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Obesity is Associated with Increased Cardiovascular Risk and Increased Prevalence of Insulin Resistance among Apparently Healthy Young Adults

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ABSTRACT

Objective: Cardiometabolic abnormalities are still prevalent in young individuals. This research aims to investigate associations between obesity, cardiometabolic risk factors, and insulin resistance (IR) in apparently healthy young adults.

Methods: This cross-sectional study involved 70 obese and 70 age/gender matched young adults with normal body weight. Serum glucose, insulin, lipids, and homocysteine were measured. IR was determined using Homeostasis Model Assessment-IR (HOMA-IR). Systolic (SBP) and diastolic (DBP) blood pressures were measured. Other data were self-reported.

Results: Obese participants exhibited higher SBP, DBP, glucose, triglycerides (TGs), cholesterol, low-density lipoprotein (LDL), insulin, and HOMA-IR, and lower high-density lipoprotein (HDL) compared to healthy weight participants (p-values<0.01). Body mass index (BMI) was correlated with SBP, DBP, glucose, insulin, HOMA-IR, cholesterol, LDL, TGs, and was inversely correlated with HDL (p-values<0.01). HOMA-IR was correlated with SBP, DBP, cholesterol, LDL, and TGs, and was inversely correlated with HDL (p-values<0.01). Participants with IR had higher BMI, SBP, DBP, cholesterol, LDL, and TGs compared to participants with normal insulin sensitivity (p-values<0.05). Obesity was associated with increased SBP, TGs, insulin and HOMA-IR (p-values<0.05). There was no significant difference in homocysteine between groups (p-value>0.05).

Conclusion: Obesity is associated with increased cardiovascular risk and increased prevalence of IR in apparently healthy young adults. Pharmacological and behavioral interventions are urgently needed to manage increased cardiovascular risks among this age group.

Keywords: Obesity, young adults, cardiovascular risk, insulin resistance.

INTRODUCTION

Obesity is defined as an excessive or abnormal body fat accumulation that presents a risk to health.[1] Overweight and obesity are increasingly prevalent because of the modern life that encourages sedentary lifestyles and consumption of unhealthy fast food and sugar-rich drinks.[2] According to the latest statistics, the worldwide prevalence of obesity has almost tripled since 1975.[3] In Jordan, age-standardized prevalence of overweight and obesity among women was 70.6% as reported in the year 2021.[4]

In addition to its adverse socioeconomic consequences,[5] obesity represents a global health concern in all age groups as it is associated with increased risk of cardiometabolic complications.[6] It increases the risk of developing cardiovascular diseases (CVDs), insulin resistance (IR), Type 2 diabetes mellitus,[7, 8] and some

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types of cancers,[9] which are considered as leading causes of mortality and morbidity.[10] It also adversely affects mental health, musculoskeletal system, and is linked to sexual dysfunction.[11-13]

Cardiovascular diseases (CVDs) are considered as a major cause of death all over the world, nearly 20.5 million people died from CVDs in the year 2021, with a rate higher in low to middle income countries.[14] Obesity is mainly associated with increased risk of heart failure, coronary artery disease, and cerebrovascular diseases.[15] The mechanisms through which obesity increases the risk of CVDs include changes in body composition that affects hemodynamics and alters heart structure.[16-18] Accumulation of visceral fat is particularly associated with increased risk of CVDs.[19]

In addition to obesity, several modifiable risk factors contribute to the development of CVDs. These include smoking, high blood pressure, elevated low-density lipoprotein (LDL), decreased high-density lipoprotein (LDL), hypercholesterolemia, hypertriglyceridemia, sedentary lifestyle, diabetes mellitus,[20] as well as hyperhomocysteinemia.[21] While non-modifiable cardiovascular risk factors include age, gender, ethnicity, race, and genetics.[22]

While increasing numbers of studies examining the correlation of metabolic parameters and cardiovascular risks in obese individuals, such correlation in healthy young subjects is not sufficiently recognized. Additionally, growing evidence suggests prevalence of cardiovascular abnormalities in apparently healthy, and particularly young individuals. Indeed, the number of young adults with cardiovascular events is increasing, and only one out of four American young adults (18 – 44 years old) had an ideal cardiovascular health.[23] Therefore, we aimed to assess cardiometabolic risk factors among young obese adults compared to age/gender matched adults with healthy body weight. The relationship between obesity and other cardiometabolic risk factors in young adults needs to be investigated to predict susceptibility to developing cardiometabolic diseases in the future. We hypothesized that obese young adults have a higher risk of developing cardiometabolic diseases compared to subjects with healthy body weight. To achieve this, we aimed to assess the relationship between obesity and cardiovascular risk variables including lipid profile, blood pressure, smoking, homocysteine, blood glucose, and insulin. Additionally, we aimed to assess IR in the study groups and its association with obesity and other cardiometabolic risk factors.

RESULTS

Differences in cardiovascular and metabolic risk factors between obese participants and participants with healthy body weight

As shown in Table 1, obese participants exhibited significantly higher levels of BMI, SBP, DBP, fasting glucose, fasting insulin, TGs, total cholesterol, LDL, and HOMA-IR, and lower levels of HDL compared to participants with healthy body weight (p-values < 0.01). Homocysteine levels of all participants were within the normal range and there was no significant difference in homocysteine between obese participants and participants with healthy body weight (p-value $= 0.34$). In addition, there was no significant difference in smoking, marital status, education, number of family members, average family income, family history of CVDs and diabetes, and doing regular exercise between obese participants and participants with healthy body weight (p-values > 0.05).

Table 1: General characteristics and differences in study variables between obese participants and participants with healthy body weight.

Variable	All participants (n= 140)	Participants with healthy body weight (BMI = 18.5-25 Kg/m^2) (n= 70)	Obese participants (BMI > 30 Kg/m^2) (n= 70)	P-value*
Age (Years)	25.44±4.30	24.91±4.03	25.96±4.52	0.15
BMI (Kg/m^2)	29.22±7.98	22.37±1.90	36.07±5.42	<0.001
Gender				
Male	70 (50)	35 (50)	35 (50)	1.00
Female	70 (50)	35 (50)	35 (50)	
Smoking				
Yes	49 (35)	27 (38.6)	22 (31.4)	0.48
No	91 (65)	43 (61.4)	48 (68.6)	
Marital status				
Single	104 (74.3)	56 (80)	48 (68.6)	0.18
Married	36 (25.7)	14 (20)	22 (31.4)	
Education				
Secondary school	34 (24.3)	17 (24.3)	17 (24.3)	1.00
University	106 (75.7)	53 (75.7)	53 (75.7)	
Employment				
Yes	80 (57.1)	30 (42.9)	30 (42.9)	1.00
No	60 (42.9)	40 (57.1)	40 (57.1)	
Number of family members	6 (4-8)	6 (4.25-8)	6 (4-8)	0.44
Average family income				
≤ 500 JD	65 (46.4)	28 (40)	37 (52.9)	0.19
501 – 1000 JD	62 (44.3)	33 (47.1)	29 (41.4)	
> 1000 JD	13 (9.3)	9 (12.9)	4 (5.7)	
Regular exercise				
Yes	40 (28.6)	17 (24.3)	23 (32.9)	0.35
No	100 (71.4)	53 (75.7)	47 (67.1)	
Family history of CVDs				
Yes	68 (48.6)	31 (44.3)	37 (52.9)	0.40
No	72 (51.4)	39 (55.7)	33 (47.1)	
Family history of DM				
Yes	72 (51.4)	32 (45.7)	40 (57.1)	0.24
No	68 (48.6)	38 (54.3)	30 (42.9)	
SBP (mmHg)	119.06±12.39	114.57±11.23	123.56±11.92	<0.001
SBP (mmHg)				
<120 mmHg	82 (58.6)	54 (77.1)	28 (40)	<0.001
≥120 mmHg	58 (41.4)	16 (22.9)	42 (60)	
DBP (mmHg)	75.91±8.51	72.66±7.78	79.16±7.99	<0.001

Variable	All participants (n= 140)	Participants with healthy body weight (BMI = 18.5-25 Kg/m^2) (n= 70)	Obese participants (BMI > 30 Kg/m^2) (n= 70)	P-value*
DBP (mmHg)				
<80 mmHg	94 (67.1)	59 (84.3)	35 (50)	<0.001
≥80 mmHg	46 (32.9)	11 (15.7)	35 (50)	
Total cholesterol (mg/dL)	169.27±32.35	159.43±26.58	179.11±34.72	<0.001
Total cholesterol (mg/dL)				
<200 mg/dL	120 (85.7)	67 (95.7)	53 (75.7)	0.001
≥200 mg/dL	20 (14.3)	3 (4.3)	17 (23.3)	
HDL (mg/dL)	48.53±11.64	50.96±12.34	46.10±10.42	0.01
HDL (mg/dL)				
≥60 mg/dL (Optimal)	24 (17.1)	17 (24.3)	7 (10)	0.01
40-60 mg/dL (At risk)	79 (56.4)	41 (58.6)	38 (54.3)	
< 40 mg/dL (Dangerous)	37 (26.4)	12 (17.1)	25 (35.7)	
LDL (mg/dL)	99.76±29.85	91.57±31.63	107.94±31.63	<0.01
LDL (mg/dL)				
<130 m/dL (Good)	122 (87.1)	67 (95.7)	55 (78.6)	<0.01
≥130 (borderline-high)	18 (12.9)	3 (4.3)	15 (21.4)	
Triglycerides (mg/dL)	94 (64.50-128.0)	77.50 (58.25-98.50)	111 (85.25-163.75)	<0.001
Triglycerides (mg/dL)				
<150 mg/dL (Optimal)	116 (82.9)	67 (95.7)	49 (70)	<0.001
≥150 mg/dL (Elevated)	24 (17.1)	3 (4.3)	21 (30)	
Glucose (mg/dL)	93.31±17.51	87.77±5.38	98.84±22.94	<0.001
Glucose (mg/dL)				
<100 mg/mL	113 (80.7)	68 (97.1)	45 (64.3)	<0.001
≥100 mg/dL	27 (19.3)	2 (2.9)	25 (35.7)	
Insulin (pg/mL)	629.34 (368.08-1011.43)	390.49 (245.60-656.42)	938.21 (621.85-1433.38)	<0.001
HOMA - IR	1.42 (0.81-2.35)	0.87 (0.54-1.42)	2.26 (1.42-3.23)	<0.001
HOMA – IR				
≤1.9 (Normal)	91 (65)	62 (88.9)	29 (41.4)	<0.001
>1.9 (IR)	49 (35)	8 (11.4)	41 (58.6)	
Homocysteine (pmol/mL)	472.91±180.81	487.47±196.23	458.35±164.08	0.34

* Statistically significant differences between study groups (p-values < 0.05) were determined using Student's t-test or Mann–Whitney U test for continuous variables and Chi-square test for categorical variables. Data are expressed as frequency (%), mean ± standard deviation or median (25th-75th percentiles). BMI; Body Mass Index, JD; Jordanian Dinar, CVDs; Cardiovascular Diseases, DM; Diabetes Mellitus, SBP; Systolic Blood Pressure, DBP; Diastolic Blood Pressure, HDL; High Density Lipoprotein, LDL; Low Density Lipoprotein, HOMA-IR; Homeostatic Model Assessment of Insulin Resistance.

Correlation between cardiovascular and metabolic biomarkers

As shown in Table 2, BMI was significantly correlated with SBP, DBP, fasting glucose, insulin, HOMA-IR, total cholesterol, LDL, TGs, and was significantly inversely correlated with HDL (P-values < 0.01). HOMA-IR was significantly correlated with SBP, DBP, total cholesterol, LDL, and TGs, and was significantly inversely correlated with HDL (P-values < 0.01). SBP was significantly correlated with DBP, insulin, HOMA-IR and TGs, and significantly inversely correlated HDL (p-values < 0.01). DBP was significantly correlated with insulin, HOMA-IR, total cholesterol, LDL and TGs (p-values < 0.01), and significantly inversely correlated with HDL (p-value < 0.05). Fasting glucose was significantly correlated with insulin, HOMA-IR, and TGs (p-values < 0.01) and was significantly inversely correlated with HDL (p-value < 0.05). Insulin was significantly correlated with HOMA-IR, total cholesterol, and TGs (p-values < 0.05). Total cholesterol was significantly correlated with LDL and TGs (p-values < 0.001). HDL was significantly inversely correlated with LDL and TGs p-values < 0.01). LDL was significantly correlated with TGs (p-value < 0.001).

Predictors of cardiovascular risk variables

The predictors of the studied cardiovascular risk variables were identified using multiple linear regression analyses (Table 3). The results showed direct associations between SBP and both BMI and DBP, and an inverse association between SBP and HDL (p-values < 0.05). LDL was directly associated with age and HOMA-IR (p-values < 0.05). HDL was inversely associated with both SBP and TGs (p-values < 0.05). TGs level was directly associated with both BMI and total cholesterol (p-values < 0.05). Total cholesterol was directly associated with age, HOMA-IR, and TGs (p-values < 0.05). Fasting glucose was directly associated with TGs and fasting insulin (P-values < 0.05). Fasting insulin was also directly associated with BMI (p-value < 0.001).

Table 2: Correlations between cardiovascular and metabolic biomarkers

	SBP (mmHg)	**DBP (mmHg)**	**Glucose (mg/dL)**	**insulin (pg/mL)**	**HOMA-IR**	**Total cholesterol (mg/dL)**	**HDL (mg/dL)**	**LDL (mg/dL)**	**Triglycerides (mg/dL)**	**Homocysteine (pmol/mL)**
Age (Years)	0.01	0.19*	0.11	0.02	0.02	0.38***	-0.15	0.36***	0.31***	-0.02
BMI (Kg/m^2)	0.37***	0.36***	0.28***	0.55***	0.58***	0.26**	-0.27**	0.24**	0.52***	-0.04
SBP (mmHg)	-	0.46***	0.06	0.26**	0.27**	0.08	-0.25**	0.13	0.26***	-0.13
DBP (mmHg)	-	-	0.08	0.30***	0.31***	0.23**	-0.20*	0.26**	0.27**	-0.13
Glucose (mg/dL)	-	-	-	0.35***	0.44***	0.09	-0.17*	<0.01	0.25**	0.01
Insulin (pg/mL)	-	-	-	-	0.99***	0.19*	-0.16	0.15	0.41***	0.08
HOMA-IR	-	-	-	-	-	0.25**	-0.23**	0.21**	0.42***	0.05
Total cholesterol	-	-	-	-	-	-	0.02	0.93***	0.46***	-0.08

	SBP (mmHg)	DBP (mmHg)	Glucose (mg/dL)	insulin (pg/mL)	HOMA-IR	Total cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Triglycerides (mg/dL)	Homocysteine (pmol/mL)
(mg/dL)										
HDL (mg/dL)	-	-	-	-	-	-	-	-0.22**	-0.48***	-0.06
LDL (mg/dL)	-	-	-	-	-	-	-	-	0.37***	-0.08
Triglycerides (mg/dL)	-	-	-	-	-	-	-	-	-	0.04

Pearson's or Spearman's correlation test (p-values < 0.05 were considered significant). BMI; Body Mass Index, SBP; Systolic Blood Pressure, DBP; Diastolic Blood Pressure, HDL; High Density Lipoprotein, LDL; Low Density Lipoprotein, HOMA-IR; Homeostatic Model Assessment of Insulin Resistance. * (P-value < 0.05), ** (P-value ≤ 0.01), and *** (P-value < 0.001).

Table 3: Predictors of cardiovascular risk variables

Cardiovascular risk variables (Dependent variables)	R^2	ANOVA	Model	B	β	P-value*
SBP (mmHg)	0.28	F (5,134) = 10.17, p-value < 0.001	Constant	96.64	-	<0.001
			BMI (Healthy body weight vs. obese)	5.50	0.22	0.02
			DBP (mmHg)	0.52	0.36	<0.001
			HOMA-IR (≤1.9 vs. >1.9)	0.16	0.01	0.94
			Log (Triglycerides (mg/dL))	-5.60	-0.09	0.32
			HDL (mg/mL)	-0.19	-0.18	0.04
DBP (mmHg)	0.30	F (7,132) = 8.21, p-value < 0.001	Constant	33.31	-	0.01
			Age (Years)	0.28	0.14	0.09
			BMI (Healthy body weight vs. obese)	2.71	0.16	0.09
			HOMA-IR (≤1.9 vs. >1.9)	1.39	0.08	0.38
			Total cholesterol (mg/dL)	0.02	0.08	0.39
			HDL (mg/mL)	-0.03	-0.04	0.63
			Log (Triglycerides (mg/dL))	0.17	<0.01	0.97
			SBP (mmHg)	0.25	0.37	<0.001
LDL (mg/dL)	0.26	F (6,133) = 7.77, p-value < 0.001	Constant	-21.76	-	0.57
			Age (Years)	2.22	0.32	<0.001

Cardiovascular risk variables (Dependent variables)	**R^2**	**ANOVA**	**Model**	**B**	**β**	**P-value***
			BMI (Healthy body weight vs. obese)	2.09	0.04	0.71
			DBP (mmHg)	0.30	0.08	0.31
			HOMA-IR (≤1.9 vs. >1.9)	13.78	0.22	0.01
			HDL (mg/mL)	-0.19	-0.08	0.38
			Log (Triglycerides (mg/dL))	16.31	0.11	0.26
HDL (mg/dL)	0.26	F (6,133) = 7.86, p-value <0.001	Constant	121.88	-	<0.001
			BMI (Healthy body weight vs. obese)	0.71	0.03	0.75
			SBP (mmHg)	-0.17	-0.18	0.04
			DBP (mmHg)	-0.01	-0.01	0.92
			HOMA-IR (≤1.9 vs. >1.9)	1.41	0.06	0.51
			LDL (mg/dL)	-0.03	-0.07	0.41
			Log (Triglycerides (mg/dL))	-26.14	-0.45	<0.001
Log (Triglycerides (mg/dL))	0.48	F (7,132) = 17.13, p-value <0.001	Constant	1.85	-	<0.001
			Age (Years)	0.01	0.10	0.18
			BMI (Healthy body weight vs. obese)	0.07	0.18	0.02
			SBP (mmHg)	<-0.01	-0.04	0.63
			DBP (mmHg)	<0.01	<0.01	0.97
			HOMA-IR (≤1.9 vs. >1.9)	0.02	0.05	0.54
			Total cholesterol (mg/mL)	<0.01	0.35	<0.001
			HDL (mg/mL)	-0.01	-0.43	<0.001
Total cholesterol (mg/dL)	0.32	F (5,134) = 12.67, p-value <0.001	Constant	-8.89	-	0.78
			Age (Years)	2.31	0.31	<0.001
			BMI (Healthy body weight vs. obese)	2.45	0.04	0.67
			DBP (mmHg)	0.14	0.04	0.63
			HOMA-IR (≤1.9 vs. >1.9)	14.37	0.21	0.01
			Log (Triglycerides (mg/dL))	44.58	0.27	<0.01
Glucose (mg/dL)	0.18	F (4,135) = 7.24, p-value <0.001	Constant	29.90	-	0.17
			BMI (Healthy body weight vs. obese)	4.57	0.13	0.17
			HDL (mg/mL)	0.00	0.00	1.00

Cardiovascular risk variables (Dependent variables)	R^2	ANOVA	Model	B	β	P-value*
			Log (Triglycerides (mg/dL))	18.60	0.21	0.03
			Log (Fasting insulin (pg/mL))	8.81	0.19	0.04
Log (Fasting insulin (pg/mL))	0.32	F (6,133) = 10.45, p-value <0.001	Constant	1.68	-	<0.001
			BMI (Healthy body weight vs. obese)	0.31	0.41	<0.001
			SBP (mmHg)	<0.01	<0.01	0.99
			DBP (mmHg)	<0.01	0.03	0.72
			Glucose (mg/dL)	<0.01	0.16	0.04
			Total cholesterol (mg/mL)	0.00	0.01	0.90
			Log (Triglycerides (mg/dL))	0.24	0.12	0.16

*Multiple linear regression analyses (p-values <0.05 were considered significant). BMI; Body Mass Index, SBP; Systolic Blood Pressure, DBP; Diastolic Blood Pressure, HDL; High Density Lipoprotein, LDL; Low Density Lipoprotein, HOMA-IR; Homeostatic Model Assessment of Insulin Resistance, B; Unstandardized Coefficient, β; Standardized Coefficient, F; F-statistic; R^2; Squared Coefficient of Determination.

Assessment of IR among study participants and association with study variables

The participants were classified into two groups based on their HOMA-IR values. The first group consisted of 91 participants with normal HOMA-IR values (≤ 1.9), while the second group consisted of 49 participants with HOMA-IR values > 1.9 (Early IR). The two groups showed significant differences in several study variables as shown in Table 4.

Table 4: Differences in study variables between participants with HOMA-IR ≤1.9 and participants with HOMA-IR > 1.9

Variable	HOMA – IR ≤ 1.9 (Normal, n= 91)	HOMA – IR > 1.9 (Early insulin resistance, n= 49)	P- value*
Age (Years)	25.75±4.50	24.86±3.88	0.24
BMI (Kg/m^2)	26.18±5.91	34.86±8.29	<0.001
Gender			
Male	45 (49.5)	25 (51)	1.00
Female	46 (50.5)	24 (49)	
Smoking			
Yes	31 (34.1)	18 (36.7)	0.85
No	60 (65.9)	31 (63.3)	
SBP (mmHg)	117.27±11.94	122.39±12.64	0.02
SBP (mmHg)			
<120 mmHg	62 (68.1)	20 (40.8)	<0.01
≥120 mmHg	29 (31.9)	29 (59.2)	
DBP (mmHg)	74.40±8.23	78.71±8.27	<0.01

Variable	HOMA – IR ≤ 1.9 (Normal, n= 91)	HOMA – IR > 1.9 (Early insulin resistance, n= 49)	P- value*
DBP (mmHg) <80 mmHg ≥80 mmHg	 70 (76.9) 21 (23.1)	 24 (49) 25 (51)	 <0.01
Total cholesterol (mg/dL)	162.59±29.13	181.67±34.61	<0.01
Total cholesterol (mg/dL) <200 mg/dL ≥200 mg/dL	 83 (91.2) 8 (8.8)	 37 (75.5) 12 (24.5)	 0.02
HDL (mg/dL)	49.38±12.42	46.94±9.94	0.24
HDL (mg/dL) ≥60 mg/dL (Optimal) 40-60 mg/dL (At risk) < 40 mg/dL (Dangerous)	 19 (20.9) 49 (53.8) 23 (25.3)	 5 (10.2) 30 (61.2) 14 (28.6)	 0.31
LDL (mg/dL)	94.01±25.91	110.43±33.79	<0.01
LDL (mg/dL) <130 m/dL (Good) ≥130 (borderline-high)	 83 (91.2) 8 (8.8)	 39 (79.6) 10 (20.4)	 0.07
Triglycerides (mg/dL)	83 (59-114)	110 (88-137)	<0.01
Triglycerides (mg/dL) <150 mg/dL (Optimal) ≥150 mg/dL (Elevated)	 77 (84.6) 14 (15.4)	 39 (79.6) 10 (20.4)	 0.49
Glucose (mg/dL)	90.70±13.76	98.14±22.27	0.02
Glucose (mg/dL) <100 mg/mL ≥100 mg/dL	 82 (90.1) 9 (9.9)	 31 (63.3) 18 (36.7)	 <0.001
Fasting insulin (pg/mL)	424.35 (271.36-603.35)	1135.24 (968.10-2026.73)	<0.001
Homocysteine (pmol/mL)	469.57±199.05	479.13±142.56	0.77

* Statistically significant differences between participants with HOMA-IR ≤1.9 and participants with HOMA-IR > 1.9 (p-values < 0.05) were determined using Student's t-test or Mann–Whitney U test for continuous variables and Chi-square test for categorical variables. Data are expressed as frequency (%), mean ± standard deviation or median (25^{th}-75^{th} percentiles). BMI; Body Mass Index, SBP; Systolic Blood Pressure, DBP; Diastolic Blood Pressure, HDL; High Density Lipoprotein, LDL; Low Density Lipoprotein, HOMA-IR; Homeostatic Model Assessment of Insulin Resistance.

related to obesity, blood pressure, glucose metabolism, and lipid profile, such as BMI, SBP, DBP, fasting glucose, total cholesterol, LDL, TG, and fasting insulin. The details of these variables are presented in Table 3.4. Participants with early IR had significantly higher levels of BMI, SBP, DBP, total cholesterol, LDL, fasting glucose, and fasting insulin and lower level of HDL compared to participants with normal HOMA-IR (p-values < 0.05).

To find predictors of IR among study participants, further binary logistic regression analysis was performed (Table 5). Results showed that early IR (HOMA-IR> 1.9) can be predicted from obesity (Odds ratio = 8.01, p-value < 0.001).

Table 5: Predictors of HOMA – IR

Variable	Value	B (SE)	Odds ratio	Confidence interval	P-value*
Constant	-	-6.09 (4.15)	-	-	<0.01
SBP (mmHg)	-	<0.01 (0.02)	1.00	0.97-1.04	0.89
DBP (mmHg)	-	0.02 (0.03)	1.02	0.96-1.08	0.57
Total cholesterol (mg/dL)	-	0.01 (0.01)	1.01	1.00-1.03	0.16
Log (Triglycerides (mg/dL))	-	0.32 (1.37)	1.38	0.10-20.15	0.81
HDL (mg/dL)		<0.01 (0.02)	1.00	0.96-1.05	0.91
BMI (Kg/m^2)	Obese Healthy body weight (reference)	2.08 (0.50)	8.01	2.99-21.45	<0.001

*Binary logistic regression (dependent variable: HOMA-IR >1.9 versus HOMA-IR ≤1.9), p<0.05 was considered statistically significant. B: coefficient (intercept); SE: standard error; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high density lipoprotein; BMI, body mass index.

DISCUSSION

This study demonstrated an association between general obesity and increased risk of cardiovascular diseases among young adults. Obese participants had significantly elevated levels of SBP, DBP, total cholesterol, TGs, and LDL, as well as lower levels of HDL. These findings indicate that obese young adults are at higher risk to develop hypertension and dyslipidemia, a leading cause of CVDs. Obese subjects also had significantly higher levels of fasting glucose, fasting insulin, and HOMA-IR. In other words, they had higher levels of IR which, if not treated, may progress to type 2 Diabetes Mellitus. Similar recent study conducted in India found that general obesity among young adults is associated with increased risk of hypertension and dyslipidemia.[24] Another study performed in Kenya to investigate hypertension risk factors among young adults found that obesity and life style factors are the main risk factors.[25] Also, a study conducted over Swedish young women revealed that overweight women showed significantly increased risk for early acute myocardial infarction and ischemic stroke while obese females showed marked increased risk.[26]

One of the main goals of this study was to counter the widespread belief that cardiometabolic disorders can be detected only in older ages. Results of this study proved that these disorders may be detected at early age especially in individuals with higher risk and combined risk factors such as obesity, family history, and sedentary lifestyle. This means that urbanization and western lifestyle with high fat diet full of industrial food along with lack of physical activity and regular exercise as well as elevated levels of stress, altogether may cause an acceleration in cardiometabolic risk development among young adults. Indeed, more research is currently focusing on identifying biological, socioeconomical and environmental factors

contributing to obesity development in young adults. [27, 28]

This knowledge opens the door for stakeholders to come up with preventative actions for fatal cardiometabolic disorders and here are some suggestions; for example, governments should raise the awareness about the importance of overall healthy lifestyles for all people and especially for younger ages. Reliable health and dietary information and statistics should be provided and updated regularly by health authorities and other concerned authorities. Also, governments must impose strict control over the food spread in the markets and its ingredients that may be an underling cause of the development of obesity and related disorders. Accessible health care facilities with dietary consultants should be available for all society segments. As applied by some countries, free places equipped for exercise should be available to encourage people to exercise regularly. Healthcare professionals should update their protocols especially with young obese adults, regular check of SBP, DBP, fasting glucose, HOMA-IR and lipid panel should be conducted at earlier ages, as early detection provides easier, more effective, and less expensive solutions. Finally, the general population should be aware of this risk, especially young adults, they should conduct serious changes to their lifestyle to reduce the elevated risk of cardiometabolic disease development.

This study also confirmed the previous knowledge about the correlation between IR (in terms of HOMA-IR) and other cardiometabolic risk factors such as SBP, DBP, total cholesterol and TGs.[29-31] Participants with IR had a significant higher number of cardiovascular risk factors, in other words, people with IR regardless of their weight status, are at high risk to develop hypertension, dyslipidemia and their correlated cardiometabolic disorders.

One of the remarkable findings of this study is that HDL levels among participants, as 56.4% of them were at risk (40 – 60 mg/dl), and only 17.1% had optimal HDL levels, which indicates an increased risk to develop CVD even among young ages, this decrease in HDL levels may be because of genetic factors, smoking, bad diet, and lack of exercise. However, serious lifestyle changes should be implemented to overcome this risk.

Homocysteine levels were within normal levels for all participants and no significant correlation between homocysteine and cardiovascular risk factors was noted as well. However, conflicting results from research were noticed regarding the correlation between homocysteine and CVDs, as it was suggested to be a marker rather than a cause of CVDs. Several factors may affect hyperhomocysteinemia prevalence among certain population including age, genetics, nutritional status, lifestyle, and environmental factors.[32] A population based cross sectional study performed in China revealed a significant effect of age, BMI, smoking and vegetable consumption on homocysteine levels.[33] Young age of our participants, folic acid fortified food and vegetable consumption may be causes of normal homocysteine levels among all participants.

Together, this study demonstrated the association between obesity among young adults and increased cardiovascular risk and IR compared to subjects with healthy body weight. Therefore, obesity should be considered as a risk factor for cardiometabolic disorders during young adulthood. The study also found an association between IR in terms of (HOMA-IR values) and increased cardiovascular risk including increased SBP, DBP, fasting glucose, total cholesterol, LDL, and TGs, and decreased HDL.

This study has some strengths including its case-control design comparing two groups of obese and healthy weight. Moreover, the selected sample size was adequate to find significant differences in cardiometabolic biomarkers between the study groups. As well, this study and up to the best of our knowledge is the first study that investigated the relationship between obesity and cardiovascular risk biomarkers in Jordan in young healthy adults. Despite these strengths, the study also has some limitations. Overweight individuals were not included because of fund limitations. Collecting information about lifestyle and family history

may affect the certainty of data obtained. Even though, we still believe that the results of this study are valid and further investigations regarding obesity and cardiometabolic risk factors among young adults should be conducted.

CONCLUSIONS

This study showed that obese participants exhibited higher blood pressure, fasting glucose, lipids, and IR compared to healthy body weight participants. IR was correlated with increased blood pressure and lipids. Participants with IR had higher BMI, SBP, DBP, cholesterol, LDL, and TGs compared to participants with normal insulin sensitivity. Increased SBP, TGs, insulin and HOMA-IR were associated with obesity. Therefore, obesity was associated with increased cardiovascular risk and increased prevalence of IR in young adults. Results suggest that obesity should be considered as a predisposing factor to cardiovascular risk and IR. Further studies should be conducted with larger sample size to detect cardiometabolic risk factors among young adults. In addition to observational clinical studies, further studies of genetic factors behind the presented correlations, as well as metabolomic studies should be conducted to find early markers able to detect cardiometabolic risk at younger age.

Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

MATERIALS AND METHODS

Study design and participants

This was a cross-sectional study that involved apparently healthy 70 obese and 70 matched adults with healthy body weight. The sample was recruited by convenience between Nov 2022 and April 2023 by advertising the study at Jordan University of Science and Technology and King Abdullah University Hospital, Irbid, Jordan. Thus, our sample was recruited from the university students, university employees, hospital employees and visitors of the hospital. Matching between controls and cases was done according to age and sex. A control was chosen and recruited each time a case was recruited. Eligible subjects were approached and informed about the study objectives. Ethical approval was obtained from the International Review Board (IRB) of Jordan University of Science and Technology (JUST, approval No.: 2022/584). The study was conducted in accordance with the World Medical Association Declaration of Helsinki and the ICH Good Clinical Practice guidelines. All subjects who agreed to participate in the study provided written informed consents. Eligibility criteria included apparently healthy young male and female adults aged from 20 to 35 years. For control group, participants' body mass index (BMI) values were between 18.5 and 25.0 Kg/m^2 (healthy weight) and for obese group, BMI values were equal to or more than 30 Kg/m^2. All participants declared that they do not have any acute or chronic illness at the time of participation. Exclusion criteria included pregnant females, patients with malignancies, chronic kidney, heart or liver diseases, patients who received medications for dyslipidemia, diabetes, or hypertension, as well as participants who received medications that affect glucose and insulin levels such as metformin or other hypoglycemic agents.

Sample size calculations

The sample size of cases and controls was calculated using the Power and Sample Size Calculation software version 3.0.34 (Vanderbilt Biostatistics, Vanderbilt University Medical Center, Nashville, USA) based on the previously reported prevalence of obesity among young adults (28.64%) [35] and assuming confidence level of 0.95, odds ratio of 5, expected proportion in controls 0.05, and power of 0.80. Accordingly, a sample size of 67 obese and 67 lean subjects was enough to find significant statistical differences between the two groups. However, we recruited 70 obese and 70 lean subjects to participate in this study.

Data collection and blood sampling

Information about age, gender, smoking, marital status, education, employment, number of family members,

average family income, physical activity, and medical history were collected by self-reporting. Participant weight in kilograms (kg) and height in meters (m) were in order to calculate BMI using the formula (BMI = weight (Kg) / [height (m)]²).[34] Systolic (SBP) and diastolic (DBP) blood pressures were measured using digital sphygmomanometer. After that 10ml of fasting venous blood samples were collected in plain tubes and serum was separated and stored at -20°C for further processing.

Biochemical analyses

All serum samples were tested for insulin and homocysteine using commercially available ELISA kits (Fine Test®, China), tests were performed according to the manufacturer's procedures, optical density (O.D.) absorbance was measured at 450nm using Diatek® microplate reader (Wuxi City, Jiangsu Province, China). All Samples and standards were run in duplicates.

Serum glucose was determined using the commercially available kit from (Bio Research®). Serum Cholesterol, TGs, and HDL were also determined using the commercially available kits from (BioMed®, Hannover, Germany. Absorbance was measured using semi-automated clinical chemistry analyzer (MISPAVIVA® by AGAPPE, Switzerland). All Samples were run in duplicates.

LDL levels were determined using the Friedewald equation [LDL Cholesterol (mg/dl) = Total Cholesterol-(Triglycerides/5) - HDL Cholesterol].[35]

Insulin resistance homeostasis model assessment (HOMA-IR) was calculated from fasting serum insulin and glucose levels using the formula [HOMA-IR = fasting insulin (mIU/mL)*fasting glucose (mg/dl)/405] to estimate IR.[36] Participants with HOMA-IR levels more than 1.9 were considered as having early IR.[37]

Statistical analyses

Statistical analyses were conducted using the IBM SPSS statistics software version 25 (Armonk,NY, USA). Statistical significance was determined at $p < 0.05$. Normality was tested first by the Shapiro-Wilk test, eye inspection of the Q-Q plot, and histogram with normal curves. Continuous variables were reported as average± standard deviation (SD) or median (25^{th}-75^{th} percentiles) as appropriate. Categorical variables were presented with frequency and percentage. The relationship between continuous variables were examined using the Pearson's or Spearman's correlation test as appropriate. Differences in categorical and continuous variables between obese participants and participants with healthy body weight were determined using Student's t-test, Mann-Whitney U-test, or Chi square test as appropriate. Differences in categorical and continuous variables between participants with HOMA-IR ≤ 1.9 and participants with HOMA-IR > 1.9 were determined using Student's t-test, Mann-Whitney U-test, or Chi square test as appropriate. Multiple linear regression analyses were used to identify predictors of cardiovascular risk parameters. Binary logistic regression analysis was used to identify predictors of HOMA-IR.

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Not applicable.

Conflict of interest

The authors declare that they have no conflict of interest.

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ارتباط السمنة بزيادة خطر الإصابة بأمراض القلب وارتفاع معدل مقاومة الإنسولين بين البالغين الشباب الأصحاء ظاهريًا

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ملخص

الهدف: دراسة العلاقة بين السمنة وعوامل خطر الأمراض القلبية والأيضية ومقاومة الأنسلين لدى البالغين الشباب الأصحاء.

الطرق: شملت هذه الدراسة المقطعية 70 بالغًا بدينًا و70 بالغًا متناسبين للعمر والجنس بوزن جسم طبيعي. تم قياس الجلوكوز في المصل، والأنسولين، والدهون، والهوموسيستئين. تم تحديد مقاومة الأنسلين باستخدام تقييم نموذج الاستقرار الذاتي.(HOMA-IR) IR- كم تم قياس ضغط الدم الانقباضي والانبساطي .

النتائج: أظهر المشاركون البالغون البدناء زيادة في قراءات ضغط الدم ومستويات الجلوكوز والتريغليسيريدات والكوليسترول واللیبوبروتين ذي الكثافة المنخفضة (LDL) والأنسولين وHOMA-IR ، وانخفاض في الليبوبروتين ذي الكثافة العالية (HDL) مقارنة بالمشاركين ذوي الوزن الطبيعي. كما كان مؤشر كتلة الجسم (BMI) مرتبطًا طردياً بـ قراءات ضغط الدم والجلوكوز والأنسولين و HOMA-IR والكوليسترول والتريغليسريدات، وكان ارتباطاً عكسياً بالكولستيرول ذو الكثافة العالية. إضافة لذلك، كان HOMA-IR مرتبطًا طردياً بقراءات الضغط والتريغليسيريدات والكولستيرول ذو الكثافة المنخفضة، وارتباطاً عكسياً بالكوليسترول ذو الكثافة العالية. كان لدى المشاركين الذين يعانون من مقاومة الانسلين قيم أعلى لمؤشر كتلة الجسم وضغط الدم والتريغليسيريدات والكولستيرول ذو الكثافة المنخفضة مقارنة بالمشاركين ذوي الحساسية الطبيعية للأنسولين. كانت السمنة مرتبطة بزيادة قراءات ضغط الدم الإنقباضي والتريغليسريدات ومستويات الأنسولين ومقاومة الأنسولين. لم يكن هناك فرق كبير في الهوموسيستئين بين المجموعات.

الاستنتاج: السمنة مرتبطة بزيادة خطر الأمراض القلبية وزيادة انتشارمقاومة الانسولين بين البالغين الشباب الأصحاء. يتطلب ذلك القيام بالتدخلات الدوائية والسلوكية بشكل عاجل لمعالجة زيادة مخاطر الأمراض القلبية في هذه الفئة العمرية.

الكلمات الدالة: السمنة؛ البالغون الشباب؛ خطر الإصابة بأمراض القلب؛ مقاومة الإنسولين.

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