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Prevalence of obesity in rheumatoid arthritis and its association with disease activity and latex positivity in a sample of patients in Erbil

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Abstract

Background and objective: The prevalence of obesity is rising across the world and it is regarded as a major health concern which is thought to be associated with a number of chronic illnesses including rheumatoid arthritis. This study aimed to find out the prevalence of obesity in patients with rheumatoid arthritis and to apprehend the association of obesity with disease activity and latex positivity.

Methods: One hundred twenty patients with rheumatoid arthritis who were regularly visiting Rizgary Teaching Hospital in Erbil were included in a cross-sectional study using specially designed mixed questionnaire. Body mass index and waist circumferences were measured, and their association with disease activity score 28 (DAS28) and clinical disease activity index (CDAI) were estimated. Furthermore, we evaluated their association with positive latex test.

Results: There was increased frequency of obesity in rheumatoid arthritis patients, and there was a positive association between body mass index and waist circumference with disease activity measured by DAS28 and CDAI (P <0.001). There was no significant association between obesity and latex positivity which has been assessed separately for males and females (P = 0.898 and 0.086, respectively).

Conclusion: Obesity is frequently found in rheumatoid arthritis patients. It is associated with higher disease activity, but not with the latex positivity in these patients.

Keywords: Obesity; Rheumatoid arthritis; BMI; latex test; Disease activity.

Introduction

Rheumatoid Arthritis (RA) is an autoimmune systemic inflammatory disorder that affects synovial joints contributing to symmetrical polyarthritis of small and large joints.[1] It occurs in women three to five times more than in men.[2] Moreover, the frequency of disease in developed countries ranges from 0.5-1% of adults, in other words, 5 to 50 per 100,000 people developing the condition each year.[3] Regarding pathophysiology of the disease, both genetic and environmental factors are implicated. Smoking is believed to be a major environmental risk factor contributing to RA.[3]. Furthermore, genetic factors comprise 50 % risk of developing RA in individuals.[3] HLA-DR4 considered as an important genetic factor. However, it's relevancy varies across different ethnic groups.[4,5] RA is linked with a reduction in life expectancy,[6] mainly due to high risk of developing cardiovascular diseases (CVD) and worst outcomes in individuals affected with RA.[7] Although the exact cause for the CVD in patients with RA is not well understood, but genetic liability,[8-11] classical CVD risk factors[12,13] as well as the impact of systemic inflammation on the blood vessels[14,15] are all presumed to relate to cardiovascular consequences.[16] RA is also believed to be associated with altered body composition. The persistent inflammation signals metabolic dearrangements[17] that cause degradation of lean tissue, particularly bulk of muscle.[18] Moreover, the presence of sedentary lifestyle further reduces the muscle mass

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and lead to a buildup of more body fat with a stable or slightly increase in the body weight.[19] Adipose tissue is not merely an energy storage depot but is also act as an active endocrine/paracrine organ that secrets several bioactive molecules known as adipokines,[20] which is known to have various functions including regulation of energy intake and expenditure.[21, 22] Similarly, many of them are involved in the regulation of the inflammatory process.[20] Generally, the more built up of adipose tissue is linked with increased in the production of pro-inflammatory molecules, likewise, decreased adiposity is related to a reduction in the level of pro-inflammatory as well as an increase in the concentration of anti-inflammatory molecules, thereby obesity is now presumed as a pro-inflammatory state.[16,23] The considerable association between obesity both with inflammation and cardiovascular disease, similarly, change in body composition seen in patients with RA heralds the study of obesity in patients with RA highly significant. Based on what is described regarding potential association between obesity and activation of pro-inflammatory pathways, one should conclude that obese RA patients have presumably a more severe and active disease.[16] To date, surprisingly very few studies explored the obesity in RA patients, the observation from general population triggers to a clear hypothesis that obesity has impact on RA patients and it influences the outcome and general health of patients.[16] This study was designed to find out the prevalence of obesity in patients with RA and to find out the association of obesity with disease activity and latex positivity in a sample of patients living in Erbil as no similar studies have been conducted before in Kurdistan region and up to my best knowledge in whole Iraq.

Methods

This cross-sectional study was carried out in the Rheumatology and Medical Rehabilitation Department of Rizgary Teaching Hospital in Erbil City. A sample of 120 patients who fulfilled EULAR-ACR-2010 and ACR 1987 criteria for RA was selected by convenience method of sampling. Those patients who had Thyroid disease, Adrenal adenoma or carcinoma, malignancy, who were pregnant and those who were on certain drugs like Insulin, sulfonylurea, antidepressants, progesterone containing drugs were excluded. Data were collected and recorded on a specially designed questionnaire after getting verbal consent from the patients. Body weight and height and waist circumference (WC) were measured for each patient. Height was measured with a digital stadiometer, and weight was measured with subjects wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight (kg) divided by height (m^2), and patients were categorized thereafter according to BMI into normal weight <25 kg/m^2, overweight 25-<30 kg/m^2, obese ≥30 kg/m^2.[19] Waist circumference was measured with a nonstretching tape measure that applies a consistent amount of tension to the tape at the midpoint between the lower border of the ribs and the iliac crest. Two measurements were taken, and the average measure was used and patients were divided into not at risk of comorbidity (WC < 80 cm for females and < 94 cm for males), increased risk of comorbidity (WC 80-<88 cm for females and 94- <102 cm for males) and substantially increased risk of comorbidity (WC ≥ 88 cm for females and ≥ 102 cm for males). The activity of disease was assessed by DAS28 and CDAI parameters (measures of disease activity in RA) which include 28 tender joint count, 28 swollen joint count and a patient global estimate of status in addition to acute-phase reactant (ESR or CRP level) in DAS28 and physician global estimate of status in CDAI. Based on DAS28 patients were graded as in remission ≤2.6, low active >2.6-3.2, moderate >3.2-5.1 and highly active >5.1 and for CDAI were entitled into in remission <2.8, low active 2.8-10,

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moderate >10-22 and highly active >22.[24] Drug therapy was noted. Erythrocyte sedimentation rate and latex test were done for all patients. The data were managed by Excel using Chi-square and Fisher's exact test. A P value less than 0.05 was considered statistically significant.

Results

One hundred twenty patients with RA were evaluated. Baseline and demographic data are shown in Table 1. 109 patients were female and 11 were male. Age of the patients ranged between 20 to 70 years, and none of them were smokers. In this study, 20% of patients had normal weight (BMI < 25), 33.33% were overweight (BMI 25-<30), and 46.66% were obese (BMI ≥ 30). 62.5% of patients were latex positive (Table 1).

Table 1: Baseline and demographic data of patients.

Demographic data		BMI					
		Normal		Overweight		Obese	
		Number	%	Number	%	Number	%
Age group/years	20-32	7	58.3	3	25	2	16.7
	33-45	7	17.5	13	32.5	20	50
	46-58	7	14.2	16	32.6	26	53.06
	59-71	3	15.7	8	42.1	8	42.1
Sex	Male	3	27.2	8	72.7	0	0.0
	Female	21	19.2	32	29.3	56	51.3
waist circumference	Normal	12	75	4	25	0	0.0
	increased risk	12	60	4	20	4	20
	substantially increased risk	0	0.0	32	38.09	52	61.9
disease duration	< 2 years	7	35	6	30	7	35
	2- 5 years	1	3.5	13	46.4	14	50
	> 5 years	16	22.2	21	29.1	35	48.6
type of treatment	Nil	6	50	2	16.6	4	33.3
	DMARD	6	13.6	15	34.09	23	52.27
	DMARD + prednisolone	6	15.7	18	47.3	14	36.8
	Biology	1	20	1	20	3	60
	DMARD + biology	5	23.8	4	19.04	12	57.1
duration of morning stiffness	Nil	8	25.8	12	38.7	11	35.4
	< 30 min	5	21.7	6	26.06	12	52.7
	30 min to 1 hr	5	13.5	12	32.4	20	54.05
	> 1 hr	6	20.6	10	34.4	13	44.8
DAS28	Remission	4	100	0	0.0	0	0.0
	Mild disease activity	13	92.8	1	7.14	0	0.0
	Moderate disease activity	7	13.2	25	47.16	21	39.6
	High disease activity	0	0.0	14	28.5	35	71.4
CDAI	Remission	8	100	0	0.0	0	0.0
	Low Disease Activity	15	55.5	11	40.7	1	3.7
	Moderate Disease Activity	1	2.4	20	48.7	20	48.7
	High Disease Activity	0	0.0	9	20.4	35	79.5
Latex test	Positive	13	17.3	30	40	32	42.6
	Negative	11	24.4	10	22.2	24	53.3

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All RA patients who were in remission by DAS28 and CDAI (who were only four patients measured by DAS28 and eight patients measured by CDAI) had a normal weight, and none of the normal weight patients had high disease activity. This is in comparison to 71.4% of patients who had high disease activity by DAS28 and 79.5% of patients with high disease activity using CDAI were obese. Fisher's exact test revealed a significant association between obesity and both DAS28 and CDAI (P value <0.001). Table 2A and 2B show this information.

Table 2A: Association of BMI with DAS28.

		BMI			Total	*P* value
		Normal	Overweight	Obese		
DAS28	Remission	4	0	0	4	<0.001
	%	100%	0.0%	0.0%	100%	
	Mild disease activity	13	1	0	14	
	%	92.8%	7.14%	0.0%	100%	
	Moderate disease activity	7	25	21	53	
	%	13.2%	47.1%	39.6%	100%	
	High disease activity	0	14	35	49	
	%	0.0%	28.5%	71.4%	100%	
Total	Count	24	40	56	120	
	%	20%	33.3%	46.6%	100.0%	

Table 2B: Association of BMI with CDAI.

		BMI			Total	*P* value
		Normal	Overweight	Obese		
CDAI	Remission	8	0	0	8	<0.001
	%	100%	0.0%	0.0%	100%	
	Low Disease Activity	15	11	1	27	
	%	55.5%	40.7%	3.7%	100%	
	Moderate disease activity	1	20	20	41	
	%	2.4%	48.7%	48.7%	100%	
	High disease activity	0	9	35	44	
	%	0.0%	20.4%	79.5%	100%	
Total	Count	24	40	56	120	
	%	20%	33.3%	46.6%	100.0%	

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Using waist circumference as an index for obesity and DAS28 as an index for disease activity 3.3% of patients were in remission of whom 50% had normal WC, in comparison to 0% of those who had WC that substantially increased the risks of comorbidities. On the other hand, 40.8% of patients had high disease activity. In this category, only 4.08% of patients had normal WC whereas 87.7% of patients had WC that increased substantially the risks of comorbidities. Thus, there was a significant association between waist circumference and DAS28. Using CDAI as a parameter for disease activity 6.6% of all patients were in remission of whom 50% had normal waist circumference and 0% with a waist circumference that increased substantially the risk of comorbidities. 36.6% of all patients had high disease activity of whom 90.90% had a waist circumference that substantially increased the risks of comorbidities (*P* <0.001) as shown in Table 3A and 3B.

Table 3A: Association of waist circumference with DAS28.

		Waist circumference				
		Normal	**Increased risks**	**Substantially increased risks**	**Total**	***P* value**
DAS28	Remission	2	2	0	4	<0.001
	%	50%	50%	0.0%	100%	
	Mild disease activity	7	7	0	14	
	%	50%	50%	0.0%	100%	
	Moderate disease activity	5	7	41	53	
	%	9.4%	13.2%	77.3%	100%	
	High disease activity	2	4	43	49	
	%	4.08%	8.16%	87.7%	100%	
Total	Count	16	20	84	120	
	%	13.3%	16.6%	70%	100%	

Table 3B: Association of waist circumference with CDAI.

		Waist circumference				
		Normal	**Increased risk**	**Substantially increased risk**	**Total**	***P* value**
CDAI	Remission	4	4	0	8	<0.001
	%	50%	50%	0.0%	100%	
	Low Disease Activity	10	9	8	27	
	%	37.03%	33.33%	29.62%	100%	
	Moderate Disease Activity	2	3	36	41	
	%	4.87%	7.31%	87.8%	100%	
	High disease activity	0	4	40	44	
	%	0.0%	9.09%	90.9%	100%	
Total	Count	16	20	84	120	
	%	13.3%	16.6%	70%	100%	

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Of all 120 patients, 75 were positive for latex test of whom 32 patients were obese, 30 patients were overweight, and 13 patients were normal in weight. Latex positivity was calculated for males and females separately. In males 66.7% of normally weighted patients had got a positive latex test versus 62.5% of all overweight patients. None of the male patients were obese. These differences were not statistically significant (Table 4A). In females, 52.4% of all normally weighted patients resulted in a positive latex test if compared to 78.1% of overweight and 57.1% of obese female patients who had a positive latex test. There difference were not statistically significant (Table 4B).

Table 4A: Association of BMI with positive latex test in men.

		BMI			Total	*P* value
		Normal	Overweight	Obese		
latex test	Positive	2	5	0	7	0.898
	%	63.6%	45.4%	0%	100%	
	Negative	1	3	0	4	
	%	25%	75%	0%	100%	
Total	Count	3	8	0	11	
	%	27.2%	72.7%	0%	100.0%	

Table 4B: Association of BMI with positive latex test in women.

		BMI			Total	*P* value
		Normal	Overweight	Obese		
latex test	Positive	11	25	32	68	0.086
	%	16.1%	36.7%	47.05%	100%	
	Negative	10	7	24	41	
	%	24.3%	17.07%	58.5%	100%	
Total	Count	21	32	56	109	
	%	19.2%	29.3%	51.3%	100.0%	

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Discussion

Obesity has turned into a major global health concern[25,26] and it is believed to be associated with a number of chronic illnesses.[26] As described above, adipose tissue poses an immunodulating impact on RA, however, the exact mechanism remains increasingly unclear.[27] Hence we investigated retrospectively the occurrence of obesity in RA patients and its association with disease activity. Furthermore, we estimated for latex test in these patients. This study showed that a large proportion (79.99%) of RA patients were overweight (33.33%) and obese (46.66%), this is close to Crowson et al. study in which 40.3% of cases were revealed to be obese.[28] But this finding is slightly more than Giles study[29] (who reported that 33% of women and 36% of men with RA were obese by BMI and 57% by DEXA scan) and a UK study that reported the prevalence of obesity to be 31% using BMI.[30] This difference could be due to potential geographical factors, lifestyle and eating habits and lack of exercise. Our study also showed a positive association between obesity and disease activity indicating higher DAS28 and CDAI in heavier patients. This is in agreement with Vidal et al. study which reported that the disease activity score in 28 joints (DAS28) appeared to be higher in obese patients than in RA patients with normal weight.[31] In QUESTA-RA study, 5161 patients with RA were compared with RA patients with normal-weight. The study concluded that obesity was associated with a rise in mean DAS28 (+0.23 points, 95% CI 0.11 to 0.34).[32] Furthermore, 1596 obese patients with early RA were monitored for a mean 9.5±3.7 years, when compared with patients with normal weight, it turn out that obesity early and during follow up was strongly related to higher disease activity (mean DAS28 3.0±1.2 vs. 2.7±1.3, *P* = 0.002), less sustained remission rate (20.5% vs 26.6%; p=0.048) and increase in the mean pain level (32.9±23.9 vs 25.8±23.8; p=0.005).[33,34] The rise in DAS28 observed in these studies appeared to be subjectively influenced (number of sore joints as well as patients overall assessment[34-36]) and not linked to C reactive protein level or ESR.[36,37] In two studies, Health Questionnaire Assessment (HAQ) was recruited to assess functional disability in RA patients. The score was significantly higher in obese patients than in normal weight patients (0.6±0.7 vs. 0.5±0.6; *P* <0.001, and +0.16 (95% CI 0.03 to 0.30) respectively).[33-35] It is important to mention that despite higher disease activity in these patients, no significant association was observed between BMI and positive latex test which might be explained by small sample size. To the extent of our knowledge, to date, few studies have addressed the association of obesity with Rheumatoid factor (RF) or anti-cyclic citrullinated peptide (ACCP) in RA patients. Two case-control studies including 515 recent RA with 769 controls and 2748 RA with 3444 controls discovered a positive association between obesity and likelihood of developing RA negative for ACCP, with an increased risk of 3.45 (1.73 to 6.87) in the first study and 1.6 (1.2 to 2.2) in women in the second study.[33,38,39] Similarly, in two cohort studies performed by Lahiri et al. and Lu et al. large number of patients with RA were studied and monitored for a long term, they found that obesity is linked to high incidence of seronegative inflammatory polyarthritis (HR 2.75; 95% CI 1.39 to 5.46) [40] and seronegative RA (HR 1.34; 95% CI 1.03 to 1.74)[41,33] respectively. Furthermore, in the Lu et al. study, the risk for patients with obesity who develop RA with onset before 55 years was much more increased in all patients with RA (seropositive and seronegative) (HR 1.65; 95% CI 1.34 to 2.05).[41,33] This could be an explanation for reduced radiographic joint damage in obese RA patients as revealed in a study of 767 patients with early stage of RA demonstrated that more joint damage is observed in normal-weight patients at inclusion and significant radiographic progression during the study is noticed

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than obese patients evaluated by the Ratingen score.[42] However, in RF- negative patients with RA. This difference in radiographic progression was not identified. Lately, in another study, 1068 participants were analyzed in two clinical trials testing Glimumab emphasized that obesity is potentially linked with a lower probability of increasing in van der Heijde-Sharp (vdHS) score at week 52 and 104, essentially independent of likely confounders.[33,43] These radiological results were proved in a study of MRI-evidenced progression in erosion score in two years' time.[43] On literature review, we came across very few studies addressing the factors contributing to obesity in RA. In a study performed in the UK, the comparison was done between the potential factors of lack of exercise, diet, and inflammation on BMI and body fat in patients with RA; obesity appeared to be associated with a lack of physical activity. However, an underweight state was linked to low energy intake. Moreover, inflammation is believed to impact body composition in RA, apparently not associated with either of them.[16, 44] It is believed that during the periods of high level of disease activity, persistent inflammation contribute to increasing in the muscle breakdown, this is further accelerated by low physical activity and decrease energy intake, similarly, during periods of reduced disease activity, muscle wasting is minimized, and less fat is stored if the patient keeps an eye on his diet and enhance his physical activity. If not, obesity may develop if exercise remains at low degree.[16] All in all, the above results highlight that high BMI is linked to a RA state known to have persistent pain and poor patient reported prognosis and presumably less responsive to treatment, while low BMI, on the other hand, is characterized by progressive joint damage.[26] There were some weak points in our study; it was a retrospective cross-sectional study, and the sample size was relatively small. Furthermore, the selection of cases was not through random sampling, and certainly, there was selection bias. Also, BMI and WC will not precisely determine the amount of body fat. Thus more accurate measures are required. Although more investigations are required to know the exact mechanisms of how obesity causes RA, and vice versa, the clinical importance of these findings are that weight reduction and regular exercises are important to prevent RA especially in high risk groups. Furthermore, avoidance of obesity is important in RA patients for better control of the disease and sustained remission state and to reduce risks of cardiovascular diseases in these patients.

Conclusion

Increasing body weight is common among RA patients which is associated with higher DAS28 and CDAI. However, no significant association was noted with latex positivity in these patients. Further longitudinal studies are required to know the exact pathophysiology of RA in obese patients and more interventional studies are required to investigate the response of disease to different treatment groups in obese RA patients.

Conflicts of interest

The authors report no conflicts of interest.

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