

Different patterns of esophageal motility disorders among patients with dysphagia and normal endoscopy

A 2-center experience

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Abstract

Esophageal motility disorders (EMDs) are the main etiology of nonobstructive dysphagia (NOD), but they are underestimated in Egypt. High-resolution manometry (HRM) with Chicago Classification version 3.0 (CC v3.0) is the current gold standard diagnostic modality to assess EMD in patients with NOD. In this HRM-based study, we aimed to classify EMD among Egyptian patients and explore the relationship between the severity of symptoms and the various groups of EMD. From January 2020 to January 2021, patients with dysphagia were subjected to diagnostic workup, which included symptom questionnaire for Eckardt score, esophagogastroduodenoscopy, barium esophagogram, and HRM. All patients were categorized based on the HRM results using CC version 3.0 after exclusion of those with obstructive esophageal lesions. Of 252 patients with dysphagia, 55 patients with NOD were analyzed according to CC version 3.0. Achalasia was diagnosed in 31 patients (56.4%) (type I: 18 [58.06%]; type II: 9 [29.03%], and type III: 4 [12.9%]), 3 patients (5.5%) with esophagogastric junction outflow obstruction, 2 patients (3.6%) with absent contractility, 4 patients (7.3%) with distal esophageal spasm, 7 patients (12.7%) with ineffective esophageal motility, and 8 patients (14.5%) with normal manometry. Patients with achalasia experienced significantly high regurgitation (96.8% vs 70.8%; $P = .016$) compared with those without achalasia. Achalasia was the most common EMD in Egyptian patients with NOD. Eckardt score was higher in patients with outflow obstruction and major motor disorder, but it could not differentiate different categories of CC of EMD. HRM is effective in characterization of EMD.

Abbreviations: CC v3.0 = Chicago Classification version 3.0, DES = distal esophageal spasm, EGD = esophagogastroduodenoscopy, EGJ = esophagogastric junction, EGJOO = esophagogastric junction outflow obstruction, EMD = esophageal motility disorder, EPT = esophageal pressure topography, HRM = high-resolution manometry, IEM = ineffective esophageal motility, IQR = interquartile range, LES = lower esophageal sphincter, NOD = nonobstructive dysphagia.

Keywords: Chicago classification, dysphagia, esophageal motility disorder, high resolution manometry

1. Introduction

Esophageal motility disorders (EMDs), including achalasia and other major and minor disorders of peristalsis, are the main etiologies of nonobstructive dysphagia (NOD), necessitating more assessment for the achievement of a correct diagnosis.^[1] These disorders are usually covered by other concurrent organic disorders, which may hide definitive diagnosis and lead to delay early clinical intervention and finally bad clinical results.^[2]

Dysphagia without visible mechanical obstructions as assessed by endoscopic examination and/or radiological methods is an arising clinical problem.^[3] High-resolution manometry (HRM) with esophageal pressure topography using Chicago

classification version 3.0 (CC v3.0) is the current gold-standard diagnostic modality to evaluate EMD in those with normal upper endoscopy.^[4]

There is paucity of data in the literature discussing the actual prevalence of EMD. However, achalasia is well studied and data from Central Chicago (USA) state that achalasia estimated yearly incidence values range from 0.77 to 1.35 per 100,000 (average, 1.07 per 100,000) and prevalence values increased progressively from 4.68 to 14.42 per 100,000 population over an 11-year period.^[5] Furthermore, In the UK, achalasia occurs in 1.99 per 100,000 population with a prevalence of 27.1 cases per 100,000 population^[6] and an incidence of 1.63 cases per 100,000 in Canada.^[7] In Europe, achalasia occurs in 1.07 to 2.2 cases per 100,000 population per

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year, with a prevalence of 10 to 15.7 cases per 100,000 population.^[8] In Algeria, the incidence is 0.27 cases per 100,000 population.^[9] Data suggest that EMD especially achalasia is increasing in incidence because of the emerging usage of HRM, which increases identification and diagnosis of such conditions.^[10]

Currently, there is a deficiency of data about the prevalence of motility disorders in Egypt. Multiple hospital visits for investigating patients with dysphagia can exhaust our medical services and lead to a considerable socioeconomic burden.^[11]

The aim of this study was to classify EMD in Egyptian patients with NOD and to explore the possible relation between the severity of symptoms and the different categories of EMD.

2. Materials and Methods

2.1. Study design

It is a cross-sectional study.

2.2. Patients

This study was carried out on patients with dysphagia who attended to both the endoscopy unit and the motility unit of university hospital, Egypt during the period from January 2020 to January 2021.

The patients were classified according to CC v3.0 into 4 main groups^[12]: group I: disorders with esophagogastric junction (EGJ) outflow obstruction, which include achalasia and EGJ outflow obstruction (EGJO), group II: major disorders of peristalsis including absence of contractility and distal esophageal spasm (DES), group III: minor disorders of peristalsis which include ineffective esophageal motility (IEM), and group IV: normal esophageal manometry.

The patients were of both sexes, >18 years old, with main esophageal symptoms >1-month duration, and normal esophagogastroduodenoscopy (EGD).

The patients with uncontrolled thyroid disease, uncontrolled diabetes, uncontrolled psychiatric illness, advanced cardiopulmonary disease, systemic sclerosis, hiatal hernia, eosinophilic esophagitis, and previous history of upper gastrointestinal surgery were excluded from this study.

All patients with NOD who attend both the endoscopy and motility units with the previous inclusion and exclusion criteria were included.

2.3. Patient assessment

Complete history taking, clinical examination, and laboratory investigation, including complete blood count, liver biochemistry (albumin, aminotransferases), random blood glucose, and renal function tests (serum urea and serum creatinine), were done on the included patients.

2.3.1. Symptom assessment. All patients were evaluated for symptoms of Eckardt score, which include dysphagia, retrosternal pain, regurgitation, and weight loss. Every index of this score was categorized into 4 degrees (none, occasionally, daily, and after every meal) with 0 to 3 points, respectively. Weight loss was categorized into 4 degrees (none, <5, 5–10, and >10kg) with 0 to 3 points, respectively. Scores ranged from 0 to 12. The higher the score was in concordance with the severity of symptoms.

2.3.2. Upper endoscopy. EGD was done in the endoscopy unit after optimal standard instructions. Evaluation of obstructive lesions, hiatal hernia, resistance over the EGJ, residual fluid or food inside the esophageal lumen, and biopsy for exclusion of eosinophilic esophagitis by senior endoscopists.

Barium esophagogram was done on patients by a senior radiologist.

2.3.3. Esophageal HRM. Medications that may affect esophageal motility were stopped for 5 to 7 days before the performance of study (eg, metoclopramide, anticholinergics, opiates, and smooth muscle relaxants).^[13] Esophageal HRM was performed for all included patients after fasting overnight by an experienced gastroenterologist using 22 water perfused pressures the Solar GI HRM catheter cover >32cm of esophagus: 13 pressures monitor the pharynx, the upper esophageal sphincter, and the esophageal body (mutual distance: 2 cm) 6 pressures monitor lower esophageal sphincter (LES) to determine its length, relaxations and resting pressure (mutual distance: 1 cm) and 1 gastric pressure placed 5 cm under LES. The catheter at the level of patients' supine body position was zeroed to atmospheric pressure. Then, the catheter was introduced transnasally in the upright position of the patients, and the upper esophageal sphincter and LES were recognized as high-pressure zones. After 5 minutes of supine position adaptation, patients were instructed to swallow ten 5-mL water at a 20-second interval.

2.4. Ethical considerations

The study was performed consistently with the proper medical practice and the declaration of Helsinki. After the approval of our hospital institutional review board committee and signing of informed consent by the patients after an explanation about the study respecting the privacy and ethical restrictions.

2.5. Statistical analysis of the data

Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percentages. The Kolmogorov–Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). Significance of the obtained results was judged at the 5% level. Chi-square test is used for categorical variables to compare different groups. Kruskal–Wallis test was used for abnormally distributed quantitative variables, to compare between >2 studied groups, and post hoc (Dunn multiple comparisons test) for pairwise comparisons.

3. Results

3.1. Demographics and clinic-laboratory characteristics of all NOD patients

During the study duration from January 2020 to January 2021, 252 patients were presented to the endoscopy unit and the motility unit of the University Hospital with dysphagia. One hundred ninety-seven patients with obstructive esophageal lesions were excluded with different etiologies as demonstrated in Figure 1.

After exclusions, 55 patients were included in our current study. The patient's group comprised 30 men (54.5%) and 25 women (45.5%) with a mean age of 42.44 years ranging from 18 to 68 years. In our cohort, almost two-thirds (32/55 patients [58.2%]) were aged >40 years. The mean weight of the studied patients was 78kg ranging from 55 to 102kg, the mean height was 172.18 cm ranging from 160 to 186 cm, and the mean body mass index was 26.19 kg/m² ranging from 23.95 to 28.4 kg/m². The most frequently described symptom other than dysphagia was regurgitation in 47 patients (85.5 %), followed by retrosternal pain in 37 patients (67.3%) and weight loss in 20 patients (36.3%), as shown in Table 1.

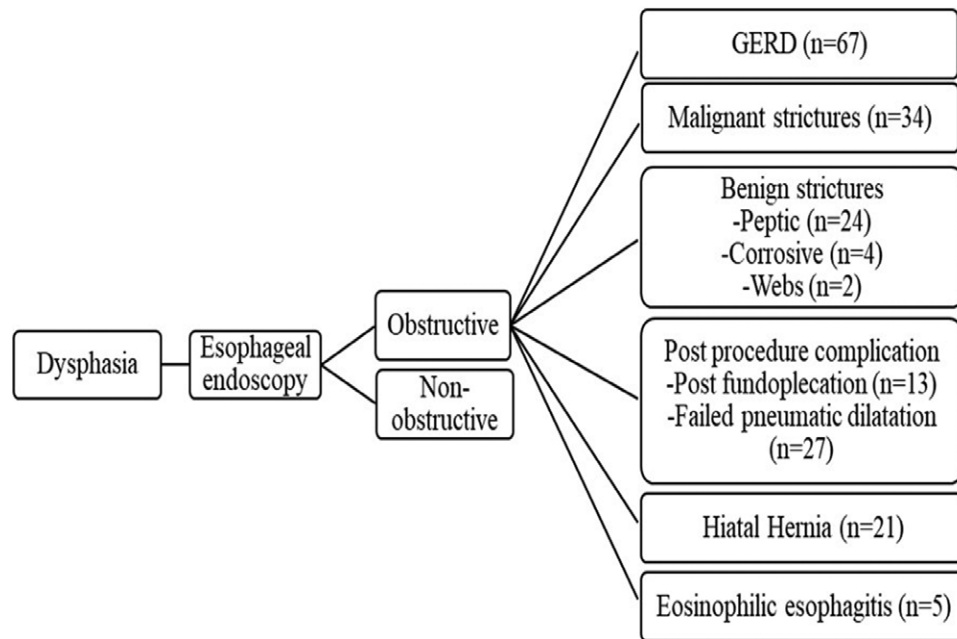


Figure 1. Classification of patients with esophageal dysphagia based on their etiology.

Table 1
Sociodemographic and clinicolaboratory characteristics of all studied patients with NOD.

Parameter	Patients (n = 55)
Age (mean ± SD)	42.44 ± 13.49
Male gender (%)	30 (54.5%)
BMI, kg/m ² (mean ± SD)	26.19 ± 3.06
Weight kg (mean ± SD)	78.0 ± 11.59
Height cm (mean ± SD)	172.18 ± 7.22
Hypertension (%)	12 (21.8%)
Diabetes mellitus (%)	2 (3.6%)
Cardiac (%)	1 (1.8%)
Smoking (%)	9 (16.4%)
Laboratory investigation (mean ± SD)	
Serum creatinine (mg/dL)	0.93 ± 0.25
Serum urea (mg/dL)	26.76 ± 9.76
Alanine transaminase (IU/L)	26.84 ± 10.30
Aspartate transaminase (IU/L)	27.18 ± 8.72
Albumin (g/dL)	4.12 ± 0.44
Hemoglobin (g/dL)	12.33 ± 1.58
Platelets (×10 ⁹ /L)	243.42 ± 70.0
White blood cells (×10 ⁹ /L)	6.21 ± 1.85
Random blood glucose (mg/dL)	97.33 ± 18.10
Associated symptoms other than dysphagia	
Weight loss (%)	20 (36.36%)
Retrosternal pain (%)	37 (67.27%)
Regurgitation (%)	47 (51.91%)
Esophagogastroduodenoscopy findings	n (%)
Spastic LES (%)	22 (40%)
Dilated esophagus (%)	19 (34.5%)
Rings (%)	3 (5.5%)
Barium delay on esophagogram (%)	34 (61.81%)

BMI = body mass index, LES = lower esophageal sphincter, NOD = nonobstructive dysphagia.

3.2. HRM classification by CC v3.0 in NOD patient

Our patients’ group were classified as followings; in the out-flow obstruction group, achalasia was diagnosed in 31 patients (56.4%) (type I: 18 [58.06%, 18/31]; type II: 9 [29.03%, 9/31], and type III: 4 [12.9%, 4/31]). EGJOO was diagnosed in 3 patients (5.5%). In the major disorders group, DES was diagnosed in 4 patients (7.3%) and absent contractility was

diagnosed in 2 patients (3.6%). In the minor disorders group, IEM was diagnosed in 7 patients (12.7%). Normal esophageal manometry was diagnosed in 8 patients (14.5%) as shown in Figures 2A and B.

3.3. Questionnaire and symptom profiles among different groups

According to the patients’ motor category group, the median Eckardt score was 5.0 (IQR, 4.0–7.0) with EGJ outflow obstruction group (achalasia: 5.0 [IQR, 4.0–6.5] and EGJOO: 6.0 [IQR, 5.0–8.0]). In major motor disorders, the median was 6.5 (IQR, 5–9) with DES: 8.0 (IQR, 5–9) and absent contractility: 5.5 (IQR, 5.0–6.0). In minor motor disorders IEM, the median score was 4.0 (IQR, 3.5–6.5). In those with normal esophageal manometry, the median Eckardt score was 3.0 (3.0–3.0) as shown in Table 2.

There was significant variation between the Eckardt scores of patients with achalasia, EGJOO, DES, and absent contractility and that of patients with normal esophageal manometry. However, there was no significant difference between the Eckardt score of patients with IEM and that of patients with normal esophageal manometry.

3.4. Comparison of symptom profiles among different groups

Because achalasia was the most frequent NOD, we compared symptoms in patients with achalasia to symptoms in other non-achalasia patients. Patients with achalasia patients had a significantly higher prevalence of regurgitation (96.8% vs 70.8%; *P* = .016) compared others. There was no significant variation in retrosternal pain, weight loss, and Eckardt score between patients with achalasia and those without (*P* = .933, .329, and .075, respective) as shown in Table 3 and Figure 3.

3.5. Endoscopic and barium findings in patients with NOD

On EGD examination, spastic LES was found in 22 patients (17 patients with achalasia, 1 patient with DES, 2 patients with EGJOO, 1 patient with IEM, and 1 patient with normal endoscopy). Fourteen of those 22 patients with spastic LES had

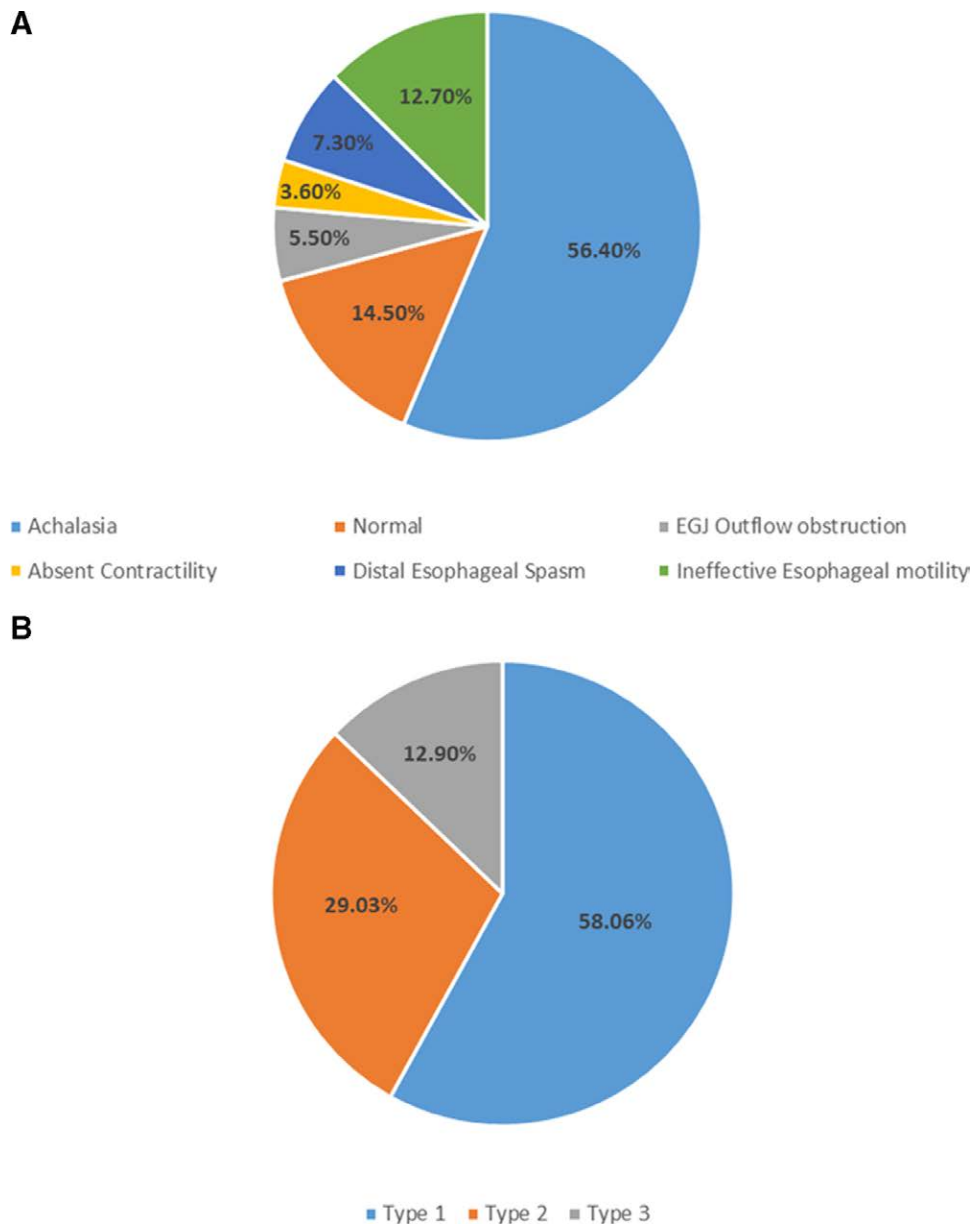


Figure 2. (A) Distribution of EMD in NOD patients according to Chicago Classification v3.0 by HRM. (B) Prevalence of different achalasia subtypes. EMD = esophageal motility disorder, HRM = high-resolution manometry, NOD = nonobstructive dysphagia.

dilated esophagus (12 patients were achalasia and 2 patients were EGJOO). Only 4 patients with achalasia and 1 patient with DES had dilated esophagus without spastic LES.

In patients with achalasia diagnosed by HRM, 80.64% (25/31) had barium stasis on barium esophagogram and EGD had features suggestive of achalasia in 64.5% (20/31) of them, as demonstrated by the existence of dilated esophagus and/or spastic LES.

4. Discussion

Dysphagia, regurgitation, and retrosternal pain are the most predominant symptoms of EMD. The barium esophagogram, EGD, and conventional esophageal manometry are traditionally used to assess patients with dysphagia. Esophageal manometry is the most accurate test for the correct diagnosis of EMD.^[14,15]

In this cross-sectional study, according to the Chicago classification, achalasia was found in (56.4%) of patients being the most common diagnosis in our Egyptian population, followed

by IEM in 12.7%, DES in 7.3%, EGJOO in 5.5%, absent contractility in 3.6%, and normal manometry in 14.5% of patients.

This was in accordance with Yeh et al^[16] who prospectively studied EMDs in Taiwanese populations and found that achalasia was the most common diagnosis (55%), followed IEM (12.5%), absent contractility (5%), EGJ outflow obstruction (5%), and Jackhammer esophagus (2.5%). Twenty percent patients had normal manometry. Also, Rehman et al^[17] who have demonstrated that achalasia was the most common diagnosis in their studied cases (35.6%) followed by DES (13.0%). Then weak peristalsis with large peristaltic defects was less common (7.9%). And, in a study by Burgess and Wyeth^[18] it was reported that achalasia was detected in 56.1% of patients, IEM in 12.2% of patients, DES in 17.1% of patients, and nutcracker esophagus in 4.9% of patients. 9.8% of patients had normal manometry studies. Abbas et al^[19] demonstrated in their study in Sudan that achalasia was the most common EMD detected in 65.38% of patients. In addition, Liu et al^[20] demonstrated that, in NOD patients, achalasia was diagnosed in 48.3% of

Table 2

Comparison among the different patient's categories according to the Eckardt Score.

Eckardt score	Chicago classification subgroups					
	Achalasia (n = 31)	EGJ outflow obstruction (n=3)	DES (n = 4)	Absent contractility (n = 2)	Ineffective motility (n = 7)	Normal (n = 8)
Median (IQR)	5.0 (4.0–0.50)	6.0 (5.0–8.0)	8.0 (5.0–9.0)	5.5 (5.0–6.0)	4.0 (3.50–6.0)	3.0 (3.0–3.0)
H (p)	16.781* (.005*)					
p ₁	<.001*	.008*	.002*	.047*	.079	

DES = distal esophageal spasm, EGJ = esophagogastric junction, IQR = interquartile range, p = P value for comparing between the different categories, p₁ = P value for comparing between group normal and each other group.

*Statistically significant at P ≤ .05.

Table 3

Comparison between achalasia and nonachalasia according to Eckardt score.

Symptoms	Achalasia (n = 31)	Nonachalasia (n = 24)	P
Weight loss (kg), n (%)	13 (41.9%)	7 (29.2%)	.329
Retrosternal pain, n (%)	21 (67.7%)	16 (66.7%)	.933
Regurgitation, n (%)	30 (96.8%)	17 (70.8%)	.016*
Eckardt score median (IQR)	5.0 (4.0–6.50)	4.0 (3.0–6.50)	.075

IQR = interquartile range.

*Statistically significant at P ≤ .05.

patients and 17.2% of patients were diagnosed with IEM, 5.2% of patients were diagnosed with EGJOO, 5.2% of patients were diagnosed with DES, 3.4% of patients were diagnosed with hypercontractile esophagus, and 5.2% of patients were diagnosed with fragmented peristalsis.

On the other hand, Wang et al^[21] in their retrospective study of NOD in the Chinese population showed that 38.6% of patients were diagnosed with IEM, which was the most common EMD followed by achalasia (19.1%) and fragmented peristalsis (16.1%) of patients. The same was demonstrated in a retrospective study from India that 43.8% of patients were diagnosed with IEM, which was the most common EMD, followed by achalasia (26.3%).^[22]

The subtypes of achalasia in our study were as follows: type I: 18 (58.06%, 18/31), which was the commonest, followed by type II: 9 (29.03%, 9/31) and type III: 4 (12.9%, 4/31). This was in accordance with Goyal et al,^[22] who have demonstrated that type I represented 54.5%, type II represented 39.4%, and type III represented 6.1% of patients with achalasia. While studies from China and Taiwan demonstrated that type II was the commonest.^[16,21] Such discrepancies emphasize the role of differences in ethnicity and dietary habits in variability of distribution of EMD spectrum.

In the current study, normal HRM was demonstrated in 14.5% of patients despite their persistent clinical symptoms. This was consistent with Goyal et al^[22] and Misra et al^[23] who demonstrated that 19.4% and 15%, respectively, had normal esophageal manometry. This could be attributed to the intermittent nature of EMD, more detailed studies like PH impedance would be useful in detecting those patients. Also, it cannot be ignored that some EMDs could be of psychiatric origin and the presence of a psychiatric specialist would help in detecting these disorders.^[24]

In our study, barium esophagogram was suggestive for the diagnosis of achalasia in 80.64% of patients. This was in accordance with Rehman et al^[17] who recorded in their cross-sectional study that barium esophagogram was sensitive for the diagnosis of achalasia proved by HRM in 63.9% of the patients. Also, Schima et al^[25] found that the diagnosis of achalasia by barium esophagogram was made in 58% of the patients with manometrically proven achalasia. Also, El-Takli et al^[26] have demonstrated that barium swallow was suggestive of achalasia in 58% patients. While O'Rourke et al^[27] found that the diagnosis of achalasia by barium esophagogram had very low sensitivity of 29%.

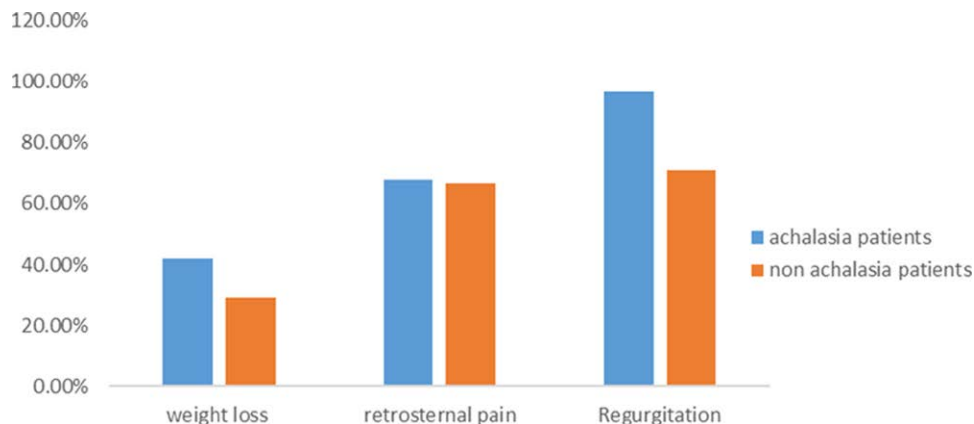


Figure 3. Comparison between achalasia and nonachalasia patients according to prevalence of the main presenting symptoms.

These findings ensure that HRM is required in the diagnosis and characterization of EMD and should be the first diagnostic modality to minimize recurrent clinic visits.

Our results showed that there was significant variation between the Eckardt scores of patients with Achalasia 5.0 (4.0–6.0), EGJOO 6.0 (5.0–8.0), DES 8 (5.0–9.0), and absent contractility 5.5 (3.5–6.0) and that of patients with normal HRM 3 (3.0–3.0). On the other hand, there was no significant difference between the Eckardt scores of patients with IEM and that of patients with normal HRM.

This came in congruence with Wang et al^[21] who have demonstrated that there was a significant variation between the Eckardt scores of patients with achalasia (4.8±0.1), type I (4.6±0.1), type II (5.0±0.2), type III (4.7±0.3), and jackhammer esophagus (4.7±0.4) and those of patients in the normal esophageal manometry group (3.9±0.1). While Yeh et al^[16] have demonstrated that patients with achalasia experienced increased vomiting (62.1% vs 31.5%) and significant weight loss (22.7% vs 7.4%) compared with nonachalasia patients. These differences could be attributed to the variability of the duration of dysphagia. So, symptoms alone could not point to a specific type of EMD.

In Egypt, we have only 6 tertiary university hospitals out of 27 equipped with motility centers and fewer private centers. Our study was a 2 tertiary center study in Egypt, so it is the first large study assessing HRM in EMD in Egypt. The practice of motility studies is also deficient in Asian countries as shown in a questionnaire-based survey assessing the status of motility units in Asian countries. Motility studies were basically used in 50% of institutions of Thailand and around 60% of institutions in Hong Kong, Japan, Korea, Philippines, and Singapore.^[28] This emphasizes the necessity of wide adoption of HRM in tertiary referral gastroenterology centers.

One of our limitations was the relatively small number of the included patients. This could be explained by the limited numbers of patients accessing the hospitals during the current pandemic restriction and prioritization of endoscopic procedures. We do recommend further studies on larger numbers of patients with longer follow-up duration for better characterization of EMD in Egypt.

In conclusion, achalasia was the most common EMD in Egyptian patients with NOD. Eckardt score was higher in patients with outflow obstruction and major motor disorder, but it could not differentiate different categories of Chicago classification of EMD. HRM is superior in characterization of EMD

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