

Differences in body mass index, waist circumference, and waist-to-hip ratio in patients with rheumatoid arthritis: association with serum adiponectin and disease parameters

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Objective

The aim of this study was to investigate differences in BMI, waist circumference (WC), and waist-to-hip ratio (WHR) in rheumatoid arthritis (RA) patients and their association with serum adiponectin and disease parameters.

Patients and methods

Fifty RA patients and 25 matched healthy controls were included. Anthropometric measurements, disease status, and serum adiponectin level were assessed.

Results

Out of 50 RA patients, 48% had normal BMI (18.5–24.9 kg/m²), 20% had BMI in the range of 25.0–29.9 kg/m², which is considered to be overweight, and 32% were obese, with BMI greater than 30 kg/m². Almost similar findings were observed by the measurements of WC – that is, 34% of patients were obese ‘abdominal obesity’. However, the percentage of obese patients increased to 42% when classified as per WHR ‘truncal obesity’. Serum adiponectin was significantly increased in RA patients compared with controls ($P=0.002$). Significant negative correlations of BMI and WC with serum adiponectin level were found ($r=-0.9$, $P\leq 0.001$; $r=-0.7$, $P\leq 0.001$, respectively). There were positive correlations of WHR with Disease Activity Score 28 ($r=0.3$, $P=0.047$), Multidimensional Health Assessment Questionnaire ($r=0.3$, $P=0.04$), and ultrasound Disease Activity Score ($r=0.4$, $P=0.04$), whereas there was a significant negative correlation with ultrasound erosion rate ($r=-0.3$, $P=0.02$).

Conclusion

BMI, WC, and WHR measurements should be used and encouraged in the RA population. Our findings suggested that WHR was better associated with disease activity, disability, and severity than with other measures.

Keywords:

anthropometric measurements, rheumatoid arthritis, serum adiponectin

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Introduction

Rheumatoid arthritis (RA) is one of the most frequent autoimmune diseases, with up to 1.3% prevalence in the world, which is also associated with a high risk for disability [1]. Body weight change in patients with RA is a complex issue. On one hand, active disease could lead to weight loss and frank wasting, termed rheumatoid cachexia, which correlates with the intensity of systemic inflammation [2]. On the other hand, some studies showed that a higher BMI is associated with less severe radiographic joint damage in the early phases of the disease [3].

These findings highlight the complex relationship between adiposity and obesity and clinical course in RA patients. Adipose tissue produces adipocytokines with various proinflammatory and anti-inflammatory effects, but the exact mechanisms behind the immunomodulatory effects of adipose tissue in RA patients are controversial [4]. Unexpectedly, accu-

mulating evidences on RA found that adiponectin was elevated in RA serum and synovial fluid; it is strongly expressed also at the synovium level and directly correlates with disease activity and radiologic progression [5].

The aim of this study was to investigate differences in BMI, waist circumference (WC), and waist-to-hip ratio (WHR) in RA patients and their correlations with serum adiponectin and disease parameters.

Patients and methods

Patients' characteristics

Fifty consecutive patients (46 female and 4 male) who fulfilled the 1987 ACR classification criteria for RA [6]

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and 25 healthy controls matched for age, sex, and BMI were enrolled for study. All patients were attending the outpatient Rheumatology Clinic, Minia University Hospital. Patients with diabetes mellitus and other endocrine disorders (Cushing syndrome or thyroid disease) were excluded from the study. Informed consent was taken from all participants in the study. The study was approved by the ethics committee of the Faculty of Medicine.

Assessment

Anthropometric measurements

BMI was calculated as weight in kilograms divided by the square of height in meters. The patients were grouped based on BMI as follows: underweight ($<18.5 \text{ kg/m}^2$), normal ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25\text{--}29.9 \text{ kg/m}^2$), and obese ($\geq 30 \text{ kg/m}^2$) [7]. To assess central adiposity, WC and WHR were measured. WC was measured at the midpoint between the lower border of the rib cage and the iliac crest. Women with WC greater than or equal to 88 cm and men with WC greater than or equal to 102 cm were initially classified as obese. Hip circumference was measured at the fullest point around the buttocks. WC was divided by hip circumference to calculate WHR. Women with WHR greater than 0.85 and men with WHR greater than 0.9 were classified as obese [8].

Disease status

Disease activity was measured using the Disease Activity Score calculated on 28 joints (DAS 28) [9]. The number of swollen/tender joints, and patient's and physician's global activity [general health (GH)] on a visual analog scale (0–100) were determined. Disability status was assessed using multidimensional health assessment questionnaire (MDHAQ; 0–3 scale) [10].

Serologic testing was performed for the following: rheumatoid factor positivity (2003; Omega Diagnostics, Latex Serology Ltd), C-reactive protein positivity (2005; Omega Diagnostics, Latex Serology Ltd, US), and erythrocyte sedimentation rate (ESR). In all patients, conventional radiography of hands, wrists, and feet was performed. Simple Erosion Narrowing Score (SENS) was used for radiographic scoring [11].

For all patients, musculoskeletal ultrasonography of the wrist, hands, and forefoot was performed with a 10–18 MHz linear scanner and middle class to high-end machine ultrasound (US) device. Conventional grey-scale ultrasound (GSUS) (B-mode) and power Doppler (PD) examinations were carried out to calculate ultrasound Disease Activity Score (US DAS), in which a power Doppler US examination of

22 joints and GSUS examination for effusion/hypertrophy (E/H) of 28 joints were performed. GSUS E/H was qualitatively graded as absent (0) or present (1) in the following joints: Metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints, wrists, elbows, shoulders, and knees (sum range: 0–28). Power Doppler was a semiquantitative score and graded in the following 22 joints: wrists, MCP joints, and MTP joints (sum range: 0–66) based on the method of Szkudlarek *et al.* [12]. The formula for US DAS is as follows:

$$\text{US DAS} = 0.56\sqrt{(\text{PD}22)} + 0.28\sqrt{(\text{E}/\text{H}28)} \\ + 0.70(\text{ESR}) + 0.014(\text{GH}).$$

GH is a measurement of a patient's response on a visual analog scale of disease activity.

Structural damage was assessed by means of US recording of ultrasound erosion count (USEC). USEC was the number of joints with erosions among the selected joints: wrists, MCP joints, PIP joints, and MTP joints. In addition to USEC, USER was also calculated by dividing the number of selected joints (where erosions were detected) with disease duration (in months).

Serum adiponectin levels were measured using an ELISA. The standard curve is generated by plotting the average optical density (450 nm) obtained for each of the standard concentrations on the vertical (*y*) axis versus the corresponding adiponectin concentration (ng/ml) on the horizontal (*x*) axis. Construct the standard curve using graph paper. The concentration read from the standard curve must be multiplied by the dilution factor. Normal value of adiponectin is 3000–14 000 ng/ml [13].

Statistical analysis

Statistical analysis was performed using SPSS (US) (version 16.0). Descriptive statistics was performed using number and percent as well as mean and SD. The analysis of variance test was used to compare the difference between more than two group means in interval and ordinal variables. Correlations were calculated using Pearson's correlation coefficient. The level of statistical significance was set at a *P* level less than 0.05.

Results

Demographic data, anthropometric measurements, and serum adiponectin level in rheumatoid arthritis patients and controls

Fifty RA patients were included in the present study. Their ages ranged from 24 to 72 years with a mean of

43.90±10.78 years, and their duration of illness ranged from 1 to 37 years with a mean of 8.70±6.11 years. Table 1 shows demographic and anthropometric measurements in all patients. Serum adiponectin level ranged from 1100 to 26 800, with a mean of 10 488±9081.1, in comparison with the control group in which adiponectin level ranged from 3600 to 6200 with a mean of 4684±757.56 with a statistically significant difference ($P=0.002$) (Table 1). Therapeutic regimens were as follows: NSAIDs in 48 (96%) patients, corticosteroids in 16 (32%) patients, methotrexate in 49 (98%) patients, antimalarial drugs in 50 (100%) patients, leflunomide in 10 (20%) patients, and sulfasalazine in two (4%) patients.

Prevalence of obesity in rheumatoid arthritis patients as per body mass index, waist circumference, and waist-to-hip ratio

Table 2 showed the prevalence of obesity as measured by BMI, WC, and WHR. Out of 50 RA patients, 48% had normal BMI (18.5–24.9 kg/m²), 20% had BMI in the range of 25.0–29.9 kg/m², which is considered to be overweight, and 32% were obese with BMI greater than 30 kg/m². Almost similar findings were observed

by the measurements of WC – that is, 34% of patients were obese ‘abdominal obesity’. However, the percentage of obese patients increased to 42% when classified according to WHR ‘truncal obesity’.

Comparison between patient groups according to body mass index

The range of BMI in RA patients was 20.9–42.6, and the patients were grouped according to WHO guidelines [7].

Patients with normal BMI had significantly higher serum adiponectin, SENS, and ultrasonographic erosion scores (USEC and USER) compared with other groups ($P<0.001$, 0.02, 0.04, and 0.04, respectively), as shown in Table 3. Hypoadiponectinemia was found in overweight and obese patients.

Correlations of anthropometric measures with serum adiponectin level and disease parameters

Significant negative correlations of BMI and WC with serum adiponectin level were found ($r=-0.9$, $P<0.001$; $r=-0.7$, $P<0.001$, respectively) (Figs 1 and 2).

There were significant positive correlations of WHR with DAS 28 ($r=0.3$, $P=0.047$), MDHAQ ($r=0.3$, $P=0.04$), and US DAS ($r=0.4$, $P=0.04$), whereas there was a significant negative correlation with USER ($r=-0.3$, $P=0.02$). All anthropometric measures (BMI, WC, and WHR) were negatively correlated with SENS ($r=-0.2$, $P=0.02$; $r=-0.1$, $P=0.049$; $r=-0.2$, $P=0.03$, respectively), as shown in Table 4. No correlations were found between BMI or WC and DAS 28, MDHAQ, and US DAS.

Table 1 Demographic data, anthropometric measurements, and serum adiponectin level in rheumatoid arthritis patients and controls

	RA patients (N=50)	Controls (N=25)	P-value
Age (years)	43.90±10.78	45.11±8.43	0.3
Sex			
Male	4 (8)	2 (8)	
Female	46 (92)	23 (92)	0.4
Duration of illness (years)	8.70±6.11	–	–
BMI (kg/m ²)	28.8±7	29.6±6.1	0.7
Waist circumference (cm)			
Male	81.0±1.83	88.05±6.43	<0.001*
Female	87.39±14.59	93.68±18.65	<0.001*
Waist-to-hip ratio			
Male	0.87±0.38	0.96±0.41	<0.001*
Female	0.87±0.65	0.97±0.52	<0.001*
Adiponectin level (ng)	10488±9081.1	4684±757.56	0.002*

Data are presented as mean (SD) or *n* (%). RA, rheumatoid arthritis. * $P<0.05$, controls versus RA patients, determined using Student's *t*-test or the χ^2 -test.

Table 2 Prevalence of obesity as per body mass index, waist circumference, and waist-to-hip ratio

	BMI [N (%)]	WC [N (%)]		WHR [N (%)]	
		Male	Female	Male	Female
Normal	24 (48)	4	33 (66)	4	29 (58)
Overweight	10 (20)	–	–	–	–
Obese	16 (32)	0	17 (34)	0	21 (42)

WC, waist circumference; WHR, waist-to-hip ratio.

Discussion

The purpose of this study was to investigate differences in BMI, WC, and WHR in RA patients and to determine whether BMI or other anthropometric measures are correlated with serum adiponectin and disease parameters. According to WHO guidelines [7], 48% of RA patients had normal BMI, 20% were classified as overweight, and 32% were classified as obese.

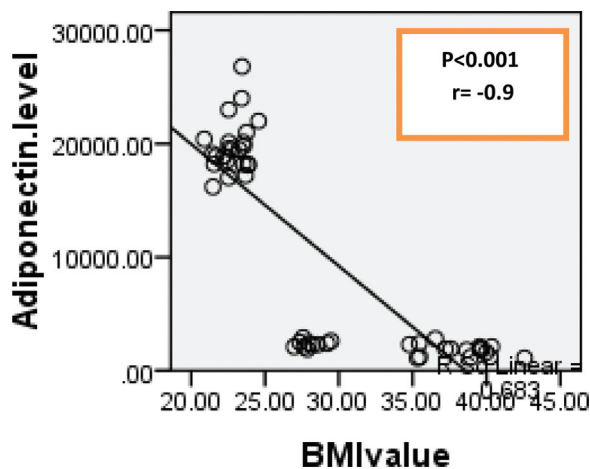
Prevalence of overweight and obesity in RA, as assessed by the general (WHO) BMI cutoff points, appears to be subject to geographical variation. A worldwide study identified 18% of RA patients as obese [14], whereas a UK-based study found a higher prevalence of 31% [15], which was nearly similar to our results.

BMI is an index that assesses obesity at the whole-body level; it takes into account total weight but it does not distinguish between different tissues that comprise it. Fat mass and other tissues (i.e. skeletal muscle, bone,

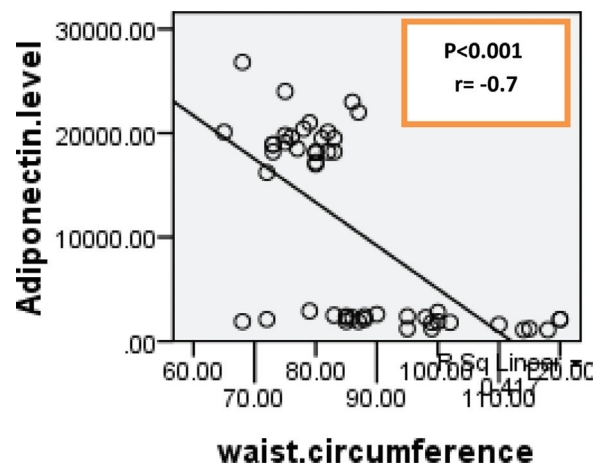
Table 3 Characteristics of rheumatoid arthritis patients according to body mass index

	Group 1: normal BMI (N=24)	Group 2: overweight (N=10)	Group 3: obese (N=16)	P-value
Age (years)	45.9±11.9	41.8±7.4	42.2±10.7	0.5
Sex				
Male	3 (12.5)	1 (10)	0	
Female	21 (87.5)	9 (90)	16 (100)	0.3
Duration of illness (years)	10.6±7.2	8.2±5.7	6.2±3.2	0.08
28 tender joint count	19.7±7.6	17.4±8.9	19.8±7.5	0.7
28 swollen joint count	9.8±4.8	9.1±6.2	9.6±5.6	0.9
Patient global assessment	5.3±1.3	4.9±1.9	5.6±1.9	0.7
Physician global assessment	5.2±2.1	4.8±1.9	5.4±1.8	0.7
DAS 28	3.5±0.8	3.3±0.8	3.6±0.7	0.7
MDHAQ	10.6±4.2	11.2±4.6	11.9±4.2	0.9
ESR (mm/h)	48.9±26.6	38.2±17.4	45.8±17.6	0.5
RF positive	17 (34)	7 (14)	10 (20)	0.9
CRP positive	18 (36)	8 (16)	13 (26)	0.9
Adiponectin level (ng)	19688±2360.1	2350±283.8	1775±510.6	<0.001*
SENS	29.2±16.7	18.8±10.7	10.6±7.9	0.02*
US DAS				
US DAS value	5.3±1.3	4.9±1.4	5.3±1.4	0.7
USEC	10.1±5.9	6.5±3.0	5.9±2.7	0.04*
USER (SD)	0.7	0.3	0.1	0.04*

CRP, C-reactive protein; DAS 28, Disease Activity Score 28; ESR, erythrocyte sedimentation rate; MDHAQ, Multidimensional Health Assessment Questionnaire; RF, rheumatoid factor; SENS, Simple Erosion Narrowing Score; US DAS, Ultrasound Disease Activity Score; USEC, ultrasound erosion count; USER, ultrasound erosion rate. Data are presented as mean (SD) or *n* (%). *P*-value is shown for ANOVA and χ^2 -tests of significance across BMI category. *Significant $P < 0.05$.

Figure 1

Correlation between BMI and adiponectin level.

Figure 2

Correlation between waist circumference and adiponectin level.

organs, skin, and blood), collectively known as fat-free mass, are components of total weight and can vary enormously between individuals [16]. In populations with altered body composition, BMI may not be a valid predictor of body fat [17]. Anthropometric measures of central adiposity, such as WC and WHR have been proposed as alternatives [18]. It is suggested that obesity should be redefined based on WHR instead of BMI [19].

In the present study, percentage of obesity increased to 34% when WC was considered as a parameter; however

it increased to 42% when the classification was based on WHR. Thus, central obesity as per WHR is more prevalent compared with general obesity. The importance of central distribution of fat has been known since decades. WC has become the preferred measure for abdominal obesity [20].

Adiponectin serum levels are increased in patients with RA compared with controls [21,22], as proved in the present study. Higher adiponectin levels were also detectable in erosive versus mild RA. In addition, serum levels of adiponectin correlated with joint

Table 4 Correlations of anthropometric measures with serum adiponectin level and disease parameters

	BMI		Waist circumference		Waist-to-hip ratio	
	<i>r</i>	<i>P</i> -value	<i>r</i>	<i>P</i> -value	<i>r</i>	<i>P</i> -value
DAS 28	0.1	0.8	0.1	0.7	0.3	0.047*
MDHAQ	0.1	0.4	0.1	0.4	0.3	0.04*
Serum adiponectin	-0.9	<0.001*	-0.7	<0.001*	-0.3	0.07
SENS	-0.2	0.02*	-0.1	0.04*	-0.2	0.03*
US DAS						
US DAS	0.04	0.8	0.1	0.678	0.4	0.04*
USEC	-0.2	0.1	-0.07	0.6	0.3	0.07
USER	0.003	0.9	-0.06	0.7	-0.3	0.02*

DAS 28, Disease Activity Score 28; MDHAQ, Multidimensional Health Assessment Questionnaire; SENS, Simple Erosion Narrowing Score; US DAS, Ultrasound Disease Activity Score; USEC, ultrasound erosion count; USER, ultrasound erosion rate. *Significant $P < 0.05$.

erosion [22,23], and plasma levels of adiponectin were higher in chronic RA compared with early RA [24].

To determine the relations between BMI and parameters of the disease activity, functional disability, or structural damage, our RA patients were grouped according to BMI as follows: group 1 'normal BMI', 24 (48%) patients; group 2 'overweight', 10 (20%) patients; and group 3 'obese', 16 (32%) patients. We found that the serum level of adiponectin was significantly higher in patients with normal BMI (group 1) than in other groups ($P < 0.001$). In agreement with our findings, Fagerer and Kullich [25] and Oranskiy *et al.* [26] demonstrated hypoadiponectinemia in patients with RA and obesity. In addition, patients with normal BMI had significantly higher radiologic and ultrasonographic erosion scores (SENS, USEC, and USER) compared with other groups.

Our results revealed a significant negative correlation of BMI and WC with serum adiponectin level ($r = -0.9$, $P \leq 0.001$; $r = -0.7$, $P \leq 0.001$, respectively). In agreement with our results, Baker *et al.* [27] found a negative correlation between BMI and adiponectin levels (Spearman's $\rho = -0.28$, $P = 0.004$), and Oranskiy *et al.* [26] investigated differences in body composition and BMI in patients with RA and their correlations with serum production of adiponectin, interleukin-6, and vascular endothelial growth factor. It was found that serum concentration of adiponectin increased in RA patients with normal BMI and underweight patients and decreased in obesity/overweight patients.

The influence of BMI and/or body fat on RA disease activity is unclear. Some studies have showed a direct association between obesity and disease activity in patients with long-time RA [28]. In advanced RA, both underweight and obese states are associated with worse disease activity; an active disease leads to loss of lean body tissue and better control of the disease is associated with weight gain [29]. Moreover, obesity

increases the physical disability [30]. These findings highlight the complex relationship between adiposity and obesity and clinical course in RA patients. Adipose tissue produces adipocytokines with various proinflammatory and anti-inflammatory effects, but the exact mechanisms behind the immunomodulatory effects of adipose tissue in RA patients are not yet explained [4].

With regard to the correlation between anthropometric measures (BMI, WC, and WHR) and parameters of disease activity or disability at the present study, we found positive correlations of WHR with DAS 28 ($P = 0.047$), MDHAQ ($P = 0.04$), and US DAS ($P = 0.04$). In agreement with our study, Ibn Yacoub *et al.* [31] and Jawaheer *et al.* [32] have reported that the obesity was associated with the activity of disease (DAS 28).

The present study demonstrated that the increased WHR was associated with less US erosion rate ($r = -0.3$, $P = 0.02$), which was not reported previously.

Our study confirms prior observations that BMI is associated with a lower prevalence of radiographic joint damage in patients with RA, as all anthropometric measures (BMI, WC, and WHR) were negatively correlated with SENS ($r = -0.2$, $P = 0.02$; $r = -0.1$, $P = 0.049$; $r = -0.2$, $P = 0.03$, respectively), but we found that adiponectin was not associated with radiologic or ultrasonographic scores and did not confound the association between BMI and joint damage.

In agreement with our study, Baker *et al.* [27] proved the negative association between BMI and joint destruction, and other studies [33,34] have found low BMI to be associated with increased erosion in small joints and decreased survival, with high BMI being protective. However, in contrast, Ibn *et al.* [31] found that increased BMI was associated with structural damage (Sharp total score) ($r = 0.297$, $P \leq 0.01$).

In conclusion, BMI with an appropriate cutoff to assess obesity, WC, and WHR measurements should be used and encouraged in the RA population. Our findings suggested that WHR was better associated with disease activity, disability, and severity than with other measures. Further research relating to possible mechanisms linking central obesity to various disease parameters in RA is recommended.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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