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"A correlative study of lipid profile and CRP in Rheumatoid Arthritis"

KEYWORDS

Rheumatoid Arthritis, CRP, Lipid profile.

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ABSTRACT Several pieces of evidence indicate that rheumatoid arthritis (RA) is a proatherogenic disease associated with increased cardiovascular (CV) ortality The objective of this study was to emphasize the need to raise awareness among healthcare professionals regarding the development of hyperlipidemia when RA is active by investigating the lipid profile and proinflammatory marker C-reactive protein (CRP) levels in rheumatoid arthritis (RA) patients, and compare them with healthy controls. Results demonstrate that the RA patients have high levels of inflammatory marker CRP which may contribute to atherosclerosis and patients also have altered lipid profile.

Introduction

Rheumatoid arthritis (RA) is chronic systemic autoimmune disorder, affecting primarily the synovium, leading to joint damage and bone destruction. RA affects between 0.5 and 1% of adults in the developed world with between 5 and 50 per 100,000 people newly developing the condition each year [1]. In 2010 it resulted in about 49,000 deaths globally [2].Onset is most frequent during middle age and women are affected 2.5 times as frequently as men. In 2013, it resulted in 38,000 deaths up from 28,000 deaths in 1990[3]. It causes significant morbidity as a result of synovial inflammation, joint destruction and associated disability [4]. Epidemiological studies have shown an increased premature mortality in patients with RA compared with the general population [5].

Under treatment of risk factors may play an important role in increasing the risk. Furthermore, accurately identifying individuals at risk for the development of RA during the preclinical phase of the illness is important, since this would allow for the primary prevention of this disease [6]. At present, little is known about markers for preclinical RA. Histological studies conducted in patients with RA have demonstrated synovitis in joints without inflammation. C-reactive protein (CRP) a potential marker for increased risk of RA is a sensitive marker of systemic inflammation and is elevated in patients with RA[7]. RA is associated with a twofold to threefold higher risk of myocardial infarction (MI) and a 50% higher risk of stroke [8]. In the general population, CRP levels >3 mg/L have been associated with increased CVD risk in RA patients. Thus, we conducted the present study to examine the association between CRP level and risk of developing incident RA.

The management of RA consists of co-ordinated multidisciplinary care, eg with physical and occupational therapy and drug treatment [9]. Successful treatment to limit joint damage and functional loss requires early diagnosis and timely initiation of disease-modifying agents [10].

Material and methods

The study was designed to evaluate lipid profile (LDL, HDL, serum cholesterol, ratio- serum cholesterol/HDL& LDL/HDL) and inflammatory marker C-reactive protein and its correlation in study group i.e. patients with Rheumatoid arthritis and normal healthy control individuals.

The study was conducted in Department of Biochemistry, Jhalawar Medical College, Jhalawar. Subjects were selected from Department of Orthopaedics of S.R.G. Hospital, Jhalawar. 100 subjects of varying age groups of both male and female, out of which Fifty subjects were fulfilling the American College of Rheumatology (ACR) 1987 criteria for RA, and early disease with disease duration of less than one year without prior use of disease modifying antirheumatic drugs (DMARDs) and or systemic steroids and fifty subjects were healthy controls without clinical symptom of rheumatoid arthritis.

We obtained general information about each patient including age, sex, weight. 55 of patients were female and 44 were male and their ages ranging from 45-50years .fasting blood sample was collected in plain vials for estimation of lipid profile and CRP from healthy subjects and patients with the sero-positive rheumatoid arthritis. Lipid Profile was measured by Fully Automated analyser (Beckman Coulter).LDL was measured by formula: - LDL = CHOLESTEROL – (HDL + VLDL) [11]. Serum cholesterol measured by cholesterol oxidase end point method and HDL by accelerative detergent end point method [12].VLDL was measured by formula VLDL= TG/5[11]. Quantitative CRP was measured by Fully Automated Analyser (MIURA 2000). Qualitative CRP was measured by manual method (CRP latex slide test method) in clinical laboratory of department of Microbiology.

Result

Among the cases women were found more prone to disease (p-Value 0.6873) (Table 1).The results in Table2 showed highly significant increase in level of serum cholesterol (p-Value 0.001) and level of TG (p value 0.007). LDL levels were also found to be increased but not much significant (p value 0.063). This pattern is mirrored in sepsis and other inflammatory states, suggesting systemic inflammation has the general effect of dyslipidaemia[13].A significant decrease in the levels of HDL was observed (p-Value 0.009) which is due to chronic inflammation which leads to oxidative changes that alter HDL structure[14]. Levels of paraoxonase-1, an antioxidant enzyme associated with HDL, are lower in patients with RA compared with healthy controls [15]. Therefore, because of inflammation there is an impairment of the normal anti-inflammatory, antioxidate and cardioprotective function of HDL cholesterol that turns out to be proinflammatory. Our understanding of the potential mechanisms behind these inflammation-associated lipid changes remains suboptimal and requires further study. The level of Serum Cholesterol/HDL ratio and LDL/HDL ratio was found to be decreased significantly (p value 0.007). Use of the total cholesterol to SC/HDL & LDL/HDL ratio as the lipid component of CVD risk scoring in patients with RA would seem appropriate given that these lipid parameters generally change in parallel with inflammation and suppression of inflammation [13]. Results displayed in Table 3 showed a highly significant increase in level of C-Reactive Protien measured quantitatively in Rheumatoid Arthritis patients (p-Value 0.003). These findings are in accordance with data from the general population that showed that CRP could be an independent predictor of CV disease with CRP values ≥3 mg/L defining high CV-risk individuals [16]. Qualitatively CRP when investigated significantly negative results were overwhelming (Table 4).

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Discussion

The result of analysis were confirmed by students t test and linear regression analysis was used to evaluate the correlation among parameters .All results were expressed as mean values ±SD; statistical significance was defined as p<0.001 and p<0.005. ERA patients exhibited increased levels of inflammatory markers that involved c-reactive protein (CRP), which increases in active disease, may contribute to atherosclerosis because it stimulates macrophages to produce tissue factor, a procoagulant that is found in atherosclerotic plaques. The presence of CRP in atheromatic lesions also suggests a 'cause and effect' relationship between this acute phase reactant and coronary events.[17]

Also ERA patients exhibited a mild dyslipidemia characterized by an increase in the serum levels of total cholesterol (TC), low density lipoprotein cholesterol (LDL) and tri glycerides as well as by decrease in the serum levels of high density lipoprotein cholesterol. Results of the current investigation were agreed with the findings of some published articles (Van Halm VP, Nielen MJ,et al 2007). They have also found approximately same the relationship between abnormalities changes of lipid pattern and inflammatory markers. Growing evidence indicates that inflammation has an important role in the pathogenesis of cardiovascular disease, particularly in atherosclerosis (Collins D, Fye CL, Anderson JW 2009).

Conclusion

We have studied lipid profile (LDL, HDL,VLDL,Triglycerides,serum cholesterol) in patients with Rheumatoid Arthritis and healthy subjects and also correlation of inflammatory marker C-Reactive Protien quantitavely and qualitatively in Rheumatoid Arthritis patients and healthy controls.

From the results of this study following conclusion can be drawn:-
Level of LDL Serum Cholesterol ratio of Serum cholesterol /HDL and ratio of LDL/HDL found to be increased in RA affected individuals as compared to healthy controls.

Level of HDL was found to be decreased in RA affected individuals as compared to healthy controls.

We concluded that the increased mortality in patients with rheumathoid arthritis (RA) is mainly due to high incidence of cardiovascular (CV) disease. CV morbidity and mortality in RA can be explained by several mechanisms: (1) chronic inflammation, (2) enhanced prevalence of traditional CV risk factors including atherogenic dyslipoproteinemia, (3) a lower use of evidence-based therapy anti rheumatic drugs (DMARD therapy). Lipid levels should be monitored and managed in patients with RA to minimize the long-term risk of cardiovascular disease.

TABLES

Table 1. Gender distribution in both the groups.

		Group		Total	Chi sq	P value
		Case	Control			
Gender	Female	29	27	56		
		58.0%	54.0%	56.0%		
	Male	21	23	44	0.162	0.6873
		42.0%	46.0%	44.0%		
Total	50	50	100			
	100.0%	100.0%	100.0%			

TABLE 2 . Distribution of Lipid Profile According to cases& controls

	Group	N	Mean	Std. Deviation	T value	P value
SERUM CHOLESTEROL	Case	50	210.1000	60.03817		
	Control	50	174.2000	48.44606	3.291	0.001*
HDL	Case	50	42.8000	14.19255		
	Control	50	50.2200	13.83030	2.648	0.009*
LDL	Case	50	138.5600	58.03383		
	Control	50	120.9000	32.51640	1.877	0.063
TRI GLYCERIDE	Case	50	136.3600	58.61001		
	Control	50	106.0400	50.55325	2.770	0.007*
SERUM CHOL/HDL	Case	50	5.4314	2.80623		
	Control	50	3.9092	2.13747	3.051	0.003*
LDL/HDL	Case	50	3.6460	2.47148		
	Control	50	2.6010	1.00389	2.770	0.007*

TABLE 3. Distribution of CRP According to cases& controls

CRP	Case	50	11.1600	7.89047		
	Control	50	4.8200	4.35042	4.975	<0.0001*

TABLE 4: Distribution of Qualitative CRP According to cases and Control

		Group		Total	Chi Sq	P value
		Case	Control			
CRP	NEGETIVE	20	31	51		
		40.0%	62.0%	51.0%		
	POSITIVE	30	19	49	4.842	0.028*
		60.0%	38.0%	49.0%		
Total	50	50	100			
	100.0%	100.0%	100.0%			

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