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Diabetic Gastroparesis: Epidemiology, Pathophysiology, Symptoms, and Clinical Consequences

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Abstract

Diabetes mellitus affects over half a billion people worldwide and is associated with numerous complications, including diabetic gastroparesis, characterized by delayed gastric emptying without mechanical obstruction. Although diabetic gastroparesis does not affect life expectancy, it significantly impairs digestion and medication absorption, complicating glucose metabolism and health management, thus reducing quality of life. The etiology of diabetic gastroparesis is multifactorial, involving autonomic neuropathy, vagus nerve dysfunction, disturbances in interstitial cells of Cajal, nitric oxide synthesis, hyperglycemia, and oxidative stress. Symptoms include early satiety, bloating, nausea, vomiting, dysphagia, and unintentional weight loss, which complicate diabetes management by causing unpredictable glycemic control. Despite advancements in understanding diabetic gastroparesis, it remains underdiagnosed due to its often-asymptomatic nature. Further research is needed to elucidate its epidemiology and pathophysiology, particularly in asymptomatic patients. This review

discusses the epidemiology, pathophysiology, symptoms, and clinical consequences of diabetic gastroparesis, highlighting the need for improved diagnostic and management strategies.

Keywords: diabetes mellitus, gastroparesis, diabetic gastroparesis, gastric emptying, autonomic neuropathy

Introduction

Diabetes mellitus (DM) is a disease, affecting over half a billion people worldwide [1]. Despite the ongoing advancements in diagnostics and treatment methods, its complications remain a serious issue, and if left untreated, they can lead to permanent disability or death [2]. One of them is diabetic gastroparesis (DG), defined as a delay in the emptying of ingested food in the absence of mechanical obstruction of the stomach or duodenum [3]. This disease, despite the demonstrated lack of impact on the life expectancy of patients with diabetes [4], significantly affects the processes of digestion and medication absorption thereby worsening glucose metabolism and complicating health management. Consequently, this can lead to serious implications and a significant reduction in the quality of life [5,6]. Its etiology is multifactorial and not solely related to diabetes. Idiopathic gastroparesis and surgically induced gastroparesis can also be distinguished [7]. Nevertheless, the role of DM in the development of gastroparesis is particularly essential, especially considering its annual increase in prevalence [8]. As many as 50-76% of individuals with longstanding diabetes struggle with the consequences of impaired gastrointestinal dynamics [9,10,11]. Older sources indicate that DG is found in approximately 30-50% of patients with longstanding diabetes, both type 1 and type 2 [12,13,14]. A meta-analysis published in 2023 revealed that the overall prevalence of gastroparesis globally is 9.3% [15]. A study from 2012 showed that patients with type 1 diabetes have a 4.4 times greater risk of developing gastroparesis compared to patients with type 2 diabetes [16]. However, in 2023, a reversal of this relationship was observed – an increased prevalence of gastroparesis as a complication of type 2 diabetes was noted [15].

Ambiguous results also concern the influence of gender on the frequency of occurrence of this condition. From a pathophysiological point of view, gastric emptying rate is slower in women than in men [17]. This was also attributed to the fourfold more frequent occurrence of

gastroparesis in women reported in 2008. However, a meta-analysis from 2023 presented different data – symptoms still occurred more frequently in women, but with a gender difference of 4.6% for women and 3.4% for men [15].

It is interesting to present the occurrence of gastroparesis depending on age. Differently from complications of DM such as coronary heart disease or lower limb ischemia, more patients with gastroparesis are found in the group age under 60 years than in the group above [15]. The first symptoms typically appear around 10 years after diabetes diagnosis, with the average age of onset of first symptoms being 34 years [18,19].

This review article discusses the epidemiology, pathophysiology, symptoms and their clinical consequences.

Pathophysiology

The passage of food content through the digestive system is a complex process. The motor functions of the stomach are regulated by the enteric nervous system (ENS), parasympathetic innervation from the vagus nerve, and the sympathetic nervous system, which interacts with the interstitial cells of Cajal (ICC) and smooth muscle cells. The ENS is a group of ganglia organized into specific plexuses that function independently but also integrate signals from the central nervous system and the autonomic nervous system. ICC are cells that are often likened to the pacemaker system of the heart – they establish the basic electrical rhythm for gastric motility. Abnormalities in this intricate network have been identified in various gastrointestinal disorders [20].

The pathogenesis of DG is not fully understood. The malfunctioning of the stomach can result from impaired relaxation of its fundus disrupted contractile activity of the gastric body and antrum, which is caused by the loss of various types of nerve cells, smooth muscle cells of the stomach wall, or disturbances in neuro-muscular coordination, and in some patients, it is caused by spastic contraction of the pylorus [21]. It is speculated that the occurrence of this condition may be attributed to vagus nerve dysfunction, pathologies in the functioning of ICC, disturbance in nitric oxide synthesis, hyperglycemia, and oxidative stress [22].

One of the causes of DG is autonomic neuropathy, which results in, among other things: decreased tone of the lower esophageal sphincter, disturbances in the contractility of the antral part of the stomach, and abnormal relaxation of the stomach fundus [23]. The cause of these pathologies is: reduced number of cells in the vagus nerve ganglia, from which motor fibers

run, decreased number of cells in sympathetic sensory ganglia, and demyelination and degeneration of vagus nerve axons both within the muscular and submucosal plexuses [24].

Many studies also indicate the significant role of ghrelin in the development of DG. Ghrelin, also known as lenomorelin, is a 28-amino acid peptide playing a significant role in regulating glucose levels in the human body. It contributes to a decrease in insulin secretion [25]. The release of ghrelin is partly regulated by impulses from the vagus nerve, which are impaired in DG due to its dysfunction. The decrease in the concentration of this peptide is likely to have a negative impact on gastric motility, and consequently, is associated with the symptoms reported by patients [26].

The functioning of the stomach requires coordinated activity of several types of cells, including ICC. Over the past few years, numerous publications have demonstrated the loss of ICC in patients with DG [27]. Abnormal gastric muscle function is associated with a reduced number of ICC in the gastric antrum and impaired communication between motor neurons and ICC located in the stomach fundus [28].

Another cause of DG development is abnormalities in nitric oxide levels. This substance is an important neurotransmitter in the intestines regulating gastric muscle function. Reduced expression and dysfunction of neuronal nitric oxide synthase (nNOS) in the smooth muscle neurons of the large intestine and potential inhibition of nNOS by advanced glycation end products lead to gastric emptying disorders and prevent proper relaxation of the pyloric sphincter [29].

Symptoms and clinical consequences

Gastroparesis is characterized by a series of symptoms resulting from impaired gastric motility and delayed emptying [30]. This includes a feeling of fullness that occurs shortly after starting a meal and persists for a longer period after eating [31]. Additionally, the accumulation of gases and fluids in the stomach causes bloating and unrelenting belching [32]. There are also nausea and vomiting, dysphagia, heartburn, and hiccups [33]. Patients suffering for a longer time may also report unintentional weight loss. This is related to both the disturbances in the absorption of nutrients present in gastroparesis and generally reduced calorie intake due to discomfort closely associated with eating [16]. This also affects a key aspect in the treatment of diabetes itself, namely proper glycemic control – consuming smaller meals, absorption disorders, and inappropriate insulin dosing relative to food intake can cause unintended spikes in blood glucose levels, even leading to ketoacidosis, and exacerbate the existing problem of

hypoglycemia in patients with gastroparesis [3]. However, this does not change the fact that obesity in the group of individuals with gastroparesis suffering from diabetes, regardless of type, remains a significant issue, despite the overall tendency to lose weight with this condition. This may be related to better tolerance of sweet, salty, and starchy foods present in gastroparesis [34,35].

The symptoms mentioned above occur with varying frequency depending on the etiology. In diabetic gastroparesis, there is a greater intensity of nausea and vomiting, while in idiopathic cases, abdominal pain and early satiety predominate [30].

From the perspective of diabetic practice, the most typical feature in the course of DG, which may be its sole symptom, is the occurrence of hypoglycemic episodes of unclear etiology – especially when they appear between the administration of short/rapid-acting insulin and meals consumed according to recommendations [5,33]. Symptoms can have a sudden onset in about 50% of those suffering from gastroparesis, while delayed gastric emptying may occur without any signs even in 60% of cases [30]. In 20% of patients, a prodromal period of infectious nature has been identified [34]. The course of the disease typically features periods of exacerbation and remission [30].

Conclusions

Diabetic gastroparesis is a condition characterized by diverse, rather nonspecific symptoms mainly associated with delayed gastric emptying in the absence of pyloric obstruction. The discomfort is burdensome for patients, comparable to inflammatory bowel diseases. However, a large group of patients remains asymptomatic, which is why in clinical practice, gastroparesis is often overlooked and diagnosed with significant delay, only after excluding diseases more common in the population, such as gastroesophageal reflux disease.

Despite the available knowledge about DG, there is still potential for further understanding of its epidemiology and pathophysiology. Research on gastroparesis is conducted at tertiary referral centers in a small group of patients presenting with moderate or severe symptoms. Considering the frequent asymptomatic nature of gastric emptying disorders, it appears necessary to conduct studies in the sensory-motor function of the gastrointestinal tract in the community of individuals with diabetes.

Disclosure

Author's Contribution:

Conceptualization, OD, PG and MD; methodology, OD and PG; check, DM; formal analysis, PG, JG, AS and MR; resources, OD, MD, DM and JM; data curation, OD; writing - rough preparation, OD, PG, MD and DM; writing - review and editing, OD, PG, MD, DM, MR, JG, JM and AS; visualization, PG and JM; supervision, OD; project administration, OD; All authors have read and agreed with the published version of the manuscript.

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