DYSLIPIDAEMIA IN RHEUMATOID ARTHRITIS AND ITS RELATION WITH DISEASE ACTIVITY

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ABSTRACT

BACKGROUND

Rheumatoid arthritis is a well-known chronic inflammatory autoimmune disease which affects multiple joints usually in a symmetrical manner. Apart from the joints, RA can affect numerous other systems of the body like cardiovascular, neurological, haematological, skin, blood vessels, etc. The most common cause of death of RA patients has been found to be cardiovascular disease due to coronary artery disease. Chronic inflammatory state and dyslipidaemia[1,2] have been proposed as the reasons for accelerated atherosclerosis in RA. There are very few studies in India about lipid profile abnormality in rheumatoid arthritis and its relationship with the severity of the disease in RA patients. There is lacuna of knowledge about this aspect of disease in Indian patients. This study aims to address this issue.

AIM

To study lipid profile abnormalities and its relationship with the severity and number of ACR criteria of Rheumatoid Arthritis.

MATERIALS AND METHODS

This cross-sectional study was conducted from August 2009 – August 2011, patients fulfilling the American College of Rheumatology 1987 criteria for Rheumatoid Arthritis.,[3] newly diagnosed and patients on treatment for Rheumatoid Arthritis are taken into consideration. Dyslipidaemia defined using the high cut-off values of National Cholesterol Education Programme-Adult Treatment Panel. Disease Activity Score DAS-28(4) was employed to calculate the disease activity. For all patients after an overnight fasting blood samples were collected and serum was separated and Fasting Lipid Profile was done enzymatically using standardised Flex® reagent cartridges for Total Cholesterol, High Density Lipoproteins, Low Density Lipoproteins and Triglycerides. RA factor was done using Latex Agglutination Test. ESR for assessing DAS 28 was done using Wintrobe's method. The significance of difference in mean between two groups were analysed by student t-test. The correlation between Lipid profile and Disease Activity, number of ACR criteria fulfilled and newly diagnosed and old cases was calculated by using the Pearson's correlation coefficient method.

Statistical significance was taken when p value < 0.05. Statistical analysis was carried out using standard formulae. Microsoft Excel 2007 and SPSS (statistical package for social sciences) version 13 software was used for data entry and analysis.

RESULTS

A total of 80 patients with Rheumatoid Arthritis (newly diagnosed and known cases) were studied. In this study, 67 (83.8%) were females and 13 (16.3%) were females, the female to male ratio is 5.15. All the 80 patients fulfilled the American College of Rheumatology 1987 criteria for the diagnosis of Rheumatoid Arthritis 25. The age of patients ranged from 24 to 80 yrs., with mean age of 44.2 ± 11.3 yrs. Out of 80 patients, 35 (43.75%) fulfilled 4 ACR criteria, 34 (42.5%) fulfilled 5 ACR criteria and 11 (13.75%) fulfilled 6&7 criteria. Out of 80 patients, 44 (55%) had Dyslipidaemia, of which 41 (51.25) had low High Density Lipoproteins. In this study, TC decreases with the increase in the activity of the disease with a P-value of 0.063. LDL decreases with the increase in the activity of the disease with a P-value of 0.091. HDL decreases with the increase in the activity of the disease with a P-value of <0.001. Triglycerides decreases with the increase in the activity of the disease with a P-value of 0.005. TC/HDL increases with the increase in the activity of the disease with a P-value of 0.0001. In this study, TC decreases with the increase in the number of ACR criteria fulfilled with a P-value of 0.024. LDL was low in patients fulfilling 6&7 ACR criteria fulfilled with a P-value of 0.056. HDL decreases with the increase in the number of ACR criteria fulfilled with a P-value of 0.014. TG decreases with the increase in the number of ACR criteria fulfilled with a P-value of 0.028. TC/HDL increases with the increase in the number of ACR criteria fulfilled with a P-value of 0.234.

CONCLUSION

Lipid Profile in Rheumatoid Arthritis patients depends on the severity of the disease. There is an inverse relationship between TC, LDL-C, HDL-C and Triglycerides and severity of the Rheumatoid arthritis. Which is statistically significant for HDL-C and Triglycerides. There is direct relationship between TC/HDL-C and severity of disease which is statistically significant. These factors in part explain the high risk of Coronary Artery Disease in patients with Rheumatoid Arthritis and the importance of effective treatment of RA.

KEYWORDS

Lipid Profile, Rheumatoid Arthritis, Disease Severity.

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INTRODUCTION: Rheumatoid arthritis is a well-known chronic inflammatory disease which affects multiple joints usually in a symmetrical manner. Autoimmunity is the mechanism proposed for the inflammation of the joints and other manifestations of rheumatoid arthritis.

Inflammation of the joints can lead to joint destruction and formation of deformities if the disease is not controlled well.

Apart from the joints RA can affect numerous other systems of the body like cardiovascular, neurological, haematological, skin blood vessels, etc.

Life expectancy in rheumatoid arthritis patients seems to be reduced compared to their normal counter parts ranging from 0.87 to 3.0. times.[4]

The most common cause of death of RA patients has been found to be cardiovascular disease. The often proposed reason being the chronic elevation of inflammatory markers leading to accelerated atherosclerosis.[5,4,6] An earlier study had showed that the incidence of coronary artery disease was about 50% higher in young females with rheumatoid arthritis.[7]

Apart from the usual risk factors like diabetes, hypertension, obesity smoking, physical inactivity, two things have been commonly implicated as the explanation for accelerated atherosclerosis in RA. Apart from the usual risk factors like diabetes, hypertension, obesity smoking, physical inactivity.

One being chronic inflammatory state and the other being dyslipidaemia.[1,2]

Most studies have shown that the lipid profile of patients with active or untreated RA is primarily characterised by a decrease in the serum levels of HDL-C. The significant reduction in HDL increases in the TC/HDL-C ratio.[8] which represents the atherogenic index and this could explain the increased CAD risk in these patients. The risk of myocardial infarction increases considerably when this ratio is higher than five, and it should ideally be four or less.[8,9] Reductions in HDL and TC also correlated with the disease activity, suggesting a potential role for inflammation in the atherogenic profile and the higher atherosclerotic risk observed in RA.[10]

However, contrasting results have been published on the serum levels of TC and LDL-C.[8,9,10,11,12,13] in RA.

The discrepancies in the lipid values observed in the various studies might be due to differences in studied populations as well as in disease activity. There are few studies in India about lipid profile abnormality in rheumatoid arthritis and its relationship with the severity of the disease in RA patients. There is lacuna of knowledge about this aspect of disease in Indian patients. This study aims to address this issue.

AIMS OF THE STUDY:

1. To study lipid profile abnormalities and its relationship with the severity of Rheumatoid Arthritis.
2. To study the relationship between the number of ACR criteria fulfilled and Lipid Profile abnormalities.
3. To study the lipid profile abnormalities in newly diagnosed and known cases of rheumatoid arthritis.

MATERIALS AND METHODS:

1. **Source of Data:** Eighty patients attending medicine and rheumatology outpatient department and patients admitted in the General Medicine Department at Sri Ramachandra Medical College.

2. **Duration of Study:** This study was conducted from August 2009 – August 2011.

3. **Study Design:** A cross-sectional study design was chosen.

4. **Inclusion Criteria:** Patients fulfilling the American College of Rheumatology 1987 criteria for Rheumatoid Arthritis.[3] Newly diagnosed and patients on treatment for Rheumatoid Arthritis are taken into consideration.

5. **Exclusion Criteria:** Patients having comorbid conditions known to influence lipids like
   - Malabsorption syndrome.
   - Nephrotic syndrome.
   - Chronic Kidney Disease.
   - Diabetes mellitus.
   - Thyroid disorders.
   - Liver disorders.
   - Coronary Artery Disease.
   - Intake drugs like.
   - Lipid modifying drugs.
   - Oral contraceptives.

6. **Methods of Study:** The study population includes 80 patients with Rheumatoid arthritis. Dyslipidaemia defined using the high cut-off values of National Cholesterol Education Programme- Adult Treatment Panel. Disease Activity Score DAS-28(4) was employed to calculate the disease activity.

Laboratory Measurements: For all patients after an overnight fasting, blood samples were collected and serum was separated and Fasting Lipid Profile was done enzymatically using standardised Flex® reagent cartridges for Total Cholesterol, High Density Lipoproteins, Low Density Lipoproteins and Triglycerides.

RA factor was done using Latex Agglutination Test.

ESR for assessing DAS 28 was done using Wintrobe's method.

Financial Support – Nil.

STATISTICAL ANALYSIS: Statistical analysis was carried out for 80 RA patients, after categorising each variable. Base line data was collected from patients - Age, sex, BMI, Fasting Lipid profile, ESR, Visual Analogue Scale (VAS) were analysed using DAS 28(4).[14,15]

Disease activity calculated using DAS 28(4)[14,15]

$DAS28=0.56\times\sqrt{TJC28}+0.28\times\sqrt{SJC28}+0.70\times Ln(ESR)+0.114XVAS.$

Tender Joint Count (TJC) and Swollen Joint Count (SJC) is measured by looking for tenderness and swelling of the 10 Metacarpophalangeal joints and 10 proximal Interphalangeal joints of upper limbs and wrists-2, elbows-2, shoulders-2, knees-2, VAS (visual analogue scale) or SA is the subjective assessment of symptoms over the past 7 days as described by the patient, DAS 28 is calculated using the above formula using DAS calculator.

≤ 3.2	Low Disease Activity
3.2 to ≤ 5.1	Moderate Disease Activity
> 5.1	High Disease Activity

Activity of the Disease based on DAS 28.[14,15]

The significance of difference in mean between two groups were analysed by student t-test. The correlation between Lipid profile and Disease Activity**,** number of ACR criteria fulfilled and newly diagnosed and old cases was calculated by using the Pearson's correlation coefficient method.

Statistical significance was taken when p value < 0.05. Statistical analysis was carried out using standard formulae. Microsoft Excel 2007 and SPSS (statistical package for social sciences) version 13 software was used for data entry and analysis.

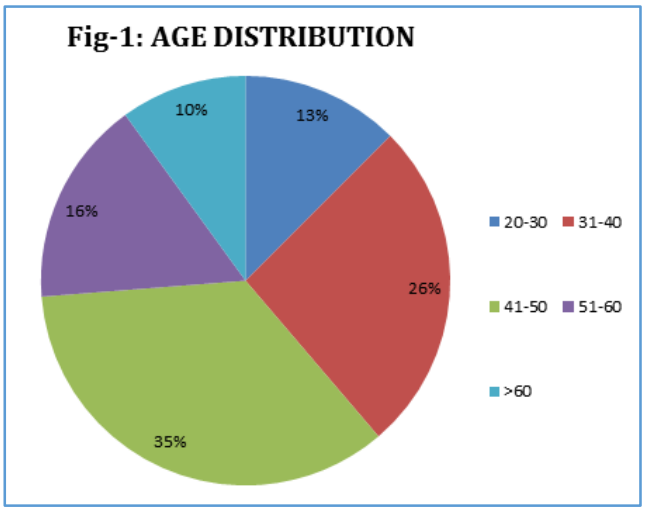
RESULTS:

Variable	Values
Age	44.2±11.307
Sex- M/F	67/13
BMI	22.747±2.562
Duration of Disease (Yrs.)	2.519±3.241
ESR	45.935±28.390
Visual Analogue scale	37.250±19.679
DAS	4.3112±1.5662
Total Cholesterol	163.100±16.573
LDL	99.162±16.884
HDL	39.112±8.027
Triglycerides	122.862±18.063
TC/HDL	4.312±0.868

Table 1: Clinical Characteristics and Lipid Profile of patients with Rheumatoid Arthritis

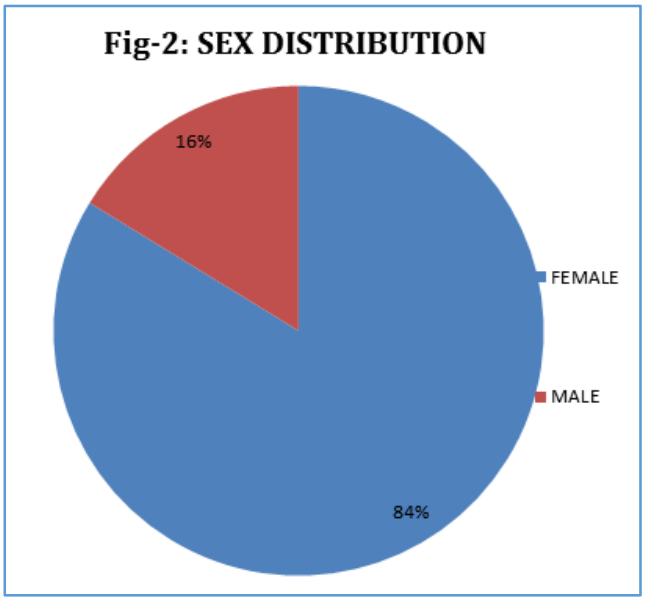
Age	Frequency	Percent
20 – 30	10	12.5
31 - 40	21	26.3
41 - 50	28	35.0
51 - 60	13	16.3
> 60	8	10.0
Total	80	100.0

Table 2: Age Distribution in the Study



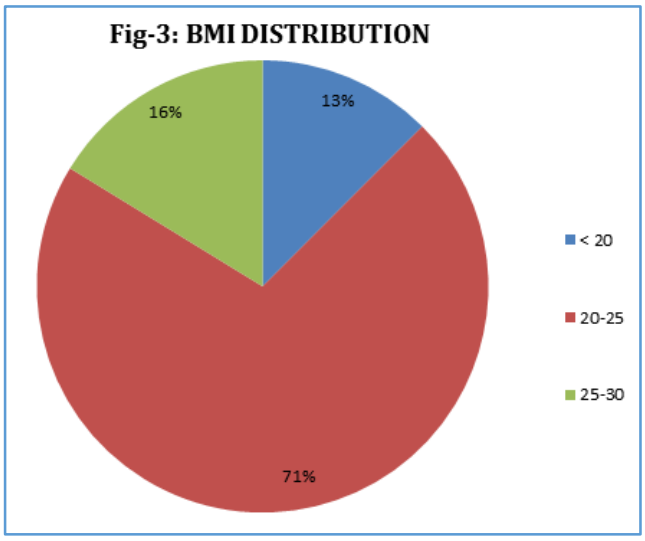
Gender	Frequency	Percent
F	67	83.8
M	13	16.3
Total	**80**	**100.0**

Table 3: Sex Distribution in the Study



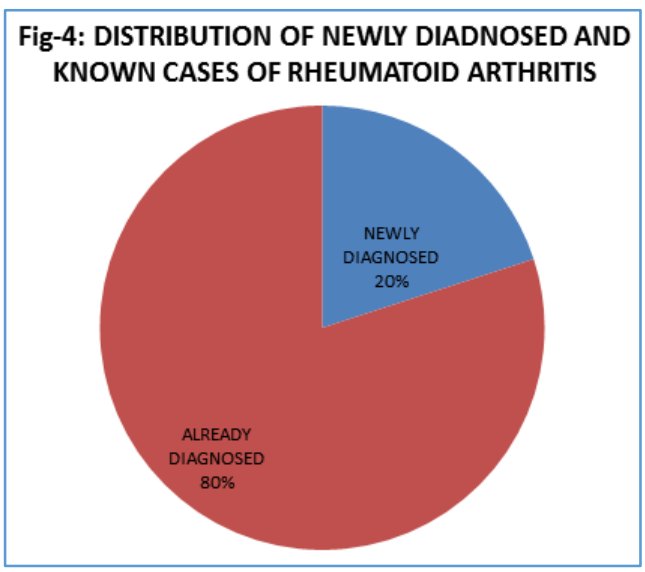
BMI	Frequency	Percent
< 20	10	12.5
20-25	57	71.3
25 - 30	13	16.3
Total	**80**	**100.0**

Table 4: Distribution of BMI in the Study



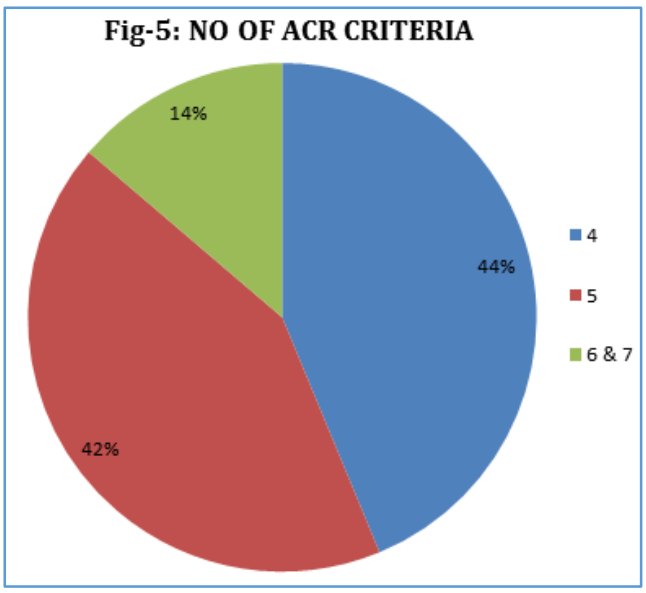
	Frequency	Percent
Newly diagnosed	16	20.0
Already Diagnosed	64	80.0
Total	80	100.0

Table 5: Distribution of newly Diagnosed and known cases of Rheumatoid Arthritis



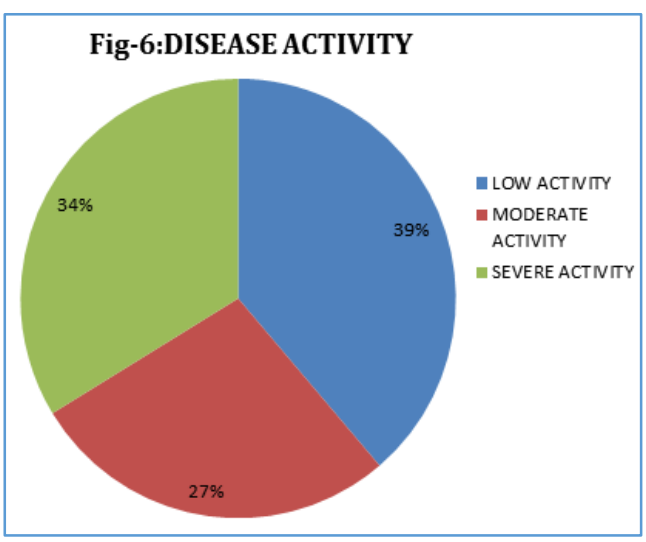
No. of ACR criteria	Frequency	Percent
4	35	43.8
5	34	42.5
6 & 7	11	13.8
Total	**80**	**100.0**

Table 6: Number of ACR 1987 Criteria Fulfilled



DAS 28	Frequency	Percent
≤ 3.2	31	38.8
3.2 to ≤5.1	22	27.5
> 5.1	27	33.8
Total	**80**	**100.0**

Table 7: Distribution of Disease Activity Score - DAS 28



DAS 28	N	Total Cholesterol Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
≤ 3.2	31	167.9355	15.50470	2.78473	162.2483	173.6227
3.2 -≤ 5.1	22	162.8636	15.94125	3.39869	155.7957	169.9316
> 5.1	27	157.7407	17.15224	3.30095	150.9555	164.5259
Total	**80**	**163.1000**	**16.57327**	**1.85295**	**159.4118**	**166.7882**

Table 8: Total Cholesterol with DAS 28

P- value- 0.63.

DAS 28	N	LDL Mean	Std. Deviation	Std. Error	95% Confidence interval for mean	
					Lower Bound	Upper Bound
≤3.2	31	102.8387	13.27930	2.38503	97.9678	107.7096
3.2 - ≤5.1	22	100.9545	14.99993	3.19800	94.3040	107.6051
> 5.1	27	93.4815	20.70372	3.98443	85.2914	101.6716
Total	**80**	**99.1625**	**16.88415**	**1.88771**	**95.4051**	**102.9199**

Table 9: LDL-C with DAS 28

P-value – 0.91.

DAS 28	N	HDL Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower bound	Upper bound
≤ 3.2	31	44.1935	6.90613	1.24038	41.6604	46.7267
3.2 - ≤5.1	22	39.4091	6.10744	1.30211	36.7012	42.1170
> 5.1	27	33.0370	6.43597	1.23860	30.4911	35.5830
Total	**80**	**39.1125**	**8.02684**	**.89743**	**37.3262**	**40.8988**

Table 10: HDL with DAS 28

P-value – <0.001.

DAS 28	N	Triglycerides Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
≤ 3.2	31	128.8710	14.95714	2.6863	123.3846	134.3573
3.2 - ≤5.1	22	125.2727	17.72053	3.7780	117.4159	133.1296
> 5.1	27	114.0000	18.71034	3.6008	106.5984	121.4016
Total	**80**	**122.8625**	**18.06300**	**2.0195**	**118.8428**	**126.8822**

Table 11: Triglycerides with DAS 28

P-value – 0.005.

DAS 28	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
≤3.2	31	3.8816	.65388	.11744	3.6418	4.1215
3.2 -≤ 5.1	22	4.1995	.58200	.12408	3.9415	4.4576
> 5.1	27	4.8978	.96719	.18614	4.5152	5.2804
Total	**80**	**4.3120**	**.86819**	**.09707**	**4.1188**	**4.5052**

Table 12: TC/HDL with DAS 28

P-value - <0.001.

No. of ACR Criteria	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
4	35	166.0571	16.76646	2.83405	160.2977	171.8166
5	34	164.0294	16.32526	2.79976	158.3333	169.7256
6 & 7	11	150.8182	11.62599	3.50537	143.0077	158.6286
Total	**80**	**163.1000**	**16.57327**	**1.85295**	**159.4118**	**166.7882**

Table 13: Total Cholesterol with Number of ACR Criteria Fulfilled

P-value – 0.024.

No. of ACR criteria	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
4	35	100.2286	15.32220	2.58992	94.9652	105.4919
5	34	101.6765	18.14040	3.11105	95.3470	108.0060
6 & 7	11	88.0000	14.33178	4.32120	78.3718	97.6282
Total	**80**	**99.1625**	**16.88415**	**1.88771**	**95.4051**	**102.9199**

Table 14: LDL with Number of ACR Criteria

P-value – 0.056.

No. of ACR criteria	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
4	35	40.9714	7.38235	1.24785	38.4355	43.5074
5	34	39.1765	8.45118	1.44937	36.2277	42.1252
6 & 7	11	33.0000	5.89915	1.77866	29.0369	36.9631
Total	**80**	**39.1125**	**8.02684**	**.89743**	**37.3262**	**40.8988**

Table 15: HDL with Number of ACR Criteria

P-value – 0.014.

No. of ACR criteria	N	Triglycerides Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
4	35	126.5714	18.72288	3.16474	120.1399	133.0030
5	34	123.1765	16.12164	2.76484	117.5514	128.8016
6 & 7	11	110.0909	17.32313	5.22312	98.4531	121.7287
Total	**80**	**122.8625**	**18.06300**	**2.01950**	**118.8428**	**126.8822**

Table 16: Triglycerides with Number of ACR Criteria

P-value – 0.028.

No. of ACR criteria	N	TC/HDL Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
4	35	4.1640	.77180	.13046	3.8989	4.4291
5	34	4.3494	.99356	.17039	4.0027	4.6961
6 & 7	11	4.6673	.67194	.20260	4.2159	5.1187
Total	80	4.3120	.86819	.09707	4.1188	4.5052

Table 17: TC/HDL with Number of ACR Criteria

P-value – 0.234.

		N	Mean	Std. Deviation	Std. Error Mean
Total Cholesterol	Newly diagnosed	16	159.1250	19.15159	4.78790
	Already Diagnosed	64	164.0938	15.87723	1.98465
LDL	Newly diagnosed	16	95.7500	24.45268	6.11317
	Already Diagnosed	64	100.0156	14.54003	1.81750
HDL	Newly diagnosed	16	33.1875	7.95168	1.98792
	Already Diagnosed	64	40.5938	7.38879	.92360
Triglycerides	Newly diagnosed	16	115.000	21.59630	5.39907
	Already Diagnosed	64	124.828	16.68718	2.08590
TC/HDL	Newly diagnosed	16	4.9994	1.12923	.28231
	Already Diagnosed	64	4.1402	.70113	.08764

Table 18: Lipid Profile with Newly Diagnosed and known cases of Rheumatoid Arthritis

P-value – Total Cholesterol - 0.156.
LDL - 0.011.
HDL - 0.676.
Triglycerides - 0.280.
TC/HDL - 0.094.

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
						Lower Bound	Upper Bound
Total Cholesterol	< 20	10	147.4000	7.47143	2.3626	142.055	152.744
	20 – 25	57	164.1930	15.95579	2.1134	159.959	168.426
	25 – 30	13	170.3846	17.59990	4.8813	159.749	181.020
	Total	**80**	**163.1000**	**16.57327**	**1.8529**	**159.411**	**166.788**
LDL	< 20	10	82.6000	5.75809	1.8208	78.480	86.719
	20 – 25	57	100.9825	17.68423	2.3423	96.290	105.674
	25 – 30	13	103.9231	11.11652	3.0831	97.205	110.640
	Total	**80**	**99.1625**	**16.88415**	**1.8877**	**95.405**	**102.919**
HDL	< 20	10	34.3000	7.34923	2.3240	29.042	39.557
	20 – 25	57	39.7193	8.00615	1.0604	37.595	41.843
	25 – 30	13	40.1538	7.89352	2.1892	35.383	44.923
	Total	**80**	**39.1125**	**8.02684**	**.8974**	**37.326**	**40.898**
Triglycerides	< 20	10	104.3000	9.58065	3.0296	97.446	111.153
	20 – 25	57	124.2982	17.35343	2.2985	119.693	128.907
	25 – 30	13	130.8462	17.54445	4.8659	120.244	141.448
	Total	**80**	**122.8625**	**18.06300**	**2.0195**	**118.842**	**126.882**
TC/HDL	< 20	10	4.4180	.96450	.3050	3.728	5.108
	20 – 25	57	4.2818	.88449	.1171	4.047	4.516
	25 – 30	13	4.3631	.77276	.2143	3.896	4.830
	Total	**80**	**4.3120**	**.86819**	**.0970**	**4.118**	**4.505**

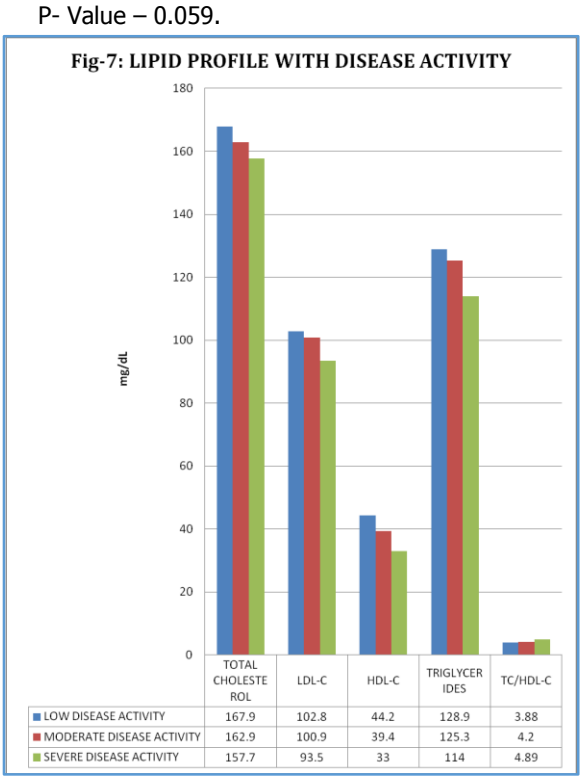
Table 19: Lipid Profile with BMI

P-value – Total Cholesterol - 0.002.
LDL - 0.003.
HDL - 0.126.
Triglycerides - 0.001.
TC/HDL - 0.879.

DAS 28	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
< 20	10	5.408	1.943	.614	4.017	6.798
20 - 25	57	4.156	1.522	.201	3.752	4.560
25 - 30	13	4.147	1.164	.323	3.443	4.851
Total	**80**	**4.311**	**1.566**	**.175**	**3.962**	**4.659**

Table 20: DAS with BMI

P- Value – 0.059.



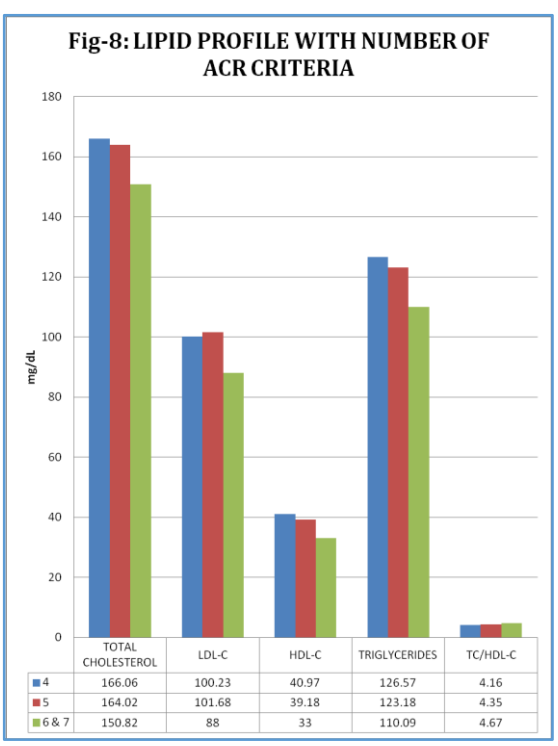
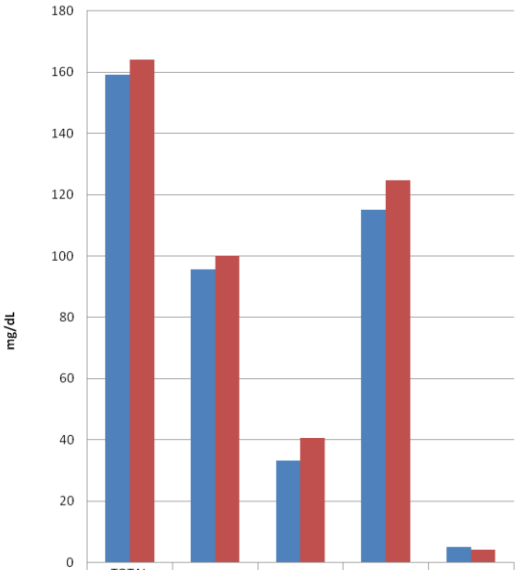
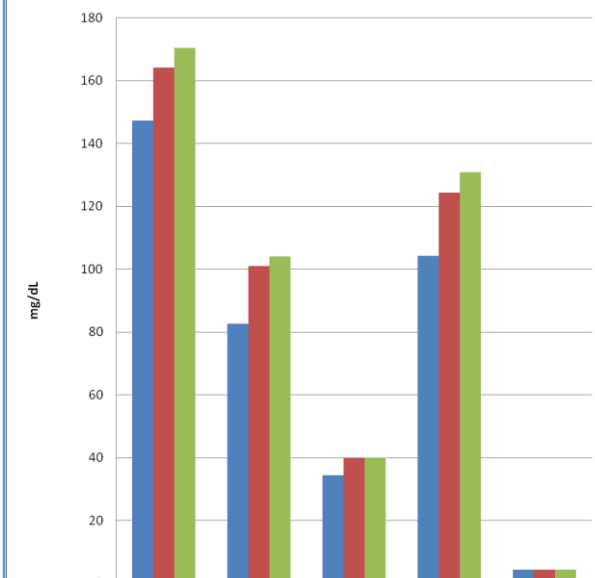


Fig-9: LIPID PROFILE WITH NEWLY DIAGNOSED AND ALREADY DIAGNOSED CASES



	TOTAL CHOLESTEROL	LDL-C	HDL-C	TRIGLYCERIDES	TC/HDL-C
NEWLY DIAGNOSED	159.1	95.7	33.2	115	4.99
ALREADY DIAGNOSED	164.1	100	40.6	124.8	4.14

Fig-10:LIPID PROFILE WITH BODY MASS INDEX



	TOTAL CHOLESTEROL	LDL-C	HDL-C	TRIGLYCERIDES	TC/HDL-C
BMI < 20	147.4	82.6	34.3	104.3	4.42
BMI 20 - 25	164.2	101	39.7	124.3	4.28
BMI 25 - 30	170.4	104	40.1	130.8	4.36

RESULTS:

- A total of 80 patients with Rheumatoid Arthritis (newly diagnosed and known cases) were studied.
- The patients were studied on the basis of the severity of the disease based on DAS 28, Duration of disease, Number of ACR 1987 criteria fulfilled with reference to the Lipid profile of the patient.
- In this study, 67 (83.8%) were females and 13 (16.3%) were females, the female to male ratio is 5.15.
- All the 80 patients have fulfilled the American College of Rheumatology 1987 criteria for the diagnosis of Rheumatoid Arthritis 25.
- The age of patients ranged from 24 to 80 yrs., with mean age of 44.2±11.3 yrs.
- Based on severity of disease, 31 (38.8%) of patients had Low Disease Activity, 22 (27.5%) patients had Moderate Disease Activity and 27 (33.8%) had Severe Disease Activity.
- 12.5% of patients had BMI <20, 71.3% of patients had BMI 20 to 25, 16.3% of patients had BMI 25 to 30, the mean BMI 22.747±2.562.
- Out of 80 patients, 20% are newly diagnosed and 80% were known cases of Rheumatoid Arthritis who are on and off treatment.
- Out of 80 patients, 35 (43.75%) fulfilled 4 ACR criteria, 34 (42.5%) fulfilled 5 ACR criteria and 11 (13.75%) fulfilled 6&7 criteria.
- Out of 80 patients, 44(55%) had Dyslipidaemia, of which 41(51.25) have low High Density Lipoproteins.

Relationship of Lipid Profile with Disease Activity:

- **Total Cholesterol (TC):** The mean TC in patients with Low Disease Activity is 167.9355± 15.5046 mg/dL, in patients with Moderate Disease Activity is 162.8636± 15.9412 mg/dL, in patients with Severe Disease Activity is 157.7407± 17.1522 mg/dL. In this study, TC decreases with the increase in the activity of the disease with a P-value of 0.063.

Among 80 patients, 1 patient had TC>200 mg/dL who has Low Disease Activity.

- **Low Density Lipoproteins (LDL):** The mean LDL in patient with Low Disease Activity is 102.8387± 13.2793 mg/dL, in patients with Moderate Disease Activity is 100.9545±14.9999 mg/dL, in patients with Severe Disease Activity is 93.4815± 20.7037 mg/dL. In this study, LDL decreases with the increase in the activity of the disease with a P-value of 0.091.
- **High Density Lipoproteins (HDL):** The mean HDL in patient with Low Disease Activity is 44.1935± 6.9061 mg/dL, in patients with Moderate Disease Activity is 39.4091± 6.1074 mg/dL, in patients with Severe Disease Activity is 33.037± 6.4359 mg/dL. In this study, HDL decreases with the increase in the activity of the disease with a P-value of <0.001.

Among patients with severe disease activity, 18 (85.18%) had low HDL levels, 13 (59.09%) with moderate activity and 5 (16.13%) with low disease activity had low HDL levels.

- **Triglycerides (TG):** The mean TG in patient with Low Disease Activity is 128.871±14.957 mg/dL, in patients with Moderate Disease Activity is 125.2727±17.7205 mg/dL, in patients with Severe

Disease Activity is 114±18.7103 mg/dL. In this study, Triglycerides decreases with the increase in the activity of the disease with a P-value of 0.005.

- **TC/HDL:** The mean TC/HDL in patient with Low Disease Activity is 3.882± 0.654, in patients with Moderate Disease Activity is 4.199± 0.582, in patients with Severe Disease Activity is 4.898± 0.967. In this study, TC/HDL increases with the increase in the activity of the disease with a P-value of 0.0001.

Relationship of Lipid Profile with Number of ACR Criteria:

- **Total Cholesterol:** The mean TC in patients who fulfilled 4 ACR criteria is 166.057±16.766 mg/dL, in patients fulfilling 5 criteria is 164.029±16.325 mg/dL, in patients fulfilling 6&7 criteria is 150.818±11.626 mg/dL. In this study TC decreases with the increase in the number of ACR criteria fulfilled with a P-value of 0.024.
- **Low Density Lipoproteins (LDL):** The mean LDL in patients who fulfilled 4 ACR criteria is 100.229± 15.322 mg/dL, in patients fulfilling 5 criteria is 101.676± 18.140 mg/dL, in patients with fulfilling 6&7 criteria is 88± 14.331 mg/dL. In this study LDL was low in patients fulfilling 6&7 ACR criteria fulfilled with a P-value of 0.056.
- **High Density Lipoproteins (HDL):** The mean HDL in patients who fulfilled 4 ACR criteria is 40.971± 7.382 mg/dL, in patients fulfilling 5 criteria is 39.176± 8.451 mg/dL, in patients with fulfilling 6&7 criteria is 33± 5.899 mg/dL. In this study HDL decreases with the increase in the number of ACR criteria fulfilled with a P-value of 0.014.
- **Triglycerides (TG):** The mean TG in patients who fulfilled 4 ACR criteria is 126.571±18.724 mg/dL, in patients fulfilling 5 criteria is 123.176±16.123 mg/dL, in patients with fulfilling 6&7 criteria is 110.09± 17.323 mg/dL. In this study TG decreases with the increase in the number of ACR criteria fulfilled with a P-value of 0.028.
- **TC/HDL:** The mean TC/HDL in patients who fulfilled 4 ACR criteria is 4.164± 0.772, in patients fulfilling 5 criteria is 4.349± 0.994, in patients with fulfilling 6&7 criteria is 4.667±0.671. In this study TC/HDL increases with the increase in the number of ACR criteria fulfilled with a P-value of 0.234.

Relationship of Lipid Profile with New and Known Cases of Rheumatoid Arthritis:

- Patients who were newly diagnosed to have RA have a mean TC of 159.125± 19.151 mg/dL and already diagnosed patients have a TC of 164.093 ±15.877 mg/dL with a P-value of 0.286.
- Patients who were newly diagnosed to have RA have a mean LDL of 95.75±24.453 mg/dL and already diagnosed patients have a TC of 100.016 ±14.54 mg/dL with a P-value of 0.369.
- Patients who were newly diagnosed to have RA have a mean HDL of 33.1875± 7.952 mg/dL and already diagnosed patients have a TC of 40.594± 7.389 mg/dL with a P-value of 0.001.
- Patients who were newly diagnosed to have RA have a mean Triglycerides of 115±21.596 mg/dL and already diagnosed patients have a TC of 124.828±16.687 mg/dL with a P-value of 0.051.
- Patients who were newly diagnosed to have RA have a mean TC/HDL of 4.999±1.129 and already diagnosed patients have a TC of 4.14± 0.701 mg/dL with a P-value of 0.051.

Disease activity and lipid profile with BMI:

- Patient with BMI < 20 had more Disease Activity 5.408± 1.943 compared to patients with BMI 20 – 25 and 25 – 30 with DAS of 4.156±1.522 and 4.147± 1.165 respectively, with a P-value of 0.059.
- Patients with BMI <20 had low TC, LDL, HDL, Triglycerides, compared to patients with BMI between 20 to 25 who had low values as compared to patients with BMI between 25 to 30, and TC/HDL is not related to the BMI. The P-values are significant for TC, LDL, Triglycerides and insignificant for HDL and TC/HDL.

The unfavourable lipid profile in our study can explain the increased cardiovascular mortality in RA patients. The explanation given by western studies for increased cardiovascular mortality in RA patients as follows.

1. The presence of circulating anti-oxidised VLDL and LDL antibodies in RA, may be responsible for the reduced level of total cholesterol and LDL cholesterol.[15]
2. Cardiovascular disease in RA may result from accelerated atherosclerosis caused by clinical or subclinical vasculitis.[9]
3. Reduced cardiovascular fitness caused by immobility.[16]
4. The inflammatory environment and disturbed antioxidant mechanisms in RA may promote LDL oxidation, thereby facilitating atherogenesis at lower ambient lipid concentrations and placing RA patients at higher cardiovascular risk.[9]
5. Lipoprotein (a), an important independent factor in atherogenesis and thrombogenesis is increased in RA correlating positively with the acute phase response.[17]
6. Increased homocysteine level,[18] and increased thrombotic factors.[19]
7. Inflammatory mechanisms responsible for synovial lesions in patients with RA may directly participate in producing atherosclerotic lesions resulting in excess cardiovascular disease in RA patients.[20]

ABBREVIATIONS:

TC - Total Cholesterol.
LDL-C - Low Density Lipoprotein cholesterol.
HDL-C - High Density Lipoprotein Cholesterol.
TG – Triglycerides.
ACR - American College of Rheumatology.
DAS 28 - Disease Activity Score of 28 joints.
ESR - Erythrocyte Sedimentation Rate.
TJC - Tender Joint Count.
SJC - Swollen Joint Count.
VAS - Visual Analogue Scale.

NCEP - National Cholesterol Education Programme.
ATP III - Adult Treatment Panel III.
ND - Newly Diagnosed.

CONCLUSION:

- Lipid Profile in Rheumatoid Arthritis patients depends on the severity of the disease.
- There is an inverse relationship between TC, LDL-C, HDL-C and Triglycerides and severity of the Rheumatoid Arthritis which is statistically significant for HDL-C and Triglycerides. There is direct relationship between TC/HDL-C and severity of disease which is statistically significant. These factors in part explain the high risk of Coronary Artery Disease in patients with Rheumatoid Arthritis and the importance of effective treatment of RA.
- There is an inverse relationship between TC, HDL-C, LDL-C and Triglycerides and the number of ACR criteria fulfilled which is statistically significant for TC, HDL-C and Triglycerides, and direct relationship between TC/HDL-C and severity of disease which is not statistically significant.
- Newly diagnosed patients have low levels of TC, HDL-C, LDL-C and Triglycerides statistically significant for HDL-C owing to the severity of the disease in patients not on treatment and the possible benefit of treatment.
- Early treatment of Rheumatoid Arthritis aimed at remission or reducing the severity of the disease has a favourable effect on the Lipid Profile of the patients with Rheumatoid Arthritis which is one of the important factors for Coronary Artery Disease which is the commonest cause of death in patients with RA.[2,3,5]

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