ORIGINAL ARTICLE

Adiponectin level changes among Egyptians with gastroesophageal reflux disease

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Abstract

Background and Aim: Visceral fat is an important endocrine organ that secretes different bioactive substances such as adipocytokines. The aim of this study was to investigate the adiponectin level changes among patients with erosive gastroesophageal reflux disease (GERD)and its consequence on pathogenesis.

Methods: In this study, 150 subjects were selected and divided into four groups: Group I ($n = 40$) were healthy individuals with an average body mass index and had no gastrointestinal tract symptoms; Group II ($n = 50$) were patients with mild to moderate erosive esophagitis; Group III ($n = 40$) were patients with severe erosive esophagitis; and finally, Group IV ($n = 20$) were patients with Barrett's esophagus. Upper gastrointestinal endoscopy was performed for Groups II, III, and IV only, and histopathological assessment was conducted for the suspicious cases of Barrett's esophagus. The measurement of serum adiponectin was performed for all groups using the ELISA test.

Results: Our results revealed that the serum level of adiponectin was significantly lower in patients with different grades of GERD as well Barrett's esophagus as compared to healthy controls (P-value < 0.001). Additionally, the serum level of adiponectin was correlated with different grades of GERD as the highest level of the adiponectin was found in the control group (11.05 ± 2.58) followed by mild to moderate GERD (6.39 ± 1.64) and then severe GERD (2.42 ± 1.00); finally, the lowest level was detected in the Barrett's esophagus group (1.99 ± 0.47). Our study showed significant correlation between body mass index, waist circumference, and waist–hip ratio on one hand and serum adiponectin level on the other hand, with a statistically significant difference (P-value < 0.001). The best cut-off value for serum adiponectin was 7.7 (μg/mL), with a sensitivity of 91.8% and specificity of 97.5%.

Conclusions: Low serum adiponectin level appears to be associated with an increased risk of erosive esophagitis, and visceral fat accumulation is related to the impaired secretion of adiponectin, which may have an influence on the pathogenesis of GERD.

Introduction

Gastroesophageal reflux disease (GERD) is defined as an abnormal reflux of gastric contents into the esophagus at least once a week due to the failure of antireflux mechanisms, leading to symptoms such as heartburn, acid regurgitation, and/or esophageal mucosal damage, which may also provoke long-term complications such as Barrett's esophagus (BE).[1] GERD is a categorical disease that manifests itself in three distinct ways: non-erosive or erosive esophagitis and Barrett's esophagus.[2] The underlying mechanism of GERD is thought to be mechanically related to an increase in intragastric pressure due to the external compression of surrounding adipose tissue resulting in the frequent relaxation of the lower esophageal sphincter and hence the development of mucosal damage in the esophagus due to

pathological acid reflux.[3] In addition to this mechanical hypothesis, metabolic factors, including the presence of metabolic syndrome, increase in insulin resistance, and decreased level of adiponectin, are also associated with GERD.[4] Visceral fat is an important endocrine organ that secretes different bioactive substances such as adipocytokines. Thus, obesity may affect the pathogenesis of GERD by adipocytokines as well as acid reflux.[5] However, current knowledge remains limited in answering why some obese patients develop this disease but others do not. Adiponectin is a peptide secreted primarily from visceral adipocytes, for which serum levels are inversely associated with obesity.[6] Furthermore, adiponectin is an adipocytokine that was isolated from the human adipose tissue. It ranges from 5 to 30 μg/mL in the human blood, and serum levels are inversely correlated with

body mass index (BMI).[7] Moreover, adiponectin has anti-inflammatory, anti-steatotic, anti-diabetic, and anti-malignant effects. Epidemiological studies have indicated that lower serum adiponectin levels are associated with various inflammatory diseases of the digestive system.[8] In accordance with these experimental and epidemiological results, we hypothesize that adiponectin is involved in the pathogenesis of GERD. Therefore, we aimed to evaluate serum adiponectin in gastroesophageal reflux patients and its role in the pathogenesis.

Methods

In our study, 150 subjects were selected from the outpatient clinic and inpatients of the Internal Medicine Department of El- Hussein University Hospital, AL-Azhar University, Cairo, Egypt, during the period October 2014 to July 2016. The included patients demonstrated GERD symptoms in the form of heartburn, regurgitation, noncardiac chest pain, dysphagia, odynophagia, dyspepsia, chronic pharyngitis, laryngitis, and asthma; therefore, they underwent esophago-gastro-duodenoscopy. The exclusion criteria of the studied groups included previous gastroesophageal surgery and previous gastroesophageal cancer. This study has been conducted in accordance with the ethical standards, and all participants gave their informed consent prior to their inclusion in the study.

Study groups. A total of 150 subjects were enrolled in this study and classified into four groups. Group I included 40 healthy individual (26.6%) with average BMI (23.7 ± 2.5) and no GIT symptoms (control group). Group II included 50 patients (33.3%) with mild to moderate erosive esophagitis confirmed by upper gastrointestinal (GI) endoscopy with grading of GERD according to Los Angeles (LA) classifications (mild to moderate GERD group). Group III included 40 patients (26.6%) with severe erosive esophagitis (severe GERD group). Group IV included 20 patients (13.3%) with Barrett's esophagus confirmed by upper GI endoscopy and histopathological assessment of biopsy specimens (Barrett's esophagus group).

Study design. All subjects were subjected to the following: full history taking, full clinical examination, and investigations, including complete blood count (CBC), fasting blood glucose (FBG), triglyceride, total cholesterol, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum creatinine. Anthropometric measurements, including body weight, body height, waist circumference (WC), and hip circumference, were obtained. BMI was calculated as weight in kilograms divided by the square of height in meters. The measurement of WC was made at the midpoint between the lowest rib and iliac crest with the subjects standing, after gentle expiration. Hip circumference was measured at the maximum circumference between the iliac crest and the crotch while the participant was standing, and was recorded in the same position. Waist–hip ratio (WHR) was calculated as WC divided by hip circumference.

Measurement of serum adiponectin. Blood samples were obtained in the morning after fasting for 12 h from all examined patients and controls before upper GI endoscopy. Blood serum was obtained after 15 min of clotting and 10 min of centrifugation at 2000 rpm. Serum was removed, frozen, and stored at −20°C. Adiponectin concentrations were measured with ELISA (Assaymax Human Adiponectin ELISA Kit, 2014).

Endoscopic procedure. All patients were offered conscious sedation with intravenous midazolam (2.5–5 mg) and/or propofol (40–200 mg) and then underwent endoscopic assessment of reflux esophagitis, with severity graded according to LA classification.[9] In our study, we defined mild to moderate erosive GERD as LA classification Grades A, B, and C, and severe erosive GERD as LA classification Grade D. To minimize the variability in the endoscopy procedure, all of the endoscopic examinations were performed by only one senior endoscopist with more than 10 years of experience in diagnostic and therapeutic endoscopy. The instruments used in this study were a video endoscope and an electronic endoscopic system (Olympus EVIS Lucera Ellit CV-290; Olympus Medical Systems, Tokyo, Japan).

Histopathological assessment. Histopathology was performed for the suspicious cases of Barrett's esophagus, and biopsy specimens were prepared according to the routine clinical protocol and interpreted by clinical histopathologists on the basis of the presence of a columnar-lined esophagus plus intestinal metaplasia to diagnosis BE.

Statistical analysis. Data were analyzed using SPSS Statistics version 21 (IBM Corp., Armonk, NY, USA). The normality of numerical data distribution was examined using the Shapiro–Wilk test. Normally distributed numerical variables were presented as mean ± SD, and intergroup differences were compared using ANOVA. The Tukey–Kramer *post hoc* test was applied when ANOVA revealed a statistically significant difference among the groups. Categorical variables were presented as number and percentage, and intergroup differences were compared using the chi-square test for trends. Correlations were tested using the Pearson correlation. The correlation coefficient (Pearson *r*) is interpreted as follows:

Correlation coefficient (Pearson *r*)	Strength of correlation
<0.2	Very weak
0.2–0.39	Weak
0.4–0.59	Moderate
0.6–0.79	Strong
0.8–1	Very strong

Receiver-operating characteristic (ROC) curve analysis was used to examine the diagnostic value of adiponectin. The area under the ROC curve (AUC) is interpreted as follows:

AUC	Diagnostic/predictive value
0.9–1.0	Excellent
0.8–0.89	Good
0.7–0.79	Fair
0.6–0.69	Poor
<0.6	Fail

Table 1 Demographic characteristics of subjects in the four study groups

Variable	Control group (*n* = 40)	Group II (*n* = 50)	Group III (*n* = 40)	Group IV (*n* = 20)	*P*-value
Gender					0.380
Male	24 (60%)	25 (50%)	20 (50%)	16 (80%)	
Female	16 (40%)	25 (50%)	20 (50%)	4 (20%)	
Age (years)	49 ± 14	46 ± 12	49 ± 8	54 ± 5	0.031
Weight (kg)	70 ± 8	75 ± 12	92 ± 17	74 ± 9	<0.001
Height (cm)	171 ± 8	172 ± 9	175 ± 8	171 ± 7	0.141
BMI (kg/m^2)	23.7 ± 2.5	25.4 ± 3.1	29.9 4.3	25.3 ± 2.7	<0.001
WC (cm)	81 ± 8	86 ± 9	99 ± 8	91 ± 7	<0.001
WHR	0.83 ± 0.05	0.83 ± 0.06	0.91 ± 0.06	0.85 ± 0.05	<0.001
DM	0 (0%)	15 (30%)	11 (27.5%)	3 (15%)	0.056

Weight and BMI were significantly higher in Group III (severe GERD) than other groups, with statistically significant differences in the control group (*P*-value < 0.001). There was an association between GERD and DM, with a statistically significant difference between the GERD group and control group.
BMI, body mass index; DM, diabetes mellitus; GERD, gastroesophageal reflux disease; WC, waist circumference; WHR, waist–hip ratio.

Multivariable binary logistic regression analysis was used to determine the relation between adiponectin and GERD adjusted for possible confounding factors. Ordinal regression was used to examine the relation between adiponectin and the severity of GERD. A *P*-value of <0.05 was considered statistically significant.

Results

A total of 150 subjects were recruited in the present study, 85 males and 65 females, and were classified into four groups. Group I included 40 subjects (26.6%), 24 males (60%) and 16 females (40%), and the mean age was 49 ± 14 years, with average BMI of 23.7 ± 2.5 (kg/m^2). Group II included 50 patients (33.3%), 25 males (50%) and 25 females (50%), and the mean age and BMI were 46 ± 12 and 25.4 ± 3.1 (kg/m^2), respectively, with mild to moderate erosive esophagitis. Group III included 40 patients (26.6%), 20 males (50%) and 20 females (50%), and the mean age and BMI were 49 ± 8 and 29.9 ± 4.3 (kg/m^2), respectively, with severe erosive esophagitis. Group IV included 20 patients (13.3%), 16 males (80%) and 4 females (20%), and the mean age and BMI were 54 ± 5 and 25.3 ± 2.7 (kg/m^2), respectively, with Barrett's esophagus (Table 1). Our results showed that weight and BMI were significantly higher in the severe GERD groups (92 ± 17 kg and 29.9 4.3 kg/m^2) than other groups, with statistically significant difference in the control group (70 ± 8 kg and 23.7 ± 2.5 kg/m^2) (*P*-value < 0.001). Additionally, WHR was significantly high in the severe GERD group (0.91 ± 0.06) compared to the control group (0.83 ± 0.05) (*P*-value < 0.001). This means that obesity, particularly abdominal obesity, was shown to be an independent risk factor for GERD and was correlated with severity. The laboratory investigation of studied groups revealed significant differences between the groups regarding FBG, serum triglyceride, and serum cholesterol. With regard to adiponectin findings in the four study groups, the highest level was detected in the control group (11.05 ± 2.58) followed by mild to moderate GERD group (6.39 ± 1.64) and severe GERD group (2.42 ± 1.00); and finally, the lowest level was found in the Barrett's esophagus group (1.99 ± 0.47) (Table 2 and Fig. 1) with a statistically

significant difference between the control group and all patient groups (*P*-value < 001), indicating that a low level of adiponectin was associated with the high prevalence of erosive esophagitis and Barrett's esophagus. Our study showed significant correlations between BMI, WC, and WHR on one hand and serum adiponectin level on the other hand, with a statistically significant difference (*P*-value < 0.001) (Table 3). ROC curve analysis for discrimination between patients with or without GERD using adiponectin showed that the best cut-off criterion was <7.7 (μg/mL) with sensitivity of 91.8% and specificity of 97.5% (Table 4). Furthermore, ROC curve analysis for discrimination between patients with severe GERD or Barrett's esophagus and those with mild or moderate GERD using adiponectin demonstrated that the best cut-off criterion was <4.24 (μg/mL) with sensitivity of 95.0% and specificity of 94.0% (Fig. 2). Multivariable binary logistic regression analysis for the relation between adiponectin and GERD as adjusted for confounding factors showed that adiponectin (odds ratio: 0.11; 95% confidence interval [CI]: 0.03–0.41; *P*-value = 0.001) and total cholesterol (odds ratio: 1.10; 95% CI: 1.01–1.21; *P*-value = 0.029) were independent predictors for GERD (Table 5). Moreover, multivariable ordinal logistic regression analysis for the relation between adiponectin and severity of GERD as adjusted for confounding factors showed that adiponectin (*P*-value < 0.001) and BMI (*P*-value < 0.001) were independent predictors for the severity of GERD.

Discussion

The prevalence of GERD has been increasing worldwide[10] and is associated with decreasing quality of life, Barrett's esophagus, and esophageal carcinogenesis.[11] Plasma adiponectin levels in humans range from 0.5 to 30 μg/mL, which is about 1000-fold higher than the concentrations of most other hormones such as leptin, insulin etc. In fact, adiponectin accounts for 0.01% of total human plasma proteins and is the most abundant adipose tissue protein.[12] In this study, we found that the serum adiponectin level was significantly decreased in GERD groups in comparison with the normal control group. Furthermore, the level decreased with increasing GERD severity (inverse relationship). Therefore, adiponectin may have a protective role against erosive

Table 2 Adiponectin findings in the four study groups

Variable	Control group (*n* = 40)	Group II (*n* = 50)	Group III (*n* = 40)	Group IV (*n* = 20)	*F* (df = 3, 147)	*P*-value
Adiponectin (µg/mL)	11.05 ± 2.58	6.39 ± 1.64	2.42 ± 1.00	1.99 ± 0.47	208.271	<0.001

The highest level of the adiponectin was in the control group followed by mild to moderate GERD group and the severe GERD group, and finally the lowest level was found in the Barrett's esophagus group.

GERD, gastroesophageal reflux disease.
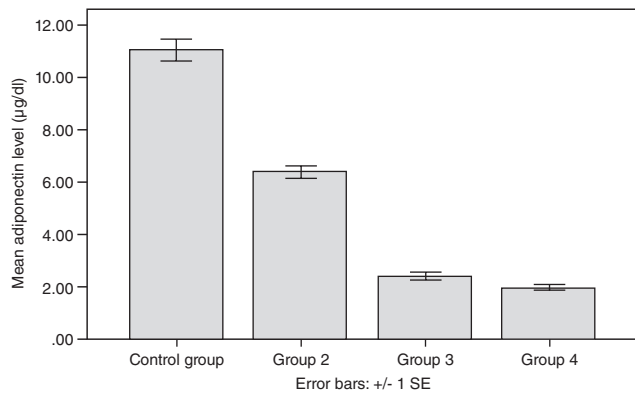
Figure 1 Mean adiponectin level in the four study groups. Error bars represent the SEM.

esophagitis. In addition to the high association of erosive esophagitis with decreasing levels of serum adiponectin, as also reported by Kato *et al.*,[12], all patients with Barrett's esophagus were diagnosed with low serum adiponectin, as also reported by the study of Lee *et al.*.[13] Our study was compatible with the study by Iwasaki *et al.*,[14], who announced that a diminished level of adiponectin was found in a patient with severe GERD assessed by video esophagography. In contrast to our study, a study by Nam *et al.*[15] showed that adiponectin had no overall relationship with reflux esophagitis. The major difference between the two studies is that our study used BMI as an indicator of obesity, but Nam *et al.* used visceral fat ratio as an indicator of central obesity and visceral adipose tissue, which is metabolically active. However, these results not only contrast with our results but also with a Japanese study by Iwasaki *et al.*,[14] who demonstrated that adiponectin is negatively associated with GERD . Another study of Taiwanese patients by Tseng *et al.*,[16] who experienced typical GERD symptoms (heartburn and/or acid regurgitation) for at least three episodes per week in the past 3 months, demonstrated a baseline assessment of symptom severity and frequency with the Reflux Disease Questionnaire and an upper endoscopy. GERD was classified into erosive esophagitis (*n* = 67), nonerosive esophagitis (*n* = 37), and BE (*n* = 8). These patients were measured for the serum levels of adipokines (adiponectin and leptin). No statistical difference was found in circulating adiponectin levels between the GERD and control groups (in contrast to our study), while BE patients had significantly lower adiponectin levels than those without BE (similar to our study). Our explanation for these results assumes that GERD by itself may be transformed in time to Barrett's

Table 3 Correlation between adiponectin and other quantitative variables

Variable	Adiponectin	
	Pearson correlation	*P*-value
Age	−0.093	0.255
Weight	−0.493	<0.001
Height	−0.144	0.078
BMI	−0.543	<0.001
WC	−0.578	<0.001
WHR	−0.389	<0.001
FBS	−0.329	<0.001
Triglycerides	−0.326	<0.001
Total cholesterol	−0.333	<0.001
ALT	0.023	0.782
AST	−0.026	0.751
Creatinine	0.151	0.065

There was a significant correlation between BMI, WC, and WHR on one hand and serum adiponectin level on the other hand.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; FBS, fasting blood sugar; WC, waist circumference; WHR, waist–hip ratio.

Table 4 ROC curve analysis for discrimination between patients with or without GERD using adiponectin

Metric	Statistic
AUC	0.986
P-value (two-tailed)	<0.0001
Best cut-off criterion (µg/mL)	<7.7
Sensitivity (%)	91.8
Lower bound (95%) (%)	84.9
Upper bound (95%) (%)	95.8
Specificity (%)	97.5
Lower bound (95%) (%)	85.7
Upper bound (95%) (%)	100.0
PPV (%)	99.0
NPV (%)	81.3
TP	101
TN	39
FP	1
FN	9
Youden index	1.893
Accuracy (%)	93.3

ROC curve analysis for discrimination between patients with or without GERD using adiponectin showed that the best cut-off criterion was <7.7 (µg/mL), with sensitivity of 91.8% and specificity of 97.5%.

AUC, area under the ROC curve; FN, false negative; FP, false positive; GERD, gastroesophageal reflux disease; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver-operating characteristic; TN, true negative; TP, true positive.
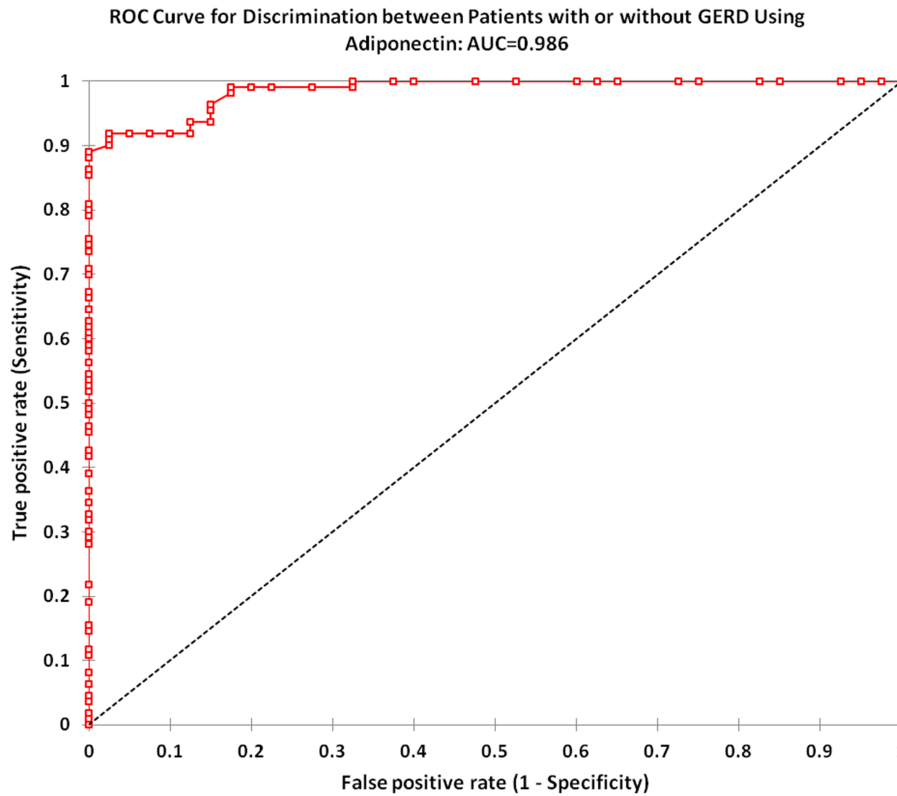
Figure 2 Receiver-operating characteristic curve analysis for discrimination between patients with severe gastroesophageal reflux disease (GERD) or Barret's esophagus and those with mild or moderate GERD using adiponectin.

esophagus. In the present study, significantly lower plasma adiponectin levels were noted in BE patients, which was comparable to the results of a case–control study conducted by Rubenstein *et al.*[17] Serum hypoadiponectinemia in BE was also shown in a

Table 5 Multivariable binary logistic regression analysis for the relation between adiponectin and GERD adjusted for confounding factors

Variable	P-value	OR	95% CI for OR Lower	95% CI for OR Upper
Adiponectin (μg/mL)	0.001	0.11	0.03	0.41
BMI (kg/m^2)	0.738	0.90	0.49	1.66
WC (cm)	0.100	1.15	0.97	1.35
FBS (mg/dL)	0.950	1.00	0.92	1.08
Triglyceride (mg/dL)	0.139	0.94	0.86	1.02
Total cholesterol (mg/dL)	0.029	1.10	1.01	1.21
Constant	0.392	60 255.89		

Adiponectin (OR: 0.11; 95% CI: 0.03–0.41; *P*-value = 0.001) and total cholesterol (OR: 1.10; 95% CI: 1.01–1.21; *P*-value = 0.029) were independent predictors for GERD. Adiponectin (*P*-value < 0.001) and BMI (*P*-value < 0.001) were independent predictors for the severity of GERD.
BMI, body mass index; CI, confidence interval; FBS, fasting blood sugar; GERD, gastroesophageal reflux disease; OR, odds ratio; WC, waist circumference.

variety of studies, such as the study by Mokrowiecka *et al.*[18] and another one by Thompson *et al.*,[19] and their results were similar to our study. Moreover, the study of Greer *et al.*[20] showed that the serum adiponectin level had an inverse association with BE. The observed associations of adiponectin with BE remained significant after adjustment of potential confounders such as age, gender, race, and obesity state, suggesting that this adipokine is associated strongly with BE and may play a biological role in the pathogenesis of esophageal columnar metaplasia. Contrary to our study, Almers *et al.*[21] conducted a case–control study evaluating the association between adiponectin (total, high, and low/medium molecular weight) and BE in the Kaiser Permanente Northern California population. Their results revealed increasing (not decreasing) serum concentrations of total adiponectin, high molecular weight and low molecular weight adiponectin. Higher adiponectin levels were independently associated with aberrant healing of esophageal injury in GERD (positive correlation not negative). Parallel to our study, another study by Chandar *et al.*[22] summarized data from nine observational studies (10 independent cohorts; 1432 patients with BE and 3550 controls). When patients with BE were matched to population controls in five studies, subjects within the highest tertile of serum adiponectin level showed decreased odds of BE (odds ratio: 0.65; 95% CI: 0.31–1.36). This association was even more pronounced in males, and after adjustment for potential confounders, such as age, gender, and race, the observed associations of adiponectin with BE remained significant. Obesity is shown to be an

independent risk factor of GERD[23] through increased transient lower esophageal sphincter relaxation, which is an important mechanism of GERD.[24] These results were compatible with our study, which demonstrated that weight and BMI was significantly high in Group III (severe GERD) in comparison to the control group. This means that obesity is shown to be independent risk factor for GERD and is correlated with severity. Several clinical studies showed decreased adiponectin levels in obese humans relative to lean subjects such as studies by Arita *et al.*[7] and Hotta *et al.*[25] For example, Arita *et al.* found a negative correlation between BMI and plasma adiponectin levels in Japanese men and women. Surprisingly, there were marked variations in adiponectin levels even among obese subjects (adiponectin concentration varied from 1.00 to 14.5 μg/mL in this study), and this finding was similar to our study (adiponectin concentration varied from 1.1 to 16.7 μg/mL).The same finding was reported by an American study by Abraham *et al.*,[26] who showed a positive association between obesity and erosive reflux esophagitis and illustrated that increasing levels of BMI are associated with a proportional increase in the erosive reflux esophagitis. This study was conducted in a multiethnic community and in both genders. Interestingly, in the present study, weight and BMI were significantly high in Group III (severe GERD) than in other groups, with statistically significant difference in the control group (P-value < 0.001). This means that obesity is shown to have a positive association with GERD and is correlated with severity in both studies. Obesity alone may be associated with the downregulation of adiponectin receptors, as stated in previous studies, like the study of Kadowaki and Yamauchi.[27] This was supported by our observation of low adiponectin levels in morbidly obese cases. With the accumulation of visceral fat, circulating levels of adiponectin, a potential anti-inflammatory adipocytokine, are decreased, while circulating levels of pro-inflammatory cytokines, such as interleukin-6 (IL-6), are increased. Low serum adiponectin levels were reported in subjects with esophago-gastro-duodenoscopic erosive esophagitis.[12] Adiponectin is one of the hormones secreted by adipose tissue. The correlation between low circulating adiponectin and obesity (especially central obesity), insulin resistance, and type 2 diabetes has been well established,[28] and our study showed the same results. Inverse correlations between plasma adiponectin levels and BMI or body fat was further supported by studies of Weyer *et al.*,[29] who performed on Caucasian and Pima Indian populations, and our study supported these data on the Egyptian people. Visceral adipose tissue is biologically active and can secrete pro-inflammatory cytokines, especially IL-6 and tumor necrosis factor-α, which lead to insulin resistance.[30] In addition, these cytokines may also be associated with a chronic inflammatory state in obesity, thus increasing the risk of erosive esophagitis.[31] Nevertheless, it remains unclear what the underlying metabolic mechanisms are and whether other humoral factors are involved in the pathogenesis of obesity-related erosive esophagitis. Previous reports demonstrated the association between GERD and type 2 diabetes mellitus (T2DM) in Japanese populations.[32] These results were consistent with our results, which found associations between GERD and diabetes mellitus, with a statistically significant difference between the GERD group and the control group (P-value = 0.05). These results indicated that the combination of metabolic syndrome and hypoadiponectinemia had a multiplicative effect on GERD and its severity. In another study, adiponectin levels were compared in three groups of subjects: nondiabetic individuals, diabetic subjects with coronary artery disease, and diabetic subjects without coronary artery disease. Plasma adiponectin levels were decreased in diabetic compared to nondiabetic individuals.[33] Adiponectin also acts on monocytes in an anti-inflammatory manner, and its deficiency has been associated with several inflammatory GI diseases, such as nonalcoholic steato hepatitis, acute pancreatitis, and inflammatory bowel diseases.[34] However, the present study was concerned by GERD and tried to link it with adiponectin. In conclusion, the coexistence of metabolic syndrome and low levels of serum adiponectin was associated with the higher prevalence of GERD symptom and correlated with severity. Adiponectin or adiponectin analogs may be effective anticancer agents and may have important therapeutic implications.[27] It was suggested that increasing the adiponectin level may be a new strategy for the prevention of colorectal cancer at an early step of carcinogenesis,[35] and we are hoping that our study results will be the key for using adiponectin as an anti-GERD and BE strategy in the future, especially in obese patients with visceral fat but more studies are required.

Conclusions

Adipose tissue is no longer considered an inert depot storage organ but an active endocrine organ. Among the various proteins released by adipocytes, adiponectin appears to be associated with an increased risk of erosive esophagitis. Furthermore, we suggest that visceral fat accumulation is associated with impaired secretion of adiponectin, which may have an influence on the pathogenesis of GERD. Supplementary studies are required to clarify the role of adiponectin in the pathogenesis of GERD.

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