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# Evaluation of obesity and various risk factors of CVD in RA patients from North India

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***ABSTRACT***

*RA is a chronic inflammatory condition leading to irreversible destruction and deformation of synovial joints. RA patients were found more prone to develop CVD as compared to normal individuals. So, the present study was designed to evaluate the various risk factors of CVD in RA patients from North India. Furthermore, the effects of obesity were also assessed on these studied parameters. The present study recruited 178 RA patients and 178 unrelated age, gender and ethnicity matched controls. Standard anthropometric measurements including weight, height, hip circumference and waist circumference were performed on each individual using standard anthropometric methodology. Body mass index (BMI), Waist hip ratio (WHR) and waist stature ratio (WSR) were calculated from the given data. Blood pressure was measured with a standard mercury sphygmomanometer. Mean arterial pressure (MAP) and pulse pressure (PP) were calculated using standard formula. Different lipid profile biomarkers and C-reactive protein (CRP) were quantified using standard reagents and kits. Lipid peroxidation was determined by quantitative analysis of serum malondialdehyde (MDA) by standard protocol. Data were analyzed using suitable statistical analysis. Present study indicated high prevalence of obesity, hypertension, inflammation, lipid peroxidation in RA patients in comparison to controls. Furthermore, obese RA patients were found to have significantly high atherogenic indices, CRP and MDA as compared to obese controls.*

***Keywords:*** *Abdominal obesity, Body Mass Index, C-reactive protein, Lipid Profile, Malondialdehyde, Rheumatoid Arthritis*

## INTRODUCTION

Rheumatoid Arthritis is a chronic inflammatory condition leading to irreversible destruction and deformation of synovial joints. The prevalence of RA is reported to be 0.7-1.5% worldwide and 0.75% in India. Epidemiological evidences have shown an increased premature mortality in RA patients, mainly attributed to cardiovascular diseases (CVD) particularly coronary atherosclerosis (Wolfe et al., 1994; Myllykangas-Luosujarvi et al., 1995). RA patients were estimated to be about 4 times more prone to develop CVD as compared to age and gender-matched subjects without RA. Both traditional as well as novel risk factors have been documented to explain the accelerated atherogenesis in RA including obesity, dyslipipdemia, hypertension, smoking and diabetes mellitus. These risk factors can play a crucial role in the development and maintenance of inflammation, which is considered to be the central event in the development of atherosclerosis (del Rincon et al., 2001; Maradit-Kremers et al., 2005; Stavropoulos-Kalinoglou et al., 2011).

The role of obesity is well documented in cardiovascular events as well as development of inflammation. The drastic increase observed in RA incidence can be partially explained by rising prevalence of obesity throughout the developed and developing countries (Myasoedova et al., 2010; Force, 2012; Crowson et al., 2013). Furthermore, obesity is associated with dyslipidemia, hypertension and diabetes mellitus, all of which are considered as traditional risk factors for cardiovascular diseases (CVD) in general population. In addition to this, obesity is considered as a pro-inflammatory state. Adipose tissue is a metabolically active entity, producing various bioactive molecules collectively called adipokines (Berg and Scherer, 2005; Trayhurn and Wood, 2005). Most of these adipokines are implicated in the production of various pro-inflammatory cytokines such as TNF-α, and IL-1, IL-6 and C-reactive protein (CRP), an acute-phase reactant (Trayhurn and Wood, 2005; Lago et al., 2007; Frannsson et al., 2010; Derdemezis et al., 2011). These adipokines as well as the molecules they induce are documented to be central in the pathogenesis and/or progression of RA. RA patientswere found to have high levels of various adipokines, TNF-α and interleukins (Klimiuk et al., 1997; Buch and Emery, 2002). CRP is considered as a powerful marker of synovial inflammation and alternation in CRP levels was considered as a useful predictor for disease activity (Singh et al., 2013). Furthermore, chronic

disease conditions including RA were also shown to be associated with increased oxidative stress (Vasanthi et al., 2009; Mishra et al., 2012). Malondialdehyde (MDA) is a stable product of oxidative degradation of lipids leads to production of lipid peroxides and is one of the most frequently used biomarkers of the overall lipid peroxidation (Kalavacherla et al., 1994; Nielsen et al., 1997).

A number of studies involving prevalence of obesity, dyslipidemia, inflammatory status as well as oxidative stress in RA patients are available. But to our knowledge, no report is available to assess all the variables in a single study and to compare the effect of obesity on all the above-mentioned variables, particularly in North India. Thus, the present study was planned to evaluate various risk factors of CVD in RA patients from North India. Furthermore, the effect of obesity was also assessed on these studied parameters.

## MATERIAL AND METHODS

**Subjects:** The present case-control study consists of 178 female RA patients from local rheumatology clinic diagnosed according to criteria of American College of Rheumatology (Arnett et al., 1988). Age, gender and ethnicity matched ($p>0.05$), 178 healthy females were also recruited as controls from adjoining areas. Information regarding demographic variables, medical history etc. was collected from all the subjects in the pre-designed proforma. The mean age of the patients and controls was 45.69±13.11 and 45.07±14.21 years respectively. All individuals were genetically unrelated North Indian residents. The pregnant women, smokers, and alcoholics were excluded from the study. The study protocol was approved by institutional ethical committee in accordance with declaration of Helsinki and the written informed consent was obtained from each individual to participate in the study.

**Anthropometric and physiometric measurements:** Standard anthropometric measurements including weight (Kg), height (m), hip circumference (cm) and waist circumference (cm) were performed on each subject using standard methodology (Weiner and Lourie, 1981). The height was measured using stadiometer, with the subject standing without shoes in the eye-ear plane. The weight of the subject was measured in kilograms by making her stand on a weighing machine in minimal clothing. Height (cm) and weight (kg) were measured to the nearest 0.1 cm

and 0.5 kg, respectively. Waist circumference (WC) was measured above the iliac crest and below the lowest rib margin at minimum respiration. Hip circumference (HC) was measured at the widest part of the hip at the level of the greater trochanter. Both circumferences were measured with a metal tape. Body mass index (BMI), Waist hip ratio (WHR) and waist stature ratio (WSR) were calculated from the given data. BMI was calculated by dividing weight in kilogram by square of height in meters. According to their BMI subjects were classified into four groups (WHO, 2000) as underweight (>18.5 $Kg/m^2$), normal weight (<18.5-22.9 $Kg/m^2$), overweight (23-24.9 $Kg/m^2$) and obese (≥25 $Kg/m^2$). The abdominal obesity was assessed by criteria for WC and WHR given by Snehalatha et al (2003). According to these criteria the subjects having WC ≥80 cm and WHR ≥0.81 were abdominally obese. The criteria used for WSR was given by Hsieh and Muto (2005) according to which the individuals having WSR ≥ 0.50 were considered to be abdominally obese.

Blood pressure was measured with a standard mercury sphygmomanometer (Pagoda, New Delhi) with an appropriate size cuff and stethoscope by following recommendations of American Heart Association (Atamen et al., 1996).Mean arterial pressure (MAP) and pulse pressure (PP) were calculated using standard formula of Peruse et al (1989).The Hypertensive status of studied subjects was assessed by using standard criteria of JNC VII (2003).

**Serum biochemical analysis:** Blood samples were collected from all the subjects in the EDTA free vials and were processed for serum isolation. The isolated serum was stored at -80$^o$ C till further use. Serum lipid profile biomarkers including total cholesterol (TC), triacylglycerols (TG) and high density lipoprotein- cholesterol (HDL-C) were quantified on semiautomatic clinical analyzer (ERBA, Germany) using standard reagents and kits using manufacturer's protocol. Very low density lipoprotein (VLDL) and low density lipoprotein-cholestrol (LDL-C) were calculated from the above mentioned lipid profile parameters by standard formulae (Friedewald et al., 1972). Non-HDL cholesterol (non-HDL C) was estimated by subtracting HDL-C from total cholesterol. Atherogenic indices i.e. TC/HDL-C, TG/HDL-C and LDL-C/HDL-C were also calculated. Inflammatory status was assessed by quantification of serum C-reactive protein (CRP) levels (n=86) using commercially available kits (Hysel India Pvt Ltd.).

Lipid peroxidation was determined by quantitative analysis of serum malondialdehyde (MDA) using MDA standard (Sigma-Aldrich, USA) by standard protocol (Buege and Aust, 1978).

**Statistical analysis** : Comparison of anthropometric variables, physiometric variables, lipid profile variables between any two different groups were done by independent't' test. Comparisons of different variables among more than two groups were done by one way ANOVA. All statistical analysis was done by Statistical Package for Social Science for windows version 16.0(SPSS inc., Chicago, IL). p values <0.05 were considered to be significant.

## RESULTS

**Table1: Comparison of different anthropometric, physiometric and serum biochemical variables of RA patients and healthy controls**

| Variables | RA patients (N=178) | Controls (N=178) | p-value |
|---|---|---|---|
| | Mean±SD | Mean±SD | |
| BMI (kg/m$^2$) | 25.77±4.79 | 23.37±3.97 | 0.001** |
| WC (cm) | 90.99±12.41 | 87.31±23.06 | 0.001** |
| WHR | 0.89±0.07 | 0.90±0.05 | 0.195 |
| WSR | 0.22±0.03 | 0.21±0.03 | 0.001** |
| SBP(mm/Hg) | 134.43±23.05 | 125.13±23.95 | 0.001** |
| DBP(mm/Hg) | 89.34±14.79 | 82.18±12.23 | 0.001** |
| MAP | 105.57±17.68 | 96.94±14.02 | 0.001** |
| PP | 45.20±16.56 | 43.57±17.56 | 0.370 |
| TC(mg/dl) | 152.87±42.83 | 148.74±45.43 | 0.343 |
| TG (mg/dl) | 135.85±52.93 | 148.74±56.96 | 0.028* |
| HDL- C (mg/dl) | 31.27±18.62 | 34.78±14.71 | 0.049* |
| LDL- C (mg/dl) | 92.35±51.75 | 90.00±44.11 | 0.644 |
| VLDL(mg/dl) | 27.00±10.61 | 29.74±11.39 | 0.019* |
| Non-HDL C (mg/dl) | 120.17±50.19 | 115.85±47.91 | 0.407 |
| TC/HDL- C | 6.66±4.74 | 4.71±2.34 | 0.001** |
| TG/HDL- C | 5.79±4.50 | 5.02±2.81 | 0.050* |
| LDL-C/HDL-C | 4.61±3.96 | 2.76±2.03 | 0.001** |
| CRP (mg/L) | 6.42±0.66 | 3.79±1.86 | 0.001** |
| MDA | 5.34±2.31 | 4.43±1.46 | 0.001** |

Significant at p<0.001**, p<0.05*; BMI: Body mass Index, WC: Waist Circumference; WHR: Waist Hip Ratio; WSR: Waist Stature ratio; SBP: Systolic blood pressure; DBP: Diastolic Blood pressure; MAP: Mean arterial pressure; PP: Pulse pressure; TG: Triacylglycerol; HDL: High density lipoprotein; LDL: Low density lipoprotein; CRP: C - reactive protein; MDA: Malondialdehyde

BMI, WC, WSR, SBP, DBP and MAP were significantly higher ($p<0.001$ each) in patients as compared to healthy subjects (Table 1)**.** Out of various serum biochemical variables tested CRP, MDA and various atherogenic indices i.e. TC/HDL-C, TG/HDL-C, LDL-C/HDL-C, were significantly ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.05$, $p<0.001$, respectively) higher in patients. However, TG, HDL-C, VLDL were found to be significantly low in patients than controls.

**Table 2: Comparison of SBP and DBP among female RA patients and healthy controls according to JNC VII guidelines.**

| **Blood Pressure (SBP mmHg)** | | | | | |
|---|---|---|---|---|---|
| **Classification** | **Count RA** | **RA** | **Count Controls** | **Control** | **p-value** |
| Normal | 51 | 106.96±16.27 | 79 | 104.48±12.67 | 0.332 |
| Pre-hypertension | 52 | 128.55±5.30 | 48 | 128.02±5.68 | 0.626 |
| Hypertension StageI | 39 | 147.97±6.10 | 32 | 149.68±6.10 | 0.844 |
| Stage II hypertension | 29 | 188.13±25.55 | 19 | 173.63±12.81 | 0.013* |
| **Blood Pressure (DBP mmHg)** | | | | | |
| Normal | 46 | 72.67±5.90 | 82 | 70.80±8.42 | 0.185 |
| Pre-hypertension | 39 | 84.12±2.13 | 45 | 84.60±2.66 | 0.378 |
| Hypertension StageI | 47 | 93.89±2.84 | 28 | 93.46±2.72 | 0.523 |
| Stage II hypertension | 39 | 119.61±18.69 | 23 | 114.61±14.15 | 0.272 |

Significant at $p<0.05$*

Out of 178 RA patients, 29.8% and 26.9% patients were found to be having normal SBP and DBP respectively as compared to 44.3% and 46.0% of controls (Table 2). There was no significant difference ($p>0.05$) in normal pre-hypertensive and stage I hypertensive category of blood pressure (SBP and DBP) between RA patients and controls. However the patients have sign ificantly high prevalence of stage II hypertension according to SBP.

Patients were segregated into underweight, normal, overweight and obese according to BMI. Out of these 63 (35.4%) and 61 (34.3%) patients were found to be overweight and obese respectively (Table 3). Significant differences in MAP, PP, TG, VLDL and MDA levels

($p<0.001$, $p<0.05$, $p<0.01$, $p<0.01$, $p<0.05$ respectively) had been observed in patients segregated according to BMI. When overall obesity (BMI) was compared between RA patients and controls (Table 4), there was more prevalence of obesity in RA patients (34.3%) as compared to healthy subjects (13%).Furthermore, the overweight and obese RA patients and controls were compared for various physiometric and biochemical parameters. Overweight patients were found to have significantly higher SBP, DBP, MAP ($p<0.05$, $p<0.001$, $p<0.001$) as compared to controls.

Significantly high TC, LDL-C, atherogenic indices, serum CRP and MDA levels were also found in overweight patients than controls ($p<0.001$, $p<0.05$, $p<0.001$, $p<0.001$, $<0.05$ respectively). Obese patients were found to have significantly high MAP, serum CRP and MDA levels as compared to obese controls ($p<0.05$, $p<0.001$, $p<0.05$) (Table 4)

**Table 3: Comparison of physiometric and serum biochemical variables within RA patients for BMI.**

| Variables | BMI | | | p-value |
|---|---|---|---|---|
| | Normal N=47 (26.4%) | Overweight N=63 (35.4%) | Obesity N=61 (34.3%) | |
| SBP(mm/Hg) | 131.50±24.79 | 139.63±33.08 | 138.23±33.81 | 0.372 |
| DBP(mm/Hg) | 88.40±16.00 | 95.14±20.54 | 90.90±20.61 | 0.183 |
| MAP | 91.00±25.25 | 110.89±27.67 | 109.49±31.64 | 0.001** |
| PP | 36.81±23.99 | 45.23±17.15 | 49.43±27.61 | 0.020* |
| TC (mg/dl) | 145.52±43.07 | 163.13±34.88 | 152.06±54.04 | 0.113 |
| TG (mg/dl) | 119.29±62.32 | 153.19±44.45 | 138.41±52.67 | 0.005* |
| HDL- C(mg/dl) | 38.33±38.07 | 36.21±32.11 | 34.14±19.42 | 0.774 |
| LDL- C (mg/dl) | 82.73±65.40 | 89.80±58.16 | 92.17±59.57 | 0.714 |
| VLDL(mg/dl) | 23.86±12.46 | 30.64±8.89 | 27.20±10.61 | 0.005* |
| Non-HDL C(mg/dl) | 108.33±62.88 | 127.11±44.06 | 119.36±54.42 | 0.201 |
| TC/HDL-C | 9.55±8.63 | 8.11±6.63 | 8.39±15.88 | 0.788 |
| TG/HDL- C | 6.86±7.45 | 7.90±7.01 | 6.93±9.76 | 0.743 |
| LDL- C /HDL- C | 5.88±6.77 | 5.22±5.63 | 6.03±14.05 | 0.887 |
| CRP (mg/L) | 6.20±2.97 | 6.31±0.74 | 7.11±2.11 | 0.227 |
| MDA | 4.42±2.41 | 5.86±3.45 | 5.56±2.72 | 0.035* |

Significant at $p<0.001$**, $p<0.05$*

**Table 4: Comparison of physiometric and serum biochemical variables between BMI overweight and obese Categories of RA patients and controls**

| Variables | BMI (Overweight) | | p-value | BMI (Obese) | | p-value |
|---|---|---|---|---|---|---|
| | RA patients N=63 (35.4%) | Controls N=79 (44.4%) | | RA patients N=61 (34.3%) | Controls N=23 (13%) | |
| SBP(mm/Hg) | 139.63±33.08 | 124.94±23.86 | 0.004* | 138.23±33.82 | 137.31±41.44 | 0.927 |
| DBP(mm/Hg) | 95.14±20.55 | 81.27±15.17 | 0.001** | 90.90±20.61 | 85.59±19.14 | 0.281 |
| MAP | 110.89±27.67 | 95.83±15.94 | 0.001** | 109.49±31.64 | 96.27±11.79 | 0.007* |
| PP | 45.23±17.14 | 43.67±20.02 | 0.616 | 49.43±27.62 | 41.81±22.34 | 0.249 |
| TC (mg/dl) | 163.14±34.88 | 132.80±43.22 | 0.001** | 152.06±54.05 | 144.28±42.06 | 0.543 |
| TG (mg/dl) | 1530.19±44.45 | 148.79±54.13 | 0.596 | 138.41±52.67 | 153.16±58.37 | 0.277 |
| HDL- C (mg/dl) | 36.21±32.11 | 37.28±14.75 | 0.808 | 34.14±19.42 | 34.72±22.10 | 0.908 |
| LDL- C (mg/dl) | 89.80±58.17 | 63.79±48.08 | 0.005* | 92.17±59.57 | 76.70±51.22 | 0.283 |
| VLDL(mg/dl) | 30.64±8.89 | 29.75±10.82 | 0.596 | 27.20±10.61 | 29.02±9.70 | 0.485 |
| Non-HDL C (mg/dl) | 127.11±44.06 | 95.52±44.73 | 0.001** | 119.85±56.52 | 122.17±51.97 | 0.867 |
| TC/HDL-C | 8.11±6.63 | 4.33±3.02 | 0.001** | 8.39±15.88 | 6.39±4.48 | 0.376 |
| TG/HDL- C | 7.90±7.01 | 4.70±2.73 | 0.001** | 7.23±5.86 | 5.29±2.72 | 0.649 |
| LDL- C /HDL- C | 5.22±5.63 | 2.33±2.74 | 0.001** | 6.93±9.76 | 5.94±4.29 | 0.534 |
| CRP (mg/L) | 6.31±0.74 | 3.33±1.63 | 0.001** | 7.11±2.11 | 3.45±2.79 | 0.001** |
| MDA | 5.87±3.44 | 4.51±1.94 | 0.006* | 5.56±2.72 | 4.28±2.29 | 0.050* |

Significant at p<0.001**, p<0.05*

**Table5: Comparison of physiometric and serum biochemical variables within RA patients for WC**

| Variables | WC | | p-value |
|---|---|---|---|
| | Normal N=3 (1.7%) | Obese N=175 (98.3%) | |
| SBP(mm/Hg) | 127.00±1.73 | 131.58±40.68 | 0.846 |
| DBP(mm/Hg) | 85.33±8.38 | 92.04±19.55 | 0.554 |
| MAP | 100.67±4.37 | 103.75±34.37 | 0.877 |
| PP | 32.33±7.37 | 41.09±26.09 | 0.563 |
| TC (mg/dl) | 162.90±87.10 | 154.88±45.32 | 0.765 |
| TG (mg/dl) | 122.00±1.73 | 136.41±54.67 | 0.001* |
| HDL- C (mg/dl) | 23.81±3.67 | 36.82±30.73 | 0.466 |
| LDL- C (mg/dl) | 100.15±19.94 | 90.06±61.78 | 0.482 |
| VLDL(mg/dl) | 24.80±2.16 | 27.11±10.96 | 0.193 |
| Non-HDL C(mg/dl) | 105.50±1.51 | 119.42±54.24 | 0.001* |
| TC/HDL-C | 5.22±1.82 | 8.33±10.91 | 0.687 |
| TG/HDL- C | 5.30±1.35 | 7.17±8.14 | 0.194 |
| LDL- C /HDL- C | 4.64±1.38 | 5.67±9.59 | 0.301 |
| CRP (mg/L) | 4.90±1.26 | 6.78±1.74 | 0.068 |
| MDA | 5.52±1.65 | 5.72±2.87 | 0.906 |

Significant at p<0.001*,

Patients were segregated into normal and obese categories according to WC (table 5). Obese subjects were found to have significantly high serum levels of TG, VLDL and non-HDL-C levels ($p<0.001$ each). Atherogenic indices i.e.TC/HDL-C, TG/HDL-C and LDL-C/HDL-C, were also higher in obese subjects, but the difference was not significant ($p>0.05$). The prevalence of abdominal obesity was also found to be higher in patients (98.3%) as compared to controls (84%) (Table 6). Obese subjects of both studied groups (patients and control) were compared for physiometric and serum parameters. Obese patients were found to have significantly high DBP ($p<0.001$), MAP ($p<0.05$), TC/HDL-C ($p<0.001$), TG/HDL-C ($p<0.001$), LDL-C/HDL-C ($p<0.001$), CRP ($p<0.001$) as well as MDA ($p<0.001$).

**Table 6: Comparison of physiometric and serum biochemical variables between WC obese Category of RA patients and controls**

| Variables | WC (Obese) | | p-value |
|---|---|---|---|
| | RA patients N=175 (98.3) | Controls N=149 (83.7%) | |
| SBP(mm/Hg) | 131.58±40.68 | 124.55±24.29 | 0.056 |
| DBP(mm/Hg) | 92.04±19.55 | 82.48±15.45 | 0.001** |
| MAP | 103.75±34.37 | 96.50±15.29 | 0.013* |
| PP | 41.09±26.09 | 42.06±23.41 | 0.725 |
| TC (mg/dl) | 154.88±45.32 | 147.21±47.97 | 0.140 |
| TG (mg/dl) | 136.41±54.67 | 147.19±57.99 | 0.088 |
| HDL- C (mg/dl) | 36.82±30.73 | 35.26±15.70 | 0.557 |
| LDL- C (mg/dl) | 90.06±61.78 | 81.07±53.86 | 0.163 |
| VLDL(mg/dl) | 27.11±10.95 | 29.44±11.59 | 0.066 |
| Non-HDL C(mg/dl) | 119.43±54.24 | 111.95±51.32 | 0.207 |
| TC/HDL-C | 8.33±10.91 | 5.23±3.37 | 0.001** |
| TG/HDL- C | 7.16±8.14 | 5.05±2.97 | 0.001** |
| LDL- C /HDL- C | 5.62±9.59 | 3.19±3.10 | 0.001** |
| CRP (mg/L) | 6.78±1.74 | 4.11±1.77 | 0.001** |
| MDA | 5.72±2.87 | 4.62±1.76 | 0.001** |

Significant at $p<0.001$*, $p<0.01$**, $P<0.05$***

Abdominal obesity was also assessed by WHR and WSR. When patients were segregated according to WHR, obese patients were found to have higher physiometric as well as

**Table 7: Comparison of physiometric and serum biochemical variables with in RA patients for WHR**

| Variables | WHR | | p-value |
|---|---|---|---|
| | Normal /non-obese N=24 (13.5%) | Obese N=154 (86.5%) | |
| SBP(mm/Hg) | 139.00±34.23 | 136.07±40.08 | 0.568 |
| DBP(mm/Hg) | 93.00±22.64 | 91.53±19.06 | 0.740 |
| MAP | 113.58±37.05 | 106.24±34.03 | 0.334 |
| PP | 46.00±16.88 | 43.90±25.33 | 0.696 |
| TC (mg/dl) | 168.56±40.82 | 157.64±46.60 | 0.280 |
| TG (mg/dl) | 138.52±49.63 | 136.83±53.70 | 0.885 |
| HDL- C (mg/dl) | 27.64±18.88 | 36.41±30.69 | 0.176 |
| LDL- C (mg/dl) | 104.17±53.17 | 91.75±62.10 | 0.354 |
| VLDL (mg/dl) | 27.70±9.93 | 26.93±10.95 | 0.745 |
| Non-HDL C (mg/dl) | 123.78±40.21 | 122.37±55.47 | 0.905 |
| TC/HDL-C | 6.94±4.22 | 8.32±11.49 | 0.560 |
| TG/HDL- C | 7.61±5.41 | 7.02±8.07 | 0.731 |
| LDL- C /HDL- C | 5.14±3.97 | 5.91±9.96 | 0.711 |
| CRP (mg/L) | 6.83±1.09 | 7.04±2.25 | 0.702 |
| MDA | 4.52±2.09 | 5.63±2.83 | 0.067 |

**Table 8: Comparison of physiometric and serum biochemical variables between WHR obese category of RA patients and controls**

| Variables | WHR (Obese) | | p-value |
|---|---|---|---|
| | RA N=154 (86.5%) | Controls N=154 (86.5%) | |
| SBP(mm/Hg) | 134.05±40.08 | 125.82±24.71 | 0.031* |
| DBP(mm/Hg) | 91.53±19.63 | 83.87±18.59 | 0.001* |
| MAP | 106.25±34.03 | 97.03±15.67 | 0.003* |
| PP | 43.90±25.33 | 42.01±23.39 | 0.498 |
| TC (mg/dl) | 157.64±46.60 | 147.31±47.29 | 0.050* |
| TG (mg/dl) | 136.83±53.70 | 147.46±58.55 | 0.098 |
| HDL- C (mg/dl) | 36.41±30.69 | 35.67±15.73 | 0.791 |
| LDL- C (mg/dl) | 91.74±62.10 | 80.75±53.22 | 0.096 |
| VLDL(mg/dl) | 26.93±10.95 | 29.49±11.71 | 0.048* |
| Non-HDL C (mg/dl) | 122.37±55.47 | 111.64±50.60 | 0.077 |
| TC/HDL-C | 8.32±11.49 | 5.17±3.33 | 0.001** |
| TG/HDL- C | 7.02±8.07 | 4.96±2.94 | 0.003* |
| LDL- C /HDL- C | 5.91±9.96 | 3.14±3.07 | 0.001** |
| CRP (mg/L) | 7.04±2.25 | 3.39±1.69 | 0.001** |
| MDA | 5.62±2.83 | 4.63±1.75 | 0.001** |

Significant at p<0.001**, p<0.05 *

biochemical variables as compared to normal ones, but the difference was not significant ($p>0.05$) (Table 7). The prevalence of abdominal obesity according to WHR showed similar prevalence of obesity in patients as well as controls (Table 8). However, obese patients were found to have significantly high SBP, DBP, MAP, TC, VLDL, atherogenic indices as well as serum CRP and MDA levels as compared to obese controls ($p<p.05$, $p<.0.001$, $p<0.05$, $p<0.05$, $p<0.05$, $p<0.001$, $p<0.001$, $p<0.001$ respectively). According to criteria of WSR, all studied subjects were found to be normal.

## DISCUSSION

The present study involves evaluation of some CVD risk factors including obesity, lipid profile, hypertension, inflammation and lipid peroxidation in RA patients and the matched healthy controls from North India. The data were further analyzed to evaluate the effect of obesity on the other CVD risk factors.

Obesity is an established risk factor for CVD in the general population. It is also considered the underlying cause of many other CVD risk factors and a potent contributor in inflammatory pathway of atherosclerosis. These findings indicate the importance of obesity in various inflammatory disease conditions including RA (Berg et al., 2005; Panoulas et al., 2007; Stavropoulos-Kalinoglou et al., 2011). The results of the present study indicate that overall as well as abdominal obesity was more prevalent in patients as compared to respective controls. The patients enrolled in the present study were found to have higher BMI, WC, WHR and WSR as compared to controls. The results indicate that prevalence of overweight and obesity according to BMI was 35.4% and 34.3% respectively. The prevalence of abdominal obesity was 98.3% and 86.5% according to WC and WHR respectively. The findings are in agreement with a recent study involving RA patients in India indicating high BMI and WC in RA patients (Deo et al., 2012). Some previous studies have examined the effect of obesity on development of RA with inconsistent results. Studies have indicated that obesity was associated with an almost 4-fold increase in the risk for developing RA, and the effect was found to be pronounced in women than men (Symmons et al., 1997; Garcia-Poma et al., 2007).In another study, obesity in RA was found to be associated with higher inflammatory activity and reduced functional capacity while no effect was observed on joint damage (Stavropoulos-Kalinoglou et al., 2011). In contrast to

these findings, other studies have found no effect of obesity on development of RA (Hernandez et al., 1990; Cerhan et al., 2002; Escalante et al., 2005; Naranjo et al., 2008). In an early study from Indian population, low BMI was found to be associated with joint damage in patients with early RA (Velpula et al., 2011), while in another study from the same population, no difference of BMI was observed between patients and controls (Mishra et al., 2012).

The results of the present study indicate significantly high levels of CRP in patients as compared to controls. This finding is in consonance with various earlier studies from India as well as other populations indicating higher serum levels of CRP in RA patients (Rani et al., 2006; Deo et al., 2012; Mullick et al., 2014).CRP is an established marker of disease activity. Furthermore, it was shown to stimulate macrophages to produce tissue factor, an important procoagulant, which was found in atheromatous plaques, suggesting a link between CRP and coronary events (Cermak et al., 1993; Ardissino et al., 1997; Torzewski et al., 1998). Obese subjects were found to have high CRP levels as compared to non-obese subjects. The results in the present study are in consonance with previous studies showing increased levels of CRP in obese subjects (Reddy et al., 2013; Dayal et al., 2014). The patients with abdominal obesity were found to have significantly higher CRP as compared to obese controls. These findings indicate that obese patients have more burden of disease.

The available literature on lipid profile in RA patients is contradictory. There have been studies reporting either increased, decreased or similar levels for TC, LDL-C and HDL-C in comparison to healthy subjects (Nurmohamed, 2007; Van Halm et al., 2007; Deo et al., 2012; Vinapamula et al., 2013). The discrepancies in various studies can be due to differences in study populations, disease activity, effect of inflammation as well as treatment (Choi et al., 2009; Toms et al., 2010).The present study showed significantly high atherogenic indices in RA patients as compared to healthy controls. It has been documented that individual lipid concentrations may show frequent variations due to variable degree of chronic inflammation and thus may change during the course of disease. Recent studies have suggested that atherogenic indices are more appropriate markers to access contribution of lipids to CV risk in RA patients being less susceptible to disease activity changes (Popa et al., 2012). Furthermore, when diseased obese individuals were compared with obese controls; obese RA patients were found to have

significantly high atherogenic indices. This finding implicate that obese RA patients were at more risk to develop CVD than their healthy counterparts. The patients were found to have significant high prevalence of hypertension stage II as compare to controls. The results of the present study are in consonance with some previous studies, which show significant high prevalence of hypertension in RA subjects as compare to controls (Panoulas et al., 2007; Chung et al., 2012) While, some other study indicate no difference in hypertension in both the studied groups (Solomon et al., 2003, 2004)

Oxidative stress is implicated in the pathogenesis of numerous diseases including RA and CVD. Oxidative stress induces peroxidation of polyunsaturated fatty acids by reactive oxygen species (ROS), leading to the formation of highly reactive molecules including MDA. The present study found significantly high levels of serum MDA in RA patients as compared to controls. This finding is in consonance with earlier studies from Indian as well as other populations (Surapneni and Gopan, 2008; Vasanthi et al., 2009). Furthermore, serum MDA levels were significantly higher in obese patients as compared to obese controls indicating enhanced lipid peroxidation in obese RA patients. These findings are in consonance with the earlier findings indicating increased peroxidation in obese individuals as well as in various disease conditions (Suzuki et al., 1999; Minoguchi et al., 2006; Park et al., 2010; Bhale et al., 2014). MDA can significantly increase inflammatory gene expression. It has been demonstrated that MDA can initiate a NF-κB and IL-6 signalling program in lymphocytes, which in turn can promote adhesion, differentiation, and vascular dysfunction and lead to cardiovascular, inflammatory, and immunological diseases (Raghavan et al., 2012; Yadavand Ramana, 2013). A recent study has demonstrated the presence of MDA in the atherosclerotic lesions (Anderson et al., 2014).

**Conclusion**

The results of the present study indicate high prevalence of obesity, hypertension, inflammation, lipid peroxidation in RA patients in comparison to controls. Obese RA patients were found to have significantly high atherogenic indices, CRP and MDA as compared to obese controls.

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