

The Clinical Significance of Endoscopic Findings of Minimal Change Esophagitis and its Diagnostic Value in Egyptian NERD Patients

Thesis

Submitted in Partial Fulfillment of Master Degree in
Internal Medicine

Presented by

Khaled Nasr El Deen Mohammed

(M.B.B.Ch.,)

Faculty of Medicine, Assiut University

Under Supervision of

Prof. Dr. Sayed Mohammad Shalaby

Professor of Internal Medicine

Faculty of Medicine, Ain Shams University

Dr. Noha Abdel-Razek El-Nakeeb

Assistant Professor of Internal Medicine

Faculty of Medicine, Ain Shams University

Dr. Maged Sami Abdel Shahid

Lecturer of Internal Medicine

Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University

2014

الدلالة الاكلينيكية لتغيرات التهاب المرىء الدقيقة المكتشفة بالمنظار ودورها التشخيصى عند المرضى المصريين المصابين بالارتجاع

رسالة

توطئة للحصول على درجة الماجستير فى الباطنة العامة

مقدمة من

طبيب / خالد نصر الدين محمد

بكالوريوس الطب والجراحة
كلية الطب – جامعة أسيوط

تحت إشراف

أ.د/ سيد محمد شلبى

استاذ أمراض الباطنة العامة
جامعة عين شمس

د/ نهى عبد الرازق النقيب

أستاذ مساعد الأمراض الباطنية
جامعة عين شمس

د/ ماجد سامى عبد الشهيد

مدرس الأمراض الباطنية
جامعة عين شمس

كلية الطب

جامعة عين شمس

2014

List of Contents

| Title | Page |
|---|------|
| ♦ List of Tables | III |
| ♦ List of Figures | IV |
| ♦ List of Abbreviations | VI |
| ♦ Introduction | 1 |
| ♦ Aim of the Work | 3 |
| ♦ Review of Literature: | |
| ♦ Chapter I: GERD | 4 |
| ▪ Theories for GERD mechanism | 7 |
| ▪ Symptoms of GERD | 8 |
| ▪ Defense mechanism against the extra esophageal symptoms of GERD..... | 21 |
| ▪ Conditions associated with GERD | 28 |
| ▪ Complications of GERD..... | 30 |
| ▪ Diagnosis of GERD | 34 |
| ▪ Treatment of GERD..... | 45 |
| ♦ Chapter II: NERD | 53 |
| ▪ Natural history of NERD | 53 |
| ▪ Endoscopic appearance of minimal change esophagitis..... | 54 |
| ▪ Endoscopic findings of NERD patients..... | 59 |

List of Contents (Cont.)

| Title | Page |
|--|-------------|
| ♦ Chapter III: Role of endoscopy in diagnosing esophagitis..... | 64 |
| ▪ Role of endoscopy in diagnosing minimal change esophagitis | 64 |
| ▪ Dye-based endoscopy..... | 65 |
| ▪ Chromoendoscopy | 66 |
| ▪ Narrow band imaging | 67 |
| ▪ Fujinon intelligent endoscopy | 72 |
| ▪ I-scan technology..... | 75 |
| ♦ Patients and Methods | 79 |
| ♦ Results | 82 |
| ♦ Discussion | 93 |
| ♦ Summary | 98 |
| ♦ Recommendations | 100 |
| ♦ References | 101 |
| ♦ Arabic Summary | -- |

List of Tables

| Table No | Title | Page |
|--------------------|--|------|
| Table (1): | GERD questionnaire..... | 35 |
| Table (2): | Efficacy of life style modification for GERD patients | 49 |
| Table (3): | Age in patients and control groups | 82 |
| Table (4): | Sex in patients and control groups | 82 |
| Table (5): | BMI in patients and control groups | 83 |
| Table (6): | Smoking in patients and control groups..... | 84 |
| Table (7): | Comparison between patients in group I as regard GERD symptoms..... | 84 |
| Table (8): | Comparison between minimal changes in patients group..... | 85 |
| Table (9): | Comparison between endoscopic signs of minimal change esophagitis and smoking in patients group..... | 86 |
| Table (10): | Comparison between state of cardia and minimal change esophagitis in patient group | 88 |
| Table (11): | Comparison between state of cardia and GERD symptoms | 90 |
| Table (12): | Comparison between endoscopic minimal change esophagitis and GERD symptoms in patient group | 91 |
| Table (13): | Comparison between minimal change esophagitis in patients group and BMI..... | 92 |

List of Figures

| Figure No | Title | Page |
|---------------------|---|------|
| Figure (1): | Effect of PPI on reflux induced asthma | 25 |
| Figure (2): | Management plan for reflux induced asthma..... | 26 |
| Figure (3): | GERD manifestations | 27 |
| Figure (4): | One or more mucosal breaks no longer than 5 mm, non of which extends between the tops of the mucosal folds | 39 |
| Figure (5): | One or more mucosal breaks more than 5 mm long, none of which extends between the tops of two mucosal folds | 39 |
| Figure (6): | Mucosal breaks that extend between the tops of two or more mucosal folds, but which involve less than 75% of the oesophageal circumference..... | 40 |
| Figure (7): | Mucosal breaks which involve at least 75% of the oesophageal circumference..... | 40 |
| Figure (8): | Suggested diagnostic gastroesophageal reflux disease (GERD) algorithm | 44 |
| Figure (9): | Endoscopic image of erythema | 56 |
| Figure (10): | Endoscopic image of Z-line blurring..... | 56 |
| Figure (11): | Endoscopic image of friability | 57 |
| Figure (12): | Endoscopic image of decreased vascularity | 57 |
| Figure (13): | Endoscopic image of white turbid discoloration | 58 |
| Figure (14): | Endoscopic image of edema or accentuation of the mucosal folds..... | 58 |

List of Figures (Cont.)

| Figure No | Title | Page |
|-----------------------|---|-------------|
| Figure (15,A): | Conventional white light endoscope..... | 73 |
| Figure (15,B): | FICE station 0..... | 74 |
| Figure (15,C): | FICE station 4..... | 74 |
| Figure (16,A): | HD mode mucosal break | 76 |
| Figure (16,B): | I-SCAN..... | 77 |
| Figure (16,C): | Lugol's stain | 77 |

List of Abbreviations

| Abbreviations |
|---------------|
|---------------|

| | |
|--------------------------|---|
| GERD |Gastro esophageal reflux disease |
| ASGE |American society of gastroenterology |
| PPI |Proton pump inhibitor |
| NERD |Non erosive reflux disease |
| EMS |Esophageal manometric studies |
| HRAs |Histamine receptor antagonist |
| DRQol |Disease related quality of life |
| IEE |Image enhanced endoscopy |
| NBI |Narrow band imaging |
| HRME |High resolution magnification endoscopy |
| LES |Lower esophageal sphincter |
| D.B.IEE |Dye based image enhanced endoscopy |
| E.B.IEE |Equipment based image enhanced endoscopy |
| LA classification | ..Los Angles calassification |
| IPCL |Intra papillary capillary loop |
| SCJ |Squamo-columnar junction |
| FICE |Fujinon intelligent color enhancement mode |
| SEM |Surface enhancement mode |
| PM |Pattern mode |
| VM |Vascular mode |
| HDC |High definition chromoendoscopy |
| NCCP |Non cardiac chest pain |
| MII |Multi channel intral luminal impidence |

INTRODUCTION

Gastroesophageal reflux disease (GERD) is defined as the reflux of gastric contents into the esophagus, leading to esophagitis, reflux symptoms sufficient to impair the quality of life, and increased risk of long-term complications (*Barlow et al., 2005*).

This definition emphasizes that gastroesophageal reflux becomes a disease when it either causes macroscopic damage to the esophagus or affects the quality of life (*Kim et al., 2011*).

GERD can be divided into erosive (ERD) and non erosive (NERD) reflux disease, and the presence or severity of erosive esophagitis at endoscopy has been defined using mucosal breaks based on the Los Angeles classification (*Caviglia et al., 2007*).

Therefore, NERD has been regarded as reflux symptoms with the absence of mucosal breaks in the esophagus at endoscopy (*Caviglia et al., 2005*). However, in the Asian literature, NERD has been divided into normal and minimal changes based on endoscopic finding (*Kim et al., 2011*), which differs from the general concept of NERD as endoscopy-negative reflux disease. Although the endoscopic findings of minimal changes are not clearly defined, some studies have reported a high rate of minimal-change lesions in NERD patients (*Kiesslich et al., 2004*).

This implies the possible over estimation of minimal-change lesions in NERD patients, irrespective of their clinical significance. Therefore, this study will evaluate the clinical significance of minimal change esophagitis by investigating whether the endoscopic findings of minimal changes have diagnostic value for NERD in a prospective study.

AIM OF THE WORK

To evaluate the clinical significance of minimal change esophagitis at endoscopy and examine whether such changes have diagnostic value in non erosive reflux disease (NERD) or not.

CHAPTER I: INTRODUCTION TO GERD

GERD is a spectrum disease, i.e., a disease composed by many patient subgroups, ranging from symptomatic disease without mucosal lesions (NERD) to the complications of erosive esophagitis, such as esophageal stricture, ulceration or Barrett's esophagus (*Pace and Porro, 2006*).

Montreal consensus defined GERD as “a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications.” Symptoms are “troublesome” if they adversely affect an individual’s wellbeing (*Pace and Porro, 2006*).

A distinguishing feature of the Montreal definition is that it does not use the term “nonerosive reflux disease” but rather subdivides esophageal syndromes into symptomatic syndromes and syndromes with esophageal injury. Hence, functional heartburn does not fit the Montreal definition of GERD, whereas it is included under the umbrella of nonerosive reflux disease. The distinction between GERD and episodic heartburn in the Montreal definition is in the word “troublesome” (*Pace and Porro, 2006*).

In the absence of esophageal injury, heartburn symptoms of insufficient frequency or severity to be perceived as troublesome by the patient (after assurance of their benign nature) do not meet the Montreal definition of symptomatic esophageal GERD syndrome (*Marrer et al., 2008*).

As far as the epidemiological features are concerned, the prevalence of at least monthly GERD symptoms ranges between 26% to 44% whereas the prevalence of endoscopic esophagitis at open access endoscopy or in symptomatic patients seem to be very high, up to 20%, with an incidence rate in the general population about hundred time lower. The principal complication, e.g., Barrett's esophagus, has a prevalence of 15-20% of the GERD population, with a rate of adenocarcinoma development of about 0.5% per patient year of follow up. Mortality for uncomplicated GERD is negligible (*Marrer et al., 2008*).

Different esophageal and extra-esophageal symptoms (even in the absence of detectable lesions), and macroscopic lesions such as erosive or ulcerative esophagitis or so-called atypical manifestations (laryngitis, pharyngitis, dental erosions, and many others). From this brief introduction is already clear that GER disease (GERD) is a broad disease, with a large clinical spectrum of signs and symptoms, interesting not only the esophageal area but many other regions of the body, including the mouth, lungs, ear, nose and throat, and which can be accompanied or not by esophageal lesions (*Pace and Porro, 2006*).

Almost all the transitions are possible amongst groups, even if the progression from one stage to the other has been described mainly based upon retrospective data.

The natural history of the disease is poorly investigated; available data would suggest that symptoms of GERD tend to persist and to worsen with time, independently from the presence and severity of mucosal lesions or the severity of esophageal acid exposure at presentation (*Fass et al., 2009*).

It is therefore evident that the epidemiology of GERD is difficult to assess because this disease encompasses at least three broad groups of patients (*Pace and Porro, 2006*):

- Those with typical symptoms, such as heartburn and regurgitation but without reflux esophagitis, so called non erosive reflux disease (NERD) patients.
- Patients with reflux esophagitis, and with or without complication, such as stricture, specialized intestinal metaplasia.
- Patients with atypical manifestations

Postulated theories of GERD mechanism:

The mechanisms by which patients with GERD develop symptoms remain incompletely understood. It is postulated that sensitization of esophageal chemoreceptors either directly by exposure to acid reflux or indirectly through release of inflammatory mediators is responsible for symptom generation in GERD (*Fass et al., 2009*). Also, morphological changes result in an increase in para cellular permeability, allowing acid to reach sensory nerve endings located within the intercellular spaces.

However, this altered permeability does not explain symptoms in GERD, specifically in NERD and in functional heartburn as most acid reflux events (95%) that occur in these patients are never perceived and symptoms occur even in the absence of acid reflux, suggesting the importance of other factors in modulating esophageal acid perception (*Fass et al., 2009*).

Reducing acid exposure in patients with GERD appears to normalize the sensitivity to acid (*Marrero et al., 2009*) However, the emergence of symptoms in patients with a normal esophageal mucosa and thus without obvious inflammation remains perplexing, particularly among patients with functional heartburn where little or no reflux actually occurs.