



## THE IMPACT OF OBESITY ON THE SEVERITY OF RHEUMATOID ARTHRITIS

## Biochemistry

**Dr. S. Michael  
Rajam Geetha**

M.D Assistant Professor, Govt. Thoothukudi Medical College

**Dr. Siva Somana\***

M.D Assistant Professor, Govt. Thoothukudi Medical College \*Corresponding Author

**Dr. V. G.  
Karpagavalli**

Associate Professor, ESIC Medical College, Coimbatore

## ABSTRACT

**Aims and Objectives:** The fat stores in our body secrete many hormones and cytokines including Leptin, an adipokine secreted in increased amounts by adipocytes in obesity that not only regulate the energy balance but also regulate the inflammatory and immune responses. This study was designed to measure the serum Leptin levels and calculate the BMI in Rheumatoid Arthritis(RA) patients and study the impact of obesity in the disease activity of Rheumatoid arthritis patients.

**Methodology:** Sixty adult RA patients and 30 sex and age matched healthy controls were selected for this case control study. Serum Leptin levels were estimated in the study subjects and compared with the Body mass index (BMI) using Quetelet index.

**Results:** RA patients showed statistically significant higher mean serum Leptin level than healthy controls (48.78 + 32.00ng/mL versus 11.94 + 6.11ng/mL respectively,  $p < 0.001$ ). The serum Leptin levels showed a statistically significant positive correlation with body mass index ( $p = 0.001$ ).

**Conclusion:** As the serum Leptin levels were significantly higher in the RA patients than in the controls it is understood that Leptin plays a pivotal role in the pathogenesis of RA as a proinflammatory cytokine. The serum Leptin levels correlated well with body mass index indicating that the body fat stores can also decide upon the incidence and progression of RA.

## KEYWORDS

Rheumatoid Arthritis, Serum Leptin, Body Mass index, Quetelet index, C-reactive protein.

## Introduction:

Rheumatoid Arthritis is an autoimmune disease affecting 0.5-1% of general population.<sup>1</sup> Women are more often affected than men in the ratio of 3:1.<sup>2</sup> Many clinical in vitro, in vivo animal and human studies suggests the involvement of Leptin and thereby obesity in the pathogenesis of Rheumatoid Arthritis. Obese individuals with body mass index of more than 30 have been found to be associated with increased incidence of Rheumatoid Arthritis.<sup>3</sup> Studies have shown that serum Leptin correlates well with BMI in humans and it is approximately four times higher in normal obese individuals than in lean healthy subjects. Also serum Leptin levels in women is approximately twice that in men due to testosterone<sup>4</sup>.

This study was designed to calculate the BMI and also measure the serum Leptin levels in Rheumatoid Arthritis(RA) patients and to compare it with healthy controls and to study the impact of obesity in the disease activity of Rheumatoid arthritis patients.

## Aim of the study:

The objectives of the study are to measure the serum Leptin concentration in rheumatoid arthritis patients and to study the effect of serum Leptin levels, and thereby the impact of obesity on the disease activity of Rheumatoid arthritis patients.

## Materials and methods:

60 Rheumatoid arthritis patients diagnosed by American College of Rheumatology (ACR) criteria 2010 with symptoms of early morning stiffness of more than 1hour, symmetrical joint involvement with pain, tenderness and swelling in the joints aged 25-55years were selected in a Tertiary Care Hospital. Patients with Diabetes Mellitus, Hypothyroidism, Hypertension, Coronary Vascular Disease, patients taking Estrogen & Statins and Pregnant and lactating women were excluded from the study. Blood samples were collected from the patients around 9.00 am to avoid diurnal variation of leptin in fasting state and for uniformity in the collection. Serum Leptin (ELISA-Sandwich method), C-Reactive protein (CRP), Rheumatoid factor (RF), Serum Uric acid, Serum Fasting Lipid profile, Serum Urea, Serum Creatinine, Erythrocyte sedimentation rate (ESR), Haemoglobin were analysed. Body mass index was calculated using "Quetelet Index". Statistical analysis including Tests of significance (5%) using Unpaired student's t-test, Pearson's correlation co-efficient and ANOVA (Analysis of Variance) were performed using SPSS software version 22.

## Results and Discussion:

**Table 1. Mean serum leptin concentration based on Body Mass Index in both patients and controls**

BMI Level	Group	S.Leptin (ng/mL)			t-Value	P-Value
		Nos.	Mean	Std.Dev		
Normal (BMI 18.5-24.9)	Case	25	35.6	24.99	5.505	<0.001
	Control	4	7.1	2.69		
	Total	29	31.6	25.22		
Over wt (BMI 25-29.9)	Case	27	50.6	33.13	5.789	<0.001
	Control	17	12.4	6.86		
	Total	44	35.8	32.16		
Obese (BMI 30 & above)	Case	8	84.0	18.99	10.248	<0.001
	Control	9	13.2	4.95		
	Total	17	46.5	38.71		
Total	Case	60	48.8	32.00	8.608	<0.001
	Control	30	11.9	6.11		
	Total	90	36.5	31.56		

## S- Significant

Table 1 shows the mean serum leptin concentration between the normal, overweight and obese groups of RA cases and apparently healthy controls. The mean serum Leptin concentration in the normal group was 35.6±24.99ng/mL in cases and 7.1±2.69ng/mL in controls, in the overweight group it was 50.6±33.13ng/mL in cases and 12.4±6.86ng/mL controls, in the obese group it was 84.0±18.99ng/mL in cases and 13.2±4.95ng/mL in controls and totally it was 48.8±32.0ng/mL in cases and 11.9±6.11ng/mL in controls. The mean difference between the cases and controls, totally and also between the groups was statistically significant with a p-value of <0.001. The study showed that patients in the normal, overweight and obese categories showed elevated S.Leptin levels when compared to the same categories in the control group and it was also statistically significant. This reveals that there is association between BMI and leptin as proved in the literature.<sup>5</sup>

**Table 2 To compare mean serum CRP concentration between patients with RA and healthy controls**

	Group	N	Mean	Std. Dev	t-Value	P-Value
CRP	Case	60	17.2872	9.25046	11.043	<0.001 S
	Control	30	3.8167	1.36257		

**S- Significant**

Table 2. shows the mean CRP concentration between cases and controls. The mean serum CRP concentration in cases was 17.29+9.25 mg/L and that of controls was 3.82+1.36 mg/L. The serum CRP concentrations was compared in both these groups using unpaired student's t-test. The difference in the mean was statistically significant with a p-value of <0.001.

**Table 3 Comparison of serum Leptin levels between CRP +ve & CRP -ve patients with RA**

Group		Sr. CRP Level	N	Mean	Std. Dev	t-Value	P-Value
Case	Leptin	Positive	51	52.0830	33.12270	3.206	0.004 S
		Negative	9	30.0478	15.22072		

**S- Significant**

Table 3. shows the mean Leptin concentration between the CRP +ve cases and CRP -ve cases with RA. The mean serum leptin concentration in CRP +ve cases was higher than that of CRP -ve cases indicating that the serum Leptin levels rise with the severity of the Rheumatoid Arthritis. On comparing the serum CRP concentration between these groups using unpaired student's t-test, the difference in the mean was statistically significant with a p-value of <0.004.

Figure 2 shows the Rheumatoid factor status in the RA patients.

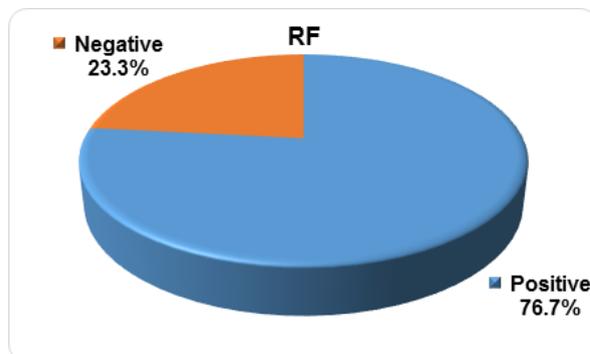


Figure.2 shows the RF status in the RA patients. Patients with RF+ve was 76.7% and those negative was 23.3%.

**Table 4. Mean serum leptin concentration between RF+ve & RF-ve patients with RA**

	RF	N	Mean	Std. Dev	t-Value	P-Value
Leptin	Positive	46	49.3528	32.37266	0.250	0.803 NS
	Negative	14	46.8879	31.86361		

**NS – Not Significant**

Table 4. shows the mean leptin concentration between the RF +ve cases and RF -ve cases with RA. The mean serum leptin concentration in RF +ve cases was 49.35+32.37ng/mL, which is slightly higher than that of RF -ve cases with leptin levels of 46.89+31.86ng/mL. The serum leptin concentrations was compared in both these groups using unpaired student's t-test and the difference was not statistically significant and the p-value was 0.803.

**Table.5 Correlation between leptin and body mass index**

BMI	Pearson Correlation	0.423
	P-Value	0.001
	N	60

Table 5. shows the correlation between leptin and BMI in RA patients. Pearsons correlation coefficient shows a moderate positive correlation between leptin and BMI with r value of 0.423 and this is statistically significant with a p-value of 0.001. A similar positive association among serum leptin concentrations and the percentage of body fat in humans was observed in the other studies too.6,7 The recent approval of Leptin for lipodystrophy emphasises how Leptin may interact with metabolic dysfunctions of obesity.

**Conclusion:**

From the above study we can come to an inference that

- Leptin has a major role in the pathogenesis of RA by its effect on both innate and adaptive immunity.
- As S.Leptin levels reflect the body fat mass, body fat stores can also decide upon the incidence and progression of RA.
- Hence the BMI can be maintained in the normal category and thereby the disease activity of Rheumatoid Arthritis can be reduced.

**References:**

1. Gary S. Firestein, Ralph C. Budd, Sherine E Gabriel, Iain B McInnes and James R O'Dell KELLEY'S Textbook of Rheumatology; Ninth edition(2012); Part 9; Chapter 69; pg1059.
2. Gary S. Firestein, Ralph C. Budd, Sherine E Gabriel, Iain B McInnes and James R O'Dell KELLEY'S Textbook of Rheumatology; Ninth edition(2012); Part 9; Chapter 69; pg1063.
3. Voigt LF, Koepsell TD, Nelson JL, Dugowson CE, Daling JR. Smoking, obesity, alcohol consumption, and the risk of rheumatoid arthritis. Epidemiology 1994;5:525-32.
4. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, et al. 1996. Serum immunoreactive leptin concentrations in normal weight and obese humans. N. Engl. J. Med. 334:292-95.
5. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, et al. 1996. Serum immunoreactive leptin concentrations in normal weight and obese humans. N. Engl. J. Med. 334:292-95
6. Hamilton BS, Paglia D, Kwan AY, Deitel M. Increased obese mRNA expression in omental fat cells from massively obese humans. Nat Med. 1995; 1:953-956. [PubMed: 7585224]
7. Considine RV, Sinha MK, Heiman ML, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. N Engl J Med. 1996; 334:292-295. [PubMed: 8532024]