Serum leptin level among Upper Egypt patients with gastroesophageal reflux disease

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ABSTRACT

Introduction: *Obesity is associated with an increased risk of esophageal disorders, including esophageal adenocarcinoma, Barrett esophagus and gastroesophageal reflux disease (GERD). Predominantly abdominal or intra-abdominal adiposity is more strongly linked with these esophageal disorders than BMI alone.* ***Aim of the work*** *is to assess if leptin have role in GERD.* ***Patient and methods:*** *total of 58 patients newly diagnosed as having GERD by upper endoscopy compared to 29 healthy volunteer as control group all are subjected to measuring BMI and serum leptin.* ***Results:*** *Serum leptin is increased as BMI increased and degree of GERD increased with p value 0.001.* ***Conclusion:*** *Positive correlation between seum leptin level, BMI and degree of GERD.*

Keywords: *Obesity, Leptin, GERD.*

INTRODUCTION

Gastroesophageal reflux disease (GERD), is the reflux of gastric contents other than air into or through the esophagus. GERD refers to reflux that produces frequent symptoms or results in damage to the esophageal mucosa or contiguous organs of the upper aerodigestive system and occasionally the lower respiratory tract **(1).**

The mechanisms underlying the association between obesity and GERD are only partly understood. Obesity-related changes in gastroesophageal anatomy and physiology (such as an increased prevalence of esophageal motor disorders, a diminished lower esophageal sphincter pressure, development of hiatal hernia, and increased intragastric pressure) might contribute to an explanation for this association **(2).**

Visceral fat is strongly different in respect to peripheral. For example, Visceral fat is more metabolically active, is characterized by a higher number of immune and inflammatory cells, and is more insulin-resistant thus leading to a higher overall mortality in respect to peripheral fat **(3).**

Leptin is a 16 kDa protein hormone that plays a key role in regulating energy intake and energy expenditure, including appetite and metabolism. It is one of the most important adipose derived hormones **(4).**

It is manufactured primarily in the adipocytes of white adipose tissue, and the level of circulating leptin is directly proportional to the total amount of fat in the body and to white adipose tissue **(5).**

Leptin acts on receptors in the hypothalamus of the brain where it inhibits appetite by **(1)** Counteracting the effects of neuropeptide Y (a potent feeding stimulant secreted by cells in the gut and in the hypothalamus); **(2)** Counteracting the effects of anandamide (another potent feeding stimulant). **(3)** Promoting the synthesis of α-melanocyte-stimulating hormone (α-MSH), an appetite suppressant **(6).**

Thus, circulating leptin levels give the brain input regarding energy storage so it can regulate appetite and metabolism.

PATIENTS AND METHODS

A case-control study in which 58 patients of GERD will be included in addition of 29 healthy peoples as a controls.

Cases which newly diagnosed as a GERD patients, who undergo an upper endoscopy for the investigation of symptoms (e.g., heartburn, acid regurgitation, atypical chest pain, and/or belching), at the gastroenterology clinics at Alazhar Assiut university hospital and Assiut university hospital from Upper Egypt governates.

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Controls were selected from the same geographic areas of those of case participants using a random method. Participants' controls will be matched to cases by age and sex, but they are GERD free peoples (clinically and endoscopically).

Study procedure

All cases and controls were subjected to:-

1. Full history taking (including any complaint, risk factors, diabetes, drugs, diseases, smoking, coffee and other habits).
2. Thorough clinical examination (including height, weight, body mass index, waist circumference …).
3. Upper endoscopy to determine whether gastro esophageal reflux disease presents (case) or not (control).
4. Measurement of serum leptin levels by ELISA

Inclusion and Exclusion criteria

For cases:

- Aged 20-60 years.
- Newly diagnosed as a GERD patient (endoscopically confirmed).
- Not previously diagnosed as a GERD patient or received GERD treatment.
- No pregnancy
- There is no drug intake by which serum leptin can be affected, e.g. corticosteroids.
- There is no chronic and/or malignant diseases by which serum leptin can be affected, e.g. G.I.T. malignancy.
- Habits: either smoking or tea and coffee ingition will be accepted but addiction and drug abuse will be excluded.

For Control:

- Selected from the same locality and matched to cases by age, sex, and other criteria but without present or previously diagnosis of gastroesophageal reflux disease (confirmed by upper endoscopy).
- A written consent were taken from the patients and controls in this study.

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- A one-way analysis of variance (ANOVA) when comparing between more than two means.
- Chi-square (X^2) test of significance was used in order to compare proportions between two qualitative parameters.
- Pearson's correlation coefficient (r) test was used for correlating data.
- Probability (P-value)
  - P-value $\leq$0.05 was considered significant.
  - P-value $\leq$0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

RESULTS

Our result revealed positive correlation between BMI and GERD (as BMI increased the degree of GERD increased) and leptin concentration shows positive correlation with the degree of GERD as shown in the tables below.

Table (1): Relation between GERD, BMI and leptin

	GERD							
	I		**II**		**III**		**ANOVA test**	
	Mean	**±SD**	**Mean**	**±SD**	**Mean**	**±SD**	**F**	**p-value**
BMI	31.80	3.78	35.44	3.22	37.80	0.42	6.426	**0.003 (S)**
Leptin	27.90	20.07	42.65	29.34	88.45	24.13	8.523	**0.001 (S)**

Table (2): Correlation between BMI and other parameters in the patients group

Parameters	BMI	
	R	p-value
Age	0.234	0.077
Wt	0.581	**<0.001**
Length	-0.344	**0.008**
GERD	0.433	**0.001**
Habit	-0.017	0.910

r- Pearson Correlation Coefficient.

There is positive correlation between (weight, GERD) and BMI, negative correlation between Length and BMI.

Table (3): Correlation between leptin level and other parameters in the patients group

	Leptin	
	R	p-value
Age	0.202	0.129
Weight	0.297	**0.024**
Length	-0.473	**<0.001**
BMI	0.820	**<0.001**

r- Pearson Correlation Coefficient.

There is positive correlation between BMI and leptin level, negative correlation between length and leptin level.

DISCUSSION

Obesity, typically defined as a body mass index (BMI) of >30 Assumed factors including genetic predisposition, increased food intake and decreased physical activity **(7).**

The prevalence of GERD and related disorders also has been steadily increasing, the reasons for this rise in GERD and its complications have not been clearly identified, and many studies have investigated whether the increase in the prevalence of obesity and GERD are related. Overall, there seems to be quite a good amount of evidence of a modest association between BMI, particularly in the obese range, and GERD symptoms **(8).**

Obese individuals may experience extrinsic gastric compression by surrounding adipose tissue, leading to an increase in intragastric pressures and subsequent relaxation of the lower esophageal sphincter, as well as increased pressure stress and anatomic disruption of the gastroesophageal junction. The anatomic disruption of the gastroesophageal junction may result in the formation of a hiatal hernia.

In our study we found that the degree of obesity as measured BMI increased the degree of GERD increased which agreed with longitudinal study by **Corley *et al., meta- analysis* (9),** who have addressed several risk factors for GERD, and indeed obesity is indicated as a potential risk factor. Interestingly, obesity has risen to epidemic levels in several regions

There was also some degree of a dose dependent relationship between BMI and these GERD related disorders and, moreover, a recent large cohort focusing on adult females reported a possible dose-response increase in the risk of GERD with a higher BMI even if within the normal range **(10).**

In agreement with this finding, in a retrospective case control study assessing BMI in relation to esophagitis and HH, it was found that obesity is strongly associated with the combined occurrence of esophagitis and HH **(11).**

A recent study has shown that the abdominal diameter measured as the waist circumference is a risk factor for GERD independently of BMI, while the association between BMI and GERD disappeared after adjustment of the abdominal diameter **(12).**

In a recent study, a large amount of visceral abdominal fat in respect to subcutaneous fat was found to be associated with a significant increase in the risk of GERD **(13).**

CONCLUSION

- Obesity appears to be involved not only in the development of GERD symptoms but, also in the occurrence of GERD complication such as erosive esophagitis, Barrett's esophagus and esophageal adenocarcinoma.
- Despite considerable evidence confirming the important role of increased esophagogastric pressure gradient, and production of inflammatory mediators by abdominal adipose tissue in the pathogenesis of GERD, the interplay between obesity and GERD is still not clear.
- Leptin one of the most important adipose derived hormones has a positive correlation with BMI and degree of GERD.

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