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Full Length Research Paper

Anthropometric measures as predictors for the occurrence of insulin resistance among obese Jordanians

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A total of 210 overweight and obese participants were recruited to investigate the association between various obesity parameters with insulin resistance (IR) in Jordanians. Weight, height, waist circumference (WC) and hip circumference were measured, and the corresponding body mass index (BMI), waist to hip ratio (WHR), and waist to height ratio (WHtR) were calculated. HOMA-IR was calculated from the corresponding fasting blood sugar and plasma insulin levels for each participant. The correlation as well as the prediction ability of obesity parameters for the occurrence of insulin resistance was evaluated statistically. Pearson and point-biserial correlation coefficients revealed that only BMI, WC and WHtR correlated with insulin resistance. However, the strength of correlation appeared to be gender-dependent. Logistic regression and ROC curve analysis showed that BMI is the best parameter to predict insulin resistance in the male population followed by WHtR. In females however, WHtR appeared to be a better classifier than BMI. In conclusion, BMI and WHtR were found to be the most significant obesity parameters for predicting insulin resistance in Jordanians male and female populations, respectively.

Key words: Obesity, body mass index, waist circumference, waist to height ratio, insulin resistance.

INTRODUCTION

Insulin resistance is a pathophysiological condition characterized by an impaired response to the presence of insulin. The exact mechanism behind the development of this condition is complex and not well understood. Several factors have been thought to play a major role in the development of insulin resistance. At the top of the list is obesity-associated exposure of tissues to elevated dietary nutrients and the resultant accumulation of toxic metabolic by-products (Kahn et al., 2006; Muoio and Newgard, 2008). The high association between obesity and insulin resistance was recognized among both males and females, and it appeared across all ethnic groups (Khan and Flier, 2000).

On the other hand, obesity is considered as an independent risk factor to type 2 diabetes mellitus (T2DM) (Carey et al., 1997; Chan et al., 1994). This association depends basically on the aforementioned link between obesity and the risk of developing insulin resistance. Insulin resistance was found to be a reputable finding among obese patient with T2DM, and considered by some authors to be the basic etiology for T2DM as most of T2DM patients shows this resistance (Reaven, 1988; Taylor, 1999; Wellen and Hotamisligil, 2005). Accordingly, obesity and insulin resistance could be used

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Abbreviations: BMI, Body mass index; **HOMA,** homeostatic model assessment; **IR,** insulin resistance; **ROC,** receiver-operating characteristic; **T2DM,** type 2 diabetes mellitus; **WC,** waist circumference; **WHR,** waist to hip ratio; **WHtR,** waist to height ratio.

Table 1. Baseline characteristics of study participants.

Characteristic	Men	Women	All participants
Participants (n)	91	119	210
Age (years)	32.82 ± 11.99	33.53 ± 11.79	33.22 ± 11.86
Weight (kg)	103.30 ± 23.69	81.03 ± 14.76	90.68 ± 22.07
Height (m)	1.73 ± 0.07	1.60 ± 0.05	1.66 ± 0.09
BMI (kg/m^2)	34.51 ± 6.7	31.55 ± 5.51	32.83 ± 6.22
WC (cm)	108.09 ± 14.73	97.66 ± 10.39	102.18 ± 13.46
WHR (kg/m)	0.92 ± 0.05	0.90 ± 0.06	0.91 ± 0.06
WHtR (kg/m)	0.63 ± 0.08	0.61 ± 0.08	0.62 ± 0.07
Fasting blood glucose level (mg/dl)	90.56 ± 11.00	88.45 ± 10.76	89.37 ± 10.89
Insulin level (mU/L)	14.11 ± 9.53	10.46 ± 6.50	12.04 ± 8.14
Insulin resistance	3.23 ± 2.43	2.32 ± 1.52	2.72 ± 2.02

used as strong predictors for the development of T2DM.

Investigation of obesity and fat accumulation as a risk factor for chronic diseases relies on obesity parameters and measurable indicators such as body mass index (BMI), waist circumference (WC), waist to hip ratio (WHR) and waist to height ratio (WHtR). Considerable attention has been given to the BMI as a universal measurable indicator of overall obesity. On the other hand, WC was found to be directly associated with the increase of the risk of insulin resistance as well as cardiovascular diseases and mortality (Koike et al., 2009; Schneider et al., 2007; 2010). The remaining two parameters, WHR and WHtR, were less investigated as compared to BMI or WC. Nevertheless, all parameters appear to increase the incidence of insulin resistance, and they are considered independent risk factors for T2DM (Kawada et al., 2010). However, the parameter that has the most predictive power of insulin resistance as well as other obesity-related health problems is not known. Apparently, the most predictive parameter is still a matter under dispute. In addition to this, many authors found that the different parameters are equally predictive with no significant difference between them (Janghorbania and Amini, 2010; Qiao and Nyamdorj, 2010; Sargeant et al., 2001; Stevens et al., 2001).

Worldwide, most researchers focused on investigating the association between obesity parameters and the incidence of T2DM as well as cardiovascular diseases (Carey et al., 1997; Schneider et al., 2007, 2010; Stevens et al., 2001). Few attempted to specifically characterize the association of these parameters with the increased risk of developing insulin resistance. To our knowledge, none has reported on the association between obesity parameters and insulin resistance in the Arab world although the prevalence of T2DM and the metabolic syndrome is high and increasing in Jordan and other Arab countries (Ajlouni et al., 2008; Khader et al., 2007). Moreover, the environmental and dietary factors which are major risk factor for diabetes-obesity end point related disease are different between Western and Arab societies. Therefore, the current work was undertaken to investigate the association between obesity parameters and insulin resistance in Jordanians as a representative Arabic community. The correlation and the ability to predict insulin resistance of BMI, WC, WHR and WHtR as reliable and measurable anthropometric obesity parameters were explored. We hope that the findings of this work will shed light on the obesity-diabetes dogma as a major public health problem and establish a simple, yet robust obesity parameter that can be used to predict and monitor obesity-related diseases in Arabic communities.

MATERIALS AND METHODS

Study subjects

This study was conducted in the Faculty of Science, Yarmouk University, Irbid, Jordan, during the period of March to September 2010. A total of 210 overweight and obese individuals were recruited for this study in order to test the relationship between insulin resistance and various obesity indicators. Participants were considered to be overweight if they have a BMI ≥ 25 and obese if their BMI was ≥ 30, according to the WHO definition of obesity and overweight. In this study group, 43% were males and 57% were females aged from 18 to 50 years and 52% of them were married. The base line characteristics of the study participants are shown in Table 1. The study was approved by the ethical and research committee of Yarmouk University and informed written consents were obtained from all participants. Medical history was taken from all individuals recruited in this study to rule out any possibility of chronic diseases. Patients who were previously diagnosed of diabetes or individuals whose fasting blood sugar was above 120 mg/dl were excluded, and they were not part of the study.

Measurements

For anthropometric measurements, participants stood and dressed in light clothing without shoes. Body weight were measured with a calibrated balance beam scale to the nearest 0.5 kg, and height with a vertical ruler to the nearest 0.5 cm. Waist and hip circumference was measured in accordance with WHO standards with a tape to the nearest 0.5 cm. WC was measured midway between lower rib margin and the iliac crest in the horizontal plane.

Table 2. The Pearson and point-biserial correlation coefficients between various anthropometric measurements and insulin resistance.

Measurement	Men		Women		All participants	
	Pearson R^2	Point-biserial R^2	Pearson R^2	Point-biserial R^2	Pearson R^2	Point-biserial R^2
BMI	0.320**	0.238*	0.228*	0.349**	0.318**	0.325**
WC	0.359**	0.181	0.173	0.329*	0.347**	0.303**
WHR	0.133	-0.155	-0.51	0.100	0.075	-0.059
WHtR	0.307**	0.185	0.221*	0.370**	0.286**	0.301**

**Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed).

Hip circumference was measured at the point yielding the maximum circumference over the buttocks.

All participants fasted for 10 to 12 h before blood sample were collected into vacuum tubes containing no preservative. Serum was separated by centrifugation at 4℃ within 1 h. Fasting blood glucose was directly measured by the hexokinase method, and the rest of the serum was stored in freezer at -20℃ for insulin level determination as well as any possible extra laboratory analysis. Fasting insulin level was measured by Enzyme Linked Immuno Sorbant Assay (ELISA) according the kit instructions provided by the supplier using standard laboratory procedures. The insulin resistance was quantified using the Homeostatic Model Assessment (HOMA) as glucose (mg/dl) × insulin (mU/L)/405 (Matthews et al., 1985). A cutoff value of 1.4 to indicate if the participant is insulin resistant or not, was used based on the common practice of endocrinologists in Jordan (Dr. Nadima Shuqom, internal medicine and endocrinologist, personal communication).

Statistical analysis

The relationship between the various obesity parameters with the HOMA insulin-resistance was systematically studied using standard statistical tests. The analysis was performed with SPSS 17 (Statistical Package for social sciences). The correlation between obesity parameters and insulin resistance was evaluated by calculating the Pearson and point-biserial correlation coefficients. The insulin-resistance predicting power of these obesity parameters was evaluated by logistic regression and three models for male participants, female participants, as well as all participants were obtained. Finally, a receiver-operating characteristic (ROC) curve analysis was used to examine the discriminatory power of the various obesity parameters. The sensitivity (true positive) and specificity (true negative) for all possible cutoff points for each parameter were simultaneously measured by performing ROC curve analysis. The ROC curves were constructed by plotting sensitivity against 1–specificity for each obesity parameters. The areas under the curve (AUCs) for each ROC curve were calculated to assess the overall performance of each anthropometric test for detecting insulin resistance.

RESULTS

The current work involved 210 overweight and obese individuals whose base line characteristics are summarized in Table 1. In this sample group, the relationship between four obesity parameters, namely BMI, WC, WHR and WHtR, with insulin resistance was evaluated. Table 2 shows the correlation between the obesity anthropometric parameters and the dependent variable under the study, the insulin resistance. The results revealed a positive correlation between BMI, WC and WHtR and the dependent variable under evaluation when the analysis was conducted for all the participants regardless of the gender. When Pearson correlation coefficient was calculated, WC was found to be more correlated with insulin resistance than BMI and WHtR. The fourth parameter on the other hand, WHR, appears to be poorly correlated with insulin resistance for that same group. However, the dependent variable in this work is dichotomous, i.e., it is categorical with only two categories as the participant is either insulin resistant or not. HOMA insulin resistance was categorized such as those values less than 1.4 indicate no insulin resistance and ≥ 1.4 indicate insulin resistance. Therefore, the relationship between the obesity parameters and insulin resistance is better investigated using the point-biserial correlation coefficient. When this correlation coefficient was calculated, BMI was the parameter that was most correlated with insulin resistance in the all participants group.

To assess the effect of the gender, the same evaluation was carried out for male and female participants separately. Strikingly, different results were obtained than those discussed before when the correlation was investigated for all the participants. In the male population, only BMI appears to be significantly correlated with insulin resistance as indicated by the point-biserial correlation coefficients calculation. Surprisingly, the other obesity parameters were poorly correlated in spite of the significant correlation shown by the Pearson correlation coefficients for these parameters when insulin resistance is treated as a continuous variable than a discrete dichotomy. Analysis of the female population on the other hand shows BMI and WHtR to be the parameters that are most correlated with insulin resistance. However, the WHtR parameter correlated better with insulin resistance than BMI as indicated by the point-biserial correlation coefficients of these two parameters shown in Table 2.

Logistic regression was also applied to find the factors (age and gender) and obesity parameters that significantly predict the incidence of insulin resistance among the various populations in the study. To start with, logistic regression for all participants was performed in

Table 3. Logistic regression analysis of insulin resistance as a function of the various obesity parameters.

Participant	Predictor	B	SE	Significance	e^B	95% CI for e^B
Men	BMI	0.179	0.064	0.005	1.196	1.056 - 1.355
	Constant	- 3.962	1.955	0.043	0.019	NA
Women	WHtR	0.154	0.041	0.000	1.167	1.078 - 1.263
	Constant	- 8.635	2.405	0.000	0.000	NA
All participant	BMI	0.138	0.062	0.027	1.148	1.016 - 1.296
	WHtR	0.209	0.089	0.019	1.232	1.035 - 1.467
	Gender	1.604	0.531	0.003	4.972	1.757 - 14.064
	Constant	- 7.081	1.920	0.000	0.001	NA

Nagelkerke R^2, Hosmer and Lemeshow χ^2 were 0.195 and 8.007, 0.203 and 5.475, 0.276 and 12.828, for male, female and all participants' models, respectively.

the backward stepwise method for insulin resistance as a function of age, gender, BMI, WC and WHtR. A significant model was obtained in which BMI, WHtR and gender were significant variables in the model (Table 3). The odd ratios (e^B) suggest that gender, as a categorical variable, has a profound effect on the model. To assess that effect, logistic regression models for individual male and female populations were constructed, and again significant models could be obtained. For the male population, BMI remained as the most significant obesity parameter for developing insulin resistance; while on the other hand, WHtR appears to be the most significant predictor in the female population.

Similar to logistic regression, the ROC curve analysis is an excellent diagnostic tool that is commonly used to establish the usefulness of particular obesity parameters for distinguishing populations with particular diseases or metabolic syndrome. The ability of the parameters to predict the response in question is classified according to the magnitude of the area under the ROC curve. The area under the ROC curve should usually range from 0.5 to 1.0 with larger values being indicative of better fit. ROC curves illustrating the performance of each obesity parameter as explained in the method section are presented in Figure 1. The calculated areas under the ROC curves (AUCs) and their 95% confidence intervals are summarized in Table 4.

In agreement with the analysis of the point-biserial correlation coefficient as well as the logistic regression for the male population, the ROC curves of BMI had the largest AUC and thus, it appears to be the most predictive obesity parameters for the development of insulin resistance in men. In the female population on the other hand, equal AUCs for BMI and WHtR were obtained indicating comparable predictive capabilities of these two parameters for the development of insulin resistance. It is worth mentioning that, in theory, no realistic classifier should have an AUC less than 0.5. Otherwise, the performance of this classifier would be worse than random guessing represented by the diagonal line between points (0,0) and (1,1) in Figure 1. The performance of the obesity parameter WHR was an example of such behavior. Clearly, WHR offers no information about the possibility of developing insulin resistance. On the contrary, this parameter may be said to predict insulin resistance incorrectly and in a reverse manner where the larger the WHR and the more obese the person is the less likely he or she might develop insulin resistance. Lastly, the ROC curve analysis for the all participant group revealed a similar pattern to that obtained by logistic regression modeling. Specifically, both parameters, BMI and WHtR are excellent classifiers with a slight superior predicting ability for BMI (AUC = 0.73) over WHtR (AUC = 0.72).

DISCUSSION

Insulin resistance gained more attention recently as researchers tried to understand the pathogenesis mechanisms of T2DM and metabolic syndrome from the insulin-resistance point view. Insulin resistance together with beta cell dysfunction leads to the appearance and gradual progression of type 2 diabetes. Accordingly, insulin resistance can be targeted to reduce the risk of diabetes and many other chronic diseases. However, HOMA insulin resistance as calculated parameter depends on two laboratory tests, fasting blood glucose and serum insulin level, which are costly and time consuming. In contrast, obesity parameters are simple and associated with fewer measurement errors and could be used as precious markers and exemplary indicators for the occurrence of insulin resistance.

Therefore, clinicians are encouraged to target obesity as a manageable health problem to prevent or delay the onset of diabetes through lifestyle intervention approaches such as weight reduction and increasing physical activity (National Institutes of Health, 2000; Qiao and

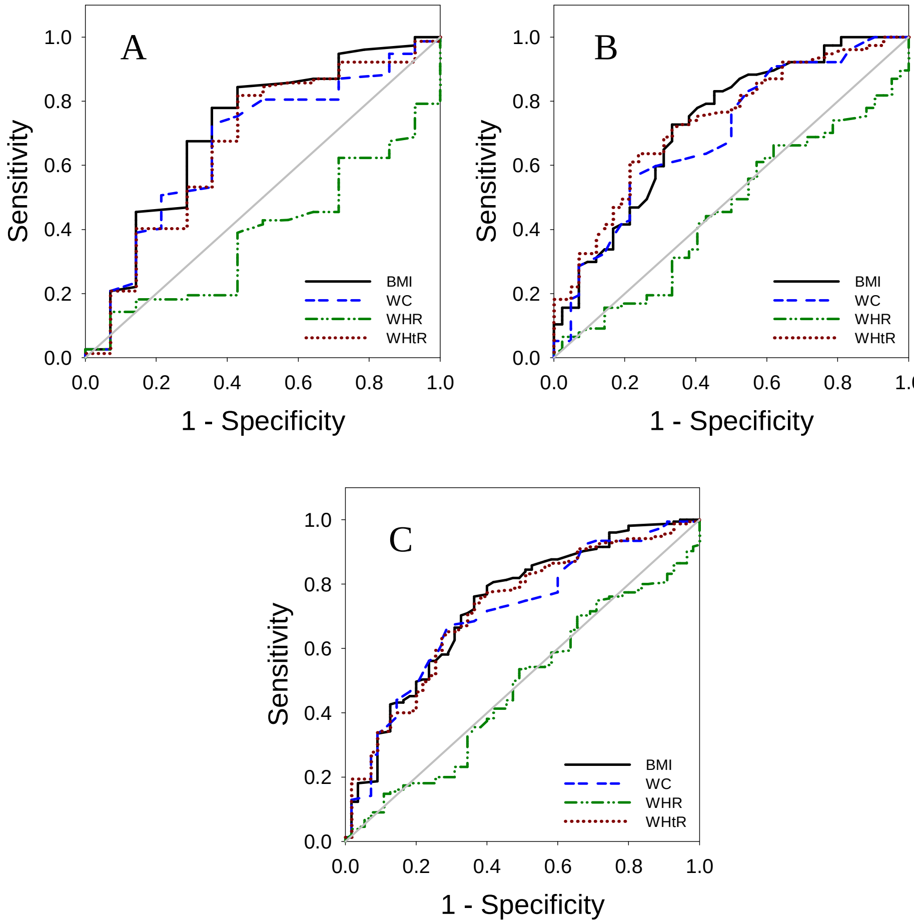

Figure 1. Receiver operating characteristic (ROC) curves to predict insulin resistance from various anthropometric measurements in (A) men, (B) women and (C) all participants.

Table 4. Areas under the receiver operating characteristic curves to predict insulin resistance from various obesity parameters.

Measurement	Men		Women		All participants	
	AUC (95% CI)	Significance	AUC (95% CI)	Significance	AUC (95% CI)	Significance
BMI	0.71 (0.55 – 0.87)	0.013	0.73 (0.63 – 0.83)	0.000	0.73 (0.65 – 0.81)	0.000
WC	0.67 (0.51 – 0.82)	0.051	0.70 (0.60 - 0.80)	0.000	0.71 (0.63 – 0.79)	0.000
WHR	0.38 (0.24 – 0.52)	0.167	0.46 (0.35 – 0.57)	0.446	0.48 (0.39 – 0.56)	0.599
WHtR	0.67 (0.51 -0. 84)	0.044	0.73 (0.64 – 0.83)	0.000	0.72 (0.64 – 0.80)	0.000

and Nyamdorj, 2010; Zimmeta et al., 2011). As mentioned previously, continuous findings for the indicative strength of various obesity parameters left clinicians nearly confused on which obesity parameter should be considered. In the Arabic and Middle Eastern societies, the situation is even vaguer as the association and the predictability of obesity parameters to the risk of insulin resistance has never been investigated.

This work presents a cross-sectional study that investigated the association between obesity parameters, namely BMI, WC, WHR and WHtR, with insulin resistance in eastern Arab society. Most of the previous studies on obesity and insulin resistance were taken in the western societies and Japan. However, dietary patterns and individual's lifestyle for eastern Arab society are different from those of the aforementioned societies. These factors directly affect the weight status and fat distribution demonstrated by the various obesity parameters. Therefore, the aim of this study was to delineate the relationship between obesity parameters with insulin resistance in Jordanian society. To this end, 210 overweight and obese individuals were recruited, and their anthropometric measurements were taken. The participant's glucose and insulin levels were measured, and the subsequent insulin resistance was calculated. The obesity parameters were statistically investigated and modeled to identify which parameter is better related to insulin resistance and thus, should be used as a predictor for the development of T2DM.

The current data suggests that BMI and WHtR are more significantly associated and correlated with the development of insulin resistance in Jordanians than WC or WHR. Estimation of correlation coefficients, logistic regression and ROC curve analysis were applied to assess the relationship between these obesity parameters and the occurrence of insulin resistance. BMI, WC and WHtR were positively correlated with insulin resistance as indicated by Pearson as well as point-biserial correlation coefficients calculated for the whole population under study. Nevertheless, when the latter correlation coefficient was calculated for the individual male and female populations, the strength of these markers appeared to be gender-dependent. While BMI was the only significantly correlated parameter with insulin resistance in males, WHtR and to a less degree BMI were the most correlated parameters with insulin resistance in females. These findings were further investigated by modeling insulin resistance as a function of age, gender, BMI, WC and WHtR using logistic regression. In agreement with correlation calculation, gender was found to have significant effect on the incidence of insulin resistance when this dependent variable was modeled in all participants. Moreover, BMI and WHtR were found to be the most significant parameters for predicting insulin resistance in the male and female populations, respectively. The goodness of fit as well as the outcome of the three logistic regression models obtained were evaluated and validated by performing ROC curve analysis. The calculated AUCs agree with the findings discussed above regarding BMI being the best obesity parameters to predict the occurrence of insulin resistance in men. In women however, both WHtR and BMI resulted in similar AUCs and thus, they are predicted to have equal classifier performance by this statistical tool.

The gender-specific behavior obtained is expected due to the vast differences in body composition between men and women. However, the combined population was always subjected to analysis in this work. This was in an attempt to explore the possibility of establishing a universal obesity parameter that has the strongest correlation and the prediction ability of insulin resistance in both genders. Apparently, this quest was not satisfactorily successful as different parameters were consistently associated with each gender.

It is also worth mentioning that our conclusions are restricted to the inability to include certain confounding factors that could affect the dependent variable under study. Such factors include individual variations in the lifestyle pattern and the nutritional habits of our participants. Limitations of resources and many social barriers are the main reasons that restricted our conclusions to include and study these factors. In conclusion, the current findings suggest that BMI and WHtR are better indicative markers for insulin resistance than other obesity parameters such as WC or WHR. Therefore, BMI in men and WHtR in women are promoted to be used as obesity parameters for many risk conditions related to insulin resistance. Moreover, clinicians in eastern Arab societies are encouraged to use them to monitor obese and diabetic patients' response to body weight reduction treatments.

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