



## GASTROINTESTINAL DISTURBANCES IN DIABETES MELLITUS

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## ABSTRACT

**AIMS AND OBJECTIVES** Studies on gastrointestinal (GI) symptoms in diabetes among patients from the South India is scarce. The aim of the study is to find the prevalence of gastrointestinal symptoms (GI) in diabetes mellitus (DM) among patients of South India and to assess the correlation between GI symptoms and glycated haemoglobin (HbA1c).

**KEYWORDS** : Diabetes mellitus, Gastrointestinal disturbances, Polyphagia, Bloating, Bowel habits

## INTRODUCTION

Diabetes is a common metabolic disease characterized by increased circulating glucose concentration associated with abnormalities in carbohydrate, fat and protein metabolism and a variety of micro vascular, macro vascular, neurologic and infectious complications (22). In diabetes defects in insulin secretion, insulin action or both are present (30).

Fundamental defects to which most of the abnormalities can be traced are on reduced entry of glucose into various peripheral tissues and on increased liberation of glucose in to circulation from the liver (9).

In type I DM there is a near or total absence of insulin secretion resulting from  $\beta$  cell destruction and the patient needs insulin for survival. This is referred to as insulin dependent diabetes mellitus (IDDM), or juvenile onset diabetes mellitus. Type I DM which is usually present prior to the age of 30-40 years most commonly seen in childhood or in adolescence. In type II DM, there is appreciable insulin but inadequate in effectiveness and is called non-insulin dependent diabetes mellitus (NIDDM). Type II DM is characterised by insulin resistance detected at the level of skeletal muscle, adipose tissue and the liver. The pathogenesis of type II DM is complex and involves the interaction of genetic and environmental factors. Genes responsible for diabetes are identified (22).

Diabetic neuropathy is one among the most common long-term complications of diabetes and is a significant source of morbidity and mortality.

It appears the most rapid deterioration of nerve function occurs soon after the onset of type I DM. In type II DM, slowing of nerve conduction velocities (NCVs) may be one of the earliest neuropathic abnormalities.

Neuropathy may be silent and go undetected while exercising its ravages or it can manifest with clinical symptoms and signs that mimic those seen in many other diseases. It is, therefore, diagnosed by exclusion.

Bytzer et al. (3) concluded that among diabetic patients an increased prevalence of upper GI symptoms, such as anorexia and vomiting. But no difference in the frequency of symptoms referable to the lower GI tract. The prevalence of GI symptoms was significantly greater in women than in men.

Ko et al. (14) had done a questionnaire study in Chinese type II

diabetic outpatients and non-diabetic control subjects and found out that about 70% of the Chinese type II diabetic outpatients have GI symptoms. This rate is much higher than in non-diabetic control subjects. They observed duration of diabetes as an important factor associated with the presence of such GI symptoms. Earlier workers reported that there is some association between gastrointestinal symptoms and diabetes mellitus (23). Of these major manifestations of gastrointestinal dysfunctions are 1) Constipation, 2) Diarrhoea 3) Oesophageal dysfunction 4) Fecal incontinence and 5) Gastro paresis diabeticorum.

**1. Constipation.** The exact pathogenesis of constipation in diabetes is not well understood. Autonomic dysfunction with a lack of synchronicity between the gut musculature and the sphincters is thought to be the major contributing factor. A solid diet containing undigestible high fiber should be avoided, since this manoeuvre may aggravate symptoms of gastro paresis.

**2. Diarrhoea.** Diabetic diarrhoea is usually chronic and intermittent and is defined as a stool volume of more than 20 g/day and usually occurs in patients with poorly controlled, long-standing diabetes. It occurs more often in men with a male to female ratio of 3:2 (2).

**3. Oesophageal dysfunction.** Oesophageal symptoms are common and when present vary from heartburn, chest pain, chest discomfort, ultimately leading to dysphagia. Motility abnormalities associated with diabetes include delayed oesophageal emptying, oesophageal dilatation and spontaneous contractions (25).

**4. Fecal incontinence.** Fecal incontinence is a particularly distressing symptom in diabetes secondary to an anal sphincter dysfunction. Patients may have incontinence either precipitated by diarrhoea or as a primary symptom. It is often not volunteered and should be elicited. Patients have been demonstrated to have a low basal anal sphincter pressure. However voluntary increments in 'squeeze' were preserved. These patterns suggest a defect in autonomic innervation of the internal sphincter (13).

**5. Gastroparesis diabeticorum.** The term "gastroparesis diabeticorum" denotes to gastric atony and delayed emptying. Vagal neuropathy as a complication of diabetes leads to impaired neural control of the myoelectric activity of

the stomach and therefore, delays gastric emptying and impairs the gastric acid response to sham feeding.

A higher prevalence of gastrointestinal symptoms has been reported among patients with diabetes and often is attributed to autonomic neuropathy (16,17,24). Upper gastrointestinal symptoms occur frequently in patients with diabetes, but are not strongly predictive of disordered gastric emptying or motility (11).

Diabetic diarrhoea is caused by increased or uncoordinated transit time in the small intestine, bacterial overgrowth, or increased intestinal secretion (20).

Quan et al. (23) found more than half of diabetic patients and 43% of the controls had at least one GI symptom during the 3 months prior to entering the study. Diabetic subjects had a significantly higher prevalence of diarrhoea when compared with controls. In addition, there was a higher prevalence of the other symptoms in the diabetic subjects when compared to controls but with no statistical significance (6).

A number of studies were carried out in the Western countries and in India to show the relationship between gastrointestinal symptoms and diabetes mellitus. Onyckwere et al. (21) set out to document features of gastrointestinal dysfunction in diabetics in an urban hospital in Nigeria and noted an increased prevalence of GI symptoms in the diabetics than controls.

The present study is an attempt in similar line to include Diabetic Patients of South India and find out the incidence and details of GI symptoms in them.

## MATERIALS AND METHODS

Present study was initiated after getting the approval of Ethical Committee of Amrita Institute of Medical Sciences and Research. A total number of 111 diabetic patients type II who were attending the Outpatient Department of Endocrinology, Amrita Institute of Medical Sciences were included in this study. They belonged to either sex and they were in the age group of 40-70 years. The height and weight of each patient was noted for BMI. Patients who were on drug for modifying gastrointestinal function or with any other chronic illnesses or underwent GI surgery were excluded. The patients were divided according to the duration of diabetes into the following groups 1. Group I with disease for  $\leq 10$  years, 2. Group II with disease for  $> 10$  years. A questionnaire each was given to patients to provide information regarding the GI symptoms for the past two months. The questionnaire included a range of parameters like epigastric pain or discomfort, nausea, regurgitation of gastric juice/ heart burn, epigastric fullness, dysphagia,odynophagia, bloating, belching, vomiting, constipation, fecal incontinence, early satiety, anorexia, heart burn, diarrhoea. The insulin requirement and drug intake of the subject at the time of sample collection were documented. The levels of FBS and PPBS were estimated using Hexokinase. HbA1c was measured using D10 HPLC. LFT (SGOT, SGPT), RFT (urea, creatinine) were done by using Olympus 2700, 680.

Statistical analysis was performed using the SPSS version 11. A 'p' value of  $< 0.05$  was considered statistically significant. Analysis was also done to find out the correlation between duration of diabetes and HbA1c using Chi-Square test but there was no significance.

## RESULTS

Comparison was done between different gastrointestinal symptoms and duration of diabetes mellitus. We found out that about 85 % of diabetic patients have any one of the GI symptoms. There is a trend to have more gastrointestinal symptoms with increasing duration of diabetes. We analysed

12 gastrointestinal symptoms out of these altered bowel habits (45%) and polyphagia (44.1%) were the most common complaints among diabetics. There is no statistically significant association between duration of diabetes and GI symptoms. Specifically, we compared altered bowel habits, polyphagia and bloating in association with duration of diabetes. It was observed that these, three are important and prevailing in this area. It is shown below according to its presence percentage wise.

GI symptoms	Percentage
Altered bowel habits	45
Polyphagia	44.1
Bloating	19.8

## Glycosylated HbA1c and Altered bowel habits

HbA1c	No. of positive cases	Total	p value
$\leq 7$	8 (33.3%)	24	NS
$> 7$	42(48.3%)	87	

## DISCUSSION

Diabetes is a 'silent killer disease' as there is no early symptom of the disease. Diabetes appears to have been a death sentence in the ancient era. Hippocrates makes no mention of this illness, which may indicate that he felt that the disease was incurable. Aretaeus did attempt to treat it but could not give a good prognosis; he commented that "Life with diabetes is short, disgusting and painful". (18).

DM is more common especially type II in the more developed countries. The greatest increase in prevalence is expected to occur in Asia and Africa, where most patients will probably be found by 2030 (28).

Diabetes is a silent epidemic and according to WHO (30) there are 246 million people in the world living with diabetes. This is almost 6% of the world's adult population. India, China, America has the maximum number of diabetics. Diabetes in Asians is five times the rate of the white population. India is the diabetes capital of the world. It is estimated that people with diabetes in India by 2025 will swell to 70 million. This would mean every fifth diabetic in the world would be Indian.

As many as 75% of patients visiting diabetes clinic report significant GI symptoms (29). The entire GI tract can be affected by diabetes from the oral cavity and oesophagus to the largest bowel and anorectal region. The common GI symptoms include; constipation, diarrhea, oesophageal dysfunction, fecal incontinence, gastro paresis diabeticorum.

Feldman et al. (8) in their review article mentioned that gastrointestinal symptoms such as vomiting, constipation, diarrhoea, and faecal incontinence occur frequently in patients with diabetes mellitus. Explanation for the cause of idiopathic diabetic diarrhoea is not known, but it is a manifestation of autonomic neuropathy. Decreased transit time in the large intestine may cause constipation or impacted stool (12). Poor glycemic control does not seem to correlate with worsening GI symptoms (4, 7, 15). Abdominal bloating/fullness but not any other upper gastrointestinal symptom is associated with diabetic gastroparesis and that gastric emptying is slower in diabetic women than in diabetic men (26).

Forty-two percentage of diabetes reported one or more GI symptoms; bloating, abdominal pain, loose stools and urgency were common (27). Diabetes Mellitus is often associated with autonomic neuropathy. Diabetic neuropathy is a set of clinical syndromes that affect distinct regions of the nervous system, singly or combined.

Schvarcz et al. (26) evaluated the prevalence of GI symptoms in a non selected, population-based cohort of 110 young adult patients with long-standing type I diabetes mellitus, compared with age- and sex-matched control subjects.

Among patients with diabetes, an increased prevalence of upper GI symptoms, such as anorexia and vomiting was present, whereas there was no difference in the frequency of symptoms referable to the lower GI tract. The prevalence of GI symptoms was significantly greater in women than in men and in those subjects with the worst glycemic control, as assessed by glycated haemoglobin (HbA1c). It has been suggested that symptoms reflect abnormal GI motility as a manifestation of irreversible autonomic neuropathy (8).

Dysfunction of the autonomic nervous system is a well-established long-term complication of diabetes mellitus. Among several patients with diabetes mellitus of prolonged duration chronic and recurrent clinical features related to the disordered motility of almost the whole GI tract including esophageal as well as epipharyngeal dysphagia, gastroparesis, constipation, diarrhoea, and fecal incontinence is seen. Diabetes can affect the motility of the gastrointestinal tract by causing changes in the intestinal smooth muscle (5). Patients with diabetes type I had more frequent and intense upper and lower GI symptoms (19).

Bytzer et al. (3) in their study mentioned the role of autonomic neuropathy in the pathogenesis of GI symptoms. Underlying autonomic neuropathy is likely to be one important factor but may not explain all GI conditions. Gastric retention in diabetes mellitus was coined the term "gastroparesis diabeticorum" to describe gastric atony and delayed emptying (2, 10).

Prolonged hyperglycaemia, and possibly hyperinsulinemia may be important in the development of GI problems in diabetes. Delayed gastric emptying has been reported with an elevation of blood glucose and insulin concentrations (1).

Feldman et al. (8) in their study found out that constipation is the major gastrointestinal complication of diabetes; about 82% diabetics had constipation along with other symptoms.

A study conducted in Chinese patients with type 2 diabetes mellitus the three commonest GI symptoms were diarrhoea (34.9%), constipation (27.5%) and epigastric fullness (16.8%) (14).

GI disorders are common among all persons, including those affected by diabetes. As many as 75% of patients visiting diabetes clinic will report significant GI symptoms (29). The entire GI tract can be affected by diabetes from the oral cavity and oesophagus to the largest bowel and anorectal region. The common GI symptoms include; constipation, diarrhea, oesophageal dysfunction, fecal incontinence, gastro paresis diabeticorum.

GI symptoms are common in patients with long standing DM, but the pathogenesis is controversial. 42% of diabetes reported one or more GI symptoms; bloating, abdominal pain, loose stools and urgency were common (27).

Recently, Schwarcz et al. (26) evaluated the prevalence of GI symptoms in a non-selected, population-based cohort of 110 young adult patients with long-standing type I diabetes mellitus, compared with age- and sex-matched control subjects.

Many GI complications of diabetes seem to be related to dysfunction of the neurons supplying the enteric nervous system and involvement of the intestinal nerves which may lead to enteric neuropathy. This is one type of autonomic neuropathy and may lead to abnormalities in intestinal motility, sensation, secretion and absorption.

### Summary

It is apparent that several syndromes involving the gastrointestinal tract itself and other para-GI organ like liver, gall bladder and pancreas occur frequently in subjects with diabetes mellitus as a consequence of autonomic dysfunction, an established long-term neuropathic complication of diabetes mellitus.

In our study we found out that gastrointestinal symptoms do occur in diabetes with increase in duration and there is no significant association between gastrointestinal symptoms and glycemic index.

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