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From Diagnosis to Recovery: The Contributing Roles of Nursing, Pharmacy, and Pathology in Managing Gastrointestinal Disorders-Diabetes as A Model.

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Abstract:

Background: Gastrointestinal disorders, particularly in patients with diabetes, are increasingly recognized as important contributors to disease burden and poor quality of life. Gastrointestinal symptoms such as gastroparesis, reflux, and dysphagia affect a large proportion of individuals with type 1 and type 2 diabetes. These disorders often complicate diabetes management and worsen glycemic control. The gastrointestinal system plays a vital role in nutrient absorption and digestion, and its dysfunctions are often exacerbated by diabetes-related complications. This paper explores the roles of nursing, pharmacy, and pathology in the management of gastrointestinal disorders in diabetes, with a focus on gastroparesis.

Aim: The aim of this article is to examine the interrelated roles of nursing, pharmacy, and pathology in managing gastrointestinal disorders, particularly gastroparesis, in diabetic patients.

Methods: This study utilized a review approach, summarizing existing research on gastrointestinal manifestations in diabetes, with a focus on gastroparesis. Data from clinical studies, diagnostic evaluations, and treatment outcomes were synthesized to assess the roles of healthcare professionals in managing these conditions.

Results: Key findings highlight the significant impact of gastrointestinal disorders like gastroparesis on diabetes management. Effective nursing interventions, such as patient education and symptom management, are crucial in improving patient outcomes. Pharmacological treatments, including prokinetic drugs, offer varying success rates, and advancements in diagnostic technologies have improved the understanding of these disorders. However, challenges remain in the standardized diagnosis and treatment of these conditions.

Conclusion: This article concludes that a multidisciplinary approach, incorporating nursing, pharmacy, and pathology, is essential for the effective management of gastrointestinal disorders in diabetes. Early diagnosis, patient-centered care, and targeted therapies are critical in alleviating symptoms and improving quality of life for affected individuals.

Keywords: Diabetes, gastrointestinal disorders, gastroparesis, nursing care, pharmacological management, pathology, glycemic control.

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Introduction:

The Gastrointestinal Tract and Diabetes

The gastrointestinal (GI) tract spans from the oral cavity to the rectum, fulfilling vital functions necessary for sustaining life. These functions encompass nutrient intake, decomposition, digestion, absorption, and the preparation and elimination of waste products. Gastrointestinal symptoms frequently occur in patients with diabetes and include characteristics such as gastroesophageal reflux, abdominal bloating, nausea, constipation, diarrhea, and fecal incontinence. Research indicates that more than 50% of patients visiting diabetic outpatient clinics encounter uncomfortable gastrointestinal problems at some stage. Moreover, gastrointestinal motility disorders are common in diabetes and may affect glucose regulation. Among these dysfunctions, gastroparesis—defined by delayed stomach emptying—possesses considerable clinical significance and will be explored in further detail. This chapter exclusively addresses the gastrointestinal manifestations linked to type 1 and type 2 diabetes, omitting other diabetes types, including those arising from cystic fibrosis.

Gastrointestinal Symptoms

Gastrointestinal symptoms are prevalent in patients with type 1 and type 2 diabetes, with the majority of research demonstrating a greater incidence in these populations relative to non-diabetic controls [1]. Nonetheless, discrepancies in results are largely attributable to changes in research techniques and patient demographics. Gastrointestinal symptoms are frequently underreported, especially those deemed socially stigmatizing, such as fecal incontinence, indicating that current prevalence estimates may not accurately reflect the actual burden. Clinical trials assessing gastrointestinal symptoms in diabetes predominantly depend on self-reported data, a method acknowledged for its shortcomings, instead of utilizing validated evaluation instruments typically employed in functional gastrointestinal diseases such irritable bowel syndrome [2]. Women with diabetes demonstrate a greater prevalence of gastrointestinal symptoms, aligning with findings in functional gastrointestinal disorders [3]. The disparity in symptom prevalence between type 1 and type 2 diabetes remains ambiguous, however the detrimental effect of these symptoms on quality of life is well documented [4]. There is a little association between symptom presence and objective assessments of gastrointestinal function, including stomach emptying rates. The natural evolution of gastrointestinal symptoms in diabetes remains inadequately characterized; yet, significant symptom variability has been noted, with around 15–25% of individuals encountering the emergence or alleviation of symptoms during a two-year timeframe [1]. This fluctuation has been linked to the onset of depression, but not to autonomic neuropathy or glycemic regulation [5].

Gastrointestinal Manifestations in Diabetes

Esophagus:

The esophagus, a muscular conduit connecting the pharynx to the stomach, enables the movement of ingested substances and is controlled by the upper and lower esophageal sphincters to avert esophago-pharyngeal and gastroesophageal reflux. Two prevalent esophageal symptoms in diabetes are heartburn, a characteristic of gastroesophageal reflux disease (GERD), and dysphagia, which may signify esophageal motility abnormalities. Esophageal motility can be assessed using conventional and high-resolution manometry; however, scintigraphy, despite its availability, lacks uniformity and is rarely employed in clinical practice. Esophageal transit exhibits a weak correlation with gastric emptying in diabetes [6]. Acute hyperglycemia has been demonstrated to compromise esophageal motility [7] and diminish lower esophageal sphincter pressure [8]. Despite being less researched than the stomach, data indicates that esophageal motility problems often coincide with gastric dysmotility and may have common underlying pathophysiological processes. This encompasses lower cholinergic activity and vagal parasympathetic

dysfunction [9], alongside anatomical alterations noted in gastroparesis, including a decrease in interstitial cells of Cajal and inhibitory intrinsic neurons [10]. A case series indicated that diffuse esophageal muscle hypertrophy was observed in two-thirds of patients with diabetes [11]. Management alternatives for esophageal issues in diabetes are constrained. General therapies encompass lifestyle alterations, including enhanced glycemic management, weight reduction, dietary changes, and consistent physical activity. Pharmacological therapies utilizing prokinetic drugs, such as metoclopramide, domperidone, cisapride, and erythromycin, exhibit inconsistent success. Botulinum toxin has demonstrated potential in preliminary tests with diabetic patients suffering from achalasia and peripheral neuropathy, enhancing peristalsis and contraction amplitude [12]. Gastroesophageal reflux disease (GERD), prevalent among the general populace and those with diabetes, is treated by lifestyle modifications, such as elevating the bed, and pharmacological therapies, including proton pump inhibitors.

Stomach: Diabetic Gastroparesis

The delayed emptying of stomach contents, termed diabetic gastroparesis, was first documented nearly a century ago. Kassander's seminal work in 1958 highlighted asymptomatic gastric retention in diabetes and introduced the term "gastroparesis diabeticorum" [16]. The study also suggested its potential adverse impact on glycemic control. Gastroparesis, defined as the abnormal delay in gastric emptying of solid food without mechanical obstruction, remains a diagnostic and therapeutic challenge in both type 1 and type 2 diabetes [17]. The rate of gastric emptying significantly influences postprandial glycemia in both health and diabetes [20]. Newer anti-diabetic agents, such as short-acting GLP-1 receptor agonists, effectively reduce postprandial glucose levels primarily by delaying gastric emptying.

Epidemiology of Diabetic Gastroparesis

The exact global incidence and prevalence of diabetic gastroparesis are ambiguous owing to discrepancies in its diagnosis, study cohorts, and methodology. Diabetes is a significant contributor, responsible for over 30% of gastroparesis cases in tertiary care research [17]. Data from the DCCT-EDIC trial indicated that 47% of type 1 diabetic patients experienced delayed stomach emptying, consistent with results from cross-sectional investigations [21]. Gastroparesis, often regarded as a consequence exclusive to advanced type 1 diabetes, is now acknowledged as prevalent in type 2 diabetes as well [16,22]. Risk factors encompass extended diabetes duration, concurrent microvascular problems, female sex, obesity, and tobacco use [17]. Community-derived data from the United States reveal an incidence of gastroparesis of roughly 5% in type 1 diabetes and 1% in type 2 diabetes, in contrast to 0.01% in control subjects [23]. Hospitalizations for diabetic gastroparesis surged by 158% from 1995 to 2004, indicating either a true increase in incidence or enhanced clinical awareness of the condition [24]. Advancements in glycemic control designed to mitigate microvascular consequences may have led to a decreased incidence of gastroparesis. Recent studies indicate that well-managed type 2 diabetes correlates with a low incidence of gastroparesis, with certain instances exhibiting moderately accelerated stomach emptying [19,25].

Diagnosis of Diabetic Gastroparesis

The diagnosis of diabetic gastroparesis necessitates a systematic approach, as gastrointestinal symptoms alone do not reliably indicate delayed gastric emptying. Clinical evidence indicates that persons experiencing severe upper gastrointestinal symptoms may demonstrate normal or even expedited gastric emptying, whereas those with considerable delays in gastric emptying may report little or no symptoms. A proper diagnosis of gastroparesis requires the assessment of gastric emptying, after ruling out mechanical obstructions at the gastric outlet or proximal small intestine. Scintigraphy, established in the 1970s, continues to be the preeminent diagnostic method. Initiatives to standardize its methodology have led to criteria established by the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine, which classify gastroparesis as intragastric retention exceeding 60% of a standardized meal at two hours and/or over 10% at four hours [26]. The standardized test meal, according to these standards, consists of two egg whites, two pieces of bread, 30 g of jam, and 120 ml of water, yielding 255 kcal primarily from carbohydrates (72%), with contributions from protein (24%), fat (2%), and fiber (2%) [26].

Notwithstanding these initiatives, the extensive global adoption of a particular test meal, especially beyond Western contexts, is improbable. Scintigraphy provides the advantage of accurate, concurrent evaluation of both solid and liquid meal constituents, although it predominantly marks the solid component in the standardized examination. Nonetheless, it is constrained by radiation exposure and the necessity for sophisticated equipment and expertise. Alternative diagnostic procedures encompass ^13C-based breath tests and ultrasonography, both of which eliminate radiation exposure; although, ultrasonography is contingent upon the operator's skill [22]. Innovative methods, like wireless motility capsules, magnetic resonance imaging (MRI), and single-photon emission computed tomography (SPECT) imaging, are also accessible. Currently, these novel technologies are regarded as less precise than scintigraphy and are predominantly confined to research applications [17].

Pathogenesis of Diabetic Gastroparesis

Gastric emptying is a sophisticated, precisely coordinated process wherein chyme is sent to the small intestine at a controlled rate. This process entails complex interactions among gastrointestinal musculature, the intrinsic and extrinsic neurological systems, the stomach pacemaker (Interstitial Cells of Cajal or ICC), immunological cells, and fibroblast-like cells that express platelet-derived growth factor receptor alpha. During fasting, a cyclic contractile pattern termed the migrating motor complex (MMC) aids in the removal of indigestible food particles and germs from the stomach to the small intestine [27]. The MMC comprises three phases: a quiescent phase (phase I) lasting roughly 40 minutes, an irregular contractile phase (phase II) enduring about 50 minutes, and a regular contractile phase (phase III) marked by rhythmic contractions occurring at approximately three per minute in the stomach and 10–12 per minute in the small intestine over a 10-minute interval [28]. Following meal consumption, the MMC shifts to a postprandial motor pattern, wherein solid food is amalgamated with gastric acid and reduced to particles smaller than 1–2 mm in the distal stomach. This process is facilitated by vagal and nitrergic processes for stomach accommodation, vagal and intrinsic cholinergic pathways for antral contractions, and nitrergic pathways for pyloric relaxation [17]. The resulting chyme is transmitted in a pulsatile fashion through the pylorus to the proximal duodenum [22,27].

The rate of stomach emptying is primarily governed by nutrient-induced inhibitory feedback from the small intestine, rather than by intragastric processes [29]. Digestible solids and nutrient-dense liquids have a linear emptying pattern, influenced by intestinal feedback mechanisms, while low- or non-nutrient liquids adhere to a volume-dependent monoexponential emptying pattern owing to diminished small intestine feedback. Various gut peptides are crucial in these mechanisms; specifically, glucagon-like peptide-1 (GLP-1), cholecystokinin (CCK), and peptide YY facilitate inhibitory feedback, whereas ghrelin and motilin, which promote stomach emptying, are diminished after meals [22,27]. The area and segment of the small intestine exposed to nutrients also affect the regulation of feedback to decelerate stomach emptying [30]. Impaired stomach emptying results from dysfunctions in multiple elements of this intricate process. Recent advancements, especially from the NIH-funded Gastroparesis Clinical Research Consortium, have elucidated the pathophysiology of diabetic gastroparesis. Histological analyses have demonstrated a decrease in the quantity of interstitial cells of Cajal, corresponding with the severity of gastric emptying delay [31]. This loss seems to be influenced by immunological infiltration, characterized by a transition from protective M2 macrophages to pro-inflammatory M1 macrophages, dysregulated heme oxygenase-1, and oxidative stress. Moreover, modifications in the expression of the Ano-1 gene, which influences ICC conduction, have been documented [32]. A decrease in inhibitory neurons that produce nitric oxide synthase worsens the situation [31].

The Role of Gastric Emptying in Glycemic Regulation and Diabetes Advancement

The rate of stomach emptying shows considerable inter-individual range, ranging from 1 to 4 kcal per minute in healthy individuals, with even greater variance observed in diabetic patients due to the occurrence of gastroparesis and, less commonly, unusually quick gastric emptying. Gastric emptying is a crucial factor influencing postprandial glycemic responses in various glucose tolerance levels, with these interactions changing over time. In people with normal glucose tolerance, the initial increase in blood

glucose (about 30 minutes) after consuming a 75 g oral glucose load is closely correlated with the pace of stomach emptying. In contrast, the conventional two-hour glucose measurement during an oral glucose tolerance test (OGTT) exhibits an inverse correlation with gastric emptying rates. In type 2 diabetes, the relationship changes, resulting in both the 30-minute and two-hour glucose levels directly correlating with the gastric emptying rate [33-35].

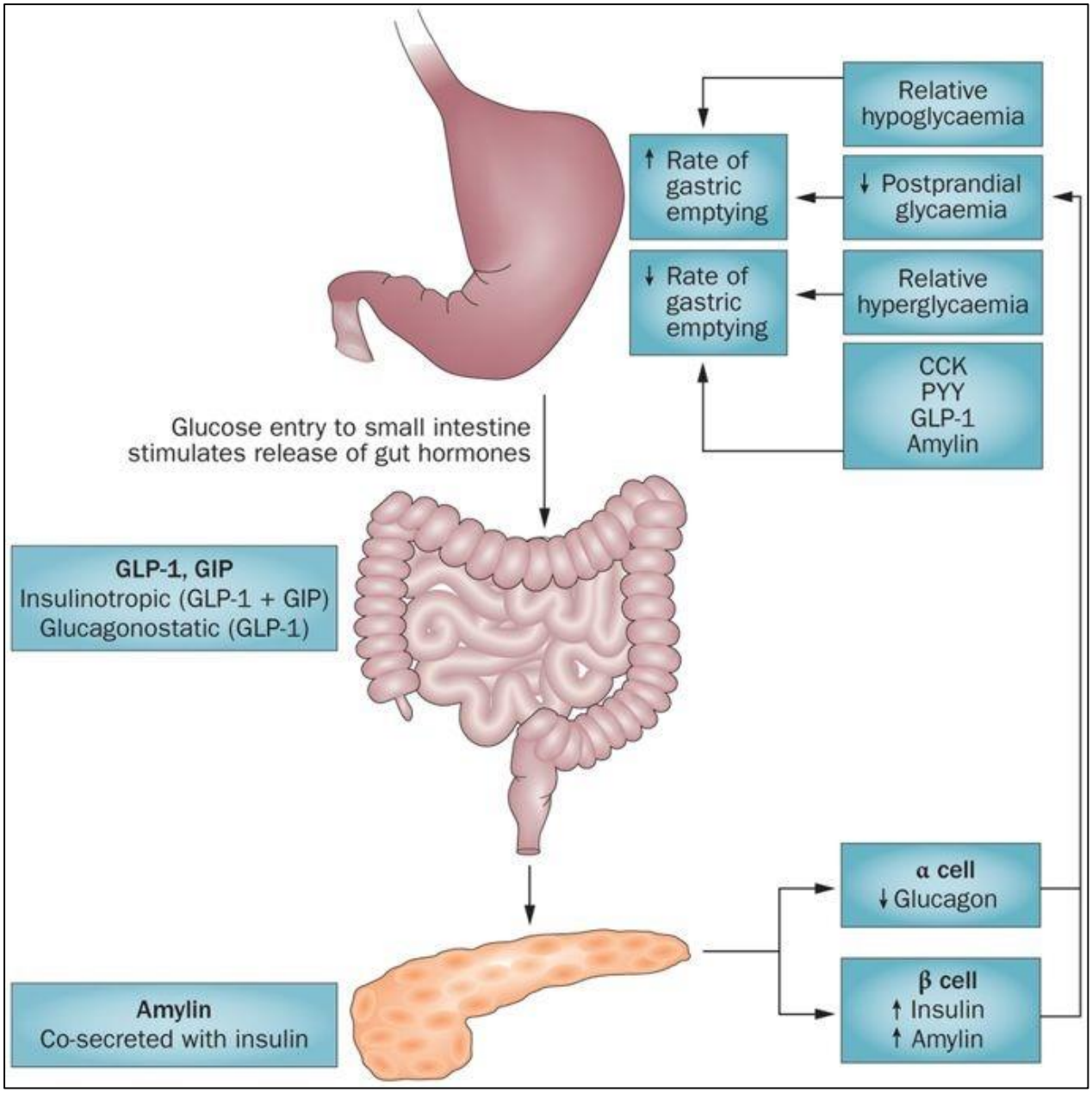

Figure 1: Bidirectional relationship between gastric emptying and glycemia.

Epidemiological studies indicate that around 50% of patients with impaired glucose tolerance (IGT) advance to type 2 diabetes, highlighting the significance of factors affecting this progression. Studies have shown that the disposition index, an essential predictor of the advancement to type 2 diabetes, is negatively correlated with gastric emptying rates [36]. Furthermore, the one-hour plasma glucose concentration during a 75 g OGTT, which is highly correlated with the risk of developing type 2 diabetes, is greatly influenced by the pace of stomach emptying [34, 35]. In type 2 diabetes, pharmacological alteration of stomach emptying directly affects postprandial glycemia. For example, the administration of drugs such as morphine, which slows stomach emptying, results in less postprandial hyperglycemia excursions,

whereas prokinetic medicines like erythromycin, which hasten gastric emptying, intensify these glycemic spikes [38]. Experimental models utilizing naso-duodenal catheters for direct glucose administration into the small intestine at regulated rates within the physiological range of gastric emptying have clarified the influence of gastric emptying on postprandial insulin secretion and the incretin effect. These investigations indicate that the contributions of incretin hormones, including glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1), fluctuate according to the rate of glucose absorption in the small intestine. GIP is predominant at lower glucose delivery rates (2 kcal/min or less), while GLP-1 gains prominence at higher delivery rates (3–4 kcal/min) [39].

Blood glucose levels influence the regulation of stomach emptying. Studies utilizing the "glucose clamp" technique have demonstrated that sudden increases in blood glucose levels impede stomach emptying in a dose-dependent fashion, where elevated glucose concentrations lead to more significant delays. For instance, when blood glucose is maintained at around 8 mmol/L (144 mg/dL), stomach emptying is considerably delayed in both healthy individuals and those with well-regulated type 1 diabetes [40]. In contrast, severe hypoglycemia, characterized by blood glucose levels of approximately 2.6 mmol/L (46.8 mg/dL), significantly enhances stomach emptying, presumably as a counter-regulatory mechanism to promote glucose absorption [42]. The dynamic regulation of stomach emptying by glucose levels underscores its potential impact on nutrient absorption and the efficacy of orally delivered drugs, a consideration that remains inadequately acknowledged in clinical practice. The effect of prolonged glycemic control on stomach emptying is still unclear and requires additional research. In individuals with insulin-dependent diabetes, regardless of type, synchronizing exogenous insulin delivery with carbohydrate availability is essential to reduce the likelihood of postprandial hypoglycemia. Delayed stomach emptying is logically linked to a reduced probability of early postprandial hypoglycemia, commonly termed "gastric hypoglycemia," succeeded by hyperglycemia in the subsequent postprandial period. Research indicates that in type 1 diabetes patients, insulin requirements during the initial 120 minutes post-meal were diminished in those with gastroparesis, although elevated during the following 180–240 minutes compared to persons with normal stomach emptying [45]. Considering the growing acknowledgment of the link between glycemic variability and negative outcomes, comprehending stomach emptying rates may provide essential insights for doctors aiming to reduce postprandial hyperglycemia fluctuations. Nevertheless, additional research is need to formally validate these prospective advantages.

Management of Symptomatic Gastroparesis

General Measures

The management of gastroparesis requires a customized strategy for each patient. Clinically, individuals are often recommended to eat smaller, more frequent meals that are low in fat and fiber, with a higher percentage of calories obtained from liquids instead of solids. Solid foods ingested should preferably fragment into little bits easily [47]. It is essential to recognize that this dietary recommendation has not undergone extensive clinical examination and may be difficult for patients to adhere to consistently. Consequently, the participation of a dietician in care planning is highly advised [48]. Although optimizing glycemic management is rational, especially considering the inhibitory impact of acute hyperglycemia on stomach emptying, evidence supporting this connection in chronic circumstances is insufficient. Recent innovations, such continuous subcutaneous insulin infusion and continuous glucose monitoring, have been suggested to improve glycemic control [49]. Concomitant medications require meticulous examination, and, where possible, drugs that may impede stomach emptying—such as opioids and anticholinergics—should be terminated. Short-acting GLP-1 receptor agonists (e.g., exenatide BD and lixisenatide) and the amylin analog pramlintide have demonstrated efficacy in enhancing chronic diabetic control, principally via their effects on stomach emptying.

Medications

Pharmacological treatments for gastroparesis mostly consist of prokinetic drugs, which, although fundamental to therapy, are linked to drawbacks like unpleasant effects and tachyphylaxis (a decline in drug

effectiveness with time). Tachyphylaxis is notably pertinent to motilin agonists, however extensive research is insufficient. Cisapride, a 5HT4 receptor agonist previously utilized for symptom control, was removed from the market due to its correlation with severe cardiac side effects, including QT interval prolongation and torsades de pointes. At present, various prokinetic agents are employed, each possessing unique attributes and possible disadvantages. Metoclopramide, a dopamine D2 receptor antagonist, facilitates stomach emptying and is accessible through oral, intranasal, and subcutaneous administration. Nonetheless, its application is constrained by central nervous system adverse effects, including the possibility of irreversible tardive dyskinesia. The U.S. Food and Drug Administration (FDA) recommends limiting its usage to 12 weeks. Emerging intranasal formulations have shown efficacy in women but not in men, suggesting that gender-specific variables may affect the appropriate route of administration [51]. Subcutaneous metoclopramide injections may be utilized to mitigate acute vomiting episodes, and it is the only FDA-approved medicine for the management of gastroparesis. Domperidone, a D2 receptor antagonist, possesses a more advantageous safety profile owing to its incapacity to traverse the blood-brain barrier. This medicine demonstrates similar efficiency to metoclopramide in enhancing gastric emptying and relieving upper gastrointestinal symptoms [48,52]. Domperidone may extend the QT interval and affect the metabolism of other medications through the CYP2D6 pathway [48]. Erythromycin, an antibiotic possessing motilin receptor agonist characteristics, has demonstrated effectiveness in expediting stomach emptying, especially in acute circumstances. It is comparatively low-cost but necessitates regular administration and presents concerns of QT interval lengthening and medication interactions via the CYP3A4 pathway [48]. Intravenous erythromycin is notably successful in markedly expediting delayed gastric emptying and may assist in the installation of neuroenteric tubes [53,54]. Nonetheless, its gastrokinetic effects are susceptible to tachyphylaxis [55].

Emerging Therapies

Numerous innovative therapeutic medicines are presently in Phase 2 and 3 clinical studies, such as ghrelin agonists and 5HT4 receptor agonists. Ghrelin, sometimes referred to as the "hunger hormone," is produced by the gastric fundus and is crucial for appetite management and nutrition detection. The exogenous infusion of ghrelin has been shown to expedite stomach emptying in both animal models and humans [56]. Initial clinical trials of the ghrelin agonist relamorelin have shown encouraging outcomes, including a decrease in upper gastrointestinal symptoms and improved stomach emptying in patients with gastroparesis, regardless of diabetes type [57]. A global Phase 3 trial is presently in progress. Moreover, selective 5HT4 receptor agonists, such velusetrag (formerly sold for constipation) and prucalopride, have demonstrated efficacy in enhancing stomach emptying rates [58,59]. A recent study of a 4-week prucalopride regimen in 32 patients with gastroparesis, including six with diabetes, demonstrated enhancements in symptoms and stomach emptying. Nonetheless, subgroup analysis of the diabetes cohort was not performed owing to the restricted sample size [59].

Treatment-Refractory Gastroparesis

The therapy of gastroparesis that does not respond to dietary and pharmacological treatments poses a considerable clinical challenge, as it greatly diminishes patient quality of life. In such instances, other nutritional support strategies, such as jejunal feeding or parenteral nutrition, may be required. Gastric electrical stimulation (GES), enabled by the "Enterra" device, first demonstrated potential in early unblinded experiments indicating symptomatic enhancement [22,48]. The FDA has sanctioned GES under a "humanitarian exemption"; nevertheless, following blinded trials did not reveal substantial differences in outcomes between periods of device activation and deactivation [22,48,60,61]. A recent randomized cross-over experiment indicated a decreased incidence of refractory vomiting over four months in gastroparesis patients (with or without diabetes) undergoing GES treatment, however it did not facilitate gastric emptying or enhance quality of life [62]. Botulinum toxin injections aimed at the pylorus have shown variable effectiveness, with superior results in uncontrolled trials compared to sham-controlled studies [22]. Surgical and endoscopic techniques, including pyloroplasty and pyloromyotomy, as well as

acupuncture, have been investigated as possible therapies; however, these methods lack substantial data from controlled research to validate their efficacy [22,48].

Gall Bladder

Gallstones are significantly more common in patients with diabetes, mostly due to the increased prevalence of risk factors such as intestinal dysmotility, obesity, and hypertriglyceridemia, especially in type 2 diabetes [63]. Other contributory causes including autonomic neuropathy, diminished gallbladder motility, cholesterol supersaturation, and elements that facilitate crystal nucleation. Ultrasound and scintigraphy are frequently utilized diagnostic techniques for assessing gallbladder motor function. Some studies indicate a higher fasting gallbladder volume in diabetic individuals, whereas others find reductions or no differences, potentially due to methodological discrepancies and the occurrence of sympathetic neuropathy. Postprandial gallbladder emptying is routinely documented as impaired in diabetes, a condition occasionally termed "diabetic cholecystoparesis" [63]. It is suspected that delayed stomach emptying contributes to poor gallbladder emptying. Acute hyperglycemia is recognized to impede gallbladder motility in a dose-dependent fashion under typical circumstances [64]. Moreover, a heightened incidence of gallbladder disorders, including cholecystitis and cholelithiasis, has been linked to the use of GLP-1 receptor agonists, possibly attributable to drug-induced delays in gallbladder refilling intervals [65,66]. Furthermore, post-bariatric surgery in obese patients, particularly those with diabetes, correlates with an increased prevalence of gallbladder disease, perhaps due to rapid weight loss [67].

Small Intestine

Although prevalent, diabetic enteropathy has received less comprehensive research attention than gastroparesis [68]. Symptoms including constipation and diarrhea, frequently associated with enteropathy, are discussed in the following section on large intestine diseases in diabetes. Historically, vagal dysfunction has been regarded as the principal underlying mechanism of diabetic enteropathy. Nevertheless, recent research underscores the essential functions of interstitial cells of Cajal and neuronal nitric oxide synthase (nNOS), mirroring observations in gastroparesis [31]. Acute hyperglycemia significantly affects postprandial small intestine motility by reducing the amplitude of duodenal and jejunal pressure waves and prolonging duodenal-cecal transit durations, effects noted in both healthy individuals and possibly in diabetic patients [69]. Small intestine bacterial overgrowth (SIBO), likely due to decreased motility, is commonly observed in diabetes, with prevalence estimates between 15% and 40% in type 1 diabetic populations. The lack of a globally recognized diagnostic criterion hinders precise evaluation. There is a paucity of data concerning small intestine glucose absorption in diabetes. Research employing animal models, particularly streptozotocin-induced diabetes in rats, indicates heightened mucosal glucose absorption [70]. Human studies indicate that glucose absorption in the small intestine of patients with type 1 diabetes without problems is equivalent to that of healthy individuals. However, this absorption is affected by duodenal motility and the glycemic context; increased blood glucose levels augment glucose absorption, while euglycemic situations result in absorption similar to controls [71]. A primary restriction in assessing the impact of stomach emptying on postprandial glycemia is the difficulty in isolating the distinct effects of gastric emptying from those of small intestine transit, which may potentially influence glycemic regulation [72].

Diagnosis of Enteropathy

Diabetic enteropathy is primarily a diagnosis of exclusion, necessitating the elimination of non-diabetes-related causes. For instance, testing for celiac disease in patients with type 1 diabetes is advised. It is important to acknowledge that gastrointestinal side effects are commonly associated with anti-diabetic medications, including metformin, GLP-1 receptor agonists (GLP-1RAs), sodium-glucose co-transporter-2 (SGLT2) inhibitors, and alpha-glucosidase inhibitors such as acarbose. Small intestinal manometry, which measures contractile activity, may provide mechanistic insights but is generally confined to specialized centers. Scintigraphy, while useful for quantifying small intestinal transit, has uncertain diagnostic significance. Emerging technologies, including ingestible wireless capsules (e.g., the SmartPill) and

continuous capsule tracking systems (e.g., 3D-Transit system), hold promise but require further validation for routine clinical use. Diagnosing small intestinal bacterial overgrowth (SIBO) involves intestinal fluid aspiration and culture or breath tests; however, both methods are limited and lack a definitive gold standard.

Management of Enteropathy

Symptomatic management with medication is common for diabetic enteropathy. Prokinetic agents used for gastroparesis are often employed to address disordered intestinal motility, though their evaluation in this context is limited. Antibiotic therapy, such as rifaximin (costly but commonly used), amoxicillin-clavulanic acid, or metronidazole, is effective in treating SIBO, though relapses are frequent.

Large Intestine

The primary function of the colon is to reabsorb water and electrolytes from intraluminal contents, solidifying waste products for elimination. Constipation, diarrhea, abdominal pain, and distension are common lower gastrointestinal symptoms in diabetes. Estimates of true prevalence vary, with chronic constipation reported in up to 25% of individuals with type 1 or type 2 diabetes, and chronic diarrhea in approximately 5% [73]. Bytzer et al. identified a higher prevalence of constipation and diarrhea among individuals with type 2 diabetes (15.6%) compared to non-diabetics (10%) [3]. Data from the US NHANES survey suggest chronic diarrhea is more frequent in diabetic populations (approximately 11%) than in non-diabetics (6%) [74].

Constipation

The multifactorial etiology of diabetic constipation includes autonomic neuropathy, which plays a significant role, particularly in patients with autonomic impairment [75]. Prolonged colonic transit time has been observed in diabetic patients with constipation [13]. Diagnostic techniques, such as colonic transit scintigraphy, radio-opaque markers, and wireless motility capsules, are available but not widely used in clinical practice [76]. Management strategies for diabetic constipation involve reviewing medication history and discontinuing causative agents if possible. For mild cases, the American Diabetes Association advocates lifestyle modifications, including increased physical activity and dietary fiber intake. Commonly prescribed over-the-counter laxatives include bulk-forming agents, osmotic agents, and stimulants like Senna and Bisacodyl. Prescription medications, such as lactulose, linaclotide, and lubiprostone, have shown efficacy. Notably, lactulose may enhance glucose-lowering effects [77], while lubiprostone has demonstrated improvement in spontaneous bowel movements and accelerated colon transit in randomized controlled trials [78]. Pyridostigmine, a cholinesterase inhibitor, showed superior outcomes in bowel function and colonic transit compared to placebo in a study of diabetic patients with chronic constipation [79].

Chronic Diarrhea

Traditionally associated with autonomic neuropathy, diabetic diarrhea is characterized by large-volume, painless, and often nocturnal episodes, occasionally accompanied by fecal incontinence [80]. Diagnosis is one of exclusion, requiring differentiation from fecal incontinence. Commonly used glucose-lowering therapies, including metformin, acarbose, and GLP-1 receptor agonists, frequently contribute to diarrhea. Optimizing glycemic control is likely beneficial but remains inadequately studied [81]. Dietary interventions, such as a low FODMAP diet under dietitian supervision, have not been specifically evaluated in diabetic populations. Symptomatic treatments include loperamide, bile acid sequestrants like cholestyramine and colesevelam, and medications such as clonidine, diphenoxylate, octreotide, and ondansetron. Cholestyramine and colesevelam also provide secondary benefits of lowering LDL cholesterol and glycated hemoglobin. Diabetes has been linked to increased risks of inflammatory bowel disease (IBD), Clostridium difficile infection, and colorectal malignancy. Metformin may exert protective effects against colorectal cancer, potentially through modulation of gut microbiota [82–84].

Rectum and Anus

Fecal incontinence is more prevalent in individuals with diabetes and correlates with disease duration and the presence of microvascular complications, such as autonomic and peripheral neuropathy [85]. Studies show that internal anal sphincter tone and anal squeeze pressures are reduced in diabetic patients compared to healthy controls [86, 87]. Diagnosis involves excluding differential conditions like colorectal malignancy and IBD [88]. Anorectal manometry, using conventional, 3D, or high-resolution techniques, is a valuable diagnostic tool, while barium defecography is useful for detecting motory, sensory, and structural abnormalities [89]. The treatment of fecal incontinence aims to alleviate symptoms and enhance quality of life. Management of fecal impaction may involve manual stool removal, enemas, bulk laxatives, dietary fiber, and toilet training. Biofeedback training, introduced by Engel et al. in 1974, remains a cornerstone in managing incontinence. This technique involves teaching patients to improve voluntary contraction of the external anal sphincter (EAS). Approximately 60% of patients benefit from biofeedback in the long term, with better outcomes in those reporting low bowel satisfaction scores and requiring digital evacuation [90, 91].

Gastrointestinal Effects Of Anti-Diabetic Medications And Their Implications For Clinical Practice

Gastrointestinal adverse effects are frequently observed among individuals receiving glucose-lowering medications for type 2 diabetes. Alpha-glucosidase inhibitors, including acarbose and miglitol, predictably result in gastrointestinal symptoms such as diarrhea and abdominal distension, attributed to carbohydrate malabsorption [92]. Significant findings have emerged regarding the gastrointestinal effects of two major medication classes: biguanides and GLP-1 receptor agonists. Metformin, a herbal-origin biguanide, remains the primary pharmacological choice for managing type 2 diabetes. Although its precise mechanisms of action are yet to be fully elucidated, it exerts multiple effects, including inhibition of hepatic gluconeogenesis, enhancement of insulin sensitivity, and modulation of gastric motility by slowing gastric emptying [93]. Approximately 25% of metformin users report gastrointestinal symptoms, primarily diarrhea and nausea. Clinical strategies to mitigate these effects include initiating therapy at a low dose (e.g., 500 mg/day), gradual dose escalation to around 2000 mg/day, employing extended-release formulations, and avoiding administration on an empty stomach. However, the robustness of evidence supporting these approaches remains limited [94].

Similarly, GLP-1 receptor agonists (unlike DPP-IV inhibitors, which modestly increase plasma GLP-1 levels) are associated with significant gastrointestinal side effects. GLP-1, a gut-derived peptide, substantially slows gastric emptying, with the degree of deceleration correlating with baseline gastric motility rates and postprandial glycemic reductions [95]. While GLP-1-induced gastric emptying deceleration partially explains upper gastrointestinal symptoms, additional effects, such as activation of central nervous system GLP-1 receptors (notably in the brainstem area postrema), may contribute. Additionally, GLP-1 receptor activation within the gastrointestinal tract may enhance motility via local mechanisms, inducing lower gastrointestinal symptoms like diarrhea [98,99]. Gastrointestinal adverse effects of GLP-1 receptor agonists, including nausea, vomiting, and diarrhea, occur in 4.5–13% of cases, with nausea being the most common (up to 25%) [100,101]. Symptoms are often dose-dependent and tend to occur during treatment initiation or dose escalation, persisting for hours or days depending on the drug's Tmax [100]. Evidence derived from scintigraphy confirms that both long-acting and short-acting GLP-1 receptor agonists delay gastric emptying, with a greater effect observed for short-acting agents [95,102-104]. Misconceptions that long-acting GLP-1 receptor agonists have negligible effects on gastric emptying during sustained use have been refuted [2]. However, clinical trials often lack validated methodologies for assessing gastric emptying, limiting comprehensive understanding [105]. Reports of GLP-1 receptor agonist-induced gastroparesis are increasing, prompting guidelines on their use before surgical procedures. The American Society of Anesthesiologists (ASA) recommends discontinuing long-acting GLP-1 agonists at least one week before surgery to mitigate aspiration risks, although robust supporting evidence is limited. Contrarily, UK experts advise individualized risk assessments over generalized discontinuation due to potential post-operative glycemic instability [107]. In individuals co-prescribed

insulin and GLP-1 receptor agonists, delayed gastric emptying may predispose to hypoglycemia by creating a mismatch between insulin availability and glucose absorption. Prescribers should exercise caution in using this combination, particularly in patients with impaired hypoglycemia awareness or suspected delayed gastric emptying.

Pancreatic Exocrine Sufficiency In Diabetes

The anatomical proximity between the endocrine and exocrine pancreatic components establishes a reciprocal relationship, with dysfunctions often coexisting. Prevalence studies indicate that pancreatic exocrine insufficiency is more common in type 1 diabetes (approximately 25–75%) than type 2 diabetes (approximately 25–50%) [109]. However, these findings predominantly arise from hospitalized cohorts, with community prevalence being considerably lower. For instance, a recent study among community-based type 2 diabetes patients reported a prevalence of 9% [110]. The etiology in type 1 diabetes involves insulin deficiency (potentially coupled with glucagon and somatostatin deficits), autoimmunity, autonomic neuropathy, and microvascular damage, whereas autonomic and microvascular dysfunction are key contributors in type 2 diabetes [109]. Symptoms of pancreatic exocrine insufficiency vary, including diarrhea (steatorrhea), abdominal pain, and failure to thrive in pediatric cases. Differentiating pancreatic from non-pancreatic causes of malabsorption is critical. Diagnostic evaluations for pancreatic exocrine function include direct and indirect methods [111]. Direct tests, involving hormone or nutrient stimulation and pancreatic secretion collection via duodenal intubation, are highly sensitive but limited by invasiveness, cost, and expertise requirements. Indirect tests, such as the 3-day fecal fat analysis, fecal elastase-1 measurement, and ^14C-triolein breath tests, are more practical. Of these, fecal elastase-1 is commonly used in clinical settings due to its non-invasiveness and affordability. Levels below 200 μg/g stool indicate mild insufficiency, while levels under 100 μg/g stool signify severe insufficiency [108]. However, the test's sensitivity (55%) and specificity (60%) are modest, and additional assessments, such as fat-soluble vitamin levels, may be warranted. Management principles for pancreatic exocrine insufficiency include dietary modifications (smaller, frequent meals and alcohol abstinence) and the involvement of experienced dietitians. Pancreatic enzyme replacement therapy (PERT) constitutes the cornerstone of treatment, although its effect on postprandial glycemic excursions in type 2 diabetes remains uncertain [110]. Adjunctive treatments, such as acid-suppressing agents, are reserved for patients with persistent symptoms despite high-dose PERT.

Role of Nursing Care:

Gastrointestinal adverse effects are a common concern in patients receiving anti-diabetic medications, particularly in those prescribed medications such as metformin and GLP-1 receptor agonists. These medications are known to cause side effects such as nausea, diarrhea, and abdominal pain, which can significantly affect a patient's quality of life and complicate their diabetes management. Nurses play a crucial role in managing these side effects, ensuring patient comfort, and educating patients on effective strategies to reduce gastrointestinal distress. One of the primary nursing goals in managing patients with gastrointestinal side effects from anti-diabetic medications is to minimize symptoms while optimizing glycemic control.

The first step in the nursing care plan involves a thorough assessment of the patient's symptoms, medication regimen, and general health status. Nurses should closely monitor gastrointestinal symptoms such as nausea, vomiting, diarrhea, and abdominal discomfort, documenting the frequency, duration, and severity of these symptoms. This assessment should be coupled with an evaluation of the patient's nutritional intake, as gastrointestinal disturbances can lead to decreased appetite, malnutrition, and dehydration. Additionally, nurses should assess the patient's understanding of their medication regimen, particularly regarding potential side effects, and gauge their compliance with prescribed treatment protocols. Understanding the patient's current health literacy allows nurses to tailor educational interventions effectively and ensure that patients understand the importance of managing their symptoms and adhering to their medication regimen. Once the assessment is complete, the nursing diagnosis should focus on the primary concerns related to the gastrointestinal adverse effects of anti-diabetic medications.

Common nursing diagnoses include Risk for Imbalanced Nutrition: Less than Body Requirements, related to gastrointestinal discomfort that reduces appetite and causes nausea and vomiting. Another pertinent diagnosis is Risk for Dehydration, which is particularly relevant for patients experiencing diarrhea, leading to significant fluid loss. The nursing diagnosis of Ineffective Health Maintenance may also apply, especially for patients who may not fully comprehend the mechanisms behind their gastrointestinal symptoms or how to mitigate them. This diagnosis highlights the importance of patient education, particularly regarding the proper use of medications and the potential benefits of dietary adjustments to minimize gastrointestinal distress.

The nursing care plan should aim to prevent further complications while improving the patient's overall quality of life. The goal is to reduce the incidence and severity of gastrointestinal symptoms, maintain proper nutritional intake, and improve adherence to the prescribed medication regimen. One of the key interventions for achieving these goals is educating patients about the proper administration of medications. For example, instructing patients to take metformin and GLP-1 receptor agonists with food, starting at a lower dose, and gradually increasing the dosage can help minimize gastrointestinal discomfort. Nurses should also educate patients about the use of extended-release formulations of these medications, which may be better tolerated by some individuals. These measures aim to reduce the intensity of adverse effects while ensuring continued glycemic control. In addition to pharmacological adjustments, nurses must also emphasize the importance of hydration and nutrition. Patients should be encouraged to increase their fluid intake to prevent dehydration, especially if they experience diarrhea or vomiting. The nurse should also collaborate with a dietitian to ensure that the patient maintains a balanced diet that supports their diabetes management while addressing any gastrointestinal symptoms. For instance, the nurse may suggest that patients eat smaller, more frequent meals to avoid overloading the digestive system and causing additional discomfort. A low-fat, easily digestible diet may also be recommended to minimize the strain on the gastrointestinal tract. For patients who continue to experience significant gastrointestinal discomfort despite these interventions, further pharmacological strategies may be required. Nurses should work closely with the healthcare team to explore alternative medications or adjunct therapies, such as antiemetics or antidiarrheal agents, to alleviate symptoms. In some cases, medication adjustments may be necessary, including switching to alternative anti-diabetic drugs that are less likely to cause gastrointestinal side effects. Monitoring the patient's progress with these interventions is essential to ensure that treatment remains effective and that the patient's quality of life improves.

Patient education is a cornerstone of the nursing care plan for managing gastrointestinal side effects from anti-diabetic medications. Nurses should provide clear and concise information about the potential side effects of medications and the steps patients can take to reduce these effects. Education should include advice on recognizing early signs of dehydration, the importance of taking medications as prescribed, and the need for regular follow-up appointments to monitor their condition. Providing patients with written materials and resources may also enhance their understanding and empower them to manage their health more effectively. Furthermore, nurses should foster open communication with patients, encouraging them to report any new or worsening symptoms promptly. Finally, nurses should emphasize the importance of individualized care for patients experiencing gastrointestinal adverse effects from anti-diabetic medications. Every patient responds differently to medication, and what works for one individual may not be suitable for another. Therefore, nurses must continuously assess the effectiveness of the interventions and make adjustments as necessary. By providing ongoing support, education, and monitoring, nurses can help patients manage the gastrointestinal effects of their medications while ensuring optimal diabetes control.

Nursing Care Plan: Pancreatic Exocrine Insufficiency in Diabetes

Pancreatic exocrine insufficiency (PEI) is a common complication in individuals with diabetes, particularly those with type 1 diabetes. The relationship between endocrine and exocrine dysfunction in the pancreas is complex, and PEI can exacerbate the challenges associated with diabetes management. The inability of the pancreas to secrete sufficient digestive enzymes leads to malabsorption of nutrients,

resulting in symptoms such as diarrhea, steatorrhea, abdominal pain, and failure to thrive in children. Effective management of PEI is critical in maintaining optimal nutritional status and improving overall health outcomes in diabetic patients. Nursing interventions must focus on diagnosing PEI, alleviating symptoms, and providing patient education to prevent complications. The first step in the nursing care plan for PEI is a comprehensive assessment of the patient's clinical presentation, including the identification of symptoms such as chronic diarrhea, abdominal bloating, and signs of malnutrition. Nurses should assess the patient's nutritional status, weight changes, and bowel patterns to detect potential signs of malabsorption. Diagnostic tests, such as fecal elastase-1 measurement, are essential for confirming the diagnosis of PEI, and nurses should ensure that these tests are performed in a timely manner. It is also important to assess the patient's history of diabetes management, as the presence of PEI may influence glycemic control and the patient's ability to absorb nutrients effectively. Once the assessment is complete, the nursing diagnosis should focus on the complications of PEI, such as Imbalanced Nutrition: Less than Body Requirements, related to malabsorption of essential nutrients and reduced food intake due to gastrointestinal discomfort. Risk for Dehydration is another relevant diagnosis, especially for patients experiencing diarrhea or vomiting. Chronic Pain may also be a diagnosis for those suffering from abdominal discomfort due to the lack of sufficient digestive enzymes. Additionally, nurses should assess for signs of vitamin deficiencies, particularly fat-soluble vitamins, which are commonly affected by PEI.

The nursing goals for managing PEI in diabetic patients are to maintain nutritional balance, alleviate gastrointestinal symptoms, and optimize overall diabetes control. Key interventions include educating patients about dietary modifications, such as eating smaller, more frequent meals and avoiding alcohol, which can exacerbate gastrointestinal symptoms. Nurses should collaborate with dietitians to develop a tailored nutrition plan that ensures adequate nutrient intake, including supplementation with fat-soluble vitamins if necessary. Furthermore, pancreatic enzyme replacement therapy (PERT) is a cornerstone of treatment for PEI, and nurses should educate patients on its proper use, including timing, dosage, and potential side effects. In addition to dietary changes and enzyme replacement, nurses must monitor the patient's response to treatment. Regular follow-up appointments are essential to assess the effectiveness of PERT and make necessary adjustments to dosage or timing. Nurses should also monitor for potential complications, such as vitamin deficiencies or fluctuations in blood glucose levels, which may be influenced by changes in the patient's digestive function. Encouraging open communication with the patient and providing ongoing support will help ensure that the patient adheres to the treatment plan and achieves optimal health outcomes. Lastly, nurses should provide patients with education on the importance of regular monitoring for signs of malabsorption and gastrointestinal distress. Teaching patients to recognize symptoms early, such as changes in stool consistency, abdominal discomfort, and weight loss, can help facilitate timely interventions and prevent further complications. By offering comprehensive care and support, nurses can significantly improve the quality of life for patients with pancreatic exocrine insufficiency, ensuring that their diabetes management remains as effective as possible.

Conclusion:

Gastrointestinal disorders in diabetes, especially gastroparesis, present a significant challenge for both patients and healthcare providers. These disorders are not only uncomfortable but can also worsen glycemic control and impact a patient's quality of life. The intricate relationship between the gastrointestinal tract and diabetes necessitates a comprehensive, multidisciplinary approach to management. Nurses, pharmacists, and pathologists play vital roles in this approach, ensuring that patients receive effective care tailored to their specific needs. Nursing professionals are often the first line of support for patients with gastrointestinal disorders. They are crucial in educating patients about their symptoms, promoting lifestyle modifications, and managing the psychosocial aspects of these conditions. The management of symptoms such as nausea, bloating, and constipation requires careful monitoring and intervention, emphasizing the importance of personalized care plans. Nurses must also be equipped to assess patients for complications and provide guidance on managing diabetes-related gastrointestinal issues. Pharmacists contribute to the management of gastrointestinal disorders through the identification and administration of appropriate medications. Prokinetic agents, including metoclopramide and

erythromycin, have shown varied efficacy in treating gastroparesis, but their use must be carefully monitored to avoid adverse effects. Pharmacists are also key in advising on the interactions between gastrointestinal medications and diabetes treatments, ensuring that glycemic control is maintained. Moreover, advancements in pharmaceutical research may lead to the development of more effective treatments for these disorders. Pathologists play a crucial role in the diagnostic process. Accurate and early diagnosis of gastrointestinal disorders, such as gastroparesis, is essential for effective treatment. Pathologists assist in identifying underlying conditions, including structural and functional abnormalities in the gastrointestinal tract. The use of diagnostic tools like scintigraphy, breath tests, and motility studies is vital in assessing gastric emptying rates and identifying complications. Pathologists' input is also necessary in the evaluation of disease progression, particularly in chronic diabetes cases where gastrointestinal symptoms may worsen over time. The collaboration between nursing, pharmacy, and pathology is fundamental in providing comprehensive care for patients with diabetes-related gastrointestinal disorders. This multidisciplinary approach not only improves patient outcomes but also enhances the quality of life for those affected. Ongoing research and advancements in diagnostic and therapeutic methods hold promise for further improving the management of these complex conditions. However, challenges remain in ensuring consistent and timely diagnosis, particularly in resource-limited settings. Continued education, patient support, and collaborative care will be essential in addressing the growing burden of gastrointestinal disorders in diabetes.

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الملخص :

الخلفية :يُعترف بشكل متزايد بأن اضطرابات الجهاز الهضمي، وخاصة لدى مرضى السكري، تُعتبر من العوامل المساهمة في عبء المرض وتدهور جودة الحياة. تؤثر الأعراض الهضمية مثل شلل المعدة، والارتجاع، وصعوبة البلع على نسبة كبيرة من الأفراد المصابين بالسكري من النوع الأول والنوع الثاني. وغالبًا ما تؤدي هذه الاضطرابات إلى تعقيد إدارة السكري وزيادة سوء التحكم في سكر الدم. يلعب الجهاز الهضمي دورًا حيويًا في امتصاص المغذيات والهضم، وغالبًا ما تتفاقم اختلالات هذا الجهاز بسبب المضاعفات المرتبطة بالسكري. تستعرض هذه الورقة الأدوار المساهمة للممارسات التمريضية، والصيدلة، وعلم الأمراض في إدارة اضطرابات الجهاز الهضمي في مرضى السكري، مع التركيز على شلل المعدة.

الهدف :الهدف من هذه المقالة هو دراسة الأدوار المترابطة للممارسات التمريضية، والصيدلة، وعلم الأمراض في إدارة اضطرابات الجهاز الهضمي، وخاصة شلل المعدة، في مرضى السكري.

الطرق :استخدمت هذه الدراسة منهج المراجعة، من خلال تلخيص الأبحاث الموجودة حول الأعراض الهضمية في مرض السكري، مع التركيز على شلل المعدة. تم دمج البيانات من الدراسات السريرية، والتقييمات التشخيصية، ونتائج العلاج لتقييم أدوار المهنيين الصحيين في إدارة هذه الحالات.

النتائج :تسلط النتائج الرئيسية الضوء على التأثير الكبير لاضطرابات الجهاز الهضمي مثل شلل المعدة على إدارة مرض السكري. تعتبر التدخلات التمريضية الفعالة، مثل تعليم المرضى وإدارة الأعراض، أمرًا حيويًا لتحسين نتائج المرضى. توفر العلاجات الدوائية، بما في ذلك الأدوية المحفزة لحركة الجهاز الهضمي، معدلات نجاح متفاوتة، وقد حسنت التقدمات في التقنيات التشخيصية من فهم هذه الاضطرابات. ومع ذلك، لا تزال هناك تحديات في التشخيص والعلاج القياسي لهذه الحالات.

الخاتمة :تختتم هذه المقالة بأن النهج متعدد التخصصات، الذي يدمج التمريض، والصيدلة، وعلم الأمراض، ضروري للإدارة الفعالة لاضطرابات الجهاز الهضمي في مرض السكري. إن التشخيص المبكر، والرعاية المتمحورة حول المريض، والعلاجات المستهدفة هي أمور حاسمة في التخفيف من الأعراض وتحسين جودة الحياة للأفراد المتأثرين.

الكلمات المفتاحية :مرض السكري، اضطرابات الجهاز الهضمي، شلل المعدة، الرعاية التمريضية، الإدارة الدوائية، علم الأمراض، التحكم في سكر الدم.