GASTROESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH LONG-TERM TYPE 1 DIABETES – DIAGNOSTIC AND THERAPEUTIC APPROACHES

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Abstract:
Gastroesophageal reflux disease (GERD) is a common gastrointestinal disorder characterized by reflux of gastric contents and associated mucosal damage. In patients with long-term type 1 diabetes mellitus (T1DM), the incidence of GERD and related complications is higher compared to the general population, which is associated with autonomic neuropathy, impaired esophageal motility, and delayed gastric emptying.
Aim: To systematize and analyze the literature data on GERD in patients with long-standing T1DM, with an emphasis on the pathophysiology, clinical characteristics and barriers to diagnosis.
Materials and methods: A systematic review of publications indexed in PubMed, ScienceDirect and Medline was conducted, using the keywords: „type 1 diabetes", „long-standing", „GERD", „autonomic neuropathy", „esophageal motility". English-language publications from the last 10–15 years were included, focusing on the pathophysiology, clinical outcomes, diagnostic approaches and their relationship to diabetic autonomic neuropathy and therapy.
Results: Literature data indicate that in patients with long-standing T1DM there is an increased frequency of GERD, even in the absence of typical symptoms associated with autonomic neuropathy. Esophageal motor dysfunction and weak lower esophageal sphincter tone have also been documented in such patients. This creates a risk of underestimation of the disease and delay of instrumental diagnostics, including esophageal manometry and 24-hour pH-metry.
Conclusion: GERD in patients with long-standing T1DM often remains undiagnosed and undertreated due to underestimation of atypical symptoms and lack of routine instrumental evaluation. An integrated approach, including gastroenterological evaluation, esophageal manometry and 24-hour pH-metry, is needed to improve diagnostic and therapeutic approaches.
Keywords: *type 1 diabetes mellitus, GERD, autonomic neuropathy, esophageal motility, diagnostics*

INTRODUCTION:

Type 1 diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia and multiple complications affecting almost all organs and systems in the human body, including the gastrointestinal tract (1). T1DM with a long history of more than 10–15 years often leads to autonomic neuropathy, which affects not only the cardiovascular system but also the gastrointestinal tract. An often underestimated but clinically significant complication of this neuropathy is gastroesophageal reflux disease (GERD). The interaction between diabetes and GERD is complex, as diabetes can exacerbate reflux through mechanisms of gastroparesis that delay gastric emptying and contribute to autonomic neuropathy that impairs lower esophageal sphincter (LES) tone and esophageal motility (2, 3).

Furthermore, patients with chronic diabetes may present with atypical or subclinical symptoms of GERD, making early diagnosis and management more difficult. In the context of long-standing T1DM, the lack of standardized screening algorithms and regular instrumental assessment (e.g., pH monitoring or manometry) may lead to underdiagnosis and undertreatment. Understanding the

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pathophysiological mechanisms of both conditions is crucial for their effective management without adverse interactions (4).

AIM:

To systematize and analyze the literature on GERD in patients with long-standing T1DM, including the role of autonomic neuropathy, with a focus on pathophysiology, clinical features, and barriers to assessment and diagnosis, to develop future integrated approaches in treatment and therapeutic practice.

MATERIAL AND METHODS:

The literature review was performed by systematically searching the PubMed, ScienceDirect and Medline databases using the following keywords: „type 1 diabetes", „long-standing", „gastroesophageal reflux disease", „autonomic neuropathy", „esophageal dysmotility". Peer-reviewed publications published up to 2024 were included, including original clinical studies, review articles, studies using manometry or pH-metry, and systematic reviews. Publications using animal models, articles with small samples without a control group, and reports with inadequate methodology were excluded.

RESULTS:

A systematic review by Kumar et al. (2024) discusses two main mechanisms that link diabetes and GERD: autonomic neuropathy and delayed gastric emptying (5). Autonomic neuropathy can lead to LES dysregulation and impaired esophageal motor function.

Additionally, patients with GERD show changes in the autonomic nervous system that affect not only the esophagus but also cardiovascular regulation. A 2024 study showed that patients with GERD have an imbalance between sympathetic and parasympathetic activity, as well as high parasympathetic tone, which correlates with autonomic symptoms (COMPASS 31))(6).

In a pilot North African study (PMC, 2022) in patients with diabetes, 23 out of 38 (≈ 60%) had abnormal esophageal motility (esophageal dysmotility) measured by manometry, but no association with symptoms (such as heartburn) was found (7), demonstrating that objective abnormalities often do not coincide with subjective complaints.

Furthermore, in a study comparing diabetic patients with controls, 28% of diabetics without GERD symptoms were found to have abnormal 24-hour pH monitoring (time with pH < 4), with the incidence being significantly higher in those with proven autonomic neuropathy (8).

In a larger study involving 81 diabetic patients (type 1 and type 2), „Motility capsules" (SmartPill) were used to measure transit times and motor indices, as well as tests of autonomic function. The results showed that certain gastrointestinal symptoms (e.g., feeling of fullness) correlated with the severity of autonomic dysfunction, but not always with motor measurements (9).

A study by Koch et al. (10) in 137 diabetic patients noted different effects of gastroparesis on gastrointestinal symptoms, with patients with type 2 diabetes experiencing greater symptom improvement than those with type 1. Finally, a study by Kinekawa et al. (11) in eight diabetics using an aldose reductase inhibitor (ARI) epalrestat significantly improved esophageal function, providing a valuable approach to the management of esophageal dysfunction in this group. Collectively, these studies advance the understanding of GERD management in the context of diabetes, advocating for personalized treatment approaches. Despite the significant frequency of abnormal motility and reflux, many patients present with atypical complaints or symptoms, making clinical interpretation difficult (12). Instrumental studies such as high-resolution manometry or 24-hour pH monitoring are not routinely used in patients with T1DM, especially those without classic GERD symptoms. There are no specific clinical algorithms or guidelines for screening for GERD in the diabetic population with long-standing T1DM.

DISCUSSION:

The review shows that autonomic neuropathy is a central mechanism for the development and maintenance of GERD in patients with long-standing T1DM. Dysfunction in autonomic regulation leads to esophageal motor abnormalities that often do not correlate with typical reflux symptoms, which

is a cause of underestimation and diagnostic errors. This is consistent with the data that in GERD patients may have impaired autonomic systems, even in the absence of clinical manifestations (13).

Interestingly, measures of autonomic function (e.g., cardiovascular tests) sometimes correlate better with symptoms than motor indices, suggesting that it is not motor dysfunction per se, but a combination of autonomic dysregulation and esophageal changes that determines the clinical picture. A similar phenomenon has been described in the SmartPill capsule study, where symptoms correlated with autonomic dysfunction but not always with objective motor data (14).

The clinical implications are significant: infrequent use of manometry or pH-metry in diabetics may lead to underestimation of GERD complications such as esophagitis, strictures, or long-term disability. Also, the therapeutic response in these patients may be different, as standard proton pump inhibitor (PPI) therapies do not address autonomic dysfunction.

It is important to consider the epidemiological profiles of GERD and diabetes mellitus to consider the clinical significance of the interaction between the two diseases. The prevalence of GERD is increasing in various regions of the world, affecting approximately 20% of the Western population, reflecting changes in dietary habits, obesity rates, and an aging population (15). On the other hand, diabetes mellitus continues to be a global health problem, with approximately 589 million adults worldwide living with the condition, according to the International Diabetes Federation (IDF Diabetes Atlas 11th Edition), and nearly half of them are unaware of it. This number is projected to reach 853 million by 2050 (16). The overlap between these two common conditions highlights the critical need for integrated clinical approaches, with a focus on treatment and quality of life for patients (17).

The understanding of the relationship between GERD and diabetes has evolved significantly in recent decades, revealing the bidirectional influence of diabetic autonomic neuropathy and GERD symptoms through impaired gastric motility (18), as well as the association of hyperglycemia and impaired lower esophageal sphincter function, further predisposing individuals to acid reflux (19). This mechanism is complex, as it not only exacerbates typical GERD symptoms but also complicates glucose control, creating difficulties in symptom management (20).

In addition, the evolving understanding of these two conditions is gradually shifting the focus of clinical practice from treating GERD and diabetes as separate entities to a more integrated approach emphasizing personalized treatment strategies that address both metabolic control and gastrointestinal health (21).

Practical recommendations and advice

- Routine screening for GERD in patients with T1DM and duration of more than 10–15 years, even in the absence of symptoms — by manometry or 24-hour pH-monitoring.
- Interdisciplinary approach including an endocrinologist and a gastroenterologist to assess autonomic function and reflux.
- Increased use of instrumental studies, such as high-resolution manometry, pH-metry and other techniques as needed.
- Consideration of combination therapy, in addition to proton pump inhibitors (PPIs), with possible inclusion of prokinetics, in patients with proven motor dysfunction and autonomic dysregulation.
- Need for prospective cohort studies in patients with long-standing T1DM to assess whether interventions based on autonomic dysfunction and motor skills reduce complications and improve quality of life.

CONCLUSION

Gastroesophageal reflux disease is a frequently unrecognized but clinically significant complication in patients with long-standing T1DM. Autonomic neuropathy plays a leading role in the pathophysiology, by disrupting esophageal motor function and esophageal sphincter regulation. Greater awareness, screening, and instrumental assessment are needed to detect and treat these patients adequately. An integrated, interdisciplinary approach and personalized therapy may improve the diagnostic process and clinical outcomes.

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