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SERUM LEPTIN, ADIPONECTIN AND APELIN IN OVERWEIGHT FEMALE SAUDI STUDENTS

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ABSTRACT

Leptin (Lep), adiponectin (APN) and apelin (APLN) are the important adipocytokines and are considered as the markers in subjects with normal weight (NW), and overweight (OW) status and a variety of diseases. A total of 121 female students (age range: 18-20 years) of NW (n: 63; BMI (kg/m^2) range: 18-24.9) and OW (n: 58; BMI range: 25-29.9) were studied and compared in the present report. Comparison of the data showed highly significant increase in serum Lep (ng/mL), and APLN (ng/mL) for OW subjects and significant decrease in serum APN (µg/mL) for OW subjects. The BMI and serum Lep showed significant positive linear correlation in NW subjects (P: 0.04) and highly significant positive linear correlation for OW subjects (P: 0.0002). The plot of BMI and APN showed negative linear correlation with P-value as 0.02 for NW and negative linear correlation with P-value as <0.0001 for OW subjects. The BMI and APLN gave positive non-significant linear correlation with P-value as 0.07 for NW and negative significant linear correlation with P-value as 0.04 for OW subjects. The results for the plot of Lep against APN showed non-significant negative linear correlation with p-value of 0.348 for NW subjects, and highly significant negative linear correlation with p-value <0.0001 for OW subjects. The plot of Lep and APLN showed non-significant negative linear correlation with p-value of 0.109 for NW subjects, and highly significant negative linear correlation with p-value 0.001 for OW subjects. Plot of APN and APLN showed non-significant negative linear correlation with p-value of 0.530 for NW subjects, and non-significant negative linear correlation with p-value 0.179 for OW subjects. This report presents the potential impact of serum Lep, APN and APLN as markers in subjects with various levels of BMI.

Keywords: Serum leptin, adiponectin, apelin, normal weight and overweight, body mass index, female students

INTRODUCTION

Adipocytokines or adipokines secreted by adipose tissue are considered as the potential biomarkers in various diseases (Blüher and Mantzoros, 2015). Leptin (Lep), adiponectin (APN) and apelin (APLN) are the important adipocytokines (Waki *et al*., 2003). The Lep and its recombinant derivatives are used for the treatment of various diseases showing leptin deficiency e.g. lipodystrophy, congenital Lep deficiencies. Several prestigious prizes were awarded related to Lep-related research (NewsMedical, 2009; The Lasker Foundation, 2010; BBVA Foundation, 2012; (KFF – KFIP – Winners, 2013) including a famous Saudi prize-King Faisal International Prize (KFF – KFIP – Winners, 2013). The Lep is a small helical protein (167 amino acids) of 16 kDa produced in white and brown adipose tissue and other body organs (Margetic *et al*., 2002). It is found in free and bound (with proteins) forms (Sinha *et al*., 1996). It regulates fat stores and a variety of other functions (Maffei *et al*., 1995), and controls the intake of food and expenditure of energy (Bełtowski, 2006). Role of Lep in various disorders has been investigated/ reviewed (Hussain, 1991; Redon, 2001; Aneja *et al*., 2004; Hussain *et al*., 2007; Sattar *et al*., 2009; Sohail *et al*., 2013; Sohail and Hussain, 2013; Taylor *et al*., 2014; Ayeser *et al*., 2016; Serafi *et al*., 2016). Recent reports reveal that serum Lep associates significantly with BMI (Ayina *et al*., 2016; Singh *et al*., 2020; Zulfania *et al*., 2020; Kosmuratova *et al*., 2021; Cheng *et al*., 2022; Alaamri *et al*., 2023).

The APN, a collagen like protein well expressing in adipose tissue, was invented in 1995 (Díez and Iglesias, 2010). It is secreted from adipose tissue and placenta during pregnancy as well (Chen *et al*., 2006)

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for controlling the glucose and fatty acids (Díez and Iglesias, 2003). It is a 244 amino acid polypeptide structure and has characteristic features in several cell types (Scherer *et al*., 1995; Matsuzawa *et al*., 2004; Lara-Castro *et al*., 2007). Tissue specificities are found in APN receptor 1 – ADIPOR1 and APN receptor 2 – ADIPOR2 and another receptor of cadherin family (T-cadherin - CDH13) (Yamauchi *et al*., 2003; Hug *et al*., 2004).

The APLN, a peptide encoded by the *APLN* gene in human is secreted from cardiovascular, CNS, urinary, digestive, pulmonary and other tissues, and is involved in controlling various physiological/ pathophysiological processes/functions e.g., blood pressure (BP), angiogenesis, cardiovascular functions/ dysfunctions, and drinking behavior.

However, the precise role of Lep, APN and APLN is controversial, e.g. it was viewed that the variations found in the concentration of Lep related with BMI might be due to race, age, specific type of obesity and other reasons (Redon, 2001). Hence, it was planned to determine and compare these adipocytokines in NW and OW subjects.

MATERIALS AND METHODS

A total of 121 female students of NW (n: 63) and OW (n: 58) were studied and compared in the present report. Age range of the subjects in NW and OW was 18-20 years. Range of the BMI (kg/m^2) in NW and OW subjects were 18-24.9 and 25-29.9 (check), respectively. The mean ± SD of the BMI, and serum levels of Lep (ng/mL), APN (µg/mL) and APLN (ng/mL) were determined and compared between both groups.

The consent of subjects for taking part in the present study was obtained. The subjects not agreed to be included were not taken in the current study. The serum adipokines were measured employing enzyme-linked immunosorbent assay (ELISA) kits. Inter-assay and intra-assay changes were in the standard levels.

The data was entered and analyzed employing SPSS software version 24. General concepts of statistical analysis were used following Zahir *et al*. (2014). The mean ± SD and student's t-test/ P-value were obtained for comparing the variables in NW and OW subjects. For analyzing the association/ linear correlation, plots of the variables were obtained that gave the positive or negative sign of slope, coefficient of determination (R^2) and P-values to find the significance level.

RESULTS

Serum leptin, adiponectin and apelin in normal weight (NW) and overweight (OW) female Saudi students were determined. The body mass index (BMI) and serum Lep, APN and APLN are given in Table 1. Comparison of the data showed highly significant increase in serum Lep, and APLN for OW subjects and significant decrease in serum APN for OW subjects.

Table 1. Serum leptin, adiponectin and apelin in normal weight and overweight women.

Variables	Normal weight and overweight Women subjects (n: 121)		P-value
	NW (n:63)	OW (n:58)	
BMI (kg/m^2)	21.65 ± 2.04	27.65 ± 1.49	< 0.0001
Serum Lep (ng/mL)	8.28 ± 5.39	17.42 ± 7.58	< 0.0001
Serum APN (µg/mL)	7.55 ± 6.21	5.71 ± 2.54	0.0387
Serum APLN (ng/mL)	2.42 ± 1.38	3.82 ± 2.76	0.0005

n: number of subjects, BMI: body mass index, Lep: leptin, APN: adiponectin, APLN: apelin, NW: normal weight, OW: overweight, values are mean ± SD

The analysis of correlations for BMI and cytokines, and among cytokines is given in Table 2. The BMI and serum Lep showed significant positive linear correlation in NW subjects (P: 0.04) and highly significant positive linear correlation (P: 0.0002). The plot of BMI and APN showed negative linear correlation with P-value as 0.02 for NW and negative linear correlation with P-value as < 0.0001 for OW subjects. The BMI

and APLN gave positive non-significant linear correlation with P-value as 0.07 for NW and negative linear correlation with P-value as 0.04 for OW subjects.

Table 2. Correlation of BMI, serum leptin, adiponectin and apelin in normal weight and overweight women.

Parameters for Correlation	Coefficient of determination (R^2) and p-values for normal weight and overweight women			
	NW		OW	
	R^2	P-value	R^2	P-value
BMI & Lep	0.066 (+ve)	0.043	0.224 (+ve)	0.0002
BMI & APN	0.085 (-ve)	0.020	0.242 (-ve)	< 0.0001
BMI & APLN	0.053 (+ve)	0.070	0.071 (+ve)	0.044
Lep & APN	0.014 (-ve)	0.348	0.342 (-ve)	< 0.0001
Lep & APLN	0.042 (+ve)	0.109	0.167 (+ve)	0.001
APN & APLN	0.007 (+ve)	0.530	0.032 (-ve)	0.179

BMI: body mass index, Lep: leptin, APN: adiponectin, APLN: apelin, NW: normal weight, OW: overweight

The results for the plot of Lep against APN showed non-significant negative linear correlation with p-value of 0.348 for NW subjects, and highly significant negative linear correlation with p-value < 0.0001 for OW subjects. The plot of Lep and APLN showed non-significant negative linear correlation with p-value of 0.109 for NW subjects, and highly significant negative linear correlation with p-value 0.001 for OW subjects. Plot of APN and APLN showed non-significant negative linear correlation with p-value of 0.530 for NW subjects, and non-significant negative linear correlation with p-value 0.179 for OW subjects.

DISCUSSION

Our results provide evidence for the previous reports that the serum levels of Lep and APN may serve as the potential biomarkers for investigating their impact on NW-BMI, OW-BMI and obese categories of BMI (Blüher and Mantzoros, 2015). It is generally suggested that Lep, APN and other adipokines are important biomarkers in various disorders (Blüher and Mantzoros, 2015). This is further verified that Lep concentration is proportional to the extent of adipose tissue, and Lep increases in subjects with obesity (Bełtowski, 2006). The impact of leptin in BMI changes was also found in other studies (Kazumi *et al*., 1999; Sattar *et al*., 2009; Kerimkulova *et al*., 2014; Caffo, *et al*., 2021; Alaamri *et al*., 2023).

The present investigation revealed the significant positive linear correlation of serum Lep with BMI. It is in agreement with other studies that indicate positive relationship of leptin plasma or serum levels with BMI (Kazumi *et al*., 1999; Hirose *et al*., 2001; Adami *et al*., 2002; Al-Sultan and Al-Elq, 2006; Antunes *et al*. 2009), and even independent significant correlation of BMI with leptin concentrations (Antunes *et al*. 2009; Nakamura *et al*., 2009; Mirrakhimov *et al*., 2014). Serum Lep correlated significantly BMI (Ayina *et al*., 2016; Singh *et al*., 2020; Zulfania *et al*., 2020; Kosmuratova *et al*., 2021; Cheng *et al*., 2022; Alaamri *et al*., 2023).

The results for serum APN in the present report can be interpreted by a previous finding that APN concentration are decreased in obese people that is controlled by posttranslational cellular mechanisms (Liu and Liu, 2012). This indicates that low levels of APN might be considered as a marker for risk factors in various disorders (Ding *et al*., 2012).

A major difference was found in the activity of Lep and APN that the former is produced in direct proportion to the fat mass, and later is produced inversely to fat mass (Nishida *et al*., 2007; Ding *et al*., 2012). The present report also provides the similar results.

The present study provides information that serum APLN increases significantly in OW compared to NW female subjects, though there are several reports that show a little or no correlation of apelin with the increase in body weight (Castan-Laurell *et al*., 2011; Reinehr *et al*., 2011; Sentinelli *et al*., 2020; Bellissimo *et al*., 2021). On the other hand, there are several investigations that provide evidence of the increased serum concentration APLN at higher BMI levels (Boucher *et al*., 2005; García-Díaz *et al*., 2007; Higuchi *et al*., 2007; Castan-Laurell *et al*., 2008; Frier *et al*., 2009; Yue *et al*., 2011; Sheibani *et al*., 2012; Ba *et al*., 2014; Kiskac *et al*., 2014; Bertrand *et al*., 2015; El Wakeel *et al*., 2018).

The present report presents the potential impact of serum Lep, APN and APLN as markers in subjects with various levels of BMI. Future research would clarify further the role of these adipokines in body weight related disorders.

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