

## Research Article

### **Nutritional Status and its Relation with Disease Activity in Rheumatoid Arthritis: A Study from North India**

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**Abstract:** This study proposed to assess the nutritional status of RA patients and to study any impact of disease activity (as assessed by DAS 28 score) on it. In this study 150 cases of RA diagnosed according to 1987 revised ACR criteria were recruited. Patients with immunocompromised state (i. e. HIV, malignancy), malabsorption syndrome, chronic disease or autoimmune disorder other than RA, metabolic syndrome and /or having cachexia due to cause other than RA were excluded from the study. From each case DAS 28 was calculated. Nutritional status was calculated by measurement of BMI, triceps skin fold thickness, serum albumin and total cholesterol. Low BMI (<25 kg/m<sup>2</sup>) and low albumin (<3.5 gm/dl) were found in 106/150 (70.67%) and 11/150 (7.33%) cases respectively. Anemia was found in 31/150 (20.67%) cases while low TSFT was present in 76/150 (50.67%) patients and low serum cholesterol in 126/150 (84%) cases. The markers of nutrition status (haemoglobin, BMI and serum albumin) showed significant change with disease activity (P<0.05 for each). Only TSFT and serum cholesterol did not have any significant alteration with DAS28 (p>0.05). Haemoglobin, BMI and serum albumin had significant negative correlation with disease activity parameters (DAS28 and ESR). This study concluded that RA patients having a higher disease activity (higher DAS28) had significantly lower hemoglobin concentration, BMI and serum albumin (p for trend <0.05). A significant negative correlation exists between markers of disease activity (DAS28 and ESR) and markers of nutrition (serum albumin, haemoglobin and BMI).

**Keywords:** Rheumatoid arthritis, nutritional status, disease activity.

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#### **INTRODUCTION**

Rheumatoid arthritis is a chronic, symmetrical, inflammatory poly arthritis associated with systemic features most commonly fatigue and cachexia.

Paget in 19<sup>th</sup> century described rheumatoid cachexia as a wasting of skeletal muscle mass in patients with inflammatory arthritis that was not due to disuse atrophy [1]. This rheumatoid cachexia is associated with an increased disease activity.

The pathologic hallmark of RA is inflammation of synovial membranes of various joints resulting in increased production of cytokines (i.e. tumor necrosis factor - $\alpha$  and interleukins). This cytokine production is proportional to the disease activity in RA. Apart from local inflammatory effects these cytokines cause higher resting energy turnovers and altered body compositions and development of cachexia when the inflammatory burden increases in RA [2].

Rheumatoid cachexia occurs in 13-15% of RA cases; but it is usually ignored in clinical practice [3]. The cachexia is associated with higher morbidity and

mortality in RA as in other systemic diseases like cancer, heart failure, critical illnesses and HIV infection [4, 5].

This study proposed to assess the nutritional status of RA patients and to study any impact of disease activity (as assessed by DAS 28 score) on it.

#### **MATERIALS AND METHODS**

This was a hospital based analytic-observational study conducted in department of medicine at a tertiary care centre in north India during the period of November 2011 to October 2012 on 150 cases of RA (diagnosed as per 1987 ACR criteria) [6] after approval of institutional ethics committee and informed consent from all the study participants. Patients who were current or ex smokers, or ethanol users, had HIV infection, malignancy, malabsorption syndrome, metabolic syndrome, chronic disease other than RA; cachexia due to any established cause other than RA or who did not given informed consent were excluded from the study.

Base line data was collected with regards to detailed disease history including drug history and then each patient was subjected to complete rheumatologic assessment inclusive of clinical examination. Various anthropometric parameters viz. height, weight, body mass index (BMI) and triceps skin fold thickness (TSFT) were recorded for each patient. After overnight fasting, blood samples of the patients were drawn and sent for complete blood count, erythrocyte sedimentation rate (ESR), fasting plasma glucose (FPG), urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), rheumatoid factor (RF), CRP, serum albumin and serum total cholesterol (TC) estimation.

TSFT was measured, with a Harpenden caliper, along the midline on the back of the triceps in both the arms, at the midpoint located between the top of the acromial process to the bottom of the olecranon process of the ulna. The skin was pinched so that the fold ran vertically. The mean of the values of the two sides was taken as TSFT value.

ESR was measured by Westergren method (normal ESR value was taken as up to 20 mm in 1<sup>st</sup> hour). Serum albumin was measured by a photometric test with a normal range of 3.5-5.5 gm/dl. Total cholesterol was estimated by sulfo-phosphovainilline assay- a colorimetry based method. Rheumatoid factor (RF) and C-reactive protein (CRP) levels were estimated by turbidimetry. A BMI range of 18.5-24.99 kg/m<sup>2</sup> was taken as normal.

RA Disease activity was calculated using disease activity score-28 (DAS-28) [7]. The DAS28 score  $\geq 5.1$

indicates high disease activity; DAS  $\geq 3.2$  to  $<5.1$  moderate disease activity and DAS  $<3.2$  low disease activity.

### Statistical analysis

Microsoft Excel® and one way anova test were used for data storage and analysis. Continuous variables were expressed as mean  $\pm$  standard deviation. Anova test was used to determine statistical difference between variables. Pearson's coefficient was used to investigate the correlation between the two variables. Statistical significance was set at p value  $< 0.05$ .

### RESULTS

The Demographic, clinical and laboratory characteristics of 150 RA cases are shown in Table 1 and Fig. 1. Low BMI ( $<25$  kg/m<sup>2</sup>) and low albumin ( $<3.5$  gm/dl) were found in 106/150 (70.67%) and 11/150 (7.33%) cases respectively. Anemia was found in 31/150 (20.67%) cases. We found low TSFT in 76/150 (50.67%) patients and low serum cholesterol in 126/150 (84%) cases.

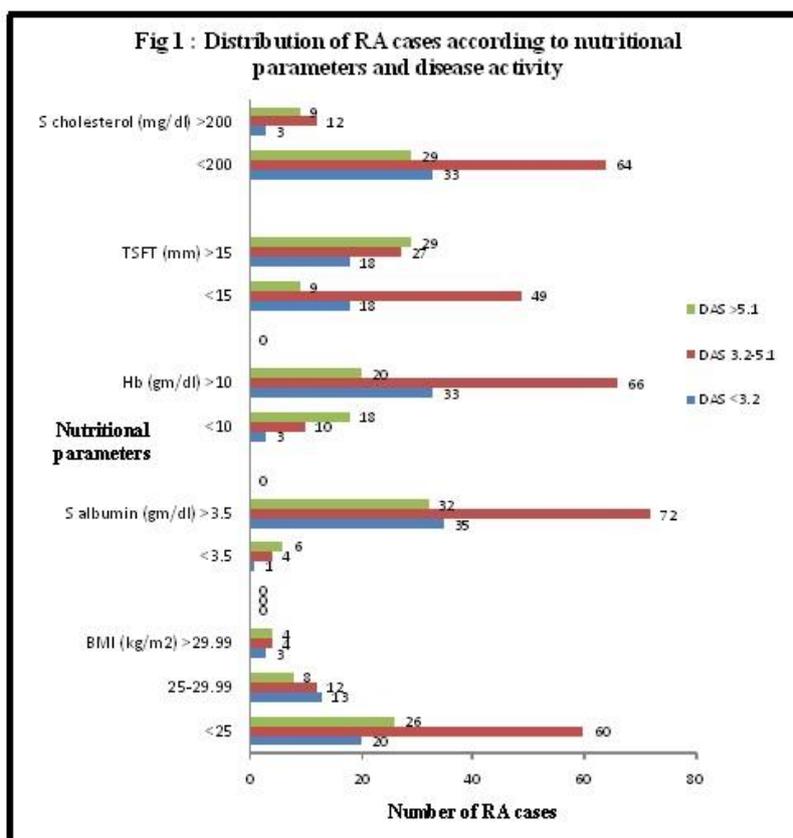
When the patients of RA were divided in groups according to their disease activity as determined by DAS28, the markers of nutrition status (haemoglobin, BMI and serum albumin) showed significant change with disease activity ( $p < 0.05$  for each). Only TSFT and serum cholesterol did not have any significant alteration with DAS28 ( $p > 0.05$ ) (Table 1).

Haemoglobin, BMI and serum albumin had significant negative correlation with disease activity parameters (DAS28 and ESR) (Table 2).

**Table 1: Demographic characteristics of 150 RA cases distributed according to DAS 28**

	Total (150)	DAS28			p value
		$<3.2$ N=36	3.2-5.1 N=76	$>5.1$ N=38	
Sex M/F	34/116	2/34	28/48	4/34	
Age (years)	43.17 $\pm$ 11.77	43.67 $\pm$ 12.55	43.29 $\pm$ 11.71	42.47 $\pm$ 11.39	$>0.05$
Duration of RA (months)	53.27 $\pm$ 40.79	57.53 $\pm$ 49.41	58.19 $\pm$ 37.43	39.39 $\pm$ 35.85	$>0.05$
RF positivity	73 (48.67%)	2 (5.55%)	38 (50%)	33 (86.84%)	
CRP positivity	78 (52%)	2 (5.55%)	44 (57.89%)	32 (84.21%)	
DAS28	4.41 $\pm$ 2.36	2.70 $\pm$ 0.24	4.17 $\pm$ 0.53	6.52 $\pm$ 3.77	$<0.05^a$
ESR (mm 1 <sup>st</sup> hour)	42.37 $\pm$ 24.56	26.64 $\pm$ 10.11	40.24 $\pm$ 19.56	61.55 $\pm$ 30.48	$<0.05^a$
Hb (gm/dl)	11.01 $\pm$ 1.41	11.25 $\pm$ 1.35	11.03 $\pm$ 1.00	10.51 $\pm$ 1.71	$<0.05^a$
BMI (kg/m <sup>2</sup> )	23.38 $\pm$ 3.73	24.66 $\pm$ 3.96	24.12 $\pm$ 3.84	22.39 $\pm$ 3.32	$<0.05^a$
TSFT (mm)	15.62 $\pm$ 5.62	17.26 $\pm$ 4.91	17.22 $\pm$ 5.96	14.03 $\pm$ 5.39	$>0.05$
Serum Albumin (gm/dl)	4.03 $\pm$ 0.34	4.11 $\pm$ 0.23	4.06 $\pm$ 0.29	3.91 $\pm$ 0.48	$<0.05^a$
Serum Cholesterol (mg/dl)	175.71 $\pm$ 36.37	167.61 $\pm$ 32.59	178.00 $\pm$ 34.60	178.79 $\pm$ 42.56	$>0.05$

a= significant



**Fig. 1: Distribution of RA cases according to nutritional parameters and disease activity**

**Table 2: Correlation of nutritional assessment parameters with disease activity in RA cases**

Parameter	Correlation with DAS 28		Correlation with ESR	
	R	p value	R	p value
Hb	-0.140	<0.05 <sup>@</sup>	- 0.346	<0.05 <sup>@</sup>
BMI	- 0.109	<0.05 <sup>@</sup>	-0.187	<0.05 <sup>@</sup>
TSFT	0.046	>0.05	0.077	>0.05
S. Albumin	-0.187	<0.05 <sup>@</sup>	-0.309	<0.05 <sup>@</sup>
S. Cholesterol	0.061	>0.05	0.121	>0.05

@=significant

## DISCUSSION

In this study effect of RA disease activity on nutritional status was assessed among 150 cases.

This study indicates that RA patients having a higher disease activity (higher DAS28) had a significantly lower hemoglobin, BMI and serum albumin levels (p for trend <0.05). The various nutritional parameters had a significant association with disease activity. Markers of disease activity (DAS28 and ESR) also had a significant but negative correlation with the indicators of the nutritional state (serum albumin, haemoglobin and BMI).

The well established relationship between inflammation (active RA) and anaemia was also confirmed in this study by a significant inverse correlation between haemoglobin concentration and DAS28, and haemoglobin concentration and ESR [8].

BMI is simple and widely used method for nutritional assessment. Low BMI has found to be associated with more active disease and higher morbidity [9, 10]. Munro and H Capell [11] also reported low BMI in patients who had active RA. This is in accordance with our observation.

TSFT provides information exclusively about fat mass and is potentially less affected by RA [12]. As muscle wasting is a common feature in RA but fat mass tends to be preserved in RA, cachexia in RA is associated with normal to slight decrease in TSFT. In a recent study, Pitt P *et al.* [13] revealed no reduction in TSFT in post-menopausal RA patients compared with controls. In our study, we also did not find any significant alteration of TSFT with disease activity. A previous study also supports our finding [12]. On the other hand, Helliwell M *et al.* [14] observed significant reduction in BMI and TSFT in RA patients compared with controls.

Serum albumin is the most useful laboratory marker for nutritional assessment as it reflects quantity of visceral protein [15]. Fukuda W *et al.* [16] in a study of 295 RA patients concluded decrease in serum albumin with increase in RA disease activity. Hypoalbuminemia was present in 24.7% Japanese RA patients. In 2001, Gomez-Vaquero *et al.* [12] observed significant inverse relation of serum albumin with disease activity parameters in RA. These findings are similar to our observation of lower serum albumin levels in RA patients with higher disease activity. Hypoalbuminemia, associated with RA, is not secondary to undernutrition [12]. Inflammation suppresses albumin synthesis and transfer albumin from the vascular to the extravascular space resulting in hypoalbuminemia [17]. RA patients also have high TNF- $\alpha$  production which is associated with higher rates of protein catabolism [18].

Serum cholesterol reflects lipid levels in the blood. Inflammation is associated with reduction in serum cholesterol. We also found reduction in mean cholesterol level with the increase in disease activity [19].

Cachexia is often found in chronic diseases with inflammatory response such as such as tuberculosis, cancer, acquired immune deficiency syndrome, cardiac failure, chronic renal failure etc. [1, 2, 20]. It usually manifests with excessive weight loss, low muscle mass and low fat mass [3, 4]. Rheumatoid cachexia is different as it is characterized by normal or increased fat mass and BMI, with concurrent loss of body protein predominantly in skeletal muscle mass, [3, 4] and therefore, it often remains undetected. Many factors are involved in the pathogenesis of rheumatoid cachexia including proinflammatory cytokines (TNF- $\alpha$ , IL-1 $\beta$ , IL-6), excessive energy expenditure, high rates of whole body protein breakdown, loss of muscle mass and strength, reduced physical activity due to joint pain and stiffness [1].

In summary, this study highlights the effect of RA disease on nutritional status of the patients and an attempt to reduce the disease activity in these patients might improve their nutritional status.

## CONCLUSION

RA patients having a higher disease activity (higher DAS28) had significantly lower hemoglobin concentration, BMI and serum albumin (p for trend <0.05). A significant negative correlation exists between markers of disease activity (DAS28 and ESR) and markers of nutrition (serum albumin, haemoglobin and BMI).

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