

Study of Gastroesophageal Reflex Disease in adult Type II Diabetes Mellitus Patients with Upper Gastrointestinal Symptoms

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Abstract

Gastrointestinal symptoms are relatively common in clinical practice in patients with type II diabetes mellitus. type II DM has been described as possible risk factor for the development of gastroesophageal reflux disease, in this study we aim to detect the prevalence of GRED in symptomatic patients with type II DM , also to see the accuracy of reflex disease questionnaire (RDQ) in the diagnosis of GERD in patients with type II DM in relation to the esophagogastroduodenoscopy finding and to study the relation of autonomic neuropathy to the prevalence and stages of GERD in diabetic patients .

Method: A ninety patients with upper gastrointestinal symptoms was divided in to tow groups according to whether had type II DM or not and then each group involved in a two stage process (a) – a RDQ , (b) – OGD .

And patients in the DM group underwent another step to detect diabetic neuropathy by a bed side clinical test .

Results: The prevalence of esophagitis in this study was higher in the DM group .

RDQ had a statistical significance in detecting esophagitis in the DM group .

There is no relation of autonomic neuropathy to the prevalence of GERD in diabetic patients . .

Conclusion: The prevalence of GERD was high in patients with type II DM , RDQ is a sensitive tool for the diagnosis of GERD in diabetic pateints , Autonomic neuropathy did not increase prevalence of esophagitis in diabetic patients .

Keywords: *diabetes mellitus ,gastro esophageal reflex disease , RDQ, Esophagogastroduodenoscopy, Esophagitis.*

Introduction

The current concept of GERD is “symptoms or complications associated with regurgitation from the stomach and or the duodenum to the esophagus”, It is estimated that 15%-30% of the general population are affected by GERD^(1,2)

GERD develops when the esophageal mucosa exposed to gastroduodenal contents for prolonged periods of time, resulting in symptoms and, in a proportion of case , esophagitis⁽²⁾.

Note that some degree of gastroesophageal reflux is normal, physiologically connected with the mechanism of belching (transient LES relaxation), but esophagitis results from excessive reflux, often accompanied by impaired clearance of the refluxed gastric juice. Restricting reflux to that which is physiologically intended depends on the anatomic and physiologic integrity of the oesphagogastric junction, a complex sphincter comprised of both the LES and the surrounding crural diaphragm. Three dominant mechanisms of esophagogastric junction incompetence are recognized: (a) transient LES relaxations (a vagovagal reflex in which LES relaxation is elicited by gastric distention),

(b) LES pressure decrease, or (c) anatomic distortion of the esophagogastric junction inclusive of hiatus hernia^(1,2).

Transient LES relaxations account for at least 90% of reflux in normal subjects or GERD patients without hiatus hernia, in many studies the first two mechanisms and other factors such as abdominal obesity, delayed gastric emptying, disruption of esophageal peristalsis, autonomic neuropathy, metabolic syndrome were thought to be a possible risk factors for the high prevalence of the typical GERD symptoms in patient with DM, but up to present, the pathogenesis of GERD in type II DM patients has not been fully clarified.^(3,4,5)

Peripheral and autonomic neuropathy especially has become a research hotspot in recent years, however,

the impact of the above factors on the presence of GERD symptoms in type II DM patients is still under debate^(3,6).

Patients with GERD may present with heartburn and regurgitation which are the major symptoms of GERD, somewhat less common are dysphagia and chest pain and a variety of other features has been described, and depending on this a clinical system of symptom-based diagnosis of GERD was made the so called reflex disease questionnaire RDQ⁽⁷⁾

RDQ comprises 6 questions assessing the frequency of heartburn, substernal chest pain, acid regurgitation, nausea, need for the medication, and trouble getting a good night sleep because of heartburn or regurgitation, per week, as shown in table 1.

Table 1: GerdQ Questionnaire

| SYMPTOM | HOW MANY TIMES DOES THIS OCCUR PER WEEK? | | | |
|--|--|-------|-------------|-------------|
| | 0 DAYS | 1 DAY | 2 OR 3 DAYS | 4 TO 7 DAYS |
| Burning feeling behind the breastbone (heartburn) | 0 | 1 | 2 | 3 |
| Stomach contents moving up to the throat or mouth (regurgitation) | 0 | 1 | 2 | 3 |
| Pain in the middle of the upper stomach area | 3 | 2 | 1 | 0 |
| Nausea | 3 | 2 | 1 | 0 |
| Trouble getting a good night's sleep because of heartburn or regurgitation | 0 | 1 | 2 | 3 |
| Need for over-the-counter medicine for heartburn or regurgitation (such as Tums, Roloids, Maalox, or other antacids), in addition to the medicine your doctor prescribed | 0 | 1 | 2 | 3 |

NOTE: Add the point values for each corresponding answer. Total score of 0 to 2 points = 0 percent likelihood of GERD; 3 to 7 points = 50 percent likelihood; 8 to 10 points = 79 percent likelihood; 11 to 18 points = 89 percent likelihood.

Several investigation used to evaluate patients with suspected having GERD of which endoscopy is the initial investigation of choice, it used for the diagnosis

and grading of GERD and to exclude other upper gastrointestinal disease that can mimic GERD and to identify complications.

Aim of the Study

To study the prevalence of GERD in symptomatic patients with type II DM in relation to non DM ,also to see the accuracy of RDQ in the diagnosis of GERD in patients with type II DM in relation to the OGD finding and to study the relation of autonomic neuropathy to the prevalence of GERD in diabetic patients present with upper gastro intestinal symptoms.

Patients and Method

This study was conducted in Alsader medical city, in Alnajaf center for gastrointestinal and hepatic diseases in which 122 adult patients referred for upper endoscopy because of upper gastrointestinal symptoms suggestive of GERD between march 2014 and march 2015 participate in this study .

Exclusion criteria were type I DM , esophageal motility disorder other than ineffective esophageal motility, patient with hiatus hernia and patient with a RDQ less than 8.

After performing the exclusion criteria a 90 patients were considered eligible for this study 31 of them were females and 59 were males.

The recruitment patients were divided into two groups according to whether had a type II DM or not , the diagnosis of type II DM based on WHO definition (Defined as fasting blood glucose ≥ 7 mmol/l or on glucose medication for raised blood glucose or with a history of diagnosis of diabetes.) (8)

the then every group involved in a two stage process (a)- Reflux disease questionnaire (RDQ) and patients with at least a minimal score of 8 had been chosen as the (RDQ) likelihood of GERD were as fellow(7) :

- 1- A total score 0 to 2 = 0 percent likelihood
- 2- A total score 3 to 7 = 50 percent
- 3- A total score 8 to 11 = 79 percent
- 4- A total score 12 to 18 =89 percent.

(b)- OGD by the use of Olympus or pentax ED-3490 TK 4.2 HOYA corporation endoscopy system , which used in the diagnosis and staging of esophagitis according to Savery-Miller classification in these patients (9)

(c)- the patients with DM group underwent another step during interview by being underwent a simple clinical test to detect the diabetic autonomic neuropathy(a bedside test for the absence respiration-associated sinus arrhythmia by monitoring the pulse rate by a pulse oximeter while the patient instructed to breathe slowly and deeply at a rate of 6 breaths per minute, heart rate normally increase with inspiration and decrease with expiration , and at a respiratory rate of 6 per minute the difference between fastest and slowest heart rate is usually more than 15 per minute , a difference of 10 beats per minute or less are observed in autonomic dysfunction(10).

Statistical Analysis:

Statistical analysis were performed using spss 16 program correlation analysis was also performed.

A P value <0.05 was considered significant.

Results

Ninety patients were included in this study and divided in to two groups a thirty patients in DM group and sixty patients in the non DM group.

In the non DM group 22 of them were females(36.66%) and 38 were males(63.33%) with a mean age of (46.7years±8.2).

In the DM group 9 were females (30%) and 21 were males (70%) with a mean age of (51.2 years±9.3). As shown in table 2.

Table-2 the demographic characters of both groups (DM and non DM)

| | Group | Result |
|----------------|--------|------------|
| Female | Non DM | 22(36.66%) |
| | DM | 9(30%) |
| Male | Non DM | 38(63.33%) |
| | DM | 21(70%) |
| Mean age years | Non DM | 51.2±9.3 |
| | DM | 46.7±8.2 |

The prevalence of esophagitis in this study were higher in the DM group as upper OGD results showed esophagitis in 32 patients of the non DM group (53.3%) and in 23 patients of the DM group(76.66%) with a statistical significant results (p value=0.03236)as shown in table3

| Group | Esophagitis | Percentage | P value 0.03236* |
|--------|-------------|------------|----------------------------|
| Non DM | 32 of 60 | 53.33% | |
| DM | 23 of 30 | 76.66% | |

Table3 (the prevalence of esophagitis by OGD in both study groups)

In comparing the RDQ which about 80% in a score level 8-11 and OGD result in detecting esophagitis in both groups the result shows that RDQ had a statistical significance in detecting esophagitis in the DM group as shown in table4.

Table 4 comparing QRS and OGD in detecting esophagitis in both study groups.

| | By QRS 80% | By OGD | P VALUE |
|---|--------------|----------------|----------|
| Number of patients in DM group with esophagitis | 24 of 30=80% | 23 of 30=76.6% | 0.00244* |
| Number of patients in non DM group with esophagitis | 48 of 60=80% | 32 of 60=53.3% | |

In the DM group the clinical bedside test for autonomic neuropathy revile an autonomic dysfunction in 16 patients of 30 (53.33%) and 14 patients show not (46.6%).

13 (81.2%) of the 16 patients with DM and autonomic dysfunction were diagnosed with esophagitis by OGD and 3 patients show no sign of esophagitis by OGD(18.7%), while in patients with DM and without autonomic dysfunction there were 10 patients of 14 (71.4%) diagnosed with osephagitis by OGD and 4 patients(28.5%) are not ,so there were no statistical significance P value=0.5287 as shown in table 5.

Table 5-previlance of esophagitis in DM patients with and without autonomic dysfunction

| Patient in DM group | Patient with esophagitis | P value |
|-------------------------------------|--------------------------|---------|
| With autonomic dysfunction no=16 | 13 of 16(81.2%) | 0.5287 |
| Without autonomic dysfunction no=14 | 10 of 14(71.4%) | |

Discussion

Diabetes is a major health problem ,as it is an important contributor to various other disease and its incidence still continues to rise. Gastrointestinal symptoms are relatively common in clinical practice in

patients with type II DM. type II DM has been described as possible risk factor for the development of GERD. Several studies reported that the prevalence of GERD symptoms in the type II DM was approximately 25%-40% in different populations^(11,12,13) , in these studies

several methods used in the diagnosis of GERD includes; RDQ which had a sensitivity of 79% in the diagnosis of GERD at 8-11 score level in non DM patients, Endoscopic examination which had high specificity but low sensitivity for the diagnosis of GERD with a sensitivity about 55% for detecting esophagitis and other complications^(14,15) and ambulatory PH monitoring which is indicated if diagnosis is unclear or surgical intervention is under consideration, although the test yields accurate and reliable information it is inconvenient for the patient and many clinicians do not have access to the appropriate instrumentation and are unable to perform this test⁽¹⁶⁾.

In this study a combination of RDQ and OGD is used to study the prevalence of GERD in patients with type II DM as a previous study by Lemeneh Tefera, B.A., Martin Fein.⁽¹⁶⁾ shows that this combination had a high proof value 98% and high specificity 97% for the diagnosis of GERD in non DM patients, in this study we found that the prevalence of GERD in adult symptomatic patient with type II DM as diagnosed by OGD were high 76.7% comparing to non DM patients 53.3% with a P value =0.03236.

We also found that the RDQ at level score >8 had a good prediction rate for esophagitis which about 80% in symptomatic patient with type II DM as the OGD result showed esophagitis in 76.66% in patients with type II DM comparing to non DM patients in regard to the sensitivity of RDQ with a P value=0.00244. and this was constant with a study by Yu Bai, Yiqi Du, Duowu Zou, Zhendong Jin and others, that suggest that the RDQ may be used for the diagnosis of GERD⁽¹⁷⁾

In previous studies neuropathy were thought of as possible risk factor for the prevalence of the typical GERD symptoms in DM patients (13,20), for example, in 2008, Wang et al.⁽¹³⁾ reported that the prevalence of GERD symptoms was higher in patients with neuropathy than in patients without neuropathy, in this study there were no significant difference in the prevalence of esophagitis in DM patients with or without neuropathy with a P value=0.05287, this results are similar to the studies of Clouse and Lustman⁽²¹⁾ and Lee et al.⁽¹⁹⁾. In 1989, Clouse and Lustman, through analyzing 114 diabetic subjects with gastrointestinal motor dysfunction symptoms, reported that gastrointestinal symptoms occurring in diabetic patients were poorly related to neuropathic complications. In 2011, Lee et al.⁽¹⁹⁾ studied 119 patients with type II DM and found that there was

no significant difference in the proportions of patients experiencing typical GERD symptoms between the two groups of type II DM with and without neuropathy.

Conclusion

The prevalence of GERD were high in patients with type II DM, RDQ is a sensitive tool for the diagnosis of GERD in those patients, Autonomic neuropathy did not increase prevalence of esophagitis in diabetic patients.

Conflicts of Interest: None of the authors have any conflicts of interest relevant to this research subject.

Ethical Clearance : the study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki. The study protocol, care of patients and subject information were reviewed and approved by a local Ethic committee.

Source of Funding: Self

References

1. J. Stephen Hauser, Dennis Kasper, Anthony Fauci, Dan Longo, Joseph Loscalzo, Jameson, Harrison's principles of internal medicine: McGraw Hill. 18th edition; 2011.
2. I.D. Penman, C.W. Lees, Davidson's principles and practice of medicine; 22^{ed}. 2014.
3. Thomas Frieling, MD Diabetic autonomic neuropathy of the gastrointestinal tract: Wolters Kluwer Health Clinical Solutions; 2015 :<http://www.uptodate.com>
4. Jacobsen B et al. Body-mass index and symptoms of gastroesophageal reflux in women. N Engl J Med. 2006; 354:2340.
5. Sehe Dong Lee, Bora Keum, Hoon Jai Chun and Young-Tae Bak. Gastroesophageal Reflux Disease in Type II Diabetes Mellitus With or Without Peripheral Neuropathy. J. Neurogastroenterology and Motility. 2011; 17(3): 274-278.
6. Huihui Sun, Lisha Yi, Ping Wu, Yingjie Li, Bin Luo, and Shuchang Xu. Prevalence of Gastroesophageal Reflux Disease in Type II Diabetes Mellitus Gastroenterology Research and Practice. 2014, Article ID 601571.
7. Jones R, Jungard O, Dent J, et al. Development of the GerdQ, a tool for the diagnosis and management of gastroesophageal reflux disease in primary care. Aliment pharmacol Ther. 2009; 30(10):1034.

8. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Geneva, World Health Organization, 1999 (WHO/NCD/NCS/99.2).
9. Ollyo JB, Fontolliet C, Lang BF: La nouvelle classification de savery des oesophagites de reflux. *Acta Endosc* .1992,;22:307-320
10. Ewing DJ, Campbell IW, Clarke BF. Assessment of cardiovascular effects in diabetic autonomic neuropathy and prognostic implications. *Ann Intern Med* .1980;92:308-311 .
11. A. Hirata, K. Kishida, H. Nakatsuji et al., “High prevalence of gastroesophageal reflux symptoms in type 2 diabetics with hypoadiponectinemia and metabolic syndrome,” *Nutrition and Metabolism*2012; vol. 9, article 4.
12. K. H. Park, S. B. Yoon, and M. H. Jo. “Clinical characteristics and analysis of risk factor for gastroesophageal reflux disease in diabetic patient,” *The Journal of Korean Diabetes Association*.2005; vol. 29, pp. 358–366.
13. X. Wang, C. S. Pitchumoni, K. Chandrarana, and N. Shah, “Increased prevalence of symptoms of gastroesophageal reflux diseases in type 2 diabetics with neuropathy,” *World Journal of Gastroenterology*.2008; vol. 14, no. 5, pp. 709–712.
14. Richter, JE. Severe reflux esophagitis. *Gastrointest Endosc Cli N Am*. 1994;4;677-698.
15. American college of physician , gastroesophageal reflux Disease , *Gastroenterology and Hepatology, MKSAP 16ed* 2012 .
16. Lemeneh Tefera, B.A., Martin Fein, M.D., PH.D, Manfred P.Ritter, M.D,prevelance of GERD in patient with type II DM .anuaal metting of the south California chapter ,American collage of surgeons ,January 1997 .
17. Yu Bai, Yiqi Du, Duowu Zou, Zhendong Jin, Xianbao Zhan, Zhao-Shen Li, Yunsheng Yang, Yulan Liu, Shutian Zhang, Jiaming Qian, Liya Zhou, Jianyu Hao, Dongfeng Chen, Dianchun Fang, Daiming Fan, Xiaofeng Yu, Weihong Sha, .Yuqiang Nie, Xiaofeng Zhang, Hong Xu, Nonghua Lv, Bo Jiang, Xiaoping Zou, Jingyuan Fang, Jiangao Fan, Yan Li, Weichang Chen, Bangmao Wang, Yiyu Zou, Youming Li, Mingjun Sun, Qikui Chen, Minhu Chen, Xiaoyan Zhao. gastro esophageal reflux questionnaire. *J Gastroenterol Hepatol*. 2013;28(4):626-631.
18. hH S Nwokediuko, U Ijoma, O Obienu, C Agunyenwa. Gastroesophageal Reflux Disease A Clinical And Endoscopic Study Of Nigerian Patients. *The Internet Journal of Gastroenterology*. 2008; Volume 8 Number 2.
19. S. D. Lee, B. Keum, H. J. Chun, and Y. T. Bak. “Gastroesophageal reflux disease in type II diabetes mellitus with or without peripheral neuropathy.” *Journal of Neurogastroenterology and Motility*.2011; vol. 17, no. 3, pp. 274–278. •
20. P. Bytzer, N. J. Talley, M. Leemon, L. J. Young, M. P. Jones, and M. Horowitz. “Prevalence of gastrointestinal symptoms associated with diabetes mellitus: a population-based survey of 15000 adults,” *Archives of Internal Medicine*.2001; vol. 161, no. 21, pp. 1989–1996.
21. R.E.Clouse and P. J. Lustman. “Gastrointestinal symptoms in diabetic patients: lack of association with neuropathy,”. *The American Journal of Gastroenterology*.1989; vol. 84, no. 8, pp. 868–872.