06)
<3 Bowel movements per week	3.1	4.2	8.6	1.88 (0.73-4.85)	1.68 (0.65-4.39)
Lumpy or hard stools	3.5	7.7	25.0	4.56 (2.18-9.56)	4.52 (2.14-9.54)
Loose or watery stools	8.4	10.6	19.4	1.71 (0.92-3.16)	1.64 (0.88-3.06)
Urgency	5.8	9.8	30.6	3.55 (1.87-6.74)	3.06 (1.89-6.87)
Fecal incontinence	0.4	5.6	2.8	3.83 (1.17-12.52)	4.02 (1.22-13.32)
Symptom complex					
Esophageal symptoms‡	10.1	16.8	40.5	3.00 (1.78-5.05)	2.89 (1.71-4.88)
Upper dysmotility symptoms§	13.2	20.3	43.2	2.58 (1.59-4.17)	2.45 (1.50-3.98)
Any bowel symptom‖	19.7	28.0	51.4	2.24 (1.46-3.44)	2.23 (1.44-3.45)
Diarrhea symptoms¶	12.3	16.1	32.4	1.97 (1.18-3.30)	1.91 (1.14-4.94)
Constipation symptoms#	7.0	13.3	27.0	2.84 (1.57-5.13)	2.72 (1.50-3.45)

*All symptoms and symptoms complexes rated often or very often. CI indicates confidence interval.
†Adjusted for age and sex.
‡Heartburn, dysphagia, or both.
§Early satiety, postprandial fullness, bloating, nausea, or vomiting.
‖Self-reported diarrhea or constipation, loose or watery stools, more than 3 bowel movements per day, urgency, fecal incontinence, fewer than 3 bowel movements per week, lumpy or hard stools, or anal blockage.
¶More than 3 bowel movements per day, urgency, or loose or watery stools.
#Fewer than 3 bowel movements per week, lumpy or hard stools, or anal blockage.

Duration of Diabetes

The period of diabetes was not correlated significantly with the incidence of symptoms of GI. Only symptomatic complex constipation (OR, 2.46; 95 percent CI, 1.32-4.56) and anal blockage symptoms (OR, 2.28; 95 percent CI, 1.12-4.67) and lumpy or hard stools (OR, 2.45; 95 percent CI, 1.14-5.27) were substantially correlated with long-standing diabetes after adjustment for age , sex, and self-reported glycemic control. In a median regression study, constipation patients reported an average period of the disease of 2.1 years longer (95 % CI, 0.17-5.33; P,.04) than patients without this complex symptom.

Type of Diabetes

After controlling for age, sex, and self-reported glycemic control, patients with type 1 diabetes mellitus appeared to have less GI symptoms than those with type 2 diabetes. However, in subjects with type 2 diabetes, in a modified model, only the symptom complex of any bowel symptom was substantially more frequent (OR, 8.33; 95 percent CI, 1.39-50.0).

Type of Diabetes Treatment

In order to examine any correlation between forms of diabetes care and the prevalence of GI symptoms, we conducted 3 separate studies. Adjustments for age, sex, and self-reported glycemic control were made in these studies. Compared to 323 non-insulin users, 77 patients who were insulin users were compared in the first study. In the prevalence of any symptom or symptom complex, we found no major variations. In the second study, there was a comparison of 198 users of oral hypoglycemic drugs with 170 patients who did not use these drugs. Only anal blockage in oral hypoglycemic drug users was slightly less frequent (OR, 0.38; 95 percent CI, 0.16-0.88). In the final study, 125 diet-only patients were compared with 275 insulin users, oral hypoglycemic drug users, or both. Postprandial fullness (OR, 2.29; 95 % CI, 1.10-4.77), anal block (OR, 2.84; 95 % CI, 1.29-6.24), and complex constipation symptoms (OR, 2.09; 95 % CI, 1.07-4.08) were substantially more common in diet-only patients.

Table 2. Prevalence Rates of Gastrointestinal Symptoms in Patients With Diabetes and Control Subjects*

	Prevalence Rates, %			
	Controls (n = 8185)	Patients With Diabetes (n = 423)	Unadjusted Odds Ratio (95% CI)	Adjusted† Odds Ratio (95% CI)
Symptom				
Abdominal pain or discomfort	10.8	13.5	1.30 (0.97-1.73)	1.63 (1.21-2.20)
Early satiety	4.3	5.2	1.22 (0.79-1.91)	1.62 (1.02-2.56)
Postprandial fullness	5.2	8.6	1.72 (1.21-2.45)	2.07 (1.43-3.01)
Bloating	11.4	12.3	1.09 (0.81-1.46)	1.51 (1.11-2.07)
Heartburn	10.8	13.5	1.30 (0.97-1.73)	1.38 (1.03-1.86)
Nausea	3.5	5.2	1.51 (0.97-2.35)	2.31 (1.45-3.68)
Vomiting	1.1	1.7	1.58 (0.73-3.44)	2.51 (1.12-5.66)
Dysphagia	1.7	5.4	3.33 (2.12-5.23)	2.71 (1.69-4.36)
Diarrhea or constipation	10.0	15.6	1.69 (1.29-2.21)	2.04 (1.54-2.71)
Anal blockage	5.0	7.7	1.60 (1.10-2.32)	1.80 (1.22-2.66)
>3 Bowel movements per day	5.3	8.4	1.64 (1.14-2.34)	1.84 (1.27-2.66)
<3 Bowel movements per week	3.6	4.3	1.19 (0.73-1.93)	1.80 (1.08-3.00)
Lumpy or hard stools	5.5	7.4	1.36 (0.93-1.98)	1.66 (1.11-2.46)
Loose or watery stools	5.4	10.0	1.95 (1.40-2.72)	2.34 (1.65-3.31)
Urgency	5.2	9.3	1.88 (1.33-2.65)	2.22 (1.55-3.17)
Fecal incontinence	0.8	2.6	3.39 (1.77-6.47)	2.74 (1.40-5.37)
Symptom complex				
Esophageal symptoms‡	11.5	15.4	1.40 (1.06-1.83)	1.44 (1.09-1.91)
Upper dysmotility symptoms§	15.3	18.2	1.24 (0.96-1.59)	1.75 (1.34-2.29)
Any bowel symptom‖	18.9	26.0	1.51 (1.21-1.89)	1.84 (1.46-2.33)
Diarrhea symptoms¶	10.0	15.6	1.67 (1.27-2.19)	2.06 (1.56-2.74)
Constipation symptoms#	9.2	11.4	1.26 (0.92-1.72)	1.54 (1.12-2.13)

*All symptoms and symptom complexes rated often or very often. CI indicates confidence interval.
†Adjusted for age and sex.
‡Heartburn, dysphagia, or both.
§Early satiety, postprandial fullness, bloating, nausea, or vomiting.
‖Self-reported diarrhea or constipation, loose or watery stools, more than 3 bowel movements per day, urgency, fecal incontinence, fewer than 3 bowel movements per week, lumpy or hard stools, or anal blockage.
¶More than 3 bowel movements per day, urgency, or loose or watery stools.
#Fewer than 3 bowel movements per week, lumpy or hard stools, or anal blockage.

Discussion:

Our perception of GI symptoms in diabetes is expanded in 2 major ways by the current findings. Our research was conducted in a community environment, unlike most previous studies, and incorporated an acceptable control group and a diverse population of diabetes subjects of all ages and grades of severity. Compared to community monitors, we found that all GI symptoms occur more frequently in subjects with diabetes, after controlling for the possible confounding factors of age and sex. In addition, we find evidence that self-reported glycemic control is associated with GI symptoms, with more symptoms in subjects with diabetes who have reported weak glycemic control. There were major methodological strengths in the present research. To detect variations in prevalence rates of 10 percent or more, we designed the survey to have sufficient strength. To diagnose diabetes mellitus in group subjects, we used a standard questionnaire and applied well-accepted criteria. We found almost equal prevalence rates of subjects with documented diabetes in the community (4.4 percent vs 4.9 percent), proportion of type 1 diabetes mellitus (7 percent vs 5.2 percent), and proportion of subjects with diabetes aged 45 years and older (83 percent vs 5.2 percent) relative to data recorded from a population-based US study, (30) using the same diagnostic criteria and type of diabetes. In our study, the prevalence of diabetes, including gestational diabetes, was only marginally higher (5.4 percent) compared to the estimates of 4.2 percent in men and 4.5 percent in women given in a recent health survey in our region (31).

The research sample therefore seems indicative of subjects in the population with documented diabetes. While we cannot preclude the possibility that people with diabetes would have been more likely than non-diabetic subjects to answer the questionnaire, it is doubtful that the results of the study will have been seriously influenced by any response bias. It is also doubtful that subjects with undiagnosed diabetes mellitus among the control subjects would have distorted the findings, since the incidence of undiagnosed diabetes in adults in Australia is only around 2 percent, according to epidemiological statistics. (32) As has been defined in other epidemiological studies, we observed the same preponderance of GI symptoms in women, in subjects with and without diabetes. (5,11,33) This disparity is likely to be due to a higher prevalence in women of functional GI disorders. A function can also be played by sex differences in levels of psychosocial distress encountered.

For instance, women have recently been shown to report a more negative impact of diabetes on everyday life compared to men. (34) In diabetes, the pathogenesis of GI symptoms has not been clearly elucidated. It has been suggested that a significant factor is neurological disability, especially autonomic neuropathy. (1,8) The role of autonomic neuropathy in the pathogenesis of GI

symptoms is not discounted by our research. However, a weak association between GI symptoms and autonomic neuropathy has been found by other investigators (9), although the latter has been tested in most studies using standardized cardiovascular reflexes rather than a complex examination of autonomic GI activity. (35,36)

In addition, GI symptoms are also present in patients with diabetes without demonstrable neuropathy (7,9,12) and it has been suggested that factors such as poor glycemic control, (5) psychiatric disorders, (12) or other diabetes-secondary metabolic derangements (4) may affect the role of GI in these patients. The present study indicates that the only factor that explains the reported higher prevalence of GI symptoms in patients with diabetes is unlikely to be permanent autonomic nerve dysfunction. We would predict a correlation with the length of established diabetes if long-term diabetic complications, such as autonomic neuropathy, were to play a major role. In the present analysis, this was checked in the diabetes cohort; only constipation-compatible symptoms were associated with long-standing diabetes.

Our results are in contrast to the findings of a recent study (7) in which the only independent risk factor for GI symptoms was the length of diabetes. However, only younger individuals (mean age, 47 years) with type 2 diabetes mellitus recruited from a tertiary referral center were included in that report. In addition, the association 's therapeutic validity is doubtful, since it was focused on the documentation of minor symptoms that did not impair everyday life.

It seems that the higher prevalence of GI symptoms in people with diabetes is not explained by the treatment of diabetes per se. Notably, after controlling for possible confounding factors , including age, gender, and self-reported glycemic control, we found no differences in the prevalence of insulin-related symptoms and only sporadic evidence of association with hypoglycemic drug treatment and diet. Researchers (37) have recently stated that in patients with diabetes, troubling GI symptoms do not seem to be triggered by the use of oral hypoglycemic drugs or other medicines, except for diarrhea and fecal incontinence, which are strongly and separately associated with the use of metformin. These findings are consistent with those of two other studies (13,38) in which diarrhea has been documented to be associated with treatment with metformin, but not with regulation of diet, use of insulin, or other forms of oral hypoglycemic medications. We did not obtain information in this study about particular types of oral hypoglycemic drugs used.

Our findings indicate that impaired glycemic regulation is closely associated with the occurrence of GI symptoms that are self-reported. The relationship between the degree of self-reported glycemic control and the prevalence rates of the 5 symptom complexes and 12 of the 16 symptoms was found to be dose-response, with higher prevalence rates correlated with weaker glycemic control. The findings of several physiological studies (15,22,23,39-41) in healthy controls and in diabetic patients who have shown that acute hyperglycemia affects GI motor activity and the perception of stimuli emanating from the GI tract support the plausibility of the results.

For instance, during hyperglycemia, the perception of nausea, occurring as a result of proximal gastric distension, is greater. (14) Acute hyperglycemia also delays the emptying of the stomach in people with diabetes, (42) decreases the lower pressure of the esophageal sphincter and the velocity of the peristalsis of the esophagus, (39) and alters the motility of the small intestine and gallbladder. (41) In healthy subjects, gastrocolic and ascending components of the colonic peristaltic reflex were inhibited during hyperglycemia (15), but in another study, colonic speech, compliance, and motor patterns were not affected. (43) While it would have been preferable to take a direct measure of glycemic regulation, this was not feasible in our epidemiological research.

However, researchers have recently shown that self-reported glycemic control of 166 subjects with diabetes (N.J.T., Johann Hammer, MD, M.P.J., and M.H., unpublished results, February 1999), using a 5-point scale similar to ours, was substantially associated with objective glycemic control steps, including glycated hemoglobin (P, 001) and plasma glucose (P = 005) levels. In the current study, no clear guidance was given to patients as to which category of average blood glucose level would correspond to the different categories of self-reported glycemic control. Therefore, it is likely that many patients have overestimated their level of good control of glycemia. This tendency toward optimism, however, will appear to reinforce the present observations. Unfortunately, the approaches used in this study did not resolve the connection between impaired glycemic control and GI symptoms. Symptoms of upper GI dysmotility, including nausea , vomiting, and early satiety, can result in a lack of glycemic control due to nutrient delivery to the small intestine that is unpredictable.

Therefore, the probability that upper GI symptoms, which are partially secondary to autonomic neuropathy, have contributed to impaired glycemic control can not be excluded. However, the increased incidence of symptoms linked to bowel dysfunction, such as constipation , diarrhea, urgency, and fecal incontinence, is not explained by this theory. To determine the course of these associations and to distinguish causes from results, a reasonable extension of this work would be to conduct longitudinal studies. However, several pathophysiological studies (15,39-41) indicate, as previously mentioned, that

poor glycemic regulation alone promotes symptoms arising from all parts of the GI tract. We were also unable to quantify other risk factors, such as diabetic complications, psychosocial distress or psychiatric comorbidity, alcohol consumption, obesity, and the use of medications other than insulin and oral hypoglycemic agents, that may be relevant in the pathogenesis of GI symptoms in diabetes. Type 2 diabetes mellitus patients are characteristically obese, and obesity in women is a risk factor for dyspepsia (broadly defined) (44), but the role of obesity in other GI symptoms remains unclear. As only 22 subjects had developed type 1 diabetes mellitus, the relative significance of the type of diabetes could not be unequivocally evaluated.

Conclusion:

This population-based research, in short, provides evidence that problematic GI symptoms are more prevalent compared to controls in subjects with diabetes, especially in those who report poor glycemic control. Our results indicate that this effect can be at least partially explained by impaired glycemic control and is not correlated with the length of diabetes or the form of treatment for diabetes.

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