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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Dyslipidemia Pattern in Rheumatoid Arthritis Patients with Correlation of Disease Activity

Romatoid Artritli Hastalarda Dislipidemi Paterni ve Hastalık Aktivitesi ile İlişkisi

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ÖZ

Amaç: Romatoid artrit (RA), bağışıklık sistemini ve nihayetinde orta yaşlı bireyleri etkileyen vücudun çeşitli dokularını etkileyen çok faktörlü bir hastalıktır. Orta Hindistan'daki RA hastalarında dislipidemi prevalansını ve paternini değerlendirmek ve dislipidemi ile hastalık aktivitesini ilişkilendirmek amaçlandı.

Materyal ve Metod: Kesitsel tipteki bu çalışma, Ocak 2014 ile Aralık 2015 tarihleri arasında, Indore'da (MP) Sri Aurobindo Tıp Bilimleri Enstitüsü ve Yüksek Lisans Enstitüsü'nde RA hastalarında gerçekleştirildi. Lipid profilleri 12 saatlik bir açlık sonrası belirlendi ve lipit profilleri ile hastalık aktivitesi ilişkisi saptanmıştır.

Bulgular: Yaş gruplarında sunulan olguların maksimum sayısı 41-50 (% 36) idi. Hastalık kadın nüfusta daha yaygındır. Maksimum hasta sayısı (34 hasta) hastalık süresi 1 ila 10 yıl arasında değişiyordu. Hastaların çoğunda hastalık aktivitesi yüksekti (% 90). Toplam kolesterol düzeyi, kadın olgularda kontrol grubuna göre anlamlı derecede yüksekti. Toplam kolestrol benzer şekilde düşük yoğunluklu lipoprotein (LDL) kolestrol kadınlarda kontrollerden daha yüksekti. Olgular ve kontroller arasında Yüksek dansiteli lipoprotein (HDL), Çok düşük dansiteli lipoprotein (VLDL) ve Trigliserid (TG) arasında anlamlı fark yoktu. Erkek olgularda ve kontrollerde ortalama lipid profili değerleri benzerdi. Hastalık aktivite skorunun (DAS)-28 ve eritrosit sedimentasyon hızı (ESR) yalnızca kadın hastalarda total kolesterol ve LDL düzeyleri ile pozitif korelasyonu gözlendi. DAS-28 ve ESR hem kadın hem de erkek hastalarda HDL, LDL ve trigliserid arasında bir korelasyon gözlenmedi.

Sonuç: Lipid profilleri hem naif hem de tedavi edilen hastalarda benzerdi. Ortalama lipid profili değerlerinde anlamlı fark yok RAF faktörüne dayalı olarak oluşturulan iki grupta HDL'nin beklendiği beklendi. Bir lipid profili değeri hastalığın süresi ile pozitif veya negatif korelasyon göstermez.

Anahtar Kelimeler: Dislipidemi, Romatoid Artrit, Hastalık Şiddeti

ABSTRACT

Aim: Rheumatoid arthritis (RA) is a multi-factorial disease which affects the immune system and ultimately various tissues in the body that typically affects middle-aged individuals. Our objectives were to evaluate prevalence of dyslipidemias and its pattern in RA patients in Central India and correlate dyslipidemia with disease activity.

Material and methods: This cross-sectional study was conducted on RA patients at Sri Aurobindo Institute of Medical Sciences and Post Graduate Institute, Indore (M.P.) between January 2014 and December 2015. Lipid profiles were determined following 12-hour overnight fasting, and the association of lipid profiles with and disease activity was determined.

Results: The maximum number of cases presented in the age group was 41-50(36%). Disease is more prevalent in female population. Maximum number of pateints (34 patients) had duration of illness ranged between 1 to 10 years. Most of the patients presented with high disease activity (90%). Total cholesterol levels were significantly higher in female cases as compared to controls. Similar to total cholesterol, Low density lipoprotein (LDL) cholesterol was significantly higher in female cases as compared to controls. There was no significant difference of High density lipoprotein(HDL), Very low density lipoprotein(VLDL) and Triglyceride(TG) between cases and controls. Mean lipid profile values were similar in male cases and controls. Positive correlation of Disease activity score (DAS)-28 Erythrocyte sedimentation rate (ESR) was observed with total cholesterol and LDL levels in female patients only. No correlation of HDL, LDL and triglyceride were observed with DAS- 28 and ESR in both male and female patients.

Conclusions: Lipid profiles were similar in both treatment naive and on treatment patients. No significant difference in mean lipid profile values expect HDL was observed in two groups created on the basis of RA factor. A lipid profile value has no positive or negative correlation with duration of illness.

Keywords: Dyslipidemia, Rheumatoid Arthritis, Disease Severity

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Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory disorder of unknown etiology which today is considered as clinical syndrome encompassing several disease subtypes rather than a single disease. It is characterized by chronic, symmetrical polyarthritis which evolves to different degrees of joint damage and joint deformities, together with functional limitations and loss of quality of life and sometimes increased mortality occurring with a female: male ratio of 3:1 and has a peak age of onset between 14 and 17 years of age [1] . In a significant proportion of patients, extra-articular features also occur (rheumatoid disease) [1,2]. Being a systemic disease, it involves number of extra-articular manifestations like rheumatoid nodules, vasculitis, heart or lung disease, anemia of chronic disease and entrapment neuropathies. Current evidences suggest that lipid metabolism is altered in RA due to inflammation [3,4]. Epidemiological studies have observed an increased risk of premature atherosclerosis and an increased mortality due to cardiovascular disease (CVD) in patients with RA [5-7].

CVD in RA may result from accelerated atherosclerosis caused by clinical or subclinical vasculitis. The main determinants of cardiovascular risk are concentrations of serum low density lipoproteins (LDL), high density lipoproteins (HDL) and triglycerides. RA-related inflammation may be responsible for synovial lesions which may be implicated in the development of accelerated atherosclerosis, leading to increased risk of CVD.[8,9] Furthermore, the magnitude and chronicity of inflammation strongly correlated with the emergence of premature atherosclerosis in RA [10,11]. Data regarding Total cholesterol(TC) and LDL levels in RA patients have been conflicting, with reports indicating increased [12], decreased [13] or similar [14] levels compared with controls. Regarding HDL-cholesterol, it has been reported that patients with active RA consistently demonstrate reduced levels [15]. Therefore this study was planned to evaluate prevalence of dyslipidemias and its pattern in RA and to correlate dyslipidemia with disease activity.

Material and Method

In this cross-sectional prospective observational study were includes 50 RA patients and 50 subjects will be healthy controls coming to out patient department of General Medicine of Sri Aurobindo Institute of Medical Sciences and Post Graduate Institute, Indore (M.P.) from January 2014 to Dec 2015. All the patients were over the 16 years and satisfying with 2010 ACR/EULAR(American college of rheumatology/European league against rheumatoid arthritis) classification were inclusion criteria. Obesity (BMI>35kg/m2), Diabetes mellitus, Hypertension (>140/90mmHg), Malignant diseases, Thyroid disorder, Other dyslipidemic disorder, Patient on lipid lowering drugs and Family history of Coronary artery disease(CAD),Diabetes mellitus(DM) , Hypertension, Thyroid disorders, kidney and liver disease were exclusion criteria.

Clinical assessment includes demographic data: age, sex, weight, height, blood pressure and duration of the disease obtained at a single time point. The patient global assessment and tender and swollen joint counts (of 28) performed. Patient global assessments of disease activity was recorded independently using the standard 100 mm visual analogue scale (VAS) in which 0 = no activity and 100 is maximal activity.DAS-28 was calculated using swollen and tender joint counts, the patient global assessment and ESR (DAS-28-ESR). After an overnight fasting, 3 ml of peripheral venous blood samples were collected under aseptic condition.. Total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, and triglyceride were measured on an automated biochemical analyser .ESR was

measured using wintrobe method. In the RA group, serum IgM rheumatoid factor was assessed by quantitative nephlometry. A concentration of IgM RF >20 IU/ml were considered positive. Data was statistically analysed the Mann Whitney U test was applied to see the difference in continuous variables in two groups. Chi Square test was applied to see the difference in frequency of discrete variables in two groups. A p value <0.05 was considered significant.

Results

A total of 100 patients were included in this study out of which 50 were cases and 50 were controls. The maximum number of cases presented in the age group was 41-50(36%). There was no significant difference of age between cases and controls (p=0.200). Amongst 50 cases, 46 patients were female and 4 were male, thus suggestive of disease is more prevalent in female population.

Maximum number of patients in this study were presented with high disease activity (90%). The mean ESR amongst female patients was 19.22±14.80 mm/hour and in control was 14.29±4.5 mm/hour whereas in male patients, it was 16.0±5.41 mm/hour and in control was 12.88±3.52 mm/hour. The p value was not significant.

Although the total cholesterol among female patients as well as controls were in normal limit yet total cholesterol level were significantly higher in female cases as compared to controls. Similar to total cholesterol, LDL cholesterol was significantly higher in female cases as compared to controls. There was no significant difference of HDL, VLDL and TG between cases and controls(Table 1). The total cholesterol, LDL, HDL and VLDL and triglyceride were in normal range in both cases and controls and there was no significant difference in mean lipid profile values in male cases and controls.

Positive correlation of DAS-28 (ESR) was observed with total cholesterol and LDL levels in female patients only(Table 2). No correlation of HDL, LDL and triglyceride were observed with DAS- 28 (ESR) in both male and female patients. Lipid profile was similar in both treatment naive and on treatment patients (Table 3)that shows Disease-modifying anti rheumatic drug(DMARD) treatment does not alter the lipid profile in rheumatoid arthritis patients.

IgM-Rheumatoid factor was found >20 IU/ml in 17 females and 1 male patient. No significant association of gender with IgM-Rheumatoid factor was observed(Table 4). No significant difference in mean lipid profile values expect HDL was observed in two groups created on the basis of IgM-Rheumatoid factor. Lipid profile values have no positive or negative correlation with duration of illness(Table 5).

Table 1: Lipid Profile in Cases and Controls

		Total cholesterol	LDL	HDL	VLDL	TG
Female	**Case**	175.20±30.77	102.04±24.05	40.28±9.54	20.70±12.93	143.57±65.0
	Control	157.29±37.4	88.95±28.41	41.95±11.49	25.69±12.18	127.64±60.84
	P value	0.016	0.022	0.459	0.266	0.240
Male	**Case**	171.50±70.56	122.25±65.59	43.25±12.99	20.0 ±8.6	100.0 ±43.78
	Control	173.13± 38.83	105.60± 35.38	39.00± 11.92	28.30± 13.29	142.25± 66.90
	P value	0.959	0.578	0.584	0.284	0.284

Table 2: Correlation of Lipid Profile with DAS - 28

		Total cholesterol	LDL	HDL	VLDL	TG
Female	**r**	0.310	0.347	-0.026	-0.011	-0.018
	P	0.036	0.018	0.861	0.943	0.905
Male	**r**	-0.638	-0.612	-0.577	-0.697	-0.700
	P	0.362	0.388	0.423	0.303	0.300

Table 3: Lipid Profile in Treatment Naive and on-Treatment Patients

	Total cholesterol	LDL	HDL	VLDL	TG
Naive	178.52±33.47	107.07 ±29.91	40.04± 9.61	30.48±15.15	152.52± 76.08
On Treatment	171.81±35.29	100.07 ±27.7	40.93± 9.99	25.89±10.22	129.48± 51.58
P value	0.496	0.344	0.753	0.210	0.211

Table 4: Lipid Profile and Rheumatoid Factor

Rheumatoid Factor	Total cholesterol	LDL	HDL	VLDL	TG
<20 IU/ml (n=32)	175.88±34.39	104.59±30.74	43.31± 9.68	27.22± 11.58	135.94± 73.27
>20 IU/ml (n=18)	173.17±35.00	102.00±25.51	35.56± 7.83	29.39± 9.02	147.44± 45.46
P value	0.792	0.763	0.006	0.570	0.550

Table 5: Correlation of Lipid Profile and Duration of Illness

	Total cholesterol	LDL	HDL	VLDL	TG
r	0.086	0.104	0.213	-0.082	-0.086
P	0.554	0.472	0.137	0.550	0.554

Discussion

In present study we observed high level of total cholesterol and LDL cholesterol in female RA patients suggesting RA may synergies dyslipidemia in female patients.

Rizzo et al [16] in 2009 reported that RA patients had higher levels of plasma triglycerides and lower levels of HDL-cholesterol concentrations as compared to controls, while total cholesterol and LDL-cholesterol concentrations were similar and about 1/3 of patients showed the complete atherogenic-lipoprotein phenotype. Ghosh et al [17] found LDL cholesterol was commonest abnormality seen in 37.2% of RA patients and concluded that lipid abnormalities are common in Indian patients with RA and low HDL-Cholesterol being the commonest abnormality. In support of the relationship between dyslipidemia and RA, Jick et al [18] found that statins may be protective against the development of RA in patients with hyperlipidemia. Toms et al [19] documented that depending on the risk stratification method, 2% to 26% of patients with RA without CVD were dyslipidemic and have sufficiently high risk to require statin therapy, and attributed altered lipid metabolism in RA to systemic inflammation, environmental lifestyle factors, drug therapy and several genetic factors and concluded that these factors may result in changes in overall lipid levels, as well as modifications of lipid/lipoprotein structure and function.

Deswal et al [20] observed an increase in lipids and lipoproteins in rheumatoid arthritis patients as compared to healthy subjects. The lipid pattern observed in RA in their study is atherogenic lipid profile. Similar atherogenic lipid profile was observed by Mullick et al [21] in early cases of RA. In present study, we found a positive correlation of total cholesterol with DAS - 28 ESR in female patients. None of the other parameter of lipid profile i.e.; HDL, LDL, VLDL and triglyceride were having any correlation with DAS - 28 (ESR). Our study also found that lipid profile were similar in treatment naive and on-treatment patients suggesting no significant effect of

DMARD's on lipid profile of RA patients. Among RA patients not receiving lipid-lowering medications, Curtis et al [22] observed that treatment with TNFi(Tumor necrosis factor inhibitor) was associated with modest increases in TC and LDL levels. This is consistent with results from other studies that observed increase in lipid levels after treatment with biological agents.

In a study done by Lakator [23] among 129 patients of RA who received treatment for 1 year (77 received glucocorticoids and 52 received Non steroidal anti-inflammatory drugs) showed increased level of triglyceride, LDL and decreased level of HDL and total cholesterol. A research done by Hafstrom et al [24] in 2007 on 67 diagnosed cases of RA who were on DMARD's and glucocorticoids showed an increased level of Total cholesterol after 5 year follow up. Sevenson et al [25] studied the effect of treatment on 33 RA patients for 9 months demonstrated increased level of total Cholesterol, Triglyceride and HDL.

Conclusion

Total cholesterol and LDL were significantly higher in female RA patients as compared to normal healthy females of similar age group. There was no effect of drug on lipid profile in RA patients. Total cholesterol was found to be positively correlated with disease activity. Our findings emphasize the need to raise awareness among healthcare professionals regarding the development of hyperlipidemia in RA patients. Screening for hyperlipidemia may be particularly important in patients with active RA to prevent cardiovascular related morbidity and mortality. Longitudinal studies are further needed for evaluating the effect of DMARD'S on Lipid Level in a dose dependent manner in RA patients. Our study has small sample size and it doesn't include the apolipoprotein levels.

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