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SERUM LEPTIN, ADIPONECTIN CONCENTRATION AND CENTRAL ADIPOSITY PARAMETERS IN EGYPTIAN PATIENT WITH BARRETT'S ESOPHAGUS AND GASTROESOPHAGEALREFLUXDISEASE

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ABSTRACT

Persons diagnosed with Barrett's esophagus (BE) are at increased risk of developing esophageal adenocarcinoma (EA). Obesity is a major risk factor for both BE and EA. The purpose of this study was to determine the extent to which the adipokines leptin and adiponectin, both of which are deregulated in obese states, mediate the obesity-BE relationship as regard waist circumference is parameter of central adiposity. In this cross sectional study based in Egypt, 49 male and 41 female compared with 18 male and 12 female as controls from the general population. Relationships between leptin and adiponectin, obesity, and BE were examined and showed that serum leptin have shown positive associations with BE that may be involved in the pathology and metaplasia after long standing GERD among Egyptian people. The study showed that there is positive relationship between serum leptin level and degree of the disease and the highest level seen in group (B) which is Barret;s group proving that leptin has positive relationship with WC and Barret's. occurance Receiver operating characteristics (ROC) curve was define the best cut off value of serum leptin between GERD and Barret's groups which was > 40 ng/ml, area under the curve = 1, with sensitivity of 100%, specificity of .% 93.3%, positive predictive value of 93.7% and negative predictive value of 100%. In the current study we found negative relationship between fasting serum adiponectin and degree of disease in the 4 groups. In the current study we found negative relationship between fasting serum adiponectin and degree of disease in the 4 groups denoting that the advanced disease the lower serum adiponectin., respectively. Our study results are consistent with the notion that circulating leptin partially mediate the obesity-BE relationship in, Egyptian. Leptin and adiponectin's role in the progression from GERD to BE and on to EA should be further studied.

KEYWORDS: Barret's Esohagus (BE), Leptin, Adiponectin, Gastro- esophageal reflux (diseaseGERD, waist circumference) WC.

INTRODUCTION

Gastro- esophageal reflux disease is condition condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications mild symptoms occurring 2 or more days a week, or moderate/severe symptoms occurring more than 1 day a week.[1] Barrett's esophagus (BE) is a premalignant condition in which the normal squamous lining of the esophagus is replaced by columnar epithelium containing intestinal metaplasia (IM), induced by recurrent mucosal injury related to gastroe- sophageal reflux disease.[2] or; metaplasia that replaces the stratified squamous epithelium of the distal esophagus and has a predisposition to develop adenocarcinoma Barrett's esophagus (BE) is the only known precursor lesion of esophageal adenocarcinoma (EAC). Endoscopically, BE appears as an area of salmon-colored mucosa in the distal esophagus.[3] Obesity in particular is emerging as a strong modifiable behavioral risk factor for BE. Six of eight epidemiologic studies published to date examining the relationship have shown a significant association between obesity and BE.[4,11] in a study designed to examine mechanisms by which obesity acts to increase BE risk, Ogunwobi and colleagues[12] established that leptin, an adipokine whose expression and secretion are upregulated in obese states[13,18], was implicated in BE pathophysiology. Recent reports suggests that leptin synegizes with acid to inhibit apoptosis promoting cellular proliferation in Barrett's –derived EA in part through activation of phosphatidylinositol 3 –kinase (P13K)/Serine/Thionine Akt[19,20] that the short form of leptin receptor is present in Barrett's epithelium[21] and that increased (serum leptin is associated with BE risk especially in men.[22]

MATERIALS AND METHODS
Patients and study design
Cross sectional study was done in Cairo in Al Azhar university(Egypt) hospitals on 90 patients and 30 healthy persons as control aging between 18 years and 55 years and their waist of circumference above 88 in females and 102 in males with history of GERD symptoms long time After informing patients and consents were taken and full history and full clinical examinations. Upper GIT endoscpy was done for each patient with multiple biopsies were taken to those suspected Barrett's esophagus for histopathology and in the same time blood samples for estimation of fasting serum Leptin and adiponectin and analysis of serum by DRG Leptin and adiponectin are ELISA kits solid phase Enzyme –linked immunosorbant assay based on sandwich principles ,according to endoscopy results patients classified into 4 groups (A):GERD –(B):Barrett's –(C):NERD Non esophageal reflux disease – (D):Normal healthy control.

Statistical analysis
Statistical analysis was performed using Microsoft Excel (Windows) version 10 Data were analyzed using Statistical Program for Social Science (SPSS) version 15.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. using the following tests **Chi-Square (X^2):** used for comparing between non-parametric data. **A one-way analysis of variance (ANOVA):** when comparing between more than two means. **Post Hoc test (Least significant difference LSD):** was used for multiple comparisons between different variables. **Pearson's correlation coefficient (r):** test was used for correlating data. **Probability (P-value)** P-value <0.05 was considered significant-. P-value <0.001 was considered as highly significant. P-value >0.05 was considered insignificant. Comparisons were elicited between 4 groups as regrd age, sex, cholesterol, Triglycerides fasting serum Leptin and Adiponectin, WC, Liver span in mid clavicular line(MCL).

RESULTS
Table (1): Comparison between groups as regard serum leptin.

| Groups Variable	Group A N = (30)		Group B N = (30)		Group C N = (30)		Group D N = (30)		ANOVA	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	F	p-value
Leptin (ng/ml)	30.7	5.8	56.3	7.3	14.5	1.9	5.5	2.04	618.1	< 0.001*

*: P-value < 0.001 is considered highly significant. This table shows highly statistical significant difference **(p-value < 0.001)** between all groups as regard serum leptin.

**Table (2): Comparison between groups as regard serum adiponectin.**

Groups Variable	Group A N = (30)		Group B N = (30)		Group C N = (30)		Group D N = (30)		ANOVA	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD	F	p-val ue
Adiponect in (ng/ml)	7.2	0.7	4.4	0.3	19.9	4.9	23.5	7.7	123.6	< 0.001**

**: P-value < 0.001 is considered highly significant.

This table shows highly statistical significant difference **(p-value < 0.001)** between all groups as regard serum adiponectin.
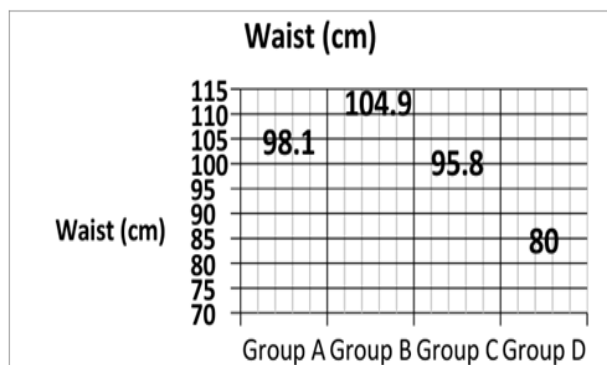
Figure (1): Comparison between groups as regard waist circumference.
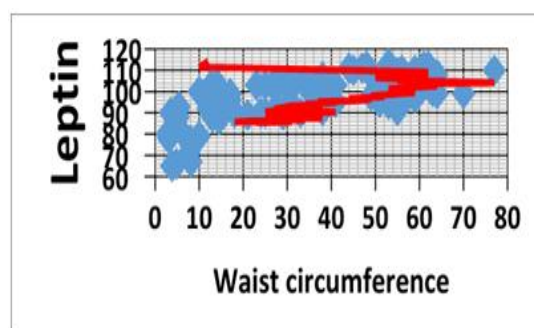
Figure (2): Positive correlation between serum leptin and waist circumference.
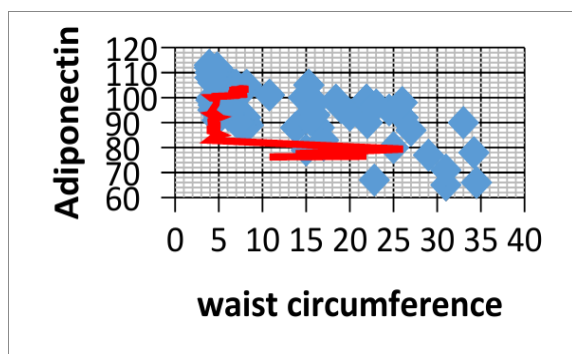
Figure (3): Negative correlation between serum adiponectin vs waist circumference.

Table (3): Demographic data of all studied patients.

	Group A Mean ±SD		Group B Mean ±SD		Group C Mean ±SD		Group D Mean ±SD	
Age (years)	42.5	10.3	40.7	11.5	41.7	13.3	40.6	10.9
Cholesterol (mg/dl)	242.3	39.5	295.6	27.7	231	26.9	161.6	16.4
LDL (mg/dl)	163.9	15	185.5	7.9	114	10	81.6	10.4
HDL (mg/dl)	29.9	5.5	30.3	5.4	21.1	3.8	57.1	3.08
TG (mg/dl)	253.7	31.3	274.1	44.8	125	15.3	136.5	9.1
Hb (g/dl)	11.1	1.5	11.2	1.6	10.8	1.7	11.4	1.7
WBCs (x10³/cmm)	4.7	1.1	4.7	1.3	4.6	0.7	4.6	0.7
Platelets (x10³/cmm)	239.7	49.6	229.2	60	232.4	34.7	230.9	72.1
Urea (mg/dl)	30.2	6.9	29.4	6.2	23.6	5.1	24	6.7
Creat. (mg/dl)	0.8	0.1	0.9	0.1	0.9	0.1	0.9	0.1
FBG (mg/dl)	94.2	10.9	93.4	9.1	89.6	11	88.6	10.2
PPG (mg/dl)	137.1	7.3	138.7	6.1	143.4	7.1	141	7.06
SGOT (U/L)	57	11.1	67.2	17.6	29.7	5.9	31	7.1
SGPT (U/L)	69.2	15.4	57.7	19.9	29.2	6.2	24.4	6.2
ALB (g/dl)	4.4	0.4	4.2	0.4	4.2	0.3	4.2	0.4
Liver span (cm)	16.6	0.6	17.4	0.8	16.8	0.7	15.1	0.3
Leptin (ng/ml)	30.7	5.8	56.3	7.3	14.5	1.9	5.5	2.04
Adiponectin (ng/ml)	7.2	0.7	4.4	0.3	19.9	4.9	23.5	7.7
Waist (cm)	98.1	6.3	104.9	6.4	95.8	4.9	80	9.4

Table (4): Diagnostic performance of serum leptin in discrimination of group B (Barrett patients) and group A (GERD patients).

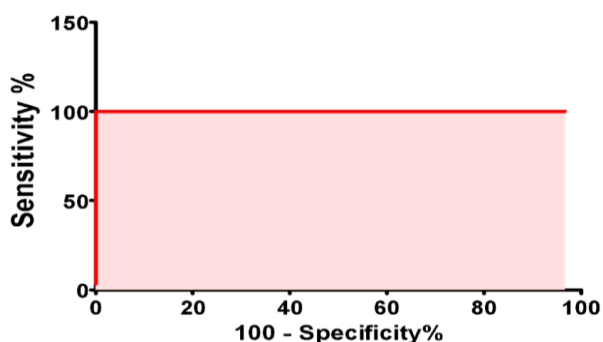| Cut off	AUC	Sensitivity	Specificity	PPV	NPV
> 40	1	100%	93.3%	93.7	100%

Figure (4): Receiver operating characteristics (ROC) curve was define the best cut off value of serum leptin which was > 40 ng/ml, area under the curve = 1, with sensitivity of 100%, specificity of 93.3%, positive predictive value of 93.7% and negative predictive value of .% 100.
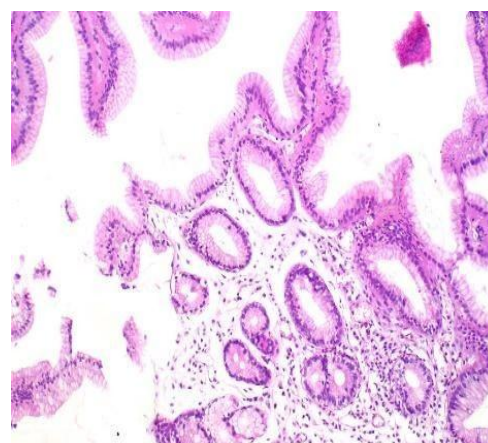

Figure (5): Barrett's esophagus with intestinal metaplasia and goblet cells (H&E) X 100.

DISCUSSION

Waist circumference is important simple parameter of central adiposity andc has important value for prediction of obesity related morbidity., WCis directly propotional to level of Leptin. Waist circumference is inversely proportional to level of adiponectin. Leptin is an important hormone produced by adipocytes and its circulating levels are proportional to total amount of fat mass. Obese individuals have markedly elevated levels of circulating leptin and they exhibit leptin resistance. At the molecular level, leptin is pro-angiogenic, proinflammatory and mitogenic. Study results on serum leptin and tissue leptin have shown positive associations with BE that may be involved in the pathology and metaplasia after long standing GERD among Egyptian people Cutoff value of fasting serum leptin was noted predicting occurance of Barrett's esophagus in Egyptian obese people needing more studies to confirm this finding and making it as important recommendation in the future. The cutoff interpretation may be helpful in prediction of Barret's occurance in long standing Egyptian GERD paients who are centrally obese. Adiponectin is a protein encoded by the ADIPOQ gene and also secreted by the white adipose tissue. It circulates in three multimeric forms: low molecular weight (LMW), middle molecular weight (MMW) and high molecular weight (HMW) adiponectin. Adiponectin plays an important role in glucose flux and energy metabolism, upregulation of uncoupling proteins and protection from endothelial dysfunction In the current study the level of serum adiponectin showed the lowest level in the Barret's group which may reveal that adiponectin may not involved in the metaplasia formation in Barrett's after long standing GERD needing further studies on wide range population or multicenter study to explain its rule with GERD for transformation in Egyptian patients suffering from GERD symptoms and confirming that it may have a protective role against metaplasia after long time GERD.

CONCLUSION

Relationships between leptin and adiponectin, obesity and BE were examined and showed that occurance of Barret's s positive relation with Leptin while negative relation ship with Adiponectin.

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