Oesophago-Gastro-Duodenoscopy (OGD) Findings and pH-Related in Patients with DM or without DM in Mosul City

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ABSTRACT

Background: The relationship between diabetes and acid related mucosal damage has been studied in many previous researches. There is no obvious idea about how much the diabetes disease can affect acidic mucosal secretions and the relation with gastric mucosal damage. Many theories about effect of diabetes disease itself or anti diabetic drugs on the gastric acid secretions and mucosa.

The aim of study: To evaluate the effect of DM on secretion of gastric acid in the stomach and the effect of DM on mucosal damage in the stomach.

Design: The study of Case-Control was adapted.

Methodology: The study of Case-Control was conducted from January 2018 till May 2018 in endoscopic unit in AL-_Salam Teaching Hospital ,database surveyed 90 patients, 43 diabetic and 47 non-diabetic patients who complain from upper GI symptoms (Gastro-esophageal reflux disease (GERD), epigastric pain, dyspepsia, upper GI bleeding) undergoing Oesophageo-Gastro-Duodenoscopy (OGD) and measurement of gastric PH by using PH kit. A multitude of acid-related afflictions have been identified, encompassing a wide range of expressions such as acid reflux, ulcers, strictures, inflammations, bile reflux, bleeding sites, and erosions.

Results: Intriguingly, despite experiencing upper GI symptoms, there were no discernible disparities in mucosal damage between the two groups. However, upon closer examination, it becomes evident that diabetic patients are at a comparable risk of acid-related damage as non-diabetic patients. Astonishingly, this risk persists even after accounting for factors such as acid reflux, gender, and age.

Conclusion: A remarkable finding emerged from our study - the risk of acid-linked mucosal damage showed no significant variation, even after accounting for potential confounding factors. Surprisingly, our data challenges the notion of a lower threshold for conducting endoscopy in diabetic patients. This discovery urges us to reevaluate our assumptions and delve deeper into the intricate relationship between acid levels and mucosal damage in this specific population.

Keywords: Diabetes Mellitus , Oesophageo-Gastro-Duodenoscopy, Upper Gastro-Intestinal Symptoms.

نتائج ناظور المعدة ومقياس الحموضة للمرضى الذين يعانون من داء السكري أو بدون داء السكري في مدينة الموصل

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الخلاصة

خلفية الدراسة: تمت دراسة العلاقة بين مرض السكري وتلف الغشاء المخاطي المرتبط بالحمض في العديد من الأبحاث السابقة. لا توجد فكرة واضحة عن مدى تأثير مرض السكري على الإفرازات المخاطية الحمضية وعلاقته بتلف الغشاء المخاطي في المعدة. هناك العديد من النظريات حول تأثير مرض السكري نفسه أو الأدوية المضادة للسكري على إفرازات حمض المعدة والغشاء المخاطي.

اهداف الدراسة: تهدف الدراسة لتقييم تاثير داء السكري على افرازات المعدة الحامضية وتاثيره على تلف الغشاء المخاطي للمعدة.

تصميم الدراسة: تم اعتماد دراسة من نوع (الحالات والشواهد).
طريقة العمل: اجريت هذه الدراسة من نوع (الحالات والشواهد) في وحدة الناظور في مستشفى السلام ,تم اختيار ٩٠ مريض ٤٣ مريض مصاب بالسكري و ٤٧ مريض غير مصاب بالسكري من الفترة كانون الثاني ٢٠١٨ الى ايار ٢٠١٨ جميعهم يعانون من اعراض اعلى جهاز الهضمي (الم المعدة ,استرجاع المرء ,سوء الهضم ,تقيأ) مع الاخذ بنظر الاعتبار عدم التدخين واستخدام العقاقير المسكنة ذات التأثير المباشر على المعدة باستخدام جهاز الناظور واشرطة قياس الحامضية وباستخدام استمارة فحص ناظور المعدة .
النتائج: اظهرت النتائج انه لا يوجد فرق كبير بين نتائج مرضى السكري ومرضى الغير مصابين بالسكري المصابين بأعراض اعلى جهاز الهضمي من حيث افراز حوامض المعدة ومن حيث نتائج الناظور .
الاستنتاج: لا يوجد تأثير مباشر لمرض السكري على امراض اعلى جهاز الهضمي وافرازات حوامض المعدة

الكلمات المفتاحية : داء السكري, تنظير المريء والمعدة والاثني عشر, اعراض الجهاز الهضمي العلوي.

INTRODUCTION

Diabetes mellitus is a complex disease caused by a deficiency of insulin, leading to elevated blood sugar levels. It results in metabolic imbalances, including changes in lipoprotein dynamics and increased levels of free fatty acids. These imbalances contribute to the development of acute and chronic complications associated with diabetes. Dysregulation of lipoprotein dynamics leads to an increase in LDL and a decrease in HDL, increasing the risk of cardiovascular disease. Diabetes also causes elevated levels of free fatty acids, which can worsen insulin resistance and hyperglycemia. The consequences of uncontrolled diabetes include symptoms such as excessive thirst and fatigue, as well as complications affecting various organs and systems of the body[1].

The gastrointestinal (GI) system is prone to various disorders, and this holds true for individuals with diabetes as well. Encountering a range of conditions like peptic ulcer disease, gallstones, irritable bowel syndrome, and food poisoning is not uncommon among patients. Surprisingly, GI symptoms affect over 75% of individuals seeking treatment at diabetes clinics. It is remarkable how diabetes can wreak havoc on the entire GI tract, from its starting point in the mouth and esophagus to its far reaches in the large bowel and ano-rectal region [2] . As a result, healthcare professionals must stay vigilant of the potential consequences of diabetes on the GI system. Diabetes can have various effects on the gastrointestinal (GI) tract, leading to symptoms such as early satiety, difficulty swallowing, reflux, abdominal pain, nausea, and vomiting. However, these symptoms can vary from person to person. Many patients with diabetes have been undiagnosed or under-treated for their GI symptoms because the GI tract has not traditionally been associated with the disease [3].

Research has shown that both acute and chronic hyperglycemia can cause specific GI complications. The severity of these complications is often related to the duration of the disease and poor blood sugar control. Recognizing the connection between diabetes and the GI tract is important for healthcare providers to provide timely diagnosis and treatment [2,3]. Patients with a history of minor complications like retinopathy, nephropathy, and neuropathy assumed that they might have GI abnormalities until proven otherwise[4] . Because recent discoveries suggest that the root cause of most GI complications in diabetes lies in the misfiring of neurons within the enteric nervous system. Just like peripheral neuropathy affects the nerves in the feet, it is entirely possible for the intestinal nerves to face same fate, giving rise to enteric neuropathy. This peculiar condition, also known as autonomic or "involuntary" neuropathy, can weaken intestinal sensations, motility, secretion, and absorption [5].

Various types of nerve fibers play a crucial role in regulating intestinal motility and function. These nerve fibers can either stimulate or inhibit the movement and activity of the intestines, ultimately affecting their overall function. The intricate network of nerves within the intestines is responsible for coordinating the rhythmic contractions that propel food and waste materials through the digestive tract. When these nerves are damaged or destroyed, it can lead to a disruption in the normal functioning of the intestines [6].

Depending on the type and extent of nerve damage, the consequences can vary. In some cases, the destruction of these nerves can result in a decrease in intestinal motility, causing a slowdown in the movement of food and waste through the digestive system. This can lead to symptoms such as constipation, bloating, and discomfort. On the other hand, destruction to these nerves can also lead to an increase in intestinal work [7] . This can result in hypermotility, where the contractions of the intestines become excessively fast and uncoordinated. This can cause symptoms such as diarrhea, urgency, and abdominal pain. Ultimately, the specific symptom complex that

arises from nerve destruction depends on the location, extent, and nature of the damage. Understanding the role of these nerve fibers and their impact on intestinal motility is crucial in diagnosing and managing gastrointestinal disorders [8].

After a while, diabetes can have a significant impact on various parts of the body, including the vagus nerve. The vagus nerve plays a crucial role in controlling the pace at which the stomach empties its contents. However, when diabetes starts to affect this nerve, it becomes impaired, leading to a condition known as gastroparesis. This condition is characterized by a delay in the digestion process, causing food to remain in the body for a longer period than it should. As a result, individuals with diabetes may experience symptoms such as bloating, nausea, early satiety, and vomiting. Gastroparesis can further complicate diabetes management, as it can affect blood sugar control and nutrient absorption [9]. Despite the fact that, it's more prevalent in people with type 1 diabetes, people with type 2 can also be effected [10].

Most individuals who suffer from gastroparesis and dyspepsia have been living with diabetes for a decade or more, and unfortunately, they often experience additional complications associated with this disease. When food lingers in the stomach for an extended period, it can become spoiled, creating a breeding ground for bacteria. This not only poses a risk to patients health but can also obstruct the natural flow of food into the small intestine. As a result, managing diabetes becomes even more challenging. Interestingly, once the food finally makes its way into the small intestine, it causes a spike in blood sugar levels as well [10,11] . The incidence of gastrointestinal (GI) symptoms has been reported to be higher in patients with diabetes mellitus (DM) compared to the general population. While there is some controversy surrounding this issue, these symptoms are not considered significant causes of mortality in patients with DM. However, they can still have a negative impact on the overall health condition and quality of life of affected individuals. GI symptoms commonly experienced by patients with DM include abdominal pain, bloating, diarrhea, constipation, and gastroparesis (delayed emptying of the stomach). These symptoms can be attributed to various factors such as autonomic neuropathy, impaired glycemic control, alteration in gut microbiota, and medication side effects. They can significantly affect the daily functioning and well-being of individuals with DM, making it important to address and manage these symptoms effectively [12] .

Multiple studies have shown a different of gastrointestinal symptoms in patients with DM, although many of these patients, especially those with the Type 1 of DM (T1DM), may appear without gastrointestinal manifestations. The fact that there are limited studies involving children and adolescents with T1DM is related, and, within patients with Type 11 of DM (T2DM), the outcomes are controversial [13]. Amongst the symptoms most currently found in DM patients; early satiety, nausea, abdominal pain, vomiting, bloating, regurgitation, dysphagia, heartburn, epigastric/abdominal discomfort and abdominal distension [14,15] . Gastroparesis, a condition characterized by delayed gastric emptying, has emerged as one of the most prevalent and well-known serious complications in patients with diabetes-linked gastrointestinal (GI) issues. It is estimated that approximately 50% of individuals experiencing GI complications related to diabetes also develop gastroparesis. This condition occurs when the muscles in the stomach fail to function properly, leading to a delay in the movement of food from the stomach to the small intestine. As a result, digestion is hindered, causing symptoms such as nausea, vomiting, bloating, and abdominal discomfort. The exact cause of gastroparesis in diabetes is not fully understood, but it is believed to be associated with nerve damage, known as neuropathy, that affects the nerves controlling the stomach muscles [16] .

The hypothesis of the disease reveals this association in a distinc manner. It is accountable for many complications, both in T1DM and T2DM, such as involvement of the GIT and diabetic neuropathy [17] . GIT dysfunction in DM is occur inferior to poor glycemic control and subsequent diabetic autonomic neuropathy, which has great impact on the motor and sensory functions of the GI-tract t from the stomach to its terminal portion[18]. The macro-vascular complications and Diabetic angiopathy are additionally inferior to chronic hyperglycemia and are linked to the pathogenesis of intestinal ischemia, nerve damage and impaired muscle function in diabetic gastroenteropathy [19].

Diabetes mellitus is a disorder attributed by hyperglycemia, deficiency of antioxidants, and changes in lipid metabolism . The impaired flow of blood vessels in the intestines, caused by a lack of oxygen and restricted blood supply, can lead to a range of issues in the gastrointestinal tract. These complications include bleeding, abdominal pain, and damage to the protective lining of the gut. Interestingly, the malfunctioning of mitochondria has also been implicated in the development of gastric neuropathy, adding another layer to the understanding of its underlying causes [20] .

The degradation of dorsal root ganglion (DRG) neurons in peripheral nerves carries immense implications for a multitude of physiological processes. It is the mitochondria within the DRG that bear the brunt of this damage, suffering particularly adverse effects. Enter advanced

glycation end products (AGE), the key culprits in this intricate dance, as they actively participate in the creation of irreversible alterations in extracellular matrix components such as laminin, type IV collagen, and vitronectin [21] . These modifications, in turn, trigger a cascade of abnormalities that affect both the quality and quantity of the extracellular matrix. Consequently, cellular growth, adhesion, and matrix aggregation are also affected. Furthermore, AGE-modified proteins interact with specific receptors on endothelial cells and macrophages, leading to changes in cell function. These alterations induce vasoconstriction, excessive matrix production, and focal thrombosis, further exacerbating the impact on overall cellular and tissue health [22] . It is related with an increased incidence of gastrointestinal tract symptoms. People with diabetes face a heightened vulnerability when it comes to the health of their gastric mucosa. This susceptibility is particularly evident in their increased risk of developing ulcers. These changes include a decline in gastric motility and secretion, which interestingly enough, are influenced by insulin but not by histamine or pentagastrin [18,22] .

The connection between diabetes mellitus and the development of peptic ulcers has caught the attention of researchers. It appears that changes in gastric acid secretion can play a role, either by decreasing it or increasing acid output. Interestingly, some studies have found no significant difference in gastric acid secretion between diabetic and non-diabetic individuals [23,24] .

It is widely recognized that diabetic autonomic neuropathy, which refers to the impairment of neurons that supply the enteric nervous system (ENS), plays a crucial role in the abnormal alterations observed in GI motility, secretion, sensation, and absorption [25,26] . The ENS is responsible for regulating important GI functions such as peristalsis, the secretion of digestive enzymes and hormones, pain sensation, and nutrient absorption [27]. When the neurons supplying the ENS are damaged or dysfunctional due to diabetic autonomic neuropathy, it disrupts the normal functioning of the GI tract, leading to a range of complications [28].

SUBJECTS AND METHODS

The study included patients selected over six month's period. To achieve the aim of the current study, A Case-control type of study was adapted. A total 90 patients aged 18 -70 years were selected from Al-Salam Teaching Hospital ,endoscopic unit, 43 diabetic patients(48%) (Case group) and 47 non-diabetic patient (Control group) (52%). All of them complain from upper GIT symptoms (epigastric pain, dyspepsia, GERD). The case group was as follow, 43 diabetic patients (25 female, 18 male) and aged 23 -70 mean age, the control group was as follow, 47 non-diabetic patients (23 female, 24 male) and aged 18 -66 mean age, matched to all patients who complain from upper GI symptom. OGD done for all patients(fibro optic scope) , during the procedure gastric acid taken by endoscopic cannula and suction syringe 50 cc , And then PH of gastric secretion by using PH kit (DF universal test paper) which can measure capacity from 1 to 14 ,and document the OGD finding as a report.

Statistical Analysis: Statistical analyses were carried out using the Microsoft Excel 2010, Statistical analyses used: t-test, compare between diabetic and no diabetic group. Chi-square for gender and PH categories comparison. P value equal to or less than 0.05 was significant statistically, p value more than 0.05 was statistically non-significant [29] .

RESULTS

A total 90 participants (43 diabetic and 47 non-diabetics) all of them complain upper GI symptoms undergo OGD were recruited in this study. The personal characteristics of the study-sampled groups according to age and gender were presented in table (1) showing non-significant difference regarding them (p=0.438) (p=0.382) respectively.

Table (1): Personal characteristics of the study-sampled groups; Mosul- Iraq, 2018.

Parameters	Cases "DM" [n = 43]	Control "No DM" [n = 47]	P-value*
Age years			
Mean ± SD	45.13 ± 10.39	43.50 ± 9.44	0.438
Range	23.0 – 70.0	18.0 – 66.0	---
Gender No. (%)			
Male	18 (41.9)	24 (51.1)	0.382
Female	25 (58.1)	23 (48.9)	

* Independent T-test of two means was applied for age differences and Chi-square for gender comparison.

Table (2): demonstrated comparison in gastric acid secretion between the two groups with non-significant differences between DM and non-DM patients regarding in PH (p= 0.491) and PH categories No. (%) (p= 0.909)

Table (2): Comparison in gastric acid secretion between the two groups.

Gastric acid secretion [PH]	Cases "DM" [n = 43]	Control "No DM" [n = 47]	Total [n = 90]	P-value*
Mean PH ± SD	3.72 ± 0.68	3.83 ± 0.79	3.78 ± 0.74	0.491
Range	2.50 – 5.00	3.00 – 5.00	2.50 – 5.00	---
PH categories No. (%)				
2.5 – 3.0	14 (32.6)	15 (31.9)	29 (32.2)	0.909
3.1 – 4.0	17 (39.5)	17 (36.2)	34 (37.8)	
4.1 – 5.0	12 (27.9)	15 (31.9)	27 (30.0)	

* Independent T-test of two means was applied for PH differences and Chi-square for PH categories comparison.

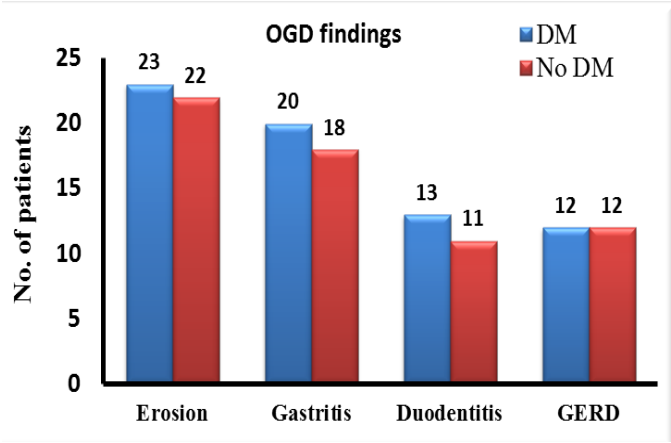

Figure (1): The number of patients of different presentations in both groups.

Table (3) shows non-significant difference in gastric acid secretions in both genders (male p=0.807, female p=0.206) in both groups.

Table (3): Gender differences in gastric acid secretion between the two groups.

Gender	**Cases "DM" [n = 43]**	**Control "No DM" [n = 47]**	**Total [n = 90]**	**P-value***
Gastric acid secretion [Mean PH ± SD]				
Male	3.72 ± 0.71	3.66 ± 0.73	**3.69 ± 0.71**	0.807
Female	3.72 ± 0.68	4.00 ± 0.83	**3.86 ± 0.76**	0.206
P- value*	0.996	0.150	0.295	---

* Independent T-test of two means was applied.

DISCUSSION

In our study, we investigated the prevalence of acid-related findings in patients who complained of upper gastrointestinal (GI) symptoms. Despite our initial assumption of a potential association between acid-linked symptoms and findings in patients with diabetes, we observed no significant difference in the risk of finding between diabetic and non-diabetic patients after accounting for multiple variables. This finding suggests that the presence of diabetes does not necessarily increase the likelihood of acid-related findings in patients with upper GI symptoms. Furthermore, our analysis revealed that the prevalence of upper GI symptoms was similar in both diabetic and non-diabetic patients. These results highlight the importance of considering various factors when assessing the risk of acid-related findings in patients with upper GI symptoms, and suggested that diabetes may not be a significant determining factor in this context.

This study covered upper GI endoscopic finding (GERD ,gastritis ,duodenitis and erosion) and their relationship with diabetes and acid secretion (PH of stomach) but after collection of data there is multiple cases of biliary gastritis which had increase PH and severe damage which conflict the result of other cases in which decreasing in PH associated with increasing severity of mucosal damage [30] .

This study compared between diabetic patients and non-diabetic patient whom their finding GERD showed a non-significant difference between them regarding occurring of GERD. Monreal-Robles and Remes-Troche (2017) Gastroesophageal reflux in [31] . The American journal of gastroenterology, showed a greater incidence of GERD observed in asymptomatic diabetic patients in comparison

with general population, the result of this study done by using long-term (24-hr duration) ambulatory esophageal pH monitoring, as well as a manometric study of the lower esophageal sphincter that wasn't use in our study .

This study compared between diabetic patients and non-diabetic whom their finding is gastritis (mild and moderate and sever) showed a statistically non-significant changes between them regarding occurring of gastritis. These result are in consistence with another study as Talebi-Taher *et al.,* 2012 [32] . Gastritis show that not to be related with diabetes mellitus or occurring of upper GI symptoms in diabetes mellitus and this similar in another study regarding upper gastrointestinal findings in diabetic outpatients at Kenyatta National Hospital, Nairobi which shown that despite of dyspepsia is common in diabetic outpatients at KNH, the endoscopic records show non-significantly changes in comparison with those of non-diabetic population [33] .

In this study that compared between diabetic patients and non-diabetic whom their finding is duodenitis, There was a non-significant statistical changes between both populations regarding occurring of duodenitis and erosion. This result similar to the result obtained from another study when upper gastrointestinal findings in diabetic outpatients done at Kenyatta National Hospital, Nairobi which demonstrated that endoscopic findings are not significantly change in diabetic outpatients at KNH in comparison with those of non-diabetic population despite of dyspepsia occurring is common [33] .

CONCLUSION

1. There was no significant difference between diabetic and non-diabetic in OGD finding in our study
2. There was no significant difference between diabetic and non-diabetic in acid secretion and PH of stomach
3. Mucosal damage is not related to gastric PH ,because in many cases bile interfere with PH of stomach and acid related mucosal damage

RECOMMENDATION

1. The study should be done to compare H. Pylori infection between diabetic and non-diabetic patients.
2. The effect of anti-diabetic drugs should be taken in consideration.
3. However, this study does not assist lower threshold to perform endoscope in diabetic patients.

Conflicts of Interest

The authors declare no conflict of interest.

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