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SIGNIFICANT EFFECT OF LOWER GASTROINTESTINAL SYMPTOMS IN THE QUALITY OF LIFE AND GLYCEMIC CONTROL IN TYPE I DIABETES PATIENTS

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Abstract:
Gastrointestinal symptoms are twice as common in type 1 diabetes and associated with poorer quality of life and glycemic control and quality of life. Lower gastrointestinal symptoms are not well characterized in people with type 1 diabetes, and the effects on quality of life and glycemic control has been studying.
Gastrointestinal (GI) symptoms represent an important and often unappreciated cause of morbidity in diabetes, although the significance of this burden across the spectrum of patients and the underlying pathophysiology, including the relationship of symptoms with glycemic control, remain poorly defined. The relevance of GI symptoms and the necessity for their accurate assessment have increased with the greater focus on the gut as a therapeutic target for glucose lowering.
This study aimed to determine the prevalence of lower gastrointestinal symptoms and the effects on glycemic control and quality of life, and to investigate for underlying causes.
Keywords: *Glycemic index, GI symptoms, diet, diabetes, quality of life.*

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INTRODUCTION:

Long-term complications cause major morbidity and mortality in type 1 diabetes mellitus. Intensive glycemic control can reduce long-term complications and improve quality of life. Even with good glycemic control, complications occur, suggesting other factors increase the risk (1). Coexisting medical problems are a significant confounding factor when managing patients' glycemic control. The association between type 1 diabetes and the gastrointestinal tract was first described in 1936 by Bargen. Classically, this has been described as *diabetic diarrhea* and most commonly occurs in patients with type 1 diabetes mellitus. Despite this historical description there have been very few studies examining patients with type 1 diabetes specifically for lower gastrointestinal symptoms (2).

Although gastrointestinal (GI) symptoms generally are accepted as more common in people with diabetes than in the general population, the reported prevalence has varied substantially, being much higher (≥70%) in most but not all outpatient samples. These inconsistencies probably reflect differences in the patient populations and the methodology used to evaluate symptoms. Whether symptom prevalence differs substantially between type 1 and type 2 diabetes is uncertain. Besides, glycemic control and gastrointestinal side effects were self-announced and no examinations were performed. In spite of these restrictions this examination detailed that both upper and lower gastrointestinal side effects were fundamentally more typical in patients with diabetes contrasted and controls. A further report found that gastrointestinal manifestations in patients with diabetes were related with poor glycemic control (glycosylated hemoglobin was estimated in a subgroup) and fringe neuropathy. This gathering has in this manner recommended no relationship between glycemic control and gastrointestinal indications. This examination just included 136 people of whom a minority (n=7) had type 1 diabetes and glycemic control was self-revealed. The idea of gastrointestinal indication cycling in patients with diabetes has been proposed and is related with mental factors instead of glycemic control (3). There is a paucity of data regarding gastrointestinal symptoms in patients with type 1 diabetes, in particular regarding prevalence, underlying causes and pathophysiology.

A few systems have been involved in the pathogenesis of gastrointestinal manifestations, including Helicobacter pylori disease, mental factors, and disabled tactile capacity. In any case, cluttered engine work coming about because of autonomic neuropathy and irregular blood glucose levels additionally appear to be essential. Intense changes in blood glucose fixations can affect engine work all through the gastrointestinal tract and regulate tactile recognition. A relationship between gastrointestinal indications and glycemic control is additionally upheld by cross-sectional epidemiologic investigations (4).

The instrument by which diabetes may prompt looseness of the bowels is believed to be multifactorial, and most theories incorporate autonomic brokenness and adjustment of administrative enterohumoral reactions. Sort 1 diabetes is likewise connected with various conditions which could prompt the runs, including celiac sickness, exocrine pancreatic inadequacy, thyroid brokenness, IgA lack and little gut bacterial abundance. In spite of the fact that these affiliations have been autonomously detailed, there has never been a binding together evaluation of an extensive partner of patients with type 1 diabetes and diabetic loose bowels (5).

This area deserves investigation as gastrointestinal symptoms are likely to impact on quality of life and glycemic control. The aims of this study were to determine the prevalence of gastrointestinal symptoms in patients with type 1 diabetes and to determine the correlation between such symptoms, glycemic control and quality of life. Furthermore, a subgroup with significant diarrhea was investigated to determine underlying causes (6).

RESULTS:

Roughly 75% of diabetic patients with a DM encounter dysfunction, likely because of motility adjustment. The predominance of indications identified with the upper GIT, for example, sickness and early satiety, is higher in the two kinds of DM patients with weakened glycemic control and engine dysfunctions (7). This fortifies the idea that the impacts of glucose focus in the impression of the upper GIT improvements are clinically essential. Changes in the GIT motility showed by postponed gastric discharging in patients with long haul T1DM and T2DM are normally connected with gastroparesis, an outcome of diabetic autonomic neuropathy. Powerless compressions of the antral stage, expanding the distance across of the postprandial gastric antrum, feeble fundic withdrawals, pyloric fits, and moderate arrhythmic waves are a portion of the discoveries showing these progressions and related with side effects in the upper GIT. Studies have demonstrated that people with a DM have a few irregularities of gastric motility: there is supper actuated disabled gastric fundus unwinding, there might be arrhythmic moderate waves, for example, bradycardia and tachygastria, smoothed example waves,

nonattendance of postprandial increment in the powers of moderate waves, diminished abundancy and recurrence of antral constrictions, decreased sufficiency of fundic withdrawals, nonappearance of antral interdigestive moving engine complex, among others (8). Disabled unwinding of gastric fundus likewise prompts hindered recurrence of spread of antral constrictions, advancement of retrograde pyloric stream, with subsequent stagnation of the bolus and weakened ingestion, adding to gastrointestinal side effects and the arrangement of bezoar (unabsorbed sustenance) that happens in DM. Another system through which hyperglycemia influences gastric motility is diminished emission and, thus, diminished serum convergence of motility administrative peptides, for example, motilin (9).

In spite of the fact that it has been little researched as far as esophageal motility, a few patients with T1DM and T2DM have anomalies of the esophageal sphincter and expanded pervasiveness of indications of gastroesophageal reflux ailment after some time.

Interstitial cells of Cajal (ICC), together with innervation and smooth muscles, assume a critical job in the control of motility. Such round muscle cells retransmit data from enteric neurons to smooth muscle cells, though in the myenteric plexus, roundabout muscle cells produce musical electrical depolarization (moderate waves), which control the recurrence and length of muscle compressions. Histopathological investigations of gastric examples in patients with T1DM uncovered: a) consumption of ICC in the myenteric plexus and smooth muscles and b) loss of neurons and lessened recoloring of different synapses and markers of ICC, bringing about disabled capacity of gastric motility. It is conceivable that comparative changes are available in different parts of the GIT, causing side effects. ICC exhaustion has been shown both in patients with DM and in research facility creature models. In a very much composed mice show with human T1DM, there was clogging 6 two months after the beginning of DM, and ICC exhaustion stretched out from distal GIT to the gastric body. Brokenness was confirming with postponed gastric discharging for solids, and electrical arrhythmia likewise happened. ICC consumption is more regularly central than diffuse and both can be distinguished in the myenteric locale or inside the muscle layers of the GIT. Injuries may prompt extremely serious clinical types of dysmotility (10-12).

In the distal colon, the loss of ICC is associated with loss of excitatory and inhibitory neuromuscular transmission. However, paradoxically in the proximal colon, the authors detected phases of activity and hyperexcitability, which were interpreted as compensatory changes developed in response to distal hypomotility that occurs as a response to severe constipation in patients with T1DM and T2DM (13).

In this manner, thinks about have emphatically shown that the loss of ICC is normal in long haul T1DM and T2DM with lacking glycemic control, and that this misfortune does not happen in seclusion, but rather joined with dystrophy of natural and extraneous nerves of the smooth muscle. Escalated changes in the cell substance of GIT tissues of patients with T1DM and T2DM are gone before by unpretentious variations from the norm that must be recognized at the sub-atomic level. These early variations from the norm, joined with different variables, for example, diseases, push, intense hyperglycemia and psychogenic elements, can prompt extreme clinical types of dysmotility. Colonic motility issue in T1DM and T2DM are showed by loose bowels or blockage. Data accessible on electrical action and colonic motility is as yet constrained. Changes in motility in the colon have not been completely seen up until now, but rather they prompt postponed intestinal travel, hindered gastrocolic reflex, irregularities of the inner butt-centric sphincter tone, impeded rectal sensation and consistence, and deferred postprandial colonic motility.14,17,35 The component of proximal colonic hypermotility stays indistinct. This system may express a type of utilitarian colonic remuneration because of distal colonic hypofunction caused by amassing of fecal material, loss of ICC, and resulting depolarization, or reaction to bacterial abundance in the small digestive tract. As of late, the impacts of loss of enteric neurons have been assessed in light of chronicle of isometric muscle groups of enteric innervation by methods for electrical field incitement (EFS) in the colons of patients with a DM (14). The reaction to withdrawals and unwinding prompted by EFS was essentially debilitated in the roundabout muscles of patients with DM. Also, it has been discovered that, within the sight of an aggressive inhibitor of L-arginine (L-NAME), a substrate for the combination of nitric oxide (inhibitory middle person of enteric neurons), the expansion in the contractile reaction was altogether lower in the colon of these patients contrasted and controls (15). This finding recommends that the number of inhabitants in inhibitory neurons is substantially littler in people with a DM and it adds to a diminished affectability to L-NAME. These discoveries show that loss of enteric neurons (enteric neuronal rebuilding), joined with oxidative worry in the colon, incites debilitated colonic motility in people with T1DM and T2DM and prompts issues, for example, blockage and looseness of the bowels in DM. In this way, it tends to be inferred that the two sorts of uncontrolled DM,

with steady hyperglycemia and chronicity, cause neuromuscular scatters of the GIT and add to sensorimotor clutters and gastrointestinal side effects. Regarding looseness of the bowels, different causes have been proposed to clarify it in diabetic patients of the two sorts notwithstanding intestinal motility issue: a) bacterial abundance; b) expanded intestinal emission because of autonomic neuropathy; c) pancreatic deficiency; d) utilization of prescriptions for treatment of T2DM, for example, metformin (this causes a decrease in the ileal assimilation of bile salts, causing overabundance in the colon); e) utilization of sweeteners, for example, sorbitol (in abundance in the eating routine, it can prompt osmotic the runs); f) visit relationship of T1DM with celiac illness (a vital reason for the runs); h) immune system hypothyroidism (a condition regularly connected with T1DM); and I) activity of hormones, for example, glucagon, somatostatin, and vasoactive intestinal peptide, which instigate the runs. In any case, these causes can be rejected in roughly 50% of patients with a DM, and anomalous motility or discharge were viewed as the doubtlessly reasons for loose bowels in patients with T2DM (16).

DISCUSSION:

This is the biggest investigation of gastrointestinal manifestations in individuals with type 1 diabetes, specifically bring down intestinal indications. A high prevalence of GI symptoms exists in the general population, which may be influenced by BMI, sex, psychological comorbidities, Helicobacter pylori infection, and age. Besides, manifestation load was fundamentally higher contrasted and controls. Facilitate investigation demonstrated that the runs, obstruction or rotating gut propensities were essentially more typical contrasted and controls, as were side effects, for example, fart and swelling, and were related with poorer personal satisfaction scores. Glycemic control was additionally fundamentally more regrettable in those with looseness of the bowels, stomach torment or exchanging entrail propensities. Notwithstanding these manifestations, just a past filled with pancreatitis was fundamentally more typical when looking at known gastrointestinal conditions. This may clarify the group of stars of stomach torment, looseness of the bowels, drifting stools and weight reduction, which could be ascribed to exocrine pancreatic ailment. Without a doubt, following examination, 6.4% of individuals with type 1 diabetes and looseness of the bowels were found to have exocrine pancreatic malady, incorporating two people with calcific pancreatitis. Both of whom had a background marked by noteworthy liquor consumption for a long time (17).

A further intriguing finding was that gastrointestinal side effects were related with expanded danger of diabetes-related entanglements. Neuropathy and stomach issues were related with any adjustment in gut propensity, while looseness of the bowels or exchanging gut propensities were related with expanded danger of all diabetes-related intricacies. These discoveries are like the underlying portrayal of diabetic loose bowels by Bargen, in which fringe neuropathy was much of the time related.

Methods for determining the presence and severity of GI symptoms have evolved substantially over recent decades, particularly in the area of functional GI disorders (e.g., irritable bowel syndrome [IBS], functional dyspepsia), which after the exclusion of structural disease, are defined exclusively by symptoms and, unlike diabetes, lack objective biomarkers. Although validated questionnaires are used widely in diabetes (e.g., to assess neuropathy) most studies, including those related to therapeutics, have not used validated tools to assess GI symptoms, and assessment has been based on self-report, which is known to be unreliable

Importantly this study detected underlying gastrointestinal disorders in those with diarrhea. To date there are no published data examining the findings of investigations for diarrhea in a large cohort of people with type 1 diabetes. Irritable bowel syndrome accounted for around one-third of all people investigated, with autonomic neuropathy being the second most common positive finding. Not all of those with autonomic neuropathy had small bowel bacterial overgrowth according to glucose hydrogen breath testing, but this may represent false-negative results. Additionally, autonomic function was tested using cardiac function rather than intestinal motility or manometry studies. The correlation between cardiac autonomic dysfunction and intestinal autonomic dysfunction is not 100%. The finding of a high prevalence of inflammatory bowel disease is novel and has been confirmed in a recent study (19).

Exocrine pancreatic disease is not unexpected and suggests that some people with diabetes may have been misclassified. A previous study by Hardt *et al* showed that around 10% of patients with type 1 or type 2 diabetes may actually have type 3c diabetes. The hypothesis is that patients present with diabetes-related symptoms for which they are treated, but they may have only subtle exocrine symptoms. Identification of these individuals is likely to be important as other therapies may be required, such as pancreatic enzyme supplementation. Furthermore, some of the newer medications such as the incretins may be more suitable for people with type 3c diabetes.

The frequency of some of the conditions identified initially appears questionable with high prevalence of both celiac disease and inflammatory bowel disease and low prevalence of lactose intolerance. However, all of these individuals had assessment for celiac disease and underwent colonoscopy, but assessment for lactose intolerance was not a first-line investigation, which would have reduced the overall prevalence. If an individual had a positive finding on the initial set of investigations, then further tests were not conducted (13).

The other diagnoses were expected except the finding of a rectal cancer. This individual was an older man who had started with looser motions over the previous few months. Colonoscopy revealed a significant lesion in the mid-rectum, which went on to be completely resected. A previous meta-analysis has shown that diabetes is a risk factor for colorectal cancer possibly due to hyperinsulinemia but is also associated with adverse outcomes following surgery for colorectal cancer. Our data suggest that diarrheal symptoms in people with type 1 diabetes deserve investigation before being ascribed nihilistically to autonomic neuropathy (9).

Despite this being such a large study with a suitable control group, there are a number of unanswered questions. This study was an epidemiologic study and not designed to establish mechanisms by which people with type 1 diabetes acquire gastrointestinal symptoms. Many of these symptoms were self-reported and not attributed to a formal diagnosis following investigations, for example, gastric problems. The focus of this study was however lower gastrointestinal symptoms. Despite this, the prevalence of gastrointestinal symptoms in the control group is in keeping with that of previous population-based studies. The prevalence of underlying diagnoses was not compared with that in the control group as these individuals were not investigated and 11 individuals with type 1 diabetes declined investigations. However, this represents less than 10% of those with type 1 diabetes and diarrhea and may represent symptom cycling. Additionally, initial assessment did not take prescribed medications into account, which may be a confounder. In those undergoing further assessment for diarrhea, a full medication history was taken but were not felt to account for any gastrointestinal symptoms. Most of the cohort were young and not on other medications other than insulin. Several conclusions can be drawn in this regard as the prevalence of irritable bowel syndrome in the general population is known to be approximately 15%. Our data support the theory that people with type 1 diabetes may perceive gastrointestinal symptoms more readily than people without diabetes suggested by the greater prevalence of gastrointestinal symptoms, including flatulence and bloating, as well as the increased prevalence of irritable bowel syndrome. Whether this is due to subtle changes in the autonomic nervous system or other intestinal hormones remains unclear. Previous studies have demonstrated that glycemic control has an effect on gastric function, but there are little data on lower gastrointestinal function. Confounding factors in previous studies have been the lack of investigation for underlying conditions, no face-to-face assessments and self-reporting of glycemic control. Additionally, previous studies have not assessed quality of life and, importantly, have not had a control group (22,23).

CONCLUSIONS:

In conclusion, we have shown for the first time that lower gastrointestinal symptoms are common in type 1 diabetes and have a significant effect on the quality of life and glycemic control. Investigation of patients with diarrhea had a high yield of treatable conditions, and therefore care for people with diabetes should encompass gastrointestinal assessments routinely. Gastrointestinal symptoms are twice as common in type 1 diabetes and associated with poorer quality of life and glycemic control. Investigation of diarrhea in people with type 1 diabetes leads to a high yield of treatable conditions and a change in management in about three-quarters.

A further interesting finding was that gastrointestinal symptoms were associated with increased risk of diabetes-related complications. Neuropathy and stomach problems were associated with any change in bowel habit, whereas diarrhea or alternating bowel habits were associated with increased risk of all diabetes-related complications. These findings are similar to the initial description of diabetic diarrhea by Bargen,4 in which peripheral neuropathy was frequently associated.

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