ALTERED PATTERN OF LIPIDS IN PLASMA AND ERYTHROCYTE MEMBRANES OF RHEUMATOID ARTHRITIS PATIENTS

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ABSTRACT

The present study has investigated the levels of lipids, lipoprotein cholesterol (HDL and LDL cholesterol), thiobarbituric acid reactive substances (TBARS) and vitamin E in plasma and erythrocyte membranes of twenty two clinically diagnosed adult rheumatoid arthritis patients and an equal number of age matched healthy subjects. The levels of lipids and lipoprotein cholesterol were markedly reduced in patients with rheumatoid arthritis as compared to healthy subjects. The altered lipid pattern may be related to decreased lipoprotein cholesterol, fatty acids and impairment in antioxidant defence mechanism.

KEYWORDS

Lipids, Lipoproteins, Rheumatoid arthritis

INTRODUCTION

Arthritis, the joint inflammation, refers to a group of diseases that cause pain, swelling, stiffness and loss of motion in the joints. Rheumatoid arthritis is a chronic systemic disorder of unknown etiology that is dominated by a serious and debilitating sequelae associated with progressive destruction of articular joints. Rheumatoid arthritis affects approximately 1 – 2% of the total world's population (1). Annual incidence rate of rheumatoid arthritis between 0.5% and 1% of total population are reported every year in both developed and developing countries (2). Lower incidences of rheumatoid arthritis are reported every year in East Asia (3). The true picture of annual incidence rate of rheumatoid arthritis in India has not been well documented.

The abnormalities in lipid and lipoprotein pattern produces number of pathological diseases including cancer (4). Altered lipid levels have been reported in various inflammatory diseases including rheumatoid arthritis (5). Increased levels of total cholesterol and LDL-cholesterol has been reported in patients with rheumatoid arthritis (6). Hypocholesterolemia has been observed in several inflammatory diseases such as rheumatoid arthritis, myelo proliferative disorders,

systemic lupus erythematosus and sarcoidosis (7). Lazarevic *et al.* (8) reported that rheumatoid arthritis patients had significantly decreased concentrations of total serum lipids, total serum cholesterol, cholesterol in low-density lipoprotein (LDL) and cholesterol in high-density lipoprotein (HDL) compared with healthy blood donors. However, the levels of lipids in plasma and erythrocyte membranes have not been simultaneously studied in rheumatoid arthritis patients. Hence, the present study is undertaken to study the levels of lipids in plasma and erythrocyte membranes of rheumatoid arthritis patients.

MATERIAL AND METHODS

Twenty two clinically diagnosed rheumatoid arthritis patients from Rajah Muthaiah Medical College and Hospital, Annamalai University, Annamalainagar, India, who had not undergone any previous treatment for their arthritis, were chosen for the study. An equal number of age matched healthy subjects were also investigated. The subjects were female ranging in age from 40 – 60 years. All the patients in the present study were clinically diagnosed as patients with rheumatoid arthritis. The presence of rheumatoid arthritis in patients was diagnosed by carrying out X-ray analysis of joint destruction, rheumatoid factor test, C-reactive protein and antinuclear antibodies test.

Fasting blood samples were obtained by antecubital vein into heparinized tubes. Plasma was separated by centrifugation at 1,000 g for 15 minutes. The buffy coat was removed and packed cells were washed three times with physiological saline. The erythrocyte membranes were prepared by the method of Dodge *et al.*, (9) modified by Quist (10).

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Total cholesterol and phospholipids were estimated by the method of Parekh and Jung (11) and Zilversmit and Davies (12) respectively. The HDL-cholesterol was estimated by heparin-manganese chloride precipitation method (13). Triglycerides and free fatty acids were estimated by the method of Foster and Dunn (14) and Falholf (15) respectively.

STATISTICAL ANALYSIS

The data are expressed as mean $\pm$ SD. Statistical comparisons were performed by Student's 't' test. The null hypothesis was rejected for $P < 0.05$.

RESULTS

The present study has analysed the levels of lipids in plasma and erythrocyte membranes of 22 rheumatoid arthritis patients and an equal number of age matched healthy subjects.

Table 1 shows the levels of plasma cholesterol, phospholipids C/P ratio, LDL and HDL cholesterol, triglycerides, free fatty acids in healthy subjects and rheumatoid arthritis patients. The levels of lipids were decreased in rheumatoid arthritis patients as compared to healthy subjects. We have observed 10 – 30% reduction in various lipid moiety of rheumatoid arthritis patients [Total cholesterol (17%), Phospholipids (13%), LDL cholesterol (16%), HDL cholesterol (29%), Triglycerides (9%) and Free fatty acids (9%)] as compared to healthy subjects.

Table 2 shows the levels of erythrocyte membranes cholesterol, phospholipid and C/P ratio in healthy subjects and rheumatoid arthritis patients. The levels of total cholesterol (15%) and phospholipids (12%) were reduced in rheumatoid arthritis patients as compared to healthy subjects.

Table 3 shows the levels of TBARS and vitamin E in plasma and erythrocyte membranes of healthy subjects and rheumatoid arthritis patients. We have observed 2 – 4 fold increase in TBARS levels and 1 – 2 fold reduction in vitamin E levels in plasma and erythrocyte membranes of rheumatoid arthritis patients as compared to healthy subjects.

DISCUSSION

In the present study, we observed a decrease in lipids and lipoprotein cholesterol levels in plasma and erythrocyte membranes of rheumatoid arthritis patients as compared to healthy subjects. Lipid and lipoproteins abnormalities play a significant role in the development and progression of various pathological diseases. Lipids may contribute to the synovitis in rheumatoid arthritis through participation in the arachidonic acid pathway within the joint space (16).

It has been reported that plasma cholesterol levels

Table 1. Plasma lipid pattern in healthy subjects and rheumatoid arthritis patients

Parameters	Healthy subjects	Rheumatoid arthritis patients
Total Cholesterol (mg/dl)	195.3 $\pm$ 18.7	162.8 $\pm$ 17.1**
Phospholipids (mg/dl)	204.7 $\pm$ 21.2	178.6 $\pm$ 18.2**
C/P ratio	0.95 $\pm$ 0.08	0.91 $\pm$ 0.07*
LDL Cholesterol (mg/dl)	112.6 $\pm$ 13.6	94.6 $\pm$ 8.2**
HDL Cholesterol (mg/dl)	49.8 $\pm$ 5.1	35.6 $\pm$ 3.8**
Triglycerides (mg/dl)	132.6 $\pm$ 11.7	120.6 $\pm$ 12.2*
Free fatty acids (mg/dl)	6.39 $\pm$ 0.52	5.82 $\pm$ 0.55*
Values are expressed as mean $\pm$ S.D; n=22.		
**Significantly different from healthy subjects, $P < 0.001$.		
*Significantly different from healthy subjects, $P < 0.01$.		

Table 2. Erythrocyte membrane lipid pattern in healthy subjects and rheumatoid arthritis patients

Parameters	Healthy subjects	Rheumatoid arthritis patients
Erythrocyte membranes		
Cholesterol (μ g/mg protein)	217.3 $\pm$ 20.7	184.3 $\pm$ 19.2**
Phospholipids (μ g/mg protein)	336.7 $\pm$ 32.1	294.7 $\pm$ 27.2**
C/P ratio	0.64 $\pm$ 0.03	0.61 $\pm$ 0.03*
Values are expressed as mean $\pm$ S.D; n=22.		
**Significantly different from healthy subjects, $P < 0.001$.		
*Significantly different from healthy subjects, $P < 0.01$.		

were significantly reduced as a result of reductions in low density and high density lipoprotein cholesterol (17). 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 (18). Elevated lipid peroxidation and depleted vitamin E has been reported in patients with rheumatoid arthritis (19, 20). The observed elevated TBARS and depleted vitamin E levels in the present study (table 3) may contribute to lowered lipid levels in plasma and erythrocyte membranes of rheumatoid arthritis patients. Thus, the observed reduction in plasma total cholesterol level in rheumatoid arthritis patients can

Table 3. Levels of TBARS and vitamin E in plasma and erythrocyte membranes of healthy subjects and rheumatoid arthritis patients

Parameters	Healthy subjects	Rheumatoid arthritis patients
Plasma		
TBARS (n mol/ml)	3.09±0.3	6.58 ±0.49**
Vitamin E (mg/dl)	1.18±0.11	0.76±0.09**
Erythrocyte membranes		
TBARS (n mol/mg protein)	0.31±0.02	1.32±0.13**
Vitamin E (µg/mg protein)	2.09±0.12	1.67±0.11**
Values are expressed as mean ± S.D; n=22. **Significantly different from healthy subjects, P<0.001.		

be correlated to the degree of inflammation, elevated oxidative stress, depleted antioxidants and decreased concentration of plasma HDL and LDL cholesterol.

Oxidative stress associated decline in phospholipids fractions has been reported in children with juvenile chronic arthritis (21). Phospholipids, the major substrate of lipid peroxidation, is decreased in rheumatoid arthritis patients due to elevated lipid peroxidation. The decrease in phospholipid levels observed in the present study can also be due to the decreased concentration of free fatty acids observed in plasma.

Altered content of cholesterol and phospholipids in the ghosts of rheumatoid arthritis has been reported (22). Mature red cells can exchange cholesterol and phospholipids with plasma due to incapability in synthesizing cholesterol and phospholipid *denovo* (23). Thus, lowered cholesterol and phospholipid concentrations observed in the erythrocyte membranes of rheumatoid arthritis patients may be a reflection of lowered plasma total cholesterol and phospholipids.

Thus, in the present study we have demonstrated a significantly altered lipid pattern in plasma and erythrocyte membranes of rheumatoid arthritis patients as compared to healthy subjects.

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