

DIABETES AND THE GASTROINTESTINAL TRACT

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Diabetes mellitus is a metabolic disease with multisystemic involvement. One of the target organs for the complications of diabetic vasculopathy, neuropathy and poor control is the gastro-intestinal tract. Gastrointestinal disorders in the diabetic may be due to many reasons.^{1,2,3}

The autonomic nervous supply to the gut is affected by long standing diabetes. These may be responsible for the disorders of the gut. Segmental demyelination, reduction in size of the neurons, altered vasoactive intestinal poly-peptide (VIP), somatostatin (SS) and substance P in these neurons supplying the gut and axonal degeneration in the meissneri plexus are the abnormalities found in diabetes.

Microangiopathy as the pathogenic mechanism has not been confirmed by experimental work. Altered glucose and electrolyte homeostasis may change the motility of the gut. Infections like tuberculosis and candidiasis in the gut may be responsible for the clinical manifestation.

Thus, it appears that the autonomic neuropathy in diabetics seems to be the key pathogenetic event in the evolution of the disorders of the **GIT**.

Complications involving the gastrointestinal tract are responsible for considerable morbidity in patients with diabetes mellitus. Diabetes results in dysfunction of the entire gastro-intestinal tract. Gastrointestinal symptoms are frequently elicited in patients attending Diabetic clinics³. Most complications of motility are secondary to neuropathy and

patients usually have peripheral neuropathy or other features of autonomic neuropathy like postural hypotension, impotency, bladder irregularities, anhidrosis etc.

Diabetes and the Esophagus

Esophageal motor dysfunction is common upto 8% in association with diabetic neuropathy and is usually asymptomatic. These disorders range from slight impairment of peristalsis to absence of coordinated peristaltic activity. In 75% of patients with diabetes secondary peristalsis in response to esophageal distension is lost^{5,6}. Delayed esophageal emptying may also occur in such patients.

Decreased resting lower esophageal sphincter pressure leads to gastroesophageal reflux and heartburn. Though reflux may be worsened by gastric stasis often it becomes less symptomatic as gastric stasis often it becomes less symptomatic as gastric hypochlorhydria supervenes. As such severe esophagitis and complications of reflux are uncommon. A significant proportion (upto 15%) of diabetics may have hyperperistalsis of the esophagus like in diffuse esophageal spasm.

Monilial esophagitis occurs most commonly in patients with an impaired immune response and may occur in uncontrolled diabetes or in patients receiving antibiotics and immuno suppressive drugs. Severe odynophagia is usually complained by these patients. Esophagoscopy reveals cheesy yellowish, exudate and a friable mucosa. Treatment is with oral nystatin suspensions. 250,000 units given every 2-4 hours.

Diabetes and the Stomach

Impaired Motor activity of the stomach is also common in patients with diabetes and gives rise to the condition known as gastroparesis diabetorum. Symptoms include nausea, vomiting early satiety, bloating and abdominal pain. Retention vomiting (of stale food) may also occur. This leads to dearrangement of diabetic control, weight loss and bezoar formation⁷.

Pathogenesis

The most likely cause is the vagal autonomic neuropathy which is almost like an autovagotomy⁸. However this is not the mechanism as patients with truncal vagotomy do not have such severe and persistent stasis. Metabolic abnormalities in the form of hyperlycemia and hyperglucogenemia and hyperkalemia also contribute to its pathogenesis⁹. Electrophysiological studies, have shown that patients with gastroparesis have a loss of the migratory motor complex as compared to asymptomatic diabetics¹⁰.
Diagnosis : A succession splash may be audible. plain x-ray of the abdomen shows dilated by a fasting residue 200 ml or a positive saline load test. Dynamic radionuclide scans are extremely useful in diagnosing and quantifying stasis.

Treatment : Patients with continuous symptoms may need hospitalisation for control of diabetes, gastric decompression and rehydration. The drug of choice is metoclopramide which acts both to accelerate gastric emptying by a 'cholinergic' effect and suppress central stimuli¹¹. The dosage is 10 mg given 4 times daily.

Incidence of low grade chronic gastritis and gastric atrophy is common. It is associated with antiparietal antibody, anti thyroid antibody in 10% cases. Gastric atrophy is

related to the patients age than severity or duration of diabetes.

Small Intestinal Dysfunction

The commonest manifestation of dysfunction is in the form of diarrhoea. Diarrhoea in diabetes is common and distressing. Half the patient may show evidence of steatorrhoea.

Diabetic Diarrhoea

Diarrhoea in diabetes is considered secondary to autonomic neuropathy and is similar to post-vagotomy diarrhoea¹². Steatorrhoea if present suggests a secondary complication like bacterial overgrowth which is secondary to disordered motility and stasis. Other causes of steatorrhoea include associated pancreatic exocrine deficiency due to chronic pancreatitis or a gluten-sensitive enteropathy which occurs more often in diabetes. In addition anal incontinence (see later) may be responsible for worsening the symptoms. Malabsorption of bile acids in the terminal ileum¹⁸ also blamed for malabsorption as is seen after vagotomy¹³. Dihydroxy bile acids produced in the colon are then responsible for causing secretion of fluid and electrolytes leading to diarrhoea. Recently excessive VIP levels in the neurons of the gut is implicated.

(Primary) Diabetic Diarrhoea

This is arbitrarily defined as the presence of diarrhoea for greater than 1 month consisting of increased frequency, small stools, often nocturnal, without evidence malabsorption. Typically the diarrhoea is episodic with bouts lasting days to weeks followed by an interval of weeks to months when even constipation may supervene. The diagnosis is primarily one exclusion and should include stool examination and screening for malabsorption. Treatment of

the condition entails strict glycaemic control of the diabetes, use of a bulk agent like ispaghula husk along with opiates like diphen-oxylate and loperamide. Trial of two weeks of tetracycline for bacterial overgrowth have been found useful in controlling diarrhoea. Cholestyramine has also been used to sequester bile salts which helps diarrhoea in some cases.

Intestinal Pseudo-Obstruction Syndrome

Diabetes mellitus is one of the secondary causes of an intestinal pseudo-obstruction syndrome. Patients may present with a chronic illness characterised by recurrent intestinal obstruction without demonstrable mechanical occlusion of the bowel. Intermittent constipation and diarrhoea is seen between the periods of symptomatic obstruction.

Constipation: This is the commonest gastrointestinal symptom. Severe constipation often requiring use of regular enemas is seen in 20% of patients with neuropathy.⁴

Pathogenesis: This is not well understood. In one electrophysiological study, it was found that though basal spike activity in the colon was preserved, the normal meal stimulated activity was blunted. The colon remained responsive to exogenous cholinergic agents suggesting a problem with the intrinsic neurohormonal transmission¹⁴.

Treatment: Conventional treatment with laxatives, stool softeners and bulking agents is indicated. Metoclopramide has been found to be useful in uncontrolled trials¹¹.

Anal 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.

Pathophysiology : 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 sphincter¹⁵.

Treatment: Opiate group of drugs should be used. Loperamide is especially useful as it produces a smaller volume of solid stool but also improves the sphincter function¹⁶.

Gastrointestinal Manifestation of Diabetic Ketoacidosis (DKA)

Nausea, vomiting and diffuse severe abdominal pain may occur in DKA. Rapid control of metabolic imbalance results in the early disappearance (4-6 hrs) of these symptoms. The differential diagnosis of such severe abdominal pain includes acute pancreatitis, acute cholecystitis and acute mesenteric ischemia. However, the diagnosis is facilitated by the early disappearance of the symptoms on correction of metabolic abnormality.

Diabetes and the Liver

a) *Fatty Liver:* This is the commonest abnormality of the liver and is seen in 20-50% of biopsies¹⁷. When present, it generally reflects uncontrolled diabetes. Obesity is another important factor. Patients may have only an enlarged liver with local tenderness. Liver function tests may show a mild elevation of alkaline phosphatase and transaminases. Biopsy shows the characteristic large vacuoles which fill the hepatocyte.

b) *Cirrhosis :* Intolerance to oral or

intravenous glucose is a common finding in patients with cirrhosis. This should be distinguished from the increased incidence of cirrhosis found in patients with diabetes as seen in autopsy, and clinical studies¹⁸. The cause of this association is unknown.

c) *Diabetes and acute viral hepatitis* : An increased incidence of adverse sequelae of viral hepatitis in the form of subacute hepatic failure, chronic hepatitis and cirrhosis apart from cholestatic hepatitis has been reported¹⁹.

d) *Hemochromatosis* : The syndrome of cirrhosis, hyperpigmentation and diabetes alongwith other systemic involvement associated with a primary iron overload state is well known in diabetes.

e) *Antidiabetic drugs--Hepatotoxicity* : Oral hypoglycemic agents are well known to produce hepatotoxicity and this was best seen with the earlier agent carbutamide. Chlorpropamide has been described to cause cholestatic hepatitis in up to 5% of treated patients, though up to 25% patients may show an elevated alkaline phosphatase²⁰.

Diabetes and Gallstones

The association of diabetes and gallstones independent of other factors like obesity is open to question. Earlier studies suggested high incidence of gallstone in diabetes²¹. Certain factors existing in diabetes predispose to gallstones formation as increased as supersaturation of bile with cholesterol, a reduction of bile acids and gall bladder hypomotility.

Acute cholecystitis is a more serious disease in these patients and occurs more often due to vascular insufficiency. Emphysematous cholecystitis secondary to gas-forming organism is a particularly dangerous condition. It is for these reasons

it is recommended that asymptomatic gallstones discovered in a diabetics should be operated electively.

Diabetes and the Pancreas

a) The most important association is a secondary diabetes resulting from chronic calcific pancreatitis, diabetes developing in this situation is often brittle and difficult to control though less prone to ketosis.

b) Acute pancreatitis is supposed to be more common in patients with diabetes. Acute pancreatitis with diabetic ketoacidosis carries a particularly high mortality²².

c) Carcinoma of the pancreas : Several studies have suggested that there is an increased incidence of pancreatic carcinoma in patients with diabetes especially women. It is often difficult to be sure whether the diabetes preceded or was caused by malignancy. In many patients it actually appears to be the result of malignancy^{23,24}. In a patient with controlled diabetes if suddenly the diabetic control go hay wire malignancy may be suspected if other causes are excluded as infection etc.

Diabetes and Vascular Disease

Patients are more likely to develop splanchnic vascular insufficiency as a consequence of atherosclerosis. This gives rise to the clinical syndrome of abdominal angina. Periumbilical pain occurs after eating and is associated with a sitophobia. Acute mesenteric arterial ischemia is one of the dreaded complications in a diabetic and early surgery is required to prevent fatal intestinal gangrene.

Diabetic Radiculopathy

This gives rise to an acute, sharp

abdominal pain which may give rise to considerable diagnostic confusion. Careful examination shows distribution along a dermatoma with cutaneous hyperaesthesia. The condition generally abates in 6-12 months²⁵.

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