T Cells and Natural Killer Cells, but not B Cells or Antibodies, are Affected in Overweight and Obese Saudi Females

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Saudi Arabia has one of the highest adult overweight and obesity rates, especially in females, leading to increased mortality, morbidity, infections, and risk for many diseases. This study determined the counts and percents of lymphocyte subtypes (CD3, CD4, CD8, and CD16 +CD56 cells) and serum IgG, IgA, and IgM concentrationsin blood samples collected from sixty-four Saudi female university employees with an age range of 24-52 years. There is only one other study on the counts/numbers of lymphocyte subtypes in overweight and obese Saudi females.Anthropometric measurements were used to categorize the subjectsinto groups according to the body mass index (BMI), waist-to-hip ratio (WHR), and waist circumference (WC).Results were all compared to the controls. Antibody concentrations were not significantly different.The CD3and CD4 counts were significantly higher for the obese BMI group and the overweight and obese BMI, respectively. The high risk WHR group had a significantly lower CD3%and a significantly higher CD16 +CD56 count. The high risk WC group had significantly higher CD3 and CD4 counts anda significantly lower CD16 +CD56%.Thus, obesity leads to changes in the cellular adaptiveand innate immune systems, while not affecting thehumoral adaptive immune system.

Keywords: Adaptive immunity, Antibodies,Innate immunity, Obesity, Overweight; Saudi females**.**

Obesity and overweight are considered major health problems in most countries of the world with developed and rich countries being affected more than poorer or underdeveloped countries. In addition, most countries are experiencing increasing rates of both overweight and obesity, with obesity being more widespread than underweight worldwide,with the exception of some African sub-Saharan and Asian countries[1]. Overweight and obesity have been increasing in the Middle East forthe last few decades, possibly due tofactors linked to changing lifestyles and modernization. Rates for overweight and obesity among adults in Saudi Arabia are among thehighest in the Middle East[2]. In Saudi Arabia, accordingto the Saudi Arabia profile published in 2016 by the World Health Organization (WHO)[3], 69.2% of females and 67.5% of males are overweight whereas39.5% of femalesand 29.5 of males are obese. Obesity and overweight lead to increased morbidity and mortality, higher infection rates, worse symptoms for some diseases, and an increased risk for many diseases, such as cardiovascular diseases, dyslipidemia, diabetes,hypertension, metabolic syndrome, liver diseases, kidney diseases,osteoarthritis,many

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types of cancers, and some psychiatric illnesses. In addition, obesity and overweight are linked to many disruptionsof and effects on different systems in the body including the immune system[4-9].

The most commonly used anthropometric adiposity measures are the body mass index (BMI), the waist-to-hip ratio(WHR), and the waist circumference (WC). They are simple ways that allow measurement of the level of overweight or obesitywith simple readily available tools. In addition, they help to specifythe distribution of fat in the body, and thus enabling to determine the presence of upper body obesity, which is highly associated with visceral fat, or lower body obesity. Upper or central obesity, which is more common in men than women, is highly linked to many of the ill health and obesity-related diseases that are more prevalent in people with this body shape. On the other hand, lower body obesity, more prevalent in women and leads to the pear shape that is common in adult women, leads to lower morbidity and obesity-related diseases.

The determination of counts and percents of lymphocyte subsets in overweight and obese subjects helps to ascertain the state of the immune system in these individuals and the extent to which the immune system is affected by increased weight. Additionally, specific lymphocyte types indicate the type(s) of immunity that maybe affected by increased weight. Therefore, CD3 cells, or T lymphocytes, are concerned with cellular adaptive immunity with the CD4 subtype, mainly helper T cells, being involved in enhancing or helping the adaptive (acquired) immune system, while the CD8 subtype, whichare cytotoxic/suppressor cells,having roles in killing unwanted or infected cells,or suppressing an adaptive reaction. CD19, or B cells, are the major cells of the humoral adaptive immune system and the cells from which plasma cells mature and finally produce antibodies. Finally, CD16 +CD56 cells, or natural killer (NK) cells, are important in the innate immune system. Thus, these cells give a good picture of the state of the immune system and may explain the altered immune response in subjects with unhealthy weight and their high incidence of diseases and mortality.

Most research studies on obesity and overweight in Saudi Arabia are epidemiological in nature. Studies[4-8]have been done on the effects of overweight and obesity on different health related parameters and cells of the immune system in Saudi females.Worldwide, studies[9-15]on the effects of overweight and obesity on the immune system and on specific types of lymphocytes are few and contradictory. After an extensive search in the internet, only one study[4]was foundon counts/percentages of lymphocyte subtypes in the circulation in overweight and obese Saudi adult females.Thus, the current study aimed to fill this knowledge gap by determining the counts and percents of immune system cells and the concentrations of antibodies in overweight and obese Saudi female university workers compared to healthy weight subjects.

MATERIALS AND METHODS

Subjects, anthropometric measurements, sample collection, and categorizations of subjects

Sixty-four randomly chosen Saudi female university employees, ages 24-52 years, were recruited from the King Abdulaziz University, Jeddah, Saudi Arabia. All subjects signed a consent form for participating in this study. None of the subjects were pregnant or menstruating at the time of blood sample collection;had any chronic diseases such as diabetes, high blood pressure, and heart diseases; nor on any medications.

Blood samples were collected from the subjects into sodium heparin vacutainer tubes for the determination ofthe types of lymphocyte subsets. In addition, blood samples were collected in plain vacutainer tubes for the determination of antibody concentrations. These tubes were centrifuged after clot formation and serum was subsequently collected. In addition, anthropometric measurements (weight, height, and waist and hips circumferences) were obtained at the same time of blood collection.

TheBMI cut off values for the BMI groups were: below 18.5 kg/m^2 for the underweight BMIgroup, 18.5-24.9kg/m^2 for the healthy BMIgroup, 25-29.9kg/m^2 for the overweight BMIgroup, and 30-39.9kg/m^2 for the obese BMIgroup. None of the subjects were morbidly obese. For the WHR groups, the low risk group subjectshad WHRs below or equal to 0.8, the moderate risk group was WHRs between 0.81 and 0.85, and finally the high risk group was subjects with a WHR above 0.85. WCs below 82.5 cm were in the WC low risk group,a WC between 82.5 and 88.9 cm was in the moderate risk group, and a WC above 88.9 cm was in the high risk group.

Determination of counts and percents of lymphocyte subsets

The counts and percents of the lymphocyte subsets were determined in whole blood using a BD FACSCanto II flow cytometer (Becton DickinsonCompany, CA, USA) using the BD Multitest 6-color TBNK reagent (BD Biosciences, CA, USA) for determining the CD markers on the surface of cells.

Determination of serum IgG, IgA, and IgM concentrations

Serum concentrations of IgG, IgA, and IgM antibodies were determined on a BN II system nephelometric analyzer (Siemens, Germany) using N antisera to human immunoglobulins (IgG, IgA, and IgM) (Siemens, Germany).

Statistical analysis

Statistical and analytical analyses of the results were done using the SPSS Statistics statistical program (version 20). To test for the presence of statistically signiûcant differences between the groups, the one-way ANOVA test was used for the normally distributed parameters while the Kruskal-Wallis H test was used for the non-normally distributed parameters. For the post hoc tests, the LSD test was used for the normally distributed parameters and the Dunnett T3test was used for the non-normally distributed parameters. The resulting P values indicate whether the differences between the groups is considered significant (P < 0.05), highly significant (P < 0.01), or non-significant(P e" 0.05).

RESULTS

Subjects and categorizations

The subjects' ages ranged from a minimum of 24 years to a maximum of 52 years. The 64 subjects had a mean age of 32.9 years and a standard deviation of 8.5 years. The weights of the subjects had a range of 39-103 kg and a mean of 64.9 kg with a standard deviation of 15.2 kg. The heights of the subjects ranged from 145.5 cm to 171 cm with a mean and standard deviation of 159.1 ± 5.6 cm. Categorizing the subjects intothe BMI, WHR, and WCgroups (Table 1) led to most subjects being in the healthy BMI group and the low risk WHR and WC groups.

Counts and percents of lymphocyte subsets and antibody concentrations

For the BMI categorization, the mean CD3 and CD4 counts (Table 2) and mean CD8 percents (Table 3) were significantly different between the groups. As for the WHR groups, the mean CD16

Table 1. Adiposity measures categorizations for the subjects

Groups	Range	N	N% of total	Minimum	Maximum	Mean	± SD
BMI** (kg/m2)							
Underweight	< 18.5	7	10.9	15.4	18.4	16.7	1.3
Healthy	18.5-24.9	21	32.8	18.7	24.8	21.4	1.9
Overweight	25-29.9	18	28.1	25.1	29.6	27.4	1.4
Obese	30-39.9	18	28.1	30.0	37.6	32.2	2.1
Total		64	100.0	15.4	37.6	25.6	5.5
WHR**							
Low	d" 0.80	34	54.8	0.47	0.80	0.7	0.1
Moderate	0.81-0.85	12	19.4	0.81	0.85	0.8	0.0
High	> 0.85	16	25.8	0.86	1.21	0.9	0.1
Total		62	100.0	0.47	1.21	0.8	0.1
WC* (cm)							
Low	< 82.5	28	45.2	49.5	82.0	71.5	7.3
Moderate	82.5-88.9	13	21.0	82.5	88.0	85.3	2.0
High	> 88.9	21	33.9	89.0	116.0	98.3	7.5
Total		62	100.0	49.5	116.0	83.5	13.6

*ANOVA one-way test, **Kruskal-Wallis testN: Number of subjects

Table 2. Statistical analysis for mean lymphocyte cell counts for the subjects using the BMI, WHR, and WC

Cell counts	Group	BMI Mean	± SD	P value	Group	WHR Mean	± SD	P value	Group	WC Mean	± SD	P value
CD3*	Underweight	1.6908	0.7853	0.023[S]	Low	1.9135	0.5554	0.873	Low	1.7596	0.5608	0.046[S]
	Healthy	1.7195	0.4636		Moderate	1.9656	0.7257		Moderate	1.9911	0.3980	
	Overweight	2.0434	0.4965		High	2.0042	0.5537		High	2.1696	0.6413	
	Obese	2.2172	0.5665									
CD4*	Underweight	0.9391	0.5071	0.015[S]	Low	1.1573	0.3363	0.954	Low	1.0642	0.3529	0.042[S]
	Healthy	1.0475	0.2854		Moderate	1.1673	0.4193		Moderate	1.1563	0.2854	
	Overweight	1.2666	0.2968		High	1.1900	0.3294		High	1.3127	0.3333	
	Obese	1.2999	0.2949									
CD8**	Underweight	0.7207	0.2714	0.066	Low	0.7121	0.2786	0.628	Low	0.6455	0.2685	0.120
	Healthy	0.6114	0.2328		Moderate	0.7081	0.3731		Moderate	0.7673	0.2173	
	Overweight	0.7122	0.2353		High	0.7514	0.2395		High	0.7944	0.3286	
	Obese	0.8524	0.3388									
CD19**	Underweight	0.0478	0.0430	0.394	Low	0.0468	0.0227	0.644	Low	0.0497	0.0253	0.883
	Healthy	0.0526	0.0190		Moderate	0.0519	0.0213		Moderate	0.0465	0.0176	
	Overweight	0.0447	0.0191		High	0.0477	0.0275		High	0.0467	0.0248	
	Obese	0.0457	0.0222									
CD16 + CD56**	Underweight	0.3196	0.1924	0.686	Low	0.2523	0.1324	0.018[S]	Low	0.2920	0.1320	0.261
	Healthy	0.2723	0.1275		Moderate	0.2113	0.0983		Moderate	0.2507	0.1508	
	Overweight	0.2918	0.1860		High	0.3538	0.1628		High	0.2544	0.1549	
	Obese	0.2511	0.1462									

*ANOVA one-way test, **Kruskal-Wallis test, S: significant difference

Table 3. Statistical analysis for mean lymphocyte cell percents for the subjects using the BMI, WHR, and WC

Cell%	Group	BMI Mean	± SD	P value	Group	WHR Mean	± SD	P value	Group	WC Mean	± SD	P value
CD3%*	Underweight	78	5	0.843	Low	78	5	0.027[S]	Low	76	5	0.401
	Healthy	76	4		Moderate	79	5		Moderate	79	5	
	Overweight	78	8		High	74	9		High	78	9	
	Obese	78	9									
CD4%*	Underweight	42	5	0.146	Low	47	6	0.177	Low	46	6	0.609
	Healthy	47	6		Moderate	47	5		Moderate	46	6	
	Overweight	48	7		High	44	7		High	48	7	
	Obese	46	7									
CD8%*	Underweight	35	5	0.041[S]	Low	29	7	0.816	Low	28	7	0.401
	Healthy	27	5		Moderate	28	8		Moderate	31	8	
	Overweight	27	7		High	28	6		High	28	7	
	Obese	30	8									
CD19%**	Underweight	7	3	0.103	Low	10	4	0.522	Low	10	4	0.509
	Healthy	11	4		Moderate	12	4		Moderate	11	4	
	Overweight	11	4		High	12	7		High	12	6	
	Obese	13	6									
CD16 + CD56%*	Underweight	14	5	0.103	Low	11	5	0.060	Low	13	5	0.020[S]
	Healthy	12	5		Moderate	9	3		Moderate	10	4	
	Overweight	11	6		High	13	5		High	9	5	
	Obese	9	5									

*ANOVA one-way test, **Kruskal-Wallis test, S: significant difference

Table 4. Statistical analysis for mean immunoglobulin concentrations for the subjects using the BMI, WHR, and WC

Concentration g/L	Group	BMI Mean	± SD	P value	Group	WHR Mean	± SD	P value	Group	WC Mean	± SD	P value
IgG*	Underweight	7.79	2.97	0.477	Low	7.43	3.10	0.510	Low	7.81	3.06	0.204
	Healthy	7.37	2.83		Moderate	7.59	2.77		Moderate	7.32	2.65	
	Overweight	6.71	3.15		High	6.50	2.47		High	6.31	2.63	
	Obese	7.26	2.69									
IgA*	Underweight	1.72	0.75	0.385	Low	1.55	0.75	0.853	Low	1.51	0.75	0.644
	Healthy	1.43	0.78		Moderate	1.58	0.47		Moderate	1.74	0.54	
	Overweight	1.49	0.75		High	1.67	0.83		High	1.60	0.81	
	Obese	1.81	0.58									
IgM**	Underweight	1.12	0.48	0.193	Low	0.87	0.54	0.864	Low	0.85	0.55	0.957
	Healthy	0.72	0.34		Moderate	0.85	0.63		Moderate	0.83	0.59	
	Overweight	0.83	0.64		High	0.75	0.43		High	0.82	0.48	
	Obese	0.86	0.57									

*ANOVA one-way test, **Kruskal-Wallis test

+CD56 counts (Table 2) and CD3 percents (Table 3) were significantly differentbetween the groups. Finally, for the WC groups, the mean CD3 and CD4 counts (Table 2) and mean CD16 +CD56 percents(Table 3) were significantly different between the groups. The remaining cell counts and percents for each obesity measure were not significantly different between the respective groups. Finally, the mean IgG, IgA, and IgM concentrations (Table 4) were not significantly different between each of the BMI, WHR, and WC groups.

The post hoc analyses were done for the significantly different cell counts and percents (Table 5). The mean CD3 count for the obese BMI group and the mean CD4 counts for the overweight and obese BMI groups were significantly higher than the mean counts for the respective healthy BMI groups (controls). The mean CD8 percent was significantly higherfor the underweight BMI group compared to the mean percent for the control group. As for the post hoc analyses for the WHR groups (Table 5), the mean CD16 +CD56 counts werenot significantly different for both the moderate and high risk groups compared to the low risk group (control), while the count for the high risk group was significantly higher compared to the count for the moderate risk group. The mean CD3 percent was significantly lower for the high risk WHR group compared to the mean percent for the control. Finally, for the post hoc comparisons for the WC groups, the mean CD3 and CD4 counts for the high risk group were both significantly higher than the respectivemean counts for the control group. The mean CD16 +CD56 percent for the WC high risk group was significantly lower than the mean percent for the control group. The remaining group comparisons for the three adiposity measures were not significantly different compared to the respective control groups.

Table 5. Post hoc statistical analysis for the significantly different parameters for the BMI, WHR, and WC

Parameter	Test	G1	G2	Mean Difference (G1-G2)	± SE	P value
			BMI			
CD3 count	LSD	Healthy	Underweight	0.0288	0.2367	0.904
			Overweight	-0.3238	0.1742	0.068
			Obese	-0.4977	0.1742	0.006S
CD4 count	LSD	Healthy	Healthy	0.1085	0.1397	0.441
			Overweight	-0.2191	0.1028	0.037S
			Obese	-0.2524	0.1028	0.017S
CD8%	LSD	Healthy	Underweight	-8	3	0.007S
			Overweight	-1	2	0.776
			Obese	-3	2	0.181
WHR						
CD16 +CD56 count	Dunnett T3	Low	Moderate	0.0410	0.0363	0.600
			High	-0.1015	0.0466	0.110
		Moderate	High	-0.1426	0.0496	0.024S
CD3%	LSD	Low	Moderate	-1	2	0.655
			High	5	2	0.016S
WC						
CD3 count	LSD	Low	Moderate	-0.2314	0.1885	0.225
			High	-0.4099	0.1622	0.014S
CD4 count	LSD	Low	Moderate	-0.0921	0.1119	0.414
			High	-0.2485	0.0963	0.012S
CD16 +CD56%	LSD	Low	Moderate	3	2	0.052
			High	4	1	0.009S

G1: group 1, G2: group 2
S: significant difference

DISCUSSION

This research study aimed to determine the status of immune system cells and antibodies in Saudi female university workers in Saudi Arabia and to determine the best measure ofadiposity to use for this cohort. Studies on immunological parameters in obese and overweight individuals from the local community are important to help determine the effects of overweight and obesity on the immune system to better educate the local population about these effects in the hope of giving more incentives for weight loss and to be able to give better guidelines on healthy weights.

For the BMI groups, the mean CD3 cell (T lymphocyte) counts were significantly higher ($P = 0.006$) for the obese BMI group compared to the healthy (control) group. The mean CD4 cell (T helper lymphocyte) counts were significantly higher for both the overweight ($P = 0.037$) and obese BMI subjects ($P = 0.017$) compared to the mean count for thehealthy BMI group. Finally, themean CD8 cell (T suppressor or T regulatory lymphocyte) percent forthe underweight BMI was significantly higher ($P = 0.007$) compared to the mean percent for the control. The remaining cells were not significantly different($P > 0.050$) for the BMI groups compared to the control.

These findings agree with the previous finding[4] of a significantly higher mean CD4 count for highly obese BMI Saudi female university students compared to healthy weight subjects. In addition, the findings of this previousstudy[4] agree with the current findings of no significant differences between themean CD8 counts, CD4 percents, and CD19 and CD16 +CD56 cell counts and percents for theBMI groupsand the control. On the other hand, the current findings disagree with the findings of the above mentioned study[4] of no significant differences for the mean CD3 counts and CD8 percents for the BMI groups compared to the control.

As for the WHR groups, only the mean CD16 +CD56 cell counts and CD3 percents showed significant differences compared to the controls. The mean CD16 +CD56 cell (natural killer lymphocyte) count for the high risk group was significantly higher ($P = 0.024$) compared to the mean count for the moderate risk group. On the other hand, both mean counts for the moderate and high risk groups were not significantly different ($P > 0.050$) from the mean count for the low risk (control) group. The mean CD3 percent for the high risk group was significantly lower ($P = 0.016$) compared to the mean count for the control.

The current findings agree with those of the above mentioned study on Saudi female university students[4] which found no significant differences for the WHR groups for the mean CD8 and CD19 counts and percents, and CD16 +CD56 percents compared to the control. On the other hand, the current findings disagree with the previous findings[4] of significantly higher CD3 count and CD4 count and percent for the moderate risk group, and none significantly different CD16 +CD56 counts for both WHR groups compared to the control.

For the WCgroups,both the mean CD3 and CD4 cell counts were significantly higher ($P = 0.014$ and 0.012, respectively) for the high risk group compared to the mean counts for the respective controls. The mean CD16 +CD56 cell percent for the high risk group was significantly lower ($P = 0.009$) compared to the mean percent for the control group. The remaining cell counts and percents were not significantly different from the controls.

The mean IgG, IgA, and IgM concentrations were not significantly different between each of the BMI, WHR, and WC groups. This agrees with previous studies[5] that also showed no significant differences in the concentrations of these antibodies in adolescent Saudi females.

The cohort of the study is considered highly educated since most of the subjects had a college degree or a higher degree. Therefore,the subjects were probably more aware than other cohorts about health and a healthy lifestyle and probably attempted to follow health and diet recommendations. This may explain the minimal differences between the overweight and obese subjects compared to the healthy weight ones.

CONCLUSIONS

All adiposity measures showed significant changes in CD3 cell (T cells) counts/percents with the highest BMI and WC being associated with significantly higher counts while the highest WHR was associated with a significantly lower percent.

CD4 counts were significantly higher for the overweight and obese BMIs and high risk WHR. On the other hand, CD16 +CD56 cell percents were significantly lower for the high WC compared to the control while not being significantly different from the controls using the BMI and WHR. Thus, higher obesity, measured by BMI and WC, is associated with higher CD3 and CD4 counts, and lower CD16 +CD56 cell percents compared to the controls. Thus, cellular adaptive immunity and innate immunity are both affected in the obese while humoral adaptive immunity is not.

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