# Study of Serum Lipid Profile and Vitamin E in Rheumatoid Arthritis.

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## ABSTRACT

**Introduction:** Rheumatoid Arthritis is a chronic systemic inflammatory disorder that may affect many tissues and organs but principally affects the joints. Our study aims to access serum lipid profile as well as atherogenic index – Total cholesterol/HDL cholesterol, LDL cholesterol/HDL cholesterol among the RA patients and compare the results with that of control group and also to estimate Vitamin E levels in cases and compare it with controls. **Methods:** Fifty diagnosed cases of Rheumatoid Arthritis and thirty healthy age and sex matched individuals were included in this study. Serum triglycerides, HDL cholesterol, LDL cholesterol, VLDL cholesterol and Vitamin E were estimated in these groups. **Results:** Among cases the values of Vitamin E were significantly lower (0.25 ± 0.06 mg/dl ± SD) as compared to controls (1.12 ± 0.23 mg/dl ± SD). S. VLDL (30.09 ± 3.33 mg/dl ± SD) and S. LDL (220.96 ± 34.19 mg/dl ± SD) values were significantly higher among cases (18.57 ± 4.63 mg/dl ± SD, 36.2 ± 15.59 mg/dl ± SD respectively in controls). The value of S. HDL was found to be significantly lower (25.04 ± 6.27 mg/dl ± SD) in cases as compared to controls (58.83 ± 11.43 mg/dl ± SD). Among cases values of Total cholesterol/HDL cholesterol (11.78 ± 3.47) and LDL cholesterol/HDL cholesterol (9.48 ± 3.18) were also higher than controls (1.99 ± 0.42, 0.66 ± 0.37 respectively). **Conclusion:** These findings strongly confirmed that patients with RA have significantly lower values of vitamin E and HDL compared to controls while higher values of other parameters of lipid profile and higher atherogenic indices.

*Keywords:* Atherogenic Index, Lipid Profile, Rheumatoid Arthritis, Vitamin E

## INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic systemic inflammatory disorder that may affect many tissues and organs but principally affect the joints. Rheumatoid Arthritis (RA) affects between 0.5 to 1% of the adult population worldwide. RA can start at any age, but the peak age of onset is between 30 and 55 years. It affects 1-2% of the total population of the world.[1] Every year 0.5% to 1% of the total population suffer from RA in both developed and developing countries.[2] However the incidence are lowered in East South Asia. Epidemiological studies have shown an increased premature mortality in patients with RA compared with general population.[3,4] There are reports of altered serum lipid levels in various inflammatory diseases including RA. Lipids may contribute to the synovitis in RA through participation in arachidonic acid pathway within the joint space.[5] Increased levels of total cholesterol (TC), Low Density Lipoprotein (LDL) and Triglycerides (TG) has been reported in patients with RA.[6]

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The serum Total Cholesterol and High Density Lipoprotein (HDL) levels in RA are inversely correlated with disease activity suggesting a potential role for inflammation in the atherogenic profile and higher atherosclerotic risk observed in RA.[7,8] As a consequence of reduction in HDL cholesterol, the atherogenic ratio of total cholesterol/HDL cholesterol as well as LDL cholesterol/HDL cholesterol were significantly higher in RA. This is so called atherogenic index is an important prognostic marker for future cardiovascular disease, the desirable ratio is four or lower.[9]

The apparent reduction of total cholesterol may result from reduced synthesis, increased clearance via the scavenger receptor pathway or increased oxidation triggered by inflammatory process.[10]

Vitamin E is the major lipid soluble anti-oxidant found in cells. Vitamin E is critical to maintain the normal function of the immune system. Elevated lipid peroxidation and depleted vitamin E has been reported in patients with RA.[11, 12] The inflammatory environment and disturbed antioxidant mechanism in rheumatoid arthritis may promote LDL oxidation thereby facilitating atherogenic and higher cardiovascular risk. The present study has been taken up to access serum lipid profile i.e. Triglyceride (TG), Total Cholesterol (TC), Very low density lipoprotein cholesterol (VLDL-C), Low density lipoprotein cholesterol (LDL-C), High density lipoprotein

cholesterol (HDL-C) as well as atherogenic index – Total cholesterol/HDL cholesterol, LDL cholesterol/HDL cholesterol among the RA patients and compare the results with that of control group. And also to estimate Vitamin E levels in cases and compare it with controls.

## MATERIALS AND METHODS

This study was conducted in Department of Biochemistry in collaboration with Department of Medicine in Regional Institute of Medical Sciences, Imphal during a period of April 2012 to March 2013. Study was approved by the institutional review board and all participants gave written informed consent.

The study group comprised of fifty diagnosed cases of Rheumatoid Arthritis either acute or chronic, who attended Rheumatic clinic, Regional Institute of Medical Sciences Hospital, irrespective of age, sex, race and socioeconomic status. For the control group, thirty healthy age and sex matched individuals from general population in Imphal, who were free from any systemic disease were included.

Those patients who had other systemic illness like diabetes mellitus, hypothyroidism, liver or kidney disease, familial dyslipidemia, obesity, cushing's syndrome and those who were receiving medication affecting lipid metabolism such as lipid lowering drugs, beta blockers, oral contraceptives, thyroxin and vitamin E were excluded from this study.

All cases and controls were aged 18 years and above. Each individual enrolled in study underwent a detailed history, clinical examination and laboratory examination designed for the study.

Five ml of venous blood was collected from each individual after an overnight fasting of twelve hours. Estimation of serum Vitamin E was done with method of Natelson S.[13] Estimation of total cholesterol was carried out by the enzymatic method of Allain CC et al.[14] Quantitative estimation of serum triglycerides was done by method adopted by Bucolo G.[15] Enzymatic determination of serum cholesterol in high density lipoprotein fractions (HDL cholesterol) was done by precipitation technique as described by Steele BW et al.[16] LDL cholesterol and VLDL cholesterol values in mg/dl were indirectly calculated by using the formulae of Friedewald WT et al.[17]

Statistical analysis: Statistical analysis was performed using SPSS version 16. Data were expressed as Mean $\pm$ SD. Statistical tests like $\chi^2$-test, independent t-test, ANOVA (F-test) and correlation coefficient 'r' were applied whenever found suitable and necessary. The P-value less than 0.05 was considered significant

## RESULTS

Table 1 shows that the mean age for developing RA in male is higher than females. But this difference was not statistically significant ($p > 0.05$). Difference in the mean age ($\pm$ SD) between RA and control cases was also not significant, indicating that both groups were of comparable age.

**Table 1:** Mean age $\pm$ SD in both control and Rheumatoid arthritis cases

| Sex | Controls (n=30) | | Rh. Arthritis cases (n=50) | |
|---|---|---|---|---|
| | No. of cases | Mean age $\pm$ SD (years) | No. of cases | Mean age $\pm$ SD(years) |
| Male | 8 | 53.5 $\pm$ 8.64 | 11 | 61.82 $\pm$ 12.38 |
| Female | 22 | 53.45 $\pm$ 9.50 | 39 | 52.77 $\pm$ 9.97 |
| Total | 30 | 53.47 $\pm$ 9.13 | 50 | 54.76 $\pm$ 11.07 |

**Table 2**: Summary of biochemical parameters in control and RA cases (values expressed in terms of Mean $\pm$ SD)

| Parameters (from serum) | Controls (n=30) Mean(mg/dl) $\pm$ SD | RA cases (n=50) Mean(mg/dl) $\pm$ SD |
|---|---|---|
| Vitamin E | 1.12 $\pm$ 0.23 | 0.25 $\pm$ 0.06* |
| S. Cholesterol | 113.6 $\pm$ 13.73 | 276.9 $\pm$ 31.84* |
| S. Triglycerides | 92.93 $\pm$ 22.77 | 154.54 $\pm$ 17.01 |
| S. HDL | 58.83 $\pm$ 11.43 | 25.04 $\pm$ 6.27* |
| S. VLDL | 18.57 $\pm$ 4.63 | 30.9 $\pm$ 3.33* |
| S. LDL | 36.2 $\pm$ 15.59 | 220.96 $\pm$ 34.19* |
| Total chol/HDL chol | 1.99 $\pm$ 0.42 | 11.78 $\pm$ 3.47* |
| LDL chol/HDL chol | 0.66 $\pm$ 0.37 | 9.48 $\pm$ 3.18* |

*p<0.001

All biochemical data are summarized in Table 2. It is evident from this table that serum total cholesterol, VLDL, LDL and atherogenic indices (i.e. Total chol/ HDL chol and LDL chol/ HDL chol) are increased in

RA cases when compared with normal controls. Increase in these parameters was statistically significant (P < 0.001). This table also shows that serum HDL and Vitamin E are decreased in RA cases compared to controls which was statistically significant (P < 0.001).

Table 3 shows comparison of vitamin E levels in RA cases and controls. Among RA cases Vitamin E levels were found to be significantly (P < 0.001) decreased both in males and females compared to controls. There was also significantly decrease (P < 0.001) in serum vitamin E levels when RA cases were compared as a whole with the controls

| Table 3 - Serum Vitamin E (mean ± SD) levels in cases and controls | | | |
|---|---|---|---|
| **Sex** | **Serum Vitamin E (mg/dl ± SD)** | | **P value** |
| | Controls (n=30) | RA Cases (n=50) | |
| **Male** | 1.2 ± 0.26 | 0.28 ± 0.07 | .008 |
| **Female** | 1.09 ± 0.22 | 0.24 ± 0.05 | .001 |
| **Total** | 1.12 ± 0.23 | 0.25 ± 0.06 | .001 |

| Table 4 - Total Chol/HDL chol (mean ± SD) in controls and RA cases | | | |
|---|---|---|---|
| **Sex** | **Total chol/HDL chol (ratio ± SD)** | | **P value** |
| | Control (n=30) | RA Cases (n=50) | |
| **Male** | 1.89 ± 0.34 | 11.58 ± 3.43 | .001 |
| **Female** | 2.03 ± 0.44 | 11.84 ± 3.52 | .001 |
| **Total** | 1.99 ± 0.42 | 11.78 ± 3.47 | .001 |

| Table 5 - LDL Chol/HDL chol (mean ± SD) in controls and RA cases | | | |
|---|---|---|---|
| **Sex** | **LDL chol/HDL chol (ratio ± SD)** | | **P value** |
| | Control (n=30) | RA Cases (n=50) | |
| **Male** | 0.61 ± 0.34 | 9.29 ± 3.13 | .001 |
| **Female** | 0.68 ± 0.39 | 9.53 ± 3.24 | .001 |
| **Total** | 0.66 ± 0.37 | 9.48 ± 3.18 | .001 |

Table 4 shows higher values of Total chol/HDL chol among RA cases than controls. This difference was found to be statistically significant (P < 0.001).Among RA patients Total chol/HDL chol was significantly (p < 0.001) increased both in males and females compared to corresponding controls.

Table 5 shows that LDL chol/HDL chol was significantly increased both in male (P < 0.001) and females (P < 0.001) among RA cases compared to controls. There was also significant increase in LDL chol/HDL chol ratio (P < 0.001) when RA cases were compared as a whole with the controls.

## DISCUSSION

The present study showed that 60% of RA cases were in age group of 51 – 60 years. The mean age ± SD of RA cases was 54.76 ± 11.07 years. The disease was found to be more prevalent in the middle aged population. These findings are similar with Georgiadis AN et al.[18] and Myasoedova E et al.[19] It may be due to higher prevalence of metabolic syndrome, a proinflammatory state which is common among the middle aged people. The expanded adipose tissue is thought to represent a source of proinflammatory cytokines (i.e. interleukin 6 and tumor necrosis factor – α). Previous studies suggest that RA disease activity correlates with metabolic syndrome, implicating a

significant role for the inflammatory burden in the evolution of metabolic disturbances in patients with RA.[20] The high prevalence of RA in middle aged population may also be due to increased fat mass and reduced physical activity.

In the present study, 78% RA patients were females and 22% were males. These findings are consistent with other studies which showed highest prevalence of RA among females.[21, 22]

Study results showed that serum vitamin E concentration was significantly decreased in RA cases as compared to normal controls. This might be due to the oxidative stress in RA patients due to an increased level of reactive oxygen species (ROS) as well as reduced anti-oxidative mechanisms.[23]

All the parameters of serum lipid profile which include Total Cholesterol (TC), Triglycerides (TG), Very Low Density Lipoprotein (VLDL) and Low Density Lipoprotein (LDL) were elevated except High Density Lipoprotein (HDL), which was diminished significantly among RA study group as compared to control group. This may be due to the fact that RA patients are genetically predisposed to the development of RA related dyslipidemia or the transcription of these genes can be altered by persistent inflammation.[24]

In the present study the atherogenic index in the form of Total Cholesterol/HDL cholesterol and LDL

cholesterol/HDL cholesterol were found to be much higher than the desirable ratio of five or lower. A higher index implies an increased cardiovascular risk and lowering this ratio has shown to decrease this risk.

## CONCLUSION

The present study showed that RA is predominantly found among the middle aged female population. Patients with RA have significantly lower values of vitamin E and HDL compared to controls. Significantly higher values of other parameters of lipid profile were found among RA patients. Higher atherogenic indices indicate higher cardiovascular risk among RA patients.

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