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Original Article

Risk stratification among metabolically unhealthy obese in independent physically inactive aged women

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ABSTRACT

Objectives: To determine whether or not adiponectin levels or basal metabolic rate (BMR) could predict worse risk stratification in patients with insulin resistance (IR) among metabolically healthy and unhealthy obese (MUHO) elderly females with Metabolic syndrome (MetS).
Methods: A cross-sectional survey was conducted on 109 elderly females in geriatric nursing home with MetS. The participants were reclassified according to adiponectin levels and IR.
Results: Group (1) (with IR, n = 41) compared to group (2) (without IR, n = 45) had lower squared adiponectin level and higher fat mass and fat percent (p value = 0.037, 0.030, and 0.035 respectively). Quadratic adiponectin level was an independent predictor for better BMR in group (2) with higher R^2 compared to linear adiponectin level (R^2 = 0.19, 0.15 consecutively, p value = 0.02, 0.008 consecutively) in group (2) rather than group (1). This revealed U-shaped relation between adiponectin level and BMR in group (2). By ROC curve, fat and lean percentages were statically significant predictors of IR between groups (1) and (2) (AUC = 0.643, 0.636; p value = 0.024, 0.032 Sensitivity = 89.2%, 72.97%; and Specificity = 55.1%, 24.48% respectively).
Conclusion: Current findings supported the possibility of risk stratification among MUHO individuals based on IR, squared adiponectin level, lean and fat percentages.

1. Introduction

The emergent of the global epidemics of severe obesity and diabetes with aging of the world's population appears as one of the major challenges to the public health worldwide especially in women [1].

However, there are individuals with long-standing obesity and even morbid obesity who can be considered healthy despite their obesity, and these subjects were referred to as metabolically healthy obese (MHO) [2]. Several definitions are used to account for MHO and most authors define MHO using measures of metabolic syndrome (MetS) and/or insulin resistance (IR) statuses [3].

Some recent researches decided to study risk differences in MHO and metabolically unhealthy obese (MUHO) in addition to discussing the potential role of adiponectin, anthropometrics and basal metabolic rate (BMR) [4].

So, the aim of this cross-sectional study was to determine whether or not adiponectin levels, anthropometrics, body composition or BMR could help better risk stratification, owing to the presence of IR, among metabolically unhealthy obese and overweight (MUHO/OW) individuals with MetS.

2. Methods

2.1. Setting of the study

A cross-sectional survey was conducted in geriatric nursing homes under Ministry of Social Affairs in Cairo, Egypt. Eight geriatric nursing homes for independent females were selected randomly from the list of total 152.

Assuming the frequency of insulin resistance rates in adults with obesity from 30 to 45%, the sample size was calculated to be 38–74 at 95% confidence interval, type 1 error 0.05 and 0.80 power of the test. It was decided to increase the size of the sample to overcome the non response.

Inclusion criteria were females, old age ≥60 yrs, overweight or obesity with BMI ≥25, physically inactive and had positive criteria for metabolic unhealthy obese [4]. None of them were taking any hormonal medications (including hormone replacement therapy,

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glucocorticoid therapy), or had thyroid diseases, Cushing's disease, or cancer. Females who were currently smoking, had fever, acute or chronic infections, refused to participate or participants with missing data were also excluded.

The study included 109 elderly female participants. Twenty three of them were excluded because either physically active (n = 9), refused to participate (n = 4) or were MHO (n = 10). Therefore, of the total sample, only 86 participants completed the study.

2.2. Data collection

Data collection regarding socio-demographics, medical history, physical activity and clinical examination, including anthropometric measures were done through an anonymous interviewer-based questionnaire. Physical activity was assessed using Rapid Assessment of Physical Activity (RAPA) questionnaire [5]. This tool was validated for older adults [6].

2.3. Anthropometric measurement

Height, weight, waist circumference (WC), hip circumference (HC), mid-thigh circumference, triceps skin fold, thigh skin fold, and abdominal fold were measured according to the instructions prescribed by Anthropometric Standardization Reference of National Health and Nutrition Examination Survey [7].

2.4. Bioelectrical impedance analysis (BIA)

Body composition was assessed by bioelectrical impedance analysis (InBody 520, Biospace, Inc., Cerritos, CA, USA), a well-established and validated technique for assessment of body composition. Measurements were performed according to the National Institutes of Health guidelines [8] and recommendation of the manufacturer. BIA is a non-invasive, inexpensive, rapid, portable, reproducible and safe technique that was widely used to assess BMR, fat mass, lean mass, and TBW in previous literatures, even in women with obesity [9].

2.5. Criteria for metabolically unhealthy obese and overweight (MUHO/OW)

All participants had positive criteria of MetS according to NCEP ATP III [10], then the participants were reclassified according to IR using the Quantitative Insulin-sensitivity Check Index (QUICKI) into two groups; Group (1) had IR (QUICKI < 0.32) [11] and group (2) had no IR and better insulin sensitivity (QUICKI ≥ 0.32).

Table 1
Participants' characteristics, body compositions, anthropometrics and laboratory analysis.

	Whole sample (n = 86)
Age	66.08 ± 9.37
Lean Percent	39.13 ± 10.14
Fat Percent	64.30 ± 11.78
Basal Metabolic Rate	1216.2 ± 156.96
Body Mass Index	35.91 ± 5.18
Waist Circumference (cm)	112.92 ± 10.53
Hip Circumference (cm)	119.72 ± 16.17
Mid-Thigh Circumference (cm)	55.76 ± 8.29
Abdominal Skin Fold (cm)	17.48 ± 7.73
Triceps Skin Fold (cm)	16.64 ± 12.75
Thigh Skin Fold (cm)	16.80 ± 8.02
Fasting Blood Sugar (mg/dl)	136.85 ± 68.78
Insulin (mIU/L)	17.16 ± 23.13
QUICKI	0.33 ± 0.06
Adiponectin (μg/mL)	25.68 ± 11.72
DM, n (%)	36 (41.9%)
Insulin Treatment, n (%)	11 (12.8%)
HTN, n (%)	49 (57.0%)

Table 2
Comparison between Group (1) with insulin resistance and Group (2) without insulin resistance.

	Group (1)(n = 41)		Group (2)(n = 45)		*P* value
Age	62.36	±8.21	69.46	±9.14	<0.001**
Systolic Blood Pressure (mmHg)	132.68	±15.85	132.33	±20.05	0.377
Diastolic Blood Pressure (mmHg)	78.78	±12.64	78.44	±15.14	0.911
Lean Amount (Kg)	32.14	±5.71	32.44	±8.28	0.838
Lean Percent	37.23	±7.16	40.87	±12.07	0.090
Fat Amount (Kg)	59.01	±14.27	51.64	±16.78	0.031*
Fat Percent	67.11	±8.60	61.76	±13.67	0.035*
Basal Metabolic Rate	1213.3	±129.63	1218.8	±179.73	0.871
Body Mass Index	36.81	±5.45	35.10	±4.86	0.130
Weight (Kg)	90.88	±14.90	84.47	±15.35	0.053
Waist Circumference (cm)	115.15	±11.13	110.89	±9.64	0.063
Hip Circumference (cm)	119.54	±20.78	119.89	±10.62	0.923
Mid-Thigh Circumference (cm)	56.41	±9.24	55.18	±7.40	0.503
Abdominal Skin Fold (cm)	16.71	±7.45	18.19	±8.01	0.929
Triceps Skin Fold (cm)	15.71	±8.86	17.80	±7.15	0.233
Thigh Skin Fold (cm)	15.71	±8.86	17.80	±7.15	0.228
Fasting Blood Sugar (mg/dl)	162.78	±75.30	113.22	±52.81	0.001**
Insulin (mIU/L)	30.62	±27.86	4.90	±2.40	<0.001**
QUICKI	0.29	±0.025	0.38	±0.04	<0.001**
Adiponectin (μg/mL)	23.48	±9.31	27.69	±13.34	0.096
Squared Adiponectin	635.84	±450.12	940.58	±815.64	0.037*
Cholesterol (mg/dl)	196.34	±39.02	201.11	±55.69	0.645
Triglycerides (mg/dl)	159.20	±67.22	148.62	±108.08	0.584
High Density Lipoprotein (mg/dl)	38.54	±4.36	38.33	±4.58	0.834
Low Density Lipoprotein (mg/dl)	135.44	±58.94	133.47	±54.81	0.873
DM, n (%)	20	(48.8%)	16	35.6%	0.21
Insulin Treatment, n (%)	7	(17.1%)	4	8.9%	0.26
HTN, n (%)	19	(46.3%)	30	66.7%	0.057

*, **P-values < 0.05 were regarded as a sign of statistical significance.

2.6. Laboratory analysis

A blood sample was collected after a fasting period for 12 h for fasting blood glucose (FBG) and lipid profile which were measured using standard laboratory methods. Insulin levels were assayed by chemiluminescence (ADVIA Centaur chemiluminescent immunoassay system; Siemens Healthcare, Deerfield, IN, USA). Serum adiponectin levels were measured by immunoassay (Millipore, Billerica, MA). Adiponectin measurements were performed in plasma samples stored at −70C.

2.7. Ethical statement

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and approved by the Institutional Ethical Committee of Ain Shams University Hospital. Informed consent was obtained from all participants.

2.8. Statistical analysis

Statistical analysis was carried out using SPSS software version 20.0 (Chicago, IL, USA). Independent t-test was used to compare between two quantitative data. Pearson correlation test was used to study linear correlation between quantitative variables. Curve estimation was used to study the linear and quadratic relation between adiponectin levels, owing to previous literatures' controversy about its beneficial level [12,13]. Squared adiponectin was used in correlation and curve estimation as an expression for the possible quadratic relation. Receiver operating characteristic (ROC) analyses were performed to evaluate the discriminatory performances of BMR, fat and lean percentages for differentiation between group (1) with IR and group (2) without IR.

3. Results

The study included 109 elderly female participants. However due to inclusion and exclusion criteria only 86 participants completed the study. Group (1) (who had positive criteria of both MetS and IR, n = 41) compared to group (2) (who had positive criteria of MetS without IR, n = 45) had lower age, squared adiponectin level and insulin sensitivity (p value < 0.001, 0.037, and 0.001 respectively). Both groups had no significant differences in all anthropometric measures except in fat mass and fat percent which were significantly lower in group (2), with better insulin sensitivity (p value = 0.030, and 0.035 respectively). (Tables 1 and 2).

Using Pearson correlation, adiponectin levels were correlated with BMR in the group (2) but not in group (1) (p value = 0.009, 0.802 respectively). (Data were not presented).

Quadratic adiponectin levels had higher R^2 than linear adiponectin levels in group (2) (R^2 = 0.19 and 0.15 consecutively, p value = 0.02, and 0.008 consecutively) with no significant relationship in group (1). This revealed U-shaped relation between adiponectin levels and BMR in group (2). In addition, using curve estimation revealed that quadratic adiponectin level had higher R^2 than linear adiponectin level for either fat or lean percent as dependent factors, with knots at18μg/ml and 40ug/ml respectively (Fig. 1).

By Pearson correlation, both adiponectin and squared adiponectin levels were only correlated with fat (%), lean (%) and BMR but not with other anthropometric measurement (Table 3).

The AUC, sensitivity, specificity of BMR, fat and lean percentages in prediction of IR between groups (1) and (2) were calculated. Only fat and lean percentages were statically significant by ROC curve (AUC = 0.643, 0.636; p value = 0.024, 0.032; Sensitivity = 89.2%, 72.97%; and Specificity = 55.1%, 24.48% respectively).

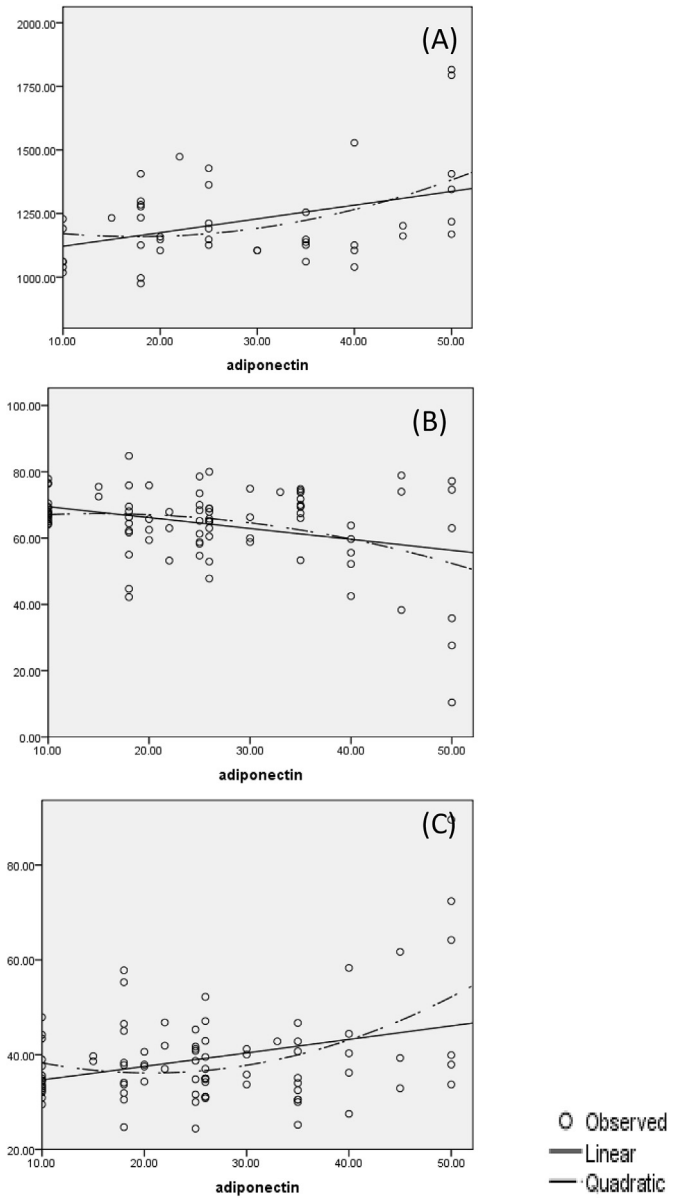

Fig. 1. Curve estimation to study quadratic vs linear relation between adiponectin level as an independent factor and BMR (A), Fat Percent (B) and Lean percent (C) as a dependent factor in group (2) with better insulin sensitivity.

4. Discussion

This study aimed to investigate the role of adiponectin level, anthropometrics, and BMR as independent predictors of superimposed IR among MUHO/OW in elderly females. To our knowledge, this is the first study aiming to stratify risk among MUHO/OW elderly females based on IR.

The significant difference between the two groups in squared adiponectin levels rather than adiponectin levels is emphasizing the importance of the U-shaped impact of adiponectin hormone on insulin sensitivity in MUHO elderly females.

Current results supported U-shaped benefit of adiponectin level, as a significant predictor of higher BMR, higher lean percent and lower fat percent in group (2) with better insulin sensitivity. BMR is the main indicator of body metabolism and any abnormalities in BMR have been associated with undesirable health problems [14].

Our finding indicates that adiponectin levels below 18 μg/ml

Table 3
Pearson correlation comparison between adiponectin and squared adiponectin levels.

		Adiponectin	Squared Adiponectin
Body Mass Index	r	−0.056	−0.064
	p value	0.611	0.556
Waist Circumference	r	−0.025	−0.043
	p value	0.823	0.692
Hip Circumference	r	0.121	0.086
	p value	0.268	0.429
Midthigh Circumference	r	−0.002	−0.024
	p value	0.987	0.825
Abdominal Skin Fold Thickness	r	−0.059	−0.095
	p value	0.588	0.382
Triceps Skin Fold Thickness	r	−0.079	−0.097
	p value	0.468*	0.373*
Thigh Skin Fold Thickness	r	0.045	0.005
	p value	0.678	0.962
Basal Metabolic Rate	r	0.276*	0.316**
	p value	0.010	0.003
Lean Mass (%)	r	0.329	0.383
	p value	0.002	<0.001
Fat Mass (%)	r	−0.326	−0.353
	p value	0.002	0.001

*P-values < 0.05 were regarded as a sign of statistical significance.

were associated with better BMR, lean and fat percents. This is supported by Kizer et al. who found the beneficial level of adiponectin below 20 μg/ml upon coronary heart disease risk was basically mediated through metabolic factors, reflecting adiponectin benefit at this level on metabolic profile [15]. Similarly, previous work in coronary heart disease showed that higher adiponectin level up to 20 μg/ml predicts lower incidence of diabetes independent of prevalent IR [16].

On the other hand, adiponectin level higher than 40 μg/ml was associated with better BMR, lean percent and fat percent. Although some authors postulated that the higher adiponectin level, at cut off 40 μg/ml, is a response to various disease processes, as aging-associated homeostatic dysregulation [15], however experimental studies showed low-affinity binding of circulating adiponectin to certain molecular patterns on apoptotic cells facilitates removal of these cells by macrophages [17]. This “mass action” of adiponectin could serve as an important anti-inflammatory function [18].

Many Authors found that adiponectin levels were lower in type 2 diabetes mellitus and MetS [19] due to associated IR. Furthermore, previous works explored that treatment with insulin-sensitizing agents; thiazolidinediones; were accounted to increased plasma adiponectin levels in humans [20] and this is further linking better insulin sensitivity to adiponectin levels.

5. Conclusion

Current findings supported the possibility of risk stratification among MUHO/OW individuals based on insulin sensitivity, squared adiponectin level, lean mass and fat mass percentages. In elderly with obesity or overweight who has both MetS and IR by QUICKI, adiponectin level below 18 μg/ml or above 40 μg/ml could predict better anthropometrics and BMR.

6. Recommendation

Future researches are warranted to confirm the beneficial U-shaped adiponectin values in those with better insulin sensitivity.

The authors declared no conflicts of interests

All authors have no financial or any other kind of conflicts with this paper.

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Conflict of interest statement: The authors whose names were listed certified that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript. The content of this paper has not been published or submitted for publication elsewhere and approved by all co-authors. All coauthors have contributed significantly and have been seen and agreed with the contents of the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.04.007.

Sponsor's role

None. There is no compliance with any research funding agency.

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