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Original Research Article

A study of lipid profile and vitamin E status in Rheumatoid Arthritis patients

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Abstract: Rheumatoid arthritis (RA) is a chronic disease characterized by inflammation and oxidative damage. Active rheumatoid arthritis patients are susceptible to dyslipidaemia, which may explain the enhanced free radicals found within the rheumatoid synovium and in the plasma of RA patients. The objective of this study is to evaluate the lipid profile and vitamin E levels in patients with RA & to compare it with healthy matched controls. Levels of serum total cholesterol (TC), high-density lipoprotein cholesterol (HDLc), triglycerides (TG), low-density lipoprotein (LDLc), very low-density lipoprotein (VLDLc), atherogenic index and vitamin E were determined in 50 diagnosed rheumatoid arthritis patients who were attending Rheumatic Clinic, RIMS Hospital between April 2011 to March 2012. These samples were compared with 30 healthy age and sex matched subjects who were free from any systemic diseases were taken as control. The mean ± SD of concentration of TC, LDL and TG in study group were 276.9±31.84 mg/dl, 220.96±34.19 mg/dl and 154.54±17.01 mg/dl respectively which found to be significantly higher ($P < 0.001$) when compared with their respective controls (TC 113.6±13.73 mg/dl, LDL 36.2±15.59 mg/dl and TG 92.93±22.77 mg/dl). There was a negative correlation between foresaid atherogenic lipid parameters with high density lipoprotein (HDL) and serum vitamin E level. Significant decrease ($P < 0.001$) of HDL and vitamin E levels were observed among RA cases compared to controls. Rheumatoid arthritis patients have a considerably more atherogenic lipid profile index and less vitamin E levels than matched controls.
Keywords: Rheumatoid Arthritis, Lipid Profile, Vitamin E

INTRODUCTION:

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease dominated by serious and debilitating sequel associated with progressive destruction of articular joints. Lipids and lipoproteins abnormalities play a significant role in the development and progression of various pathological diseases including RA [1]. Its etiology is unknown but it is presumed to be an immunologic disease with genetic [2-3], hormonal [4-6] and environmental risk factors such as cigarette smoking [7-9]. Oxidative damage has been implicated in the pathogenesis of RA, and free radicals have been found within the rheumatoid synovium[10-13] and in the plasma of patients with RA[14]. Such molecules may induce endothelial cell damage and promote the production of pro-inflammatory cytokines and adhesion molecules, thereby contributing to the ongoing inflammatory response in RA.

Lipids may contribute to the synovitis in RA through participation in the arachidonic acid pathway within the joint space [15]. Increased levels of total cholesterol, LDL cholesterol and triglyceride have been reported in patients with rheumatoid arthritis [16]. However, Lazarevic *et al.;* [17] reported decreased concentration of total serum lipids, serum total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol among the patients with rheumatoid arthritis when compared with healthy controls. The serum total cholesterol and HDL cholesterol levels in rheumatoid arthritis are inversely correlated with disease activity suggesting a potential role for inflammation in the atherogenic profile and higher atherosclerotic risk observed in RA [18, 19]. 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.

It has been suggested that low vitamin E and impairment of the antioxidant protection may contribute to low serum cholesterol levels in juvenile chronic arthritis [20]. Elevated lipid peroxidation and depleted vitamin E has been reported in patients with rheumatoid arthritis [21, 22]. The inflammatory environment and disturbed antioxidant mechanisms in rheumatoid arthritis may promote LDL oxidation thereby facilitating atherogenesis and higher cardiovascular risk.

The antioxidant enzymes are reported to contribute little extracellular antioxidant defense in RA [23]. Also the reports of the altered lipid and lipoprotein level in serum are variable and contradictory between different studies conducted by various investigators. It is with this view in mind that it is planned to study lipid profile i.e., triglyceride, total cholesterol, VLDL cholesterol, LDL cholesterol, HDL cholesterol, total cholesterol/HDL cholesterol ratio, LDL cholesterol/HDL cholesterol ratio as well as chain breaking antioxidant vitamin E among the patients with rheumatoid arthritis.

The objectives of the study are to study the lipid profile along with the different atherogenic indices and vitamin E status among RA patients and to compare it with the healthy matched controls.

MATERIALS AND METHODS

This study included 50 (fifty) cases of already diagnosed rheumatoid arthritis either acute or chronic who were attended Rheumatic Clinic, RIMS Hospital. The patients were selected irrespective of age, sex, race and socioeconomic status. For the control group, healthy 30 (thirty), age and sex matched individuals who are free from any systemic diseases were included.

This study was carried out in the Department of Biochemistry, Regional Institute Of Medical Sciences (RIMS) , Imphal in collaboration with the Department of Medicine, RIMS, Imphal , Manipur during a period of 12 (twelve) months from April 2011 to March 2012. The study was done after obtaining the approval from Institutional Ethical Committee, RIMS.

A proforma of all the patients were maintained, wherein a brief history of clinical information regarding the, sex, dietary habits, occupation, history of diabetes, past illness, etc are recorded. Complete general, physical and systemic examinations carried out were also recorded. Routine investigations, if done were also recorded in the proforma.

Those patients who exhibited diseases of other systems like diabetes mellitus, hypothyroidism, liver or kidney disease, Cushing's syndrome, obesity, familial dyslipidemia were excluded from the study. Patients were also excluded if they had a history of receiving medications affecting lipid metabolism such as lipid lowering drugs, beta blockers, oral contraceptives (estrogen, progestins etc.), thyroxine and vitamin E.

Blood samples will be collected in a plain as well as heparin vials after overnight fast and was centrifuged at 700g × 5 minutes and the sera thus separated was used for analysis. The estimation of vitamin E is based on the reduction of ferric ions to ferrous ions by tocopherols after xylene extraction and subsequent reaction of ferrous ions with bipyridyl to give red colour which could be measured at 520 nm (Method of Natelson S) [24].

Serum lipid profile were estimated by Enzymatic Colorimetric Test with lipid clearing factor (LCF) by using kits marketed by Human Gesellschaft fur Biochemica und Diagnostica mbH through its Indian branch supply [25-27].

RESULTS

It is evident from Figure 1, that the majority of rheumatoid arthritis cases (60%) occurred in the age group of 51 to 60 years, followed by 14% in both the age groups of 41 to 50 years and 61 to 70 years. Among the control cases, majority of the cases (60%) are in the age group of 41-50 years, followed by 27% in the age group of 61-70 years, 10% in the age group of 51-60 years, 3% in the age group of more than 70 years.

Figure 2 shows that both rheumatoid arthritis cases and control groups, females outnumbered the males. Around 78% of rheumatoid arthritis cases are females.

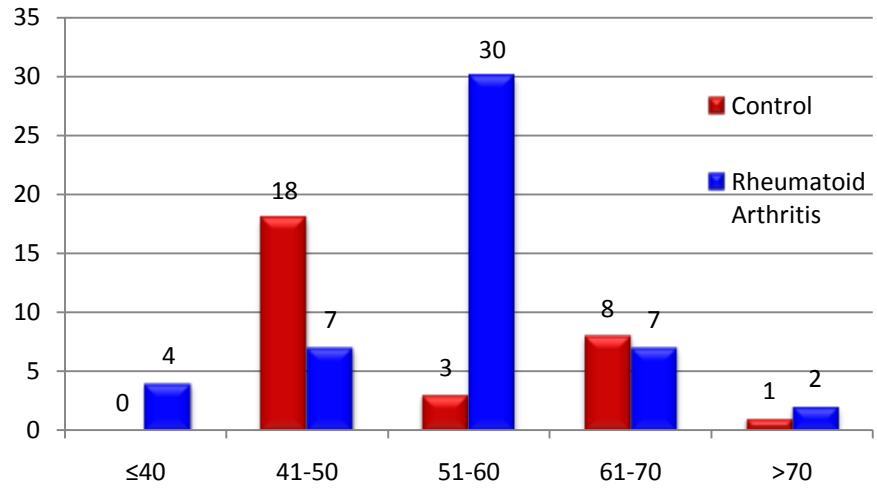

Fig. 1: Age-wise distribution of Control and Rheumatoid Arthritis Cases

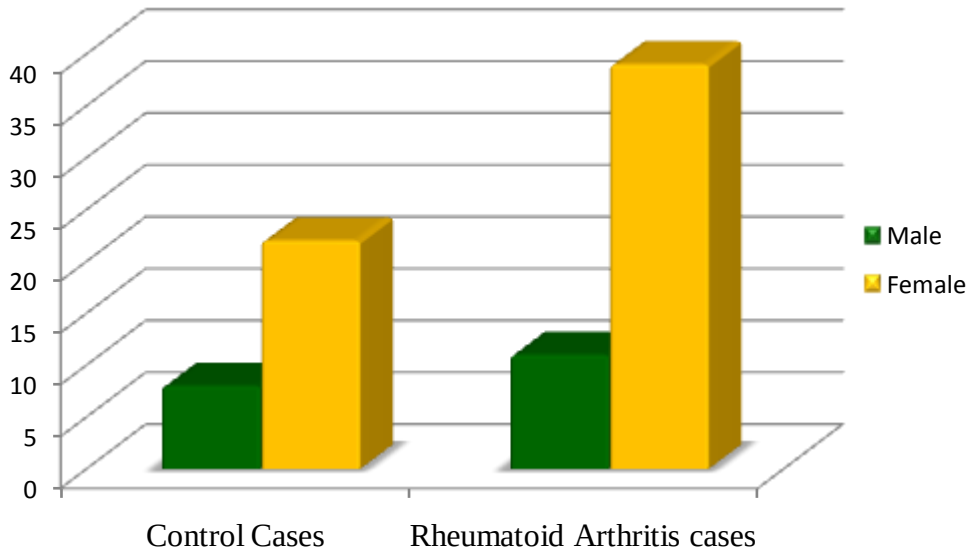

Fig. 2: Sex-wise distribution of Control and Rheumatoid Arthritis Cases

Table 1: Serum Vitamin E (Mean ± SD) level in Control and Rheumatoid Arthritis Cases by sex

Sex	Serum Vitamin E (mg/dl ± SD)		P value
	Control cases (n=30)	Rh. Arthritis cases (n=50)	
Male	1.2 ± 0.26	0.28 ± 0.07	.008
Female	1.09 ± 0.22	0.24 ± 0.05	.000
Both	1.12 ± 0.23	0.25 ± 0.06	.000

Table 1 shows that serum vitamin E concentration (expressed as mean ± SD) is significantly decreased both in male (P <0.01) and female (P <0.001) rheumatoid arthritis cases when compared with corresponding control cases. There is also significant decrease in serum vitamin E level (P <0.001) when rheumatoid arthritis cases are compared as a whole with the control cases.

Table 2: Serum cholesterol, Serum Triglyceride and HDL concentration (Mean ± SD) level in Control and Rheumatoid Arthritis Cases by sex

Sex	Serum Total Cholesterol (mg/dl ± SD)		P value	Serum Triglyceride (mg/dl ± SD)		P value	Serum HDL Cholesterol (mg/dl ± SD)		P value
	Control cases (n=30)	Rh. Arthrit-is cases (n=50)		Control cases (n=30)	Rh. Arthrit-is cases (n=50)		Control cases (n=30)	Rh. Arthrit-is cases (n=50)	
Male	120.75± 16.91	277.55± 34.63	.017	88.5± 27.19	154.82± 15.48	.02	64.75± 9.51	25.27± 5.27	.05
Female	111.00± 11.77	276.71± 31.49	.000	94.55± 21.44	154.46± 17.61	.2	56.68± 11.49	24.97± 6.58	.001
Both	113.6± 13.73	276.9± 31.84	.000	92.93± 22.77	154.54± 17.01	.02	58.83± 11.43	25.04± 6.27	.001

Table 2 shows that serum cholesterol concentration (expressed as mean ± SD) is significantly increased both in male (P <0.05) and female (P <0.001) rheumatoid arthritis cases when compared with corresponding control cases. There is also significant increase in serum cholesterol level (P <0.001) when rheumatoid arthritis cases are compared as a whole with the control cases. Moreover serum triglyceride concentration (expressed as mean ± SD) is increased significantly in male (P <0.05) but the increase in female rheumatoid arthritis cases are insignificant (P>0.05) when compared with corresponding control cases. There is also significant increase in serum triglyceride level (P <0.05) when rheumatoid arthritis cases are compared as a whole with the control cases. Serum HDL cholesterol concentration (expressed as mean ± SD) is significantly decreased both in male (P <0.05) and female (P <0.001) rheumatoid arthritis cases when compared with corresponding control cases. There is also significant decrease in serum HDL cholesterol level (P <0.001) when rheumatoid arthritis cases are compared as a whole with the control cases

Table 3: Serum VLDL and LDL level in Control and Rheumatoid Arthritis Cases by sex

Sex	Serum VLDLc (mg/dl ± SD)		P value	Serum LDLc (mg/dl ± SD)		P value
	Control cases (n=30)	Rh. Arthritis cases (n=50)		Control cases (n=30)	Rh. Arthritis cases (n=50)	
Male	17.75±5.5	31±3.13	.02	38.25±20.4	221.27±36.75	.024
Female	18.86±4.38	30.87±3.43	.129	35.45±13.96	220.87±33.94	.000
Both	18.57±4.63	30.9±3.33	.01	36.2±15.59	220.96±34.19	.000

Table 3 shows that serum VLDL concentration (expressed as mean ± SD) is significantly increased in male (P <0.05) but increased insignificantly in female (P >0.05) rheumatoid arthritis cases when compared with corresponding control cases. There is also significant increase in serum VLDL level (P <0.01) when rheumatoid arthritis cases are compared as a whole with the control cases. Moreover serum LDL concentration (expressed as mean ± SD) is significantly increased both in male (P <0.05) and female (P <0.001) rheumatoid arthritis cases when compared with corresponding control cases. There is also significant increase in serum LDL level (P <0.001) when rheumatoid arthritis cases are compared as a whole with the control cases.

Table 4: Total cholesterol/HDL and LDL/HDL cholesterol ratio in Control and Rheumatoid Arthritis Cases by sex

Sex	Total cholesterol/HDL cholesterol (ratio ± SD)		P value	LDL cholesterol/HDL cholesterol ratio (ratio ± SD)		P value
	Control cases (n=30)	Rh. Arthritis cases (n=50)		Control cases (n=30)	Rh. Arthritis cases (n=50)	
Male	1.89±0.34	11.58±3.43	.000	0.61±0.34	9.29±3.13	.000
Female	2.03±0.44	11.84±3.52	.000	0.68±0.39	9.53±3.24	.000
Both	1.99±0.42	11.78±3.47	.000	0.66±0.37	9.48±3.18	.000

Table 4 shows that total cholesterol/HDL cholesterol ratio (expressed as mean ± SD) is significantly increased both in male (P <0.001) and female (P <0.001) rheumatoid arthritis cases when compared with corresponding control cases. There is also significant increase in total cholesterol/HDL cholesterol ratio (P <0.001) when rheumatoid arthritis cases are compared as a whole with the control cases. Moreover LDL cholesterol/HDL cholesterol ratio (expressed as mean ± SD) is significantly increased both in male (P <0.001) and female (P <0.001) rheumatoid arthritis cases when compared with corresponding control cases. There is also significant increase in LDL cholesterol/HDL cholesterol ratio (P <0.001) when rheumatoid arthritis cases are compared as a whole with the control cases.

DISCUSSION

The present study shows that 60% of the rheumatoid arthritis cases are in the age group of 51-60 years, 14% each in the age group of 41-50 years and 61-70 years, followed by 8% in the group of <40 years and 4% above 70 years (Fig. I). The mean age ± SD of rheumatoid arthritis case is 54.76 ± 11.07 yrs (Fig. II). The disease is most prevalent in the middle aged population. This finding is similar with the findings of Georgiadis AN *et al.;* [28] and Myasoedova E *et al.;* [29] In the present study, 78% of rheumatoid arthritis patients are females and 22% are males (Fig. II). Thus, highest prevalence of rheumatoid arthritis is occurring in females. This finding is consistent with the findings of Masi AT [30] and Weyand CM *et al.;*[31] According to Masi AT, serum DHEAS, an adrenal androgen, was impressively decreased among women with premenopausal onset of RA.

In this study, it has been found that the level of serum vitamin E (mean ± SD mg/dl) in the control group is 1.12 ± 0.23 and that of the study case is 0.25 ± 0.06 (Table I). This variation between the two groups was statistically significant (P <0.001). This finding is similar to the findings of Heliovaara M *et al.;* [32] and Comstock GW *et al.;* [33] who had also found the decrease in the mean level of serum vitamin E in rheumatoid subjects although not significant when compared to the control groups. This may be due to the small number of incident cases of RA as well as long period of storage between the baseline examination and the time for the serum analyses. This concordance reduces the likelihood that this is a chance finding and suggests that low concentrations of vitamin E may in some way be related to the development of RA, either directly or as associates of an aetiological factor.

In the present study, it has been found that the level of serum total cholesterol (mean ± SD mg/dl) in the study case is 276.9±31.84 and that of the control group is 113.6±13.73 (Table II). This variation between the two groups was statistically significant (P <0.001). This finding is similar to the findings of Georgiadis AN *et al.;* [30] and Van Halm VP *et al.;* [35] who had also found a significant increase in the mean level of serum total cholesterol in rheumatoid subjects when compared to the control groups. The level of serum triglyceride (TG) (mean ± SD mg/dl) in the study case is 154.54±17.01 and that of the control group is 92.93±22.77. This variation between the two groups was statistically significant (P <0.05). This findings highlighted hypertriglyceridemia in the study group which is in accordance with the report of Hahn BH [36] and Lourida ES *et al.;* [37]. The level of serum HDL-C (mean ± SD mg/dl) in the study cases is 25.04±6.27 and that of the control group is 58.83±11.43. This variation between the two groups was statistically significant (P <0.001). These findings are in agreement with the report of Lazarevic MB *et al.;* [38] and Park YB *et al.;* [22].

The total cholesterol/HDL cholesterol ratio (expressed as mean ± SD mg/dl) in control group (Table IV) is 1.99±0.42 and that of the study group is 11.78±3.47. This variation between the two groups was statistically significant (P <0.001).

This increased ratio is also reported by the study of Boers M *et al.;* [21] Park YB *et al.;* [39] and Georgiadis AN *et al.;* [30]. As most of the RA patients in this study have total cholesterol/HDL cholesterol ratio

more than 5 they have high risk of developing CVD. LDL cholesterol/HDL cholesterol ratio is significantly increased both in male (P <0.001) and female (P <0.001) rheumatoid arthritis cases when compared with corresponding control cases with values (expressed as mean ± SD mg/dl) in case of study group is 9.48±3.18 compared to 0.66±0.37 in controls group. This variation between the two groups was statistically significant (P <0.001). This elevated ratio is also found in the study done by Allanore Y *et al.;* [40] and Dahlquist S R *et al.;* [41].

CONCLUSION

This study result shows that serum vitamin E concentration is significantly decreased in rheumatoid arthritis cases as compared to normal controls. This might be due to the elevated oxidative stress in RA patients due to an elevated level of reactive oxygen species (ROS) as well as from reduced antioxidative mechanisms. Mostly all the parameters of the serum lipid profile which includes total cholesterol (TC), triglyceride (TG), very low density lipoprotein cholesterol (VLDL-C), low density lipoprotein cholesterol (LDL-C) are elevated except high density lipoprotein cholesterol (HDL-C) which 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.

In the present study the atherogenic index in the form of total cholesterol/HDL cholesterol, LDL cholesterol/HDL cholesterol found to be much higher than the desirable ratio of five or lower. A higher index implies an increased in cardiovascular risk and lowering this ratio has been shown to decrease this risk.

Therefore, it can be concluded that serum lipid profile in the form of total cholesterol (TC), triglyceride (TG), very low density lipoprotein cholesterol (VLDL-C), low density lipoprotein cholesterol (LDL-C) except high density lipoprotein cholesterol (HDL-C) which has positive correlation with serum vitamin E and atherogenic index - total cholesterol/HDL cholesterol, LDL cholesterol/HDL cholesterol has negative correlation to the level of serum vitamin E in this study group of rheumatoid arthritis.

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