ORIGINAL ARTICLE

# Insulin Resistance and Lipid Profile in Rheumatoid Arthritis Patients in Bangladesh

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**Abstract:**

*There has been a great deal of research activity focusing on the relationship between insulin resistances (IR), hyperlidemia and Rheumatic arthritis (RA). It appears to be a general agreement that IR and hyperlipidaemia are commonly seen in patients with RA. A case-control study was done among 45 RA patients and 42 healthy controls. The study was conducted in the outpatient department of Bangabandhu Sheikh Mujib Medical University (BSMMU). A structured questionnaire was used to collect data through face-to-face interview. TG and LDL were significantly higher and HDL was lower in comparison to those of control and associated with IR. Hyperlipidemias are associated with RA in Bangladeshis.*

## Introduction:

Rheumatoid arthritis (RA) is a systemic immune and chronic inflammatory disease. Its prevalence is remarkably consistent worldwide. Its prevalence is 0.6% in Bangladeshi population[1] and 0.8% in western population. In addition to articular manifestations of RA, there is growing recognition of excess mortality, which is predominantly due to increased coronary artery atherosclerosis[2].

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Rheumatoid arthritis is now considered as an important component of metabolic syndrome. RA patients experience a markedly increased prevalence of cardiovascular disease[3], a comorbidity that may be partly mediated through insulin resistance[4]. An independent association of insulin resistance with carotid as well as coronary artery atherosclerosis has been reported in RA[5]. Insulin resistance (IR) seems to be the main metabolic abnormality that alters glucose metabolism, decreases the sensitivity of peripheral tissues to insulin in patients with rheumatoid arthritis and complicating rheumatic disease via an increase in atherosclerotic disease risk and pre-diabetic state[6].

In RA, the primary site of inflammation is the synovial tissue, from which cytokines can be released into the systemic circulation. Insulin insensitivity also shows cytokine production and other markers of inflammation. Pro-inflammatory cytokines like Interleukin-1, Interleukin-6 and Tumor necrosis factor – α

(TNF- α) are major modulators of these events. TNF- α leading to accumulation of serum triglycerides and decrease in serum HDL cholesterol and increased LDL cholesterol might be result of hampered insulin action[7].Under their influence, elevation of blood lipids, enhanced gluconeogenesis, catabolic hormone production and decreased insulin sensitivity occurs. Similar events, however, occur during the course of inflammatory diseases such as RA[8,9]. In RA patients, disease activity is associated with elevated levels of LDL and insulin resistance[10].

Thus, in western population it is evident that hyperlipidaemia seems to be an important feature in insulin resistant RA patients. So far, in Bangladesh, no study has yet been done to explore the role of hyperlipidaemia and insulin resistance, in rheumatic arthritis patients. The present study has been undertaken to evaluate the association of IR and lipid profile among RA patients.

## Materials and method:

The present case-control study was carried out in the department of biochemistry of BSMMU. In this study, 87 subjects with age ranged from 34-45years of both sexes were included. Among them 45 patients were of RA fulfilling the American College of Rheumatology (ACR) criteria. The RA patients were further divided into two groups; untreated group of 19 RA patients and treated group of 26 patients who were on disease modifying anti-rheumatic agents (DMARD). Forty two apparently healthy volunteers, not having DM and MI, were also selected as control. The objectives and benefits of the study were explained to all the subjects to ensure their voluntary participation and written informed consent was taken from each subject prior to the study.

From each subject, blood was drawn for determination of IR and lipid profile. IR was calculated from fasting plasma glucose (mmol/l) and fasting serum insulin (pmol/l) values by the Homeostasis Model Assessment (HOMA) model, using HOMA-2 software[11]. Plasma total cholesterol was measured by enzymatic endpoint method (cholesterol oxides / peroxides). Plasma triglyceride was measured by enzymatic colorimetric (GPO-PAP) method. Plasma high density lipoprotein (HDL-c) was measured by enzymatic colorimetric (cholesterol CHOD-PAP) method. Plasma LDL-cholesterol level was calculated by using Friedewald's formula.

Statistical analysis was done using SPSS software for Windows version 12.0. Data were expressed as Mean ± SD, Median (Range) or as number (%). Statistically significance of differences between mean and median values was assessed by Student's unpaired t-test, Mann-Whitney U-test, where appropriate. A two-tailed p-value of $< 0.05$ was considered statistically significant.

## Results:

The study subjects were age and BMI matched. RA patients with treatment showed significantly higher triglyceride z=0.02 and RA patients without treatment showed significantly higher triglyceride z=0.009 than the controls and in RA patients with treated vs untreated. Lower high-density lipoprotein (HDL) in treated RA group and in untreated RA group than the controls and in RA patients with treated vs. untreated. Results are

expressed as mean ± SD. Unpaired Student's t-test was done.

**Table-I:** Age and BMI distribution of the study subjects

| Study subjects | Age in years | BMI |
|---|---|---|
| RA patients (n = 45) | 33.89 ± 10.89 | 22.17 ± 4.34 |
| Control (n = 42) | 31.79 ± 9.22 | 22.67 ± 3.7 |
| Test of significance t / P | 0.97 / 0.34 | 0.58 / 0.56 |

have abnormal lipid profiles as evidenced by global reduction of all lipid subsets and also increased triglyceride[11]. Some studies report the disease activity of RA is associated with both low LDL and HDL cholesterol and both lipoproteins increase upon suppression of disease activity[12].

Reason behind such findings in Bangladeshi patients can be due to different food habit, life style etc. Replacing carbohydrates by monounsaturated fats as a source of calories

**Table II:** Comparison of lipid profile and insulin resistance

| Parameters | With treatment (n=26) | Without treatment (n=19) | Control (n=42) | Test of Significance z / p | | |
|---|---|---|---|---|---|---|
| | | | | Control vs treated | Control vs untreated | treated vs untreated |
| T. Cholesterol | 173(120-259) | 176(130-225) | 170(125-273) | .207/.836 | .745/. 456 | .548/. 583 |
| TG | 110(52-185) | 139(42-320) | 93(34-262) | 2.20/0.02 | 2.62/0.009 | 1.25/. 20 |
| HDL | 25(17-37) | 26(15-37) | 38(24-51) | 5.6/0.0001 | 5.04/0.0001 | 1.31/. 18 |
| LDL | 123(62-200) | 120(87-178) | 115(40-199) | 1.03/.30 | .99/. 32 | .28/. 77 |
| HOMA%B | 88 (1-238) | 105(33-303) | 91(47-189) | .64 /. 51 | .55/. 57 | 1.05/. 29 |
| HOMA%S | 141(27-317) | 121(35-315) | 140 (24-289) | .03/. 97 | 1.5 / .11 | .98/. 32 |

Results are expressed as Median (range). Mann-Whitney test was done. n= number of subjects.
RA= Rheumatoid arthritis: TG= Triglyceride; HDL= High density lipoprotein; LDL= Low density lipoprotein

## Discussion:

Insulin resistance has been considered as a main metabolic abnormality in patients with RA leading to alteration in glucose metabolism caused by decreased sensitivity of peripheral tissues to insulin. In western population, it is evident that IR seems to be an important feature in RA patients[7,11]. Association between IR and lipid profile in RA subjects was evaluated in this study.

In this study, IR was associated with higher level of cholesterol, higher triglycerides and lower HDL level in RA patients. These findings are supported by many studies where it has been found that patients with active RA raises HDL- cholesterol without effecting LDL- cholesterol and also improve insulin sensitivity. For conclusive results, further study with greater population with dietary intervention is recommended.

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