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Research Article

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High Levels of Inflammatory Adipokines and C-reactive protein, and Minimal Changes in Immune Cells in Overweight and Obese Saudi Female University Students

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ABSTRACT

Increased body weight affects the whole body including the immune response, and leads to a state of non-specific inflammation, which leads to increased incidence of inflammatory diseases. The aim of this study was to determine the relationship between adiposity and the hematological profile, and serum concentrations of glucose, C-reactive protein (CRP), some pro-inflammatory [leptin, resistin, interlukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α)] and anti-inflammatory (adiponectin) adipokines in 112 healthy Saudi female university students. Adiposity was determined using the body mass index (BMI), waist-to-hip ratio (WHR), and waist circumference (WC). The results showed that the mean total white blood cell counts were significantly higher for the high risk WHR group, and the mean platelet and red blood cell counts were higher for the obese/morbidly obese BMI group compared to the respective controls. The white blood cell types and hemoglobin did not show any significant differences. Mean serum CRP, leptin, resistin, and IL-6 concentrations were significantly higher for the obese/morbidly obese BMI and high risk WC subjects compared to the healthy weight subjects. The only significant difference for the WHR groups was a significantly higher mean resistin level for the moderate risk group compared to the control. Mean glucose, TNF-α and adiponectin concentrations were not significantly different among the groups. Thus, it may be concluded that the immune system cells and the hematological profile in subjects with high adiposity were minimally affected compared to the healthy weight subjects. They also had higher platelet counts, and CRP, leptin, resistin, and IL-6 concentrations, which are inflammatory effectors/markers, thus confirming that obese subjects had heightened inflammation and a higher risk for inflammatory diseases.

Key words: *Immune System Cells, Adipokines, Inflammation, Obesity, C-Reactive Protein, Leptin, Resistin, Interlukin-6 (IL-6), And Tumor Necrosis Factor Alpha (TNF-A).*

INTRODUCTION

The prevalence of overweight and obesity has been increasing in developed countries and in most developing countries for the last few decades. According to the latest World Health Organization statistics [1], of the worldwide adult population in 2016, 39% were overweight and around 13% were obese, with females outnumbering males. In addition, the prevalence of obesity worldwide has nearly tripled between the years 1975 and 2016. Overweight and obesity have been increasing in Saudi Arabia for the last two to three decades with rates that continue to increase, especially in females, making Saudi Arabia one of the top countries for the prevalence of obesity and obesity-related diseases [2].

Increased body fat content affects many functions and systems of the body leading to poor health in general, increased mortality, increased infection rates, and enhanced risk for many diseases, such as hypertension, dyslipidemia, cardiovascular diseases, insulin resistance, type 2 diabetes, and some types of cancers. Chronic low-grade inflammation has been linked to increased weight and obesity and to many of the so-called obesity-related diseases [3], also called obesity-related inflammatory diseases, such as type 2 diabetes, atherosclerosis, fatty liver diseases, osteoarthritis, rheumatoid arthritis, cancer, cardiovascular diseases, insulin resistance, and

even some mental illnesses [4]. Thus, it may be that the detrimental effects of increased weight and obesity are mediated partially or mainly through inflammation.

In addition to inflammation being linked to increased weight and obesity, it is an important part of the immune response. The immune system is known to be very sensitive to changes in the body and general health, and is one of the systems of the body are affected by increased body weight [5, 6]. Many unhealthy conditions in the body, including obesity, smoking, and stress, may activate or deactivate the immune response and lead to chronic inflammation [5-8]. Overweight and obesity have been found to affect the immune system by influencing some immune functions and immune cells and molecules, although there is no consensus on the type and extent of these effects [5-7].

The major cells in adipose tissue are the adipocytes, which may also be found anywhere in the body. Adipocytes are important in many functions, including energy homeostasis, inflammation, and insulin sensitivity [9]. In addition, they secrete cytokines, termed adipokines, which are hormone-like molecules with specific functions that affect other cells. Cytokines have many functions including the regulation of glucose and lipid metabolism, energy balance, and regulation and mediation of some functions of the immune system [9, 10]. Of special interest is their effect on inflammation with some cytokines being pro-inflammatory, such as leptin, resistin, interlukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α); or anti-inflammatory, such as adiponectin. Excess lipids or fats in the body are stored in adipocytes leading to increased size and/or number of these cells and increased weight. This leads to the increased production and subsequently higher concentrations of cytokines, resulting in a state of chronic active inflammation along with an increased susceptibility to inflammatory diseases that are commonly associated with overweight and obesity [11].

The C-reactive protein (CRP), which is secreted by adipose tissue, hepatocytes and other cell types [12], is an acute phase protein that is involved in the immune response and it increases in cases of tissue injury, obesity, cardiovascular diseases, stroke, infection, and inflammation in the body [13]. Therefore, it is used as a marker for inflammation and obesity-linked inflammatory diseases, and it has been shown [14, 15] to be pro-inflammatory by inducing the production of cytokines that may be inflammatory.

The body mass index (BMI) is one of the most commonly used and widely accepted methods to estimate body fat content to determine overweight and obesity without the use of specialized equipment. Other measures of body fat, although less popular and newer, include the waist-to-hip ratio (WHR), and waist circumference (WC). Only the WHR determines the body shape of the subject, with higher WHRs and WCs indicating the presence of more fat around the waist (abdominal or central obesity), rather than on the hips that lead to the apple or android shape. This central fat distribution is considered unhealthy and carries a high risk for inflammation and many diseases [5-7, 16]. On the other hand, lower WHRs and WCs are more favorable healthwise, and indicate a higher proportion of lower body obesity (wider hips circumference) or what is termed as the pear or gynoid shape which carries less risk for overweight and obesity-related diseases, mortality, and metabolic problems [5-7, 16-18].

Previous studies [3, 5-8, 11, 16, 17] have shown that increased weight and obesity are linked to inflammation and an altered immune system, although not all studies concur and studies are lacking in some populations. There have not been many studies done in Saudi Arabia that compared the levels of adipokines and cells of the immune system in healthy overweight and obese subjects with lean non-obese ones. Therefore, this study aimed to determine the effects of overweight and obesity, measured using the BMI, WHR, and WC, on the immune system, inflammation, and general health in a cohort of healthy Saudi female university students, and to investigate the status of adipokines and non-specific inflammation in Saudi females. To achieve this, the differential complete blood counts (CBC); the concentrations of some pro-inflammatory (leptin, resistin, IL-6, and TNF-α) and anti-inflammatory (adiponectin) adipokines important in obesity, the immune response, and insulin resistance and regulation; and the concentrations of the inflammatory marker C-reactive protein (CRP) and glucose were determined in blood samples.

MATERIALS AND METHODS

Subjects and inclusion criteria

A total of 112 healthy Saudi female students at King Abdulaziz University, Jeddah, Saudi Arabia, ages 18-28 years, were used in this study. The subjects filled a consent form and a general questionnaire for health status assessment. None of the subjects had diabetes, heart disease, blood diseases, or any type of allergy. In addition,

none were taking any medications, including birth control and hormones. Finally, any subject with a glucose level not within the normal range (70-100 mg/dl) and a white blood count (WBC) more than 20 x $10^{-3}/\mu L$ were excluded from the study.

Blood Collection

Fasting (a minimum of 8 hours) blood samples were collected from all the subjects. Blood samples were collected in ethylene diamine tetra-acetic acid (EDTA) tubes, and used within three hours of collection, for the determination of the differential CBC. Blood samples were also collected in plain tubes for the determination of all the remaining parameters. These blood samples were allowed to stand at room temperature until a clot was formed, after which, the tubes were centrifuged at 3,000 rpm for 10 minutes, and the serum was stored at -20^{o}C until use.

Anthropometric measurements

Anthropometric measurements (weight, height, and waist and hip circumferences) were obtained for all the subjects on the same day of blood collection. The subjects were weighed using a regular household scale; and the height, waist (at the naval) and hips (at the fullest point) circumferences were measured using a measuring tape.

Categorizations of subjects

The subjects were categorized using three different measures of body fat, namely the BMI, WHR, and WC. The BMI was used to divide the subjects into four groups, which were underweight (BMI < 18.5 kg/m^2), normal (BMI = 18.5 to 24.9), overweight (BMI = 25 to 29.9), and obese/morbidly obese (BMI ≥ 30). The WHR was used to assign the subjects into one of three risk groups. The groups were low risk (WHR ≤ 0.80), moderate risk (WHR = 0.81-0.85), and high risk (WHR > 0.85). Finally, the WC of subjects was used to distribute the subjects into three risk groups according to the accepted reference ranges for each group. The low risk group was the subjects with a WC lower than 32.5 inches, a WC between 32.5 and 35 inches was considered moderate risk, while the high risk group were subjects with a WC higher than 35 inches.

Determination of blood glucose levels

Glucose levels were determined in blood samples of the subjects using a Bayer Contour blood glucose meter (Bayer, New York, U.S.A) and single use Contour strips (Bayer AG, Basel, Switzerland).

Differential complete blood counts

Total WBC counts and the differential CBC were done using a CELL-DYN Sapphire Hematology System (Abbott Company, Illinois, U.S.A.) at King Abdulaziz Medical City-Western Region, Jeddah, Saudi Arabia.

Determination of serum C-reactive protein concentrations

The CardioPhase high sensitivity CRP reagent (Siemens Company, Marburg, Germany) was used for the quantitative determination of CRP in serum samples of the subjects by means of particle-enhanced immunonephelometry using the BN II/BN ProSpec system instrument (Siemens Company, Berlin, Germany) at King Abdulaziz University Hospital, Jeddah, Saudi Arabia .

Determination of serum leptin, adiponectin, resistin, IL-6, and TNF-α concentrations

The concentrations of serum leptin, adiponectin, resistin, IL-6, and TNF-α were determined for all samples using high sensitivity human ELISA kits specific for each adipokine (BioVendor–Laboratorni Medicina a. s. Company, Brno, Czech Republic). The kits were done according to the manufacturer's instructions and the final products were measured at wavelengths of 450 and 630 nm using an ELx808 Microplate Reader (BioTek, Bedfordshire, United Kingdom).

Statistical methods

The SPSS Statistics 20 statistical program was used to obtain the descriptive and analytical statistics. A P value lower or equal to 0.05 was considered significant, and a P value lower than 0.01 was considered highly significant. For the normally distributed parameters, the ANOVA one-way test was used to test for the presence of overall significant differences between the groups for each parameter. In the case of the presence of a significant difference, the Tukey or LSD (least significant difference) post hoc tests were used for determining the significant differences between the groups. For the parameters that were not normally distributed, the Kruskal-Wallis H test was used for determining the overall differences between the groups, and for the post hoc comparisons between the groups, the Mann-Whitney U test was used.

RESULTS

Subjects and categorizations

The 112 Saudi female university students had an age range of 18-28 years and, as previously reported [16], a mean age of 22.23 years (SD = ± 2.44). It was also previously found that the subjects' BMIs ranged from 13.51 to 45.17 Kg/m^2, the WHRs ranged from 0.61 to 1.53 cm, and the WC ranged from 19.68-70.86 inches [16].

Adiposity groups and the differential complete blood counts

Statistical analysis of the data (Table 1) showed no statistically significant differences between the BMI groups for the mean total and differential WBC counts and hemoglobin concentrations in the blood. On the other hand, the mean platelet and red blood cell (RBC) counts for the BMI groups were significantly different. Compared to the mean counts for the respective normal (control) BMI groups (Table 2), the mean platelet and RBC counts for the obese/morbidly obese BMI group were significantly higher, while for both of the underweight and overweight BMI groups, there were no significant differences.

The mean total WBC counts for the WHR groups were significantly different (Table 1). The mean WBC count for the high risk group was highly significantly higher, while for the moderate risk group it was not significantly different compared to the mean count for the low risk (control) group (Table 3). The remaining components of the differential CBC did not show any significant differences among the WHR groups. Finally, the mean total and differential WBC counts, platelet counts, and RBC and hemoglobin concentrations were not significantly different among the WC groups (Table 1).

Table 1: Descriptive statistics and test of significance for the differential complete blood count for the BMI, WHR and WBC groups.

Parameter	BMI				WHR				WC			
	BMI group	Mean	± SD	P value	Risk group	Mean	± SD	P value	Risk group	Mean	± SD	P value
WBC[1,1,1] (10^3cell/µ)	Underweight	6.950	1.798	0.262^{NS}	Low	7.128	1.960	0.021^{S}	Low	6.921	1.856	0.062^{NS}
	Normal	7.025	1.990		Moderate	6.988	1.536		Moderate	7.317	2.168	
	Overweight	7.331	2.119		High	8.921	3.176		High	7.994	2.372	
	Obese/Morbidly obese	8.025	2.461									
Basophil[2,2,2] (10^3cell/µ)	Underweight	0.081	0.060	0.282^{NS}	Low	0.068	0.047	0.920^{NS}	Low	0.068	0.049	0.326^{NS}
	Normal	0.058	0.038		Moderate	0.068	0.052		Moderate	0.051	0.051	
	Overweight	0.068	0.042		High	0.059	0.052		High	0.068	0.034	
	Obese/Morbidly obese	0.065	0.040									
Eosinophil[2,2,1] (10^3cell/µ)	Underweight	0.193	0.122	0.686^{NS}	Low	0.201	0.143	0.569^{NS}	Low	0.191	0.147	0.180^{NS}
	Normal	0.204	0.204		Moderate	0.173	0.126		Moderate	0.165	0.121	
	Overweight	0.179	0.136		High	0.091	0.303		High	0.245	0.244	
	Obese/Morbidly obese	0.238	0.100									
Monocyte[1,1,1] (10^3cell/µ)	Underweight	0.561	0.150	0.667^{NS}	Low	0.551	0.147	0.524^{NS}	Low	0.535	0.147	0.363^{NS}
	Normal	0.525	0.166		Moderate	0.532	0.181		Moderate	0.554	0.121	
	Overweight	0.565	0.150		High	0.598	0.173		High	0.584	0.187	
	Obese/Morbidly obese	0.568	0.158									
Neutrophil[2,2,2] (10^3cell/µ)	Underweight	3.332	1.483	0.465^{NS}	Low	3.440	1.462	0.301^{NS}	Low	3.307	1.421	0.227^{NS}
	Normal	3.384	1.364		Moderate	3.432	1.314		Moderate	3.734	1.551	
	Overweight	3.571	1.571		High	4.618	2.285		High	3.967	1.770	
	Obese/Morbidly obese	4.086	1.886									
ocyte[2,2,2] (10^3cell	Underweight	2.807	0.639	0.707^{NS}	Low	2.875	0.756	0.310^{NS}	Low	2.827	0.738	0.288^{NS}
	Normal	2.856	0.844		Moderate	2.778	0.641		Moderate	2.814	0.764	
	Overweight	2.934	0.750		High	3.371	1.034		High	3.116	0.842	

	Obese/Morbidly obese	3.068	0.856									
Platelets[1,2,1] (10^3cell/µ)	Underweight	277.77	36.93		Low	296.10	76.99		Low	287.17	72.45	
	Normal	286.05	83.25		Moderate	299.62	68.12	0.458^{NS}	Moderate	295.65	57.99	0.062^{NS}
	Overweight	289.48	64.78	0.014^{S}	High	322.45	94.03		High	326.52	89.27	
	Obese/Morbidly obese	338.86	79.36									
RBC[1,1,1] ($x10^6$/µL)	Underweight	4.759	0.401		Low	4.693	0.368		Low	4.659	0.380	
	Normal	4.627	0.408	0.008^{HS}	Moderate	4.677	0.391	0.972^{NS}	Moderate	4.606	0.377	0.122^{NS}
	Overweight	4.554	0.272		High	4.709	0.435		High	4.805	0.351	
	Obese	4.887	0.314									
HGB[2,2,2] (g/dL)	Underweight	13.269	1.150		Low	13.024	1.021		Low	13.005	1.079	
	Normal	12.803	1.096		Moderate	12.749	2.724	0.618^{NS}	Moderate	12.771	0.922	0.535^{NS}
	Overweight	12.863	0.670	0.131^{NS}	High	13.009	0.890		High	13.011	1.081	
	Obese/Morbidly obese	13.033	1.216									

Superscripts on parameters indicate the test used for the significance x_1,x_2,x_3: x_1 test used for the BMI, x_2 test used for the WHR, x_3 test used for the WC

[1]The ANOVA one way test was used for the significance test

[2]The Kruskal-Wallis test was used for the significance test

HS: Highly significant (P < 0.01), S: significant (P ≤ 0.05), NS: Not significant (P > 0.05)

Number of subjects = 112

Table 2: Multiple comparisons between the normal BMI and other BMI groups for the significantly different parameters of Tables 1 and 2.

Parameter	Test	BMI Group	Mean difference (Normal BMI - BMI group)	± SE	P value
Platelets	LSD	Underweight	8.285	17.978	0.646^{NS}
(10^3cell/µ)		Overweight	-3.427	17.786	0.848^{NS}
		Obese/Morbidly obese	-52.809	18.893	0.006^{HS}
RBC	Tukey	Underweight	-0.132	0.920	0.484^{NS}
($x10^6$/µL)		Overweight	0.073	0.091	0.854^{NS}
		Obese/Morbidly obese	-0.260	0.097	0.041^{S}
CRP	Tukey	Underweight	0.567	0.417	0.910^{NS}
(mg/L)		Overweight	-0.402	0.520	0.694^{NS}
		Obese/Morbidly obese	-4.353	0.454	0.000^{HS}
Leptin	Tukey	Underweight	28.135	5.365	0.000^{HS}
(ng/ml)		Overweight	-24.499	5.306	0.000^{HS}
		Obese/Morbidly obese	-38.142	5.644	0.000^{HS}
Resistin	Mann–Whitney	Underweight	-0.112	0.233	0.519^{NS}
(ng/ml)		Overweight	-0.549	0.233	0.018^{S}
		Obese/Morbidly obese	-0.545	0.242	0.030^{S}
IL-6	Tukey	Underweight	-0.007	0.093	1.000^{NS}
(ng/ml)		Overweight	-0.459	0.220	0.522^{NS}
		Obese/Morbidly obese	-1.470	0.504	0.000^{HS}

HS: highly significant (P < 0.01), S: significant (P ≤ 0.05), NS: not significant (P > 0.05)

LSD: least significant difference test

Table 3: Multiple comparisons between the low risk WHR and the other WHR groups for the significantly different parameters of Tables 1 and 2.

Parameter	Test	WHR Group	Mean difference (Low risk WHR - WHR group)	± SE	P value
WBC	LSD	Moderate risk	-0.139	0.499	0.780^{NS}
($x10^6$/µL)		High risk	-1.793	0.654	0.007^{HS}
Resistin	LSD	Moderate risk	-0.446	0.223	0.049^{S}
(ng/ml)		High risk	-0.532	0.299	0.078^{NS}

HS: highly significant (P < 0.01), S: significant (P ≤ 0.05), NS: not significant (P > 0.05)

LSD: least significant difference test

Adiposity groups and CRP and glucose levels

The mean serum CRP concentrations were significantly different for the BMI and WC groups but not for the WHR groups (Table 4). Compared to the mean CRP concentration for the normal BMI group, the mean CRP concentration for the obese/morbidly obese BMI group was highly significantly higher, while for the underweight and overweight BMI groups, the mean concentrations were not significantly different (Table 2). For the WC risk groups, the high risk group was highly significantly higher, while the moderate risk group was not significantly different compared to the mean concentration of the low risk WC group (Table 5). The mean serum glucose levels were not significantly different between each of the BMI, WHR, and WC groups (Table 4).

Table 4: Descriptive statistics and test of significance for the CRP, glucose, and adipokines concentrations for the BMI, WHR and WBC groups.

Parameter	BMI				WHR				WC			
	BMI group	Mean	± SD	P value	Risk group	Mean	± SD	P value	Risk group	Mean	± SD	P value
CRP[1,2,1] (mg/L)	Underweight	2.230	0.000	0.000^{HS}	Low	2.747	1.898	0.091^{NS}	Low	2.558	1.936	0.000^{HS}
	Normal	2.797	2.534		Moderate	4.368	4.122		Moderate	3.429	1.804	
	Overweight	3.199	1.616		High	8.515	7.592		High	5.908	5.851	
	Obese/Morbidly obese	7.150	6.536									
Leptin[1,2,1] (ng/ml)	Underweight	26.674	18.714	0.000^{HS}	Low	57.333	32.856	0.082^{NS}	Low	46.457	28.609	0.000^{HS}
	Normal	54.809	24.146		Moderate	72.024	26.070		Moderate	76.035	22.894	
	Overweight	79.307	20.468		High	73.500	26.080		High	85.218	22.739	
	Obese/Morbidly obese	92.950	18.024									
Adiponectin[2,2,2] (ng/ml)	Underweight	39695.4	11572.6	0.109^{NS}	Low	39509.5	11319.4	0.246^{NS}	Low	39667.67	11759.8	0.245^{NS}
	Normal	41988.7	10764.2		Moderate	36560.1	9818.9		Moderate	38717.4	9469.2	
	Overweight	37128.7	10740.2		High	37361.1	13480.3		High	37036.5	11190.2	
	Obese/Morbidly obese	35771.7	11476.2									
Resistin[2,1,1] (ng/ml)	Underweight	2.671	0.950	0.049^{S}	Low	2.694	0.887	0.049^{S}	Low	2.621	0.820	0.029^{S}
	Normal	2.559	0.753		Moderate	3.140	0.853		Moderate	3.069	1.016	
	Overweight	3.109	0.871		High	3.226	0.978		High	3.100	0.933	
	Obese/Morbidly obese	3.104	0.998									
IL-6[1,1,1] (ng/ml)	Underweight	0.082	0.257	0.000^{HS}	Low	0.306	0.722	0.294^{NS}	Low	0.169	0.550	0.000^{HS}
	Normal	0.075	0.351		Moderate	0.963	1.983		Moderate	0.426	0.786	
	Overweight	0.535	0.900		High	1.043	1.617		High	1.171	1.867	
	Obese/Morbidly obese	1.545	2.054									
TNF-α[2,2,2] (ng/ml)	Underweight	1.538	3.720	0.345^{NS}	Low	1.674	4.024	0.096^{NS}	Low	2.025	4.457	0.945^{NS}
	Normal	1.816	3.457		Moderate	1.759	2.981		Moderate	3.314	10.195	
	Overweight	0.440	1.375		High	2.969	4.390		High	1.689	3.547	
	Obese/Morbidly obese	2.195	3.911									
se[2,2] (m	Underweight	75.65	9.273	0.993^{NS}	Low	76.69	10.54	0.753^{NS}	Low	76.81	10.89	0.777^{NS}
	Normal	76.7	12.106		Moderate	76.14	13.95		Moderate	76.88	10.95	

	Overweight	77.52	12.075		High	76.68	13.68		High	75.84	13.08	
	Obese/Morbidly obese	76.18	12.469									

Superscripts on parameters indicate the test used for the significance x1,x2,x3: x1 test used for the BMI, x2 test used for the WHR, x3 test used for the WC

[1]The ANOVA one way test was used for the significance test

[2]The Kruskal-Wallis test was used for the significance test

HS: highly significant ($P < 0.01$), S: significant ($P \leq 0.05$), NS: not significant ($P > 0.05$)

Number of subjects for parameters = 112 except for adiponectin = 86, resisitin = 106, IL-6 = 79 and TNF-α = 87

Table 5: Multiple comparisons between the low risk WC and other WC groups for the significantly different parameters of Table 2.

Parameter	Test	WC Group	Mean difference (Low risk WC - WC group)	± SE	P value
CRP	Tukey	Moderate risk	-0.871	0.500	0.630^{NS}
(mg/L)		High risk	-3.350	1.078	0.000^{HS}
Leptin	Tukey	Moderate risk	-29.578	7.179	0.000^{HS}
(ng/ml)		High risk	-38.761	5.758	0.000^{HS}
Resistin	Tukey	Moderate risk	-0.447	0.243	0.162^{NS}
(ng/ml)		High risk	-0.479	0.198	0.046^{S}
IL-6	Tukey	Moderate risk	-0.257	0.242	0.764^{NS}
(ng/ml)		High risk	-1.002	0.398	0.003^{HS}

HS: highly significant ($P < 0.01$), S: significant ($P \leq 0.05$), NS: not significant ($P > 0.05$)

Adiposity groups and concentrations of adipokines

The mean serum adiponectin and TNF-α concentrations were not significantly different between each of the BMI, WHR, and WC groups (Table 4). The mean leptin concentrations were highly significantly different for the BMI and WC groups, but not for the WHR groups (Table 4). The mean leptin concentrations for the overweight and obese/morbidly obese BMI groups (Tables 2) each were highly significantly higher than the mean concentration for the control BMI group. As for the underweight BMI group, the mean serum leptin concentration was highly significantly lower compared to the mean concentration for the normal BMI group. Finally, the mean leptin concentrations for the high and moderate risk WC groups were highly significantly higher compared to the mean leptin concentration for the low risk WC group (Table 5).

The mean serum resistin concentrations were significantly different for the BMI, WHR, and WC groups (Table 4). The mean resistin concentrations were significantly higher for the overweight and obese/morbidly obese BMI groups (Tables 2), moderate risk WHR group (Table 3), and high risk WC group (Table 5) comparing each group to its respective control group. The remaining groups, underweight BMI, high risk WHR, and moderate risk WC, were not significantly different compared to the respective control groups.

The mean serum IL-6 concentrations were significantly different for the BMI and WC groups, but not significantly different for the WHR groups (Table 4). The mean IL-6 concentrations were highly significantly higher for the obese/morbidly obese BMI group (Tables 2) and the high risk WC group (Table 5) compared to the respective control groups. On the other hand, the mean serum IL-6 concentrations for the underweight and overweight BMI groups, and moderate WC group showed no significant differences compared to the mean concentrations for the respective control groups.

DISCUSSION

This study investigated the effects of overweight and obesity on the immune system and non-specific inflammation in healthy Saudi female university students, using the BMI, WHR and WC as methods of weight assessment and categorization. To this end, the differential complete blood counts and the concentrations of glucose; CRP; and the adipokines leptin, adiponectin, resitin, IL-6, and TNF-α were determined. These adipokines and CRP are all associated with obesity, the immune response, insulin resistance and regulation, and inflammation [19, 20].

The mean total WBC counts were not significantly different between each of the BMI and WC groups (both $P > 0.05$). On the other hand, the mean total WBC counts for the WHR groups were significantly different ($P =$

0.021) with the mean count for the high risk group (Mean ± SD: 8.921 ± 3.176) being highly significantly higher (P = 0.007) than the mean count for the low risk (control) group (7.128 ± 1.960), while the mean count for the moderate risk group was not significantly different from the control. The mean basophils, eosinophils, monocytes, neutrophils, and lymphocytes counts were all not significantly different (all P > 0.05) between each of the BMI, WHR, and WC groups.

The findings of the current study are consistent with previous research studies done on Saudi female adolescents [6] and young female adults [5] that found higher WBC counts for the high risk WHR group. On the other hand, these studies found no significant differences between the BMI [5, 6], WHR [5, 6], and WC groups [6] for basophil, eosinophil, and monocyte cell counts; and for the WHR groups for lymphocyte counts [5], each compared to the respective healthy weight control groups. On the other hand, the current findings disagree with some previous studies [5, 6], where researchers found higher cell counts for neutrophils and lymphocytes for the obese and morbidly obese BMI, moderate and high risk WHR, and high risk WC groups; and for lymphocyte counts for the morbidly obese BMI group when each was compared to the respective controls. Also in contrast to the current results, the findings of other studies showed that WBC [21-24], lymphocyte [22, 24], monocyte [21, 24], neutrophil [21-24], and granulocyte [21] cell counts significantly increased with increasing BMI or increasing obesity. This increase in WBC and WBC types is expected since these cells play major roles in inflammation and since obesity has been considered by many researchers to be an inflammatory disease.

Mean platelet counts were highly significantly associated with obesity measured by BMI (P = 0.014) but not with WHR or WC (both P > 0.05). The mean platelet counts for both the underweight and overweight BMI groups were not significantly different (both P > 0.05) compared to the mean platelet count for the BMI control group. On the other hand, the mean platelet count for the obese/morbidly obese group (338.86 ± 79.36) was highly significantly higher (P = 0.006) compared to the mean count for the control (286.05 ± 83.25).

It was not surprising that the mean platelet count was higher for the obese/morbidly obese groups since platelets have important effector roles in both the immune response and inflammation [25, 26], both of which are affected by obesity. Additionally, the higher platelet count and its role in releasing inflammatory mediators further confirm its role in inflammation in obesity.

These results support the findings of many other studies [27-30] that showed that platelet counts were affected by body weight, obesity and WHR. Platelet counts were shown [5] to be significantly higher in young Saudi adult females with overweight, obese, and morbidly obese BMIs compared to the control, and this is in partial agreement with the current findings. In addition, the researchers found that platelet counts were not significantly different between the WHR groups, which is in agreement with the current results. This effect of obesity on platelet counts, in turn, affected immunological functions.

The results for the mean RBC counts were significantly different (P = 0.008) for the BMI groups, but not for the WHR and WC groups (P > 0.05). The mean RBC count for the obese/morbidly obese BMI group (4.887 ± 0.314) was significantly higher (P = 0.041) compared to the mean RBC count for the control group (4.627 ± 0.408). There were no significant differences (P > 0.05) between the mean RBC counts for both the underweight and overweight BMI groups compared with the count for the control. The results for the mean hemoglobin concentrations were not significantly different (all P > 0.05) between each of the BMI, WHR and WC groups.

The present results are in agreement with a study by Zhang et al. [31] that showed higher RBC counts in the obese, but it is contradictory with their findings of a higher hemoglobin level for the obese group compared to the non-obese group. Other researchers showed that obese subjects [32] and overweight adolescent girls [33] had lower hemoglobin concentrations compared to non-obese subjects. Another study [34] found no differences in hemoglobin concentrations for overweight and obese subjects compared to normal weight subjects.

All BMI, WHR, and WC groups had higher mean CRP concentrations, except for the underweight BMI group that had a lower concentration, although not all the concentrations were significantly different compared to the respective controls. The mean serum CRP concentrations for the groups were highly significantly related (both P = 0) to the BMI and WC groups, while they were not significantly related to the WHR groups (P > 0.05). The mean serum CRP levels were highly significantly higher (P = 0.036) for the obese/morbidly obese BMI group (7.150 ± 6.536) compared with the normal BMI group (2.797 ± 2.534), while the levels for the other BMI groups were not significantly different (P > 0.05) from the normal group. As for the WC groups, compared with the mean level for the low risk control group (2.558 ± 1.936), the mean serum CRP level for the high risk group

(5.908 ± 5.851) was highly significantly higher (P = 0), while there was no significant difference for the moderate WC group.

The findings of the current study were consistent with those of a previous study [7] that found highly significantly higher CRP levels in young females with overweight and obese BMI, and high risk WHR and WC compared to the healthy weight subjects. In addition, other researchers [12, 35-39] found that serum CRP concentrations were significantly higher for overweight and obese females and males with high BMI and WC compared to the normal weight subjects.

The results show that the mean serum leptin concentrations were highly significantly related to the BMI, and WC groups (both P = 0). For the BMI, the mean serum leptin levels were highly significantly higher (both P = 0) for both the overweight (79.307 ± 20.468) and obese/morbidly obese BMI groups (92.950 ± 18.024), and highly significantly lower (P = 0) for the underweight group (26.674 ± 18.714) compared with the mean level for the normal BMI group (54.809 ± 24.146). As for the WC groups, both the moderate and high risk WC groups had highly significantly higher (both P = 0) mean serum leptin levels (76.035 ± 22.894, and 85.218 ± 22.739, respectively) compared with the mean level for the control group (46.457 ± 28.609). As for the WHR groups, both the moderate and high risk groups had higher leptin levels, although not significantly higher, compared to the level for the control.

The current findings agree with a previous study by Mahassni and Sebaa [7] who also found highly significantly higher mean serum leptin concentrations for the overweight and obese BMI, and moderate and high risk WHR and WC groups compared to the respective controls. Several other studies also found significantly higher serum leptin levels in overweight and obese subjects [12, 38, 40, 41], and in subjects with high BMI, WHR, and WC [40-42] compared to healthy weight subjects.

Mean serum resistin concentrations were significantly related to the BMI, WHR and WC groups (P = 0.049, 0.049, and 0.029, respectively). Compared to the mean resistin serum concentration for the control BMI group (2.559 ± 0.753), both the overweight and obese/morbidly obese BMI groups had a significantly higher (P = 0.018 and 0.030, respectively) mean serum resistin level (3.109 ± 0.871, and 3.104 ± 0.998, respectively), while the mean concentration for the underweight group was none significantly higher. For the WHR groups, only the moderate risk group had a significantly different (higher) (P = 0.049) mean serum resistin concentration (3.140 ± 0.853) compared to the mean level for the control group (2.694 ± 0.887). Finally, the high risk WC group had a significantly higher (P = 0.046) mean serum resistin concentration (3.100 ± 0.933) while the moderate risk WC group was none significantly higher when both groups were compared to the mean resistin concentration for the control group (2.621 ± 0.820).

These results are in agreement with other studies [20, 43-45] that demonstrated that obese subjects had significantly higher serum resistin levels than none obese subjects. On the other hand, other studies [43, 46], in disagreement with the current findings, found unchanged resistin levels in the obese compared to non-obese subjects.

The mean serum IL-6 concentrations were higher for all BMI, WHR, and WC groups compared to the respective controls, although not all were significantly higher. The mean serum IL-6 concentrations were highly significantly different (P = 0 for both) between the BMI and WC groups each, but not significantly different between the WHR groups. The obese/morbidly obese BMI group had a significantly higher (P = 0.044) mean serum IL-6 concentration (1.545 ± 2.054) compared with the control group mean concentration (0.075 ± 0.351). On the other hand, the mean IL-6 concentrations for both the underweight and overweight BMI groups were not significantly different from the mean concentration for the control BMI group. The mean serum IL-6 concentration for the high risk WC group (1.171 ± 1.867) was highly significantly higher (P = 0.003), while for the moderate risk group it was not significantly different, comparing both with the mean concentration for the control (0.169 ± 0.550).

Previous research studies [37, 47-50] agreed with the current findings of significantly higher IL-6 levels in obese subjects and subjects with high BMI and WC compared to non-obese subjects. Other research studies [39, 51] found that serum IL-6 concentrations did not correlate significantly with the BMI and WC, thereby disagreeing with the current findings.

The results show that the mean serum adiponectin, TNF-α, and glucose concentrations were not significantly affected (all P > 0.05) by overweight and obesity measured by BMI, WHR and WC. It is worth nothing that the mean adiponectin concentrations were lower, although none significantly, for all BMI, WHR, and WC groups

compared to the respective controls. On the other hand, the mean TNF-α concentrations for the BMI, WHR, and WC groups, compared to the respective controls, did not all behave the same way. Finally, the lack of differences in the mean glucose levels for the groups compared to the controls was expected since only the subjects that had a glucose level within the normal range were included in the study.

In contrast to the current findings, several studies [7, 52-55] have shown significantly lower serum adiponectin concentrations in obese subjects and subjects with high BMI, WHR, and WC compared to the healthy weight subjects. The findings of the current study were consistent with other research studies [39, 51] that found that serum TNF-α concentrations did not correlate significantly with the BMI and WC, while others found them to be significantly correlated with the BMI and WC [37]. Also in disagreement with the current results, other researchers found plasma and serum TNF-α concentrations [40, 51] to be higher in obese subjects, and lower for subjects with higher WHR [39] compared to non-obese subjects.

CONCLUSIONS AND RECOMMENDATIONS

Overall, the BMI was the adiposity measure that displayed more significant differences between the groups and the control for the measured parameters, followed by the WC, and finally the WHR that showed differences in only two parameters (total WBC counts and resistin concentration). Thus, it is recommended to use the BMI to ascertain the effects of obesity on the subjects.

The concentrations of the pro-inflammatory CRP and adipokines, except TNF-α, were all significantly higher for the obese/morbidly obese using the BMI and WC and non-significantly higher for the WHR compared to the non-obese. As for the concentrations of the anti-inflammatory adipokine adiponectin, they were not significantly different, although they were lower, for the obese/morbidly obese groups of the three adiposity measures compared to the non-obese.

Therefore, it might be concluded that the overweight and obese/morbidly obese subjects had minimal changes in the immune system and blood profile but they had major effects on the CRP and pro-inflammatory adipokines. Thus, the overweight and obese/morbidly obese would be at a greater risk for heightened inflammation and obesity-related inflammatory diseases. Finally, it is important to study other age categories and carry the same study on Saudi males to determine the differences that may be present between the sexes and age groups.

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