



## Correlative study of RA and Diabetic Mellitus in cardio vascular diseases in Gujarat Population

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### Abstract

**Background-** Although RA is due to genetic factors but aggregated by environmental and nutritional status and mainly has linkages with DM and CVD. Hence attempt was made to study the clinical profile of RA and DM, CVD was corrected with controlled group,

**Method-** RA with DM and CVD were studied (CARRE) study having DM with CVD risk and Hoorn study was also studied. RA +ve, ESR, CRP, lipid profile was also noted

**Results-** Apart-from significant different CVD, systolic BP, Diastolic BP, HTN lipid profile, CRP studies , Different grades of DM studied Grade II had 2.3(SD±1.10), DM 3.13 (SD±1.40) RA 't' test was 4.43 P< 00.1 (highly significant) similarly In grade-III, 2.20 (SD±0.88) DM, 2.74 (SD±1.20) RA 't' test was 4.71 and P<0.001(P value was highly significant

**Conclusion-** This study RA with DM with CVD has significant correlative Parameters can prognoses the morbidity and mortality of affected patients.

**Keywords:** - RA= Rheumatoid Arthritis, DM= Diabetic mellitus, CVD= cardio vascular diseases, CARRE, Hoorn study, HTN= Hypertensive

## Introduction

RA (Rheumatoid Arthritis) epidemiology is suggestive of a genetic effect. Prevalence of RA is increasing globally at high rate<sup>(1)</sup>. It is also predicted that apart from genetic inheritance, environment factors also contribute for prevalence of RA in India and abroad<sup>(2)</sup>

The important familial recurrence risk a key factor in determining the power of genetic linkage studies like diabetic mellitus (DM) and cardio vascular diseases because RA affects the valves of heart and blood vessels. While DM will mainly affect the macro and micro – Vascularity, Due to hyperglycemia there is more viscosity in the blood. Hence reduction in the blood flow leads to lesser, least blood in the macro/micro vascular system results vasculities ischemia infarction, gangrene etc moreover lipids also create obstruction in blood flow in the blood vessels, causing multiple CVD<sup>(3)</sup><sup>(4)</sup>. Hence attempt was made to study the correlative of risk factors of cardio- vascular diseases in RA and DM patients.

## Material and Methods

95 RA with CVD and 95 DM patients, aged between 45 to 60 years, who were regularly visiting cancer society medical college hospital Ahmadabad were selected for study and their all parameters were compared with normal 100 (control group) people.

**Inclusive criteria-** The patients diagnosed and confirmed RA with CVD, DM included in the study.

**Exclusion criteria** – The patients have congenital heart anomalies, juvenile diabetic, patients undergone bypass cardiac surgery, history of malignancy, Immune-compromised patients were excluded from the study.

**Method-** The RA patients associated with CVD (CARRE study) patients having glucose metabolism with CVD risk (Hoorn study). Every patient was investigated for RA +ve, ESR, C- reactive protein, lipid profile and present medication status of the patients was also noted. The duration of study was April 2018 to December 2019.

**Statistical analysis-** Parameters of DM, RA were compared with controlled group, various grades of DM, RA were also compared by using soft were 2007. The ratio of male and female were 2:1

### Observation and Results

**Table-1** –In the study of CVD 14 controller groups 26(27%) DM group, 39 (41%) patients in RA, In coronary artery disease study 11 were in control group, 13(13.6%) in DM, 24(25.2%) in RA, In cerebral arterial disease study 3 in controlled 9(9.47%) in DM, 15(15.7%) in RA . In peripheral arterial disease 2 were in control, 12 (12.6%) in DM patients, 6 (6.3%) in RA patients. In the study of CVD risk factors systolic BP- Was 130( $\pm$ 16) in controls, 146( $\pm$ 18) in DM patients 143( $\pm$ 20) in RA patients, in diastolic BP-80( $\pm$ 11) in controlled, 84 ( $\pm$ 10) in DM, 83( $\pm$ 7) in RA patients. The patients on anti HTN drugs were 15 in controls, 43 (45.2%) in DM, 26(27.3%) in RA patients. In the study of HTN patients 36 in controls, 78 (82%) in DM, 59(62.1%) in RA patients

**Table-2-** Comparative study of laboratory finding were- Creatinine (mg/dl) was 93 in controls, 94 in DM, 89 in RA patients, Cockcroft- Gault (ml/min): 70 in controllers 78 in DM, 76 in RA patients. Total cholesterol was 25(mg/dl) in control 32, in DM, in RA patients HDL (mg/dl) was 6.5( $\pm$ 1.3) in control 6.7( $\pm$ 1.4) in DM, 5.9( $\pm$ 1.3) in RA LDL (mg/dl) 1.5 ( $\pm$ 0.4) in controls, 1.3 (0.4) in DM, 1.6 ( $\pm$ 0.7)in RA patients Triglycerides 4.5( $\pm$ 1.2) in controls, 4.2 ( $\pm$ 1.3) in DM, 3.9( $\pm$ 1.1 to 1.2) in RA patients. Statins (%):

1.7 (1.0-1.9) in controls, 2.1 ( $\pm 1.3-2.9$ ) in DM, 1.4( $\pm 1.0-1.9$ ) in RA patients In the CRP (mg/dL) analysis 2( $\pm 1.4$ ) in controls, 3( $\pm 1.5$ ) in DM patients 7( $\pm 3.17$ ) in RA patients. IGM- RF $\geq$ IU/ml was 73( $\pm 2.5$ ) in RA patients. Anti CCP  $\geq$  50Au/ml (%) was 56 ( $\pm 3-6$ ), Erosion of joints viewed radiologically

**Table-3-** study of number of patients on anti -RA treatment -48 (50.2%) were on methotrexate, 17(17.8%) were sulfasalazine, 5(5.26%) were on hydrochlorine, 16(16.8%) were on prednisolone, 09(9.47%) were on herbal treatment. Comparison of mean values of different grades of DM and RA in control groups, Grade-I- Study - Mean value of 2.60 (SD $\pm$ 1.22) in DM, 2.84 (SD $\pm$ 1.44) in RA and 't' test was 1.23 and P value was 0.10 (P $<$ 0.01), Grade-II- 2.32 (SD $\pm$ 1.10) in DM. 3.13(SD $\pm$ 0.88) in RA, 't' test value was 4.43 0.01(P $<$ 0.01) P value was highly significant, Grade-III- 2.02(SD $\pm$ 0.88) in DM 2.74(SD $\pm$ 1.20) in RA and 't' test value was 't' test value -4.71 and P value was highly significant (P $<$ 0.01)

## Discussion

In the present study of RA and DM in CVD patients CVD 14 control groups 26(27%) DM group, 39 (41%) patients in RA In coronary artery disease study 11 were in control group, 13(13.6%) in DM, 24(25.2%) in RA patients. In the study of cerebral arterial disease study 3 in controlled 9(9.47%) in DM, 15(15.7%) in RA patients.

In peripheral arterial disease 2 were in control, 12 (12.6%) in DM patients, 6 (6.3%) in RA patients. In the study of CVD risk factors systolic BP- Was 130( $\pm 16$ ) in controls, 146( $\pm 18$ ) in DM patients 143( $\pm 20$ ) in RA patients. The patients on anti HTN drugs were 15 in controls, 43 (45.2%) in DM, 26(27.3%) in RA patients. In the study of HTN patients 36 in controls, 78 (82%) in DM 59(62.1%) in RA patients (Table-1) In the study of laboratory finding were.- Creatinine (mg/dL)]was 93 in control, 94( $\pm 1-3$ ) in , 89 ( $\pm 1-2$ )in RA patients. Cockcroft- Gault (ml/min) 70 in control 78( $\pm 1.4$ ) in DM, 76( $\pm 1.2$ ) in RA patients, Total cholesterol was 25(mg/dL) in control 32,(SD $\pm 1.4$ ) in DM, in RA patients HDL (mg/dL) was 6.5( $\pm 1.3$ ) in control 6.7( $\pm 1.4$ ) in DM,

5.9( $\pm$ 1.3)in RA patients. LDL (mg/dL)1.5 ( $\pm$ 0.4) in controls, 1.3 (0.4) in DM, 1.6 ( $\pm$ 0.7)in RA patients. Triglycerides (mg/dL) 4.5( $\pm$ 1.2) in controls, 4.2 ( $\pm$ 1.3) in DM, 3.9( $\pm$ 1.1 to 1.2) in RA patients, Statins (%): 1.7 (1.0-1.9) in controls 2.1 ( $\pm$ 1.3-2.9) in DM, 1.4( $\pm$ 1.0-1.a) in RA patients, CRP (mg/dl) analysis 2( $\pm$ 1.4) in controls, 3( $\pm$ 1.5) in DM patients 7( $\pm$ 3.17) in RA patients, IGM- RF $\geq$ IU/ml was 73( $\pm$ 2.5)in RA patients. Anti CCP  $\geq$  50Au/ml (%) was 56 in RA patients Erosion of joints (viewed in radiology) was 4.12( $\pm$ 1.4) in RA patients (Table-2). study of number of patients on anti -RA treatment -48 (50.2%) were on methotrexate, 17(17.8%) were sulfa salazine, 5(5.26%) were on hydrochlorine, 16(16.8%) were on prednisolone, 09(9.47%) were on herbal treatment.(Table-3).In the comparison of mean values of different grades of DM and RA in control groups, Grade-I- Study -Mean value of 2.60(SD $\pm$ 1.22) in DM, 2.84 (SD $\pm$ 1.44) in RA and't' test was 1.23 and P vale was 0.10 (P<0.01) Grade-II- 2.32 (SD $\pm$ 1.10) in DM. 3.13(SD $\pm$ 0.88) in RA, 't' test value was 4.43 0.01(P<0.01) P value was highly significant Grade-III- 2.02(SD $\pm$ 0.88) in DM 2.74(SD $\pm$ 1.20) in RA 't' test value was 't' test value -4.71 and P value was highly significant (P<0.01)(Table-4) These findings were more or less in agreement with previous studies <sup>(5)(6)(7)</sup>

Such types of study was carried out previously, the method was called CARRE study- CARRE is a Dutch acronym for Cardiovascular and Rheumatoid Arthritis <sup>(8)</sup>. Similarly the Hoorn study was also Dutch study, related to glucose metabolism and other cardio-vascular risk factors (9). The risk of CVD patients have multiple cardio-vascular diseases RA itself should be regarded as strong independent cardio-vascular risk factors as good as Diabetic mellitus <sup>(10)</sup>. Moreover clinical and laboratory investigations also shown elevated stage of atherosclerosis and inflammatory profiles which contribute increased CVD risk Inflammation is known to cause deterioration of fatty streaks into unstable plaques, plaques raptures and compliment activation <sup>(11)</sup>. Inflammation is also associated with higher systolic Blood pressure and adverse lipid profile <sup>(12)</sup>. Hence it can be expected that CVD occurs more frequently in diseases with high inflammation in RA patients associated with DM.

It was also reported that, elevation of CRP is an indication of thickness of carotid intima<sup>13</sup>. This plays vital role in chemoreceptor and Baro-receptors, which has important contribution role in CVD. Although NSAID, cox-2 inhibitor and diseases modifying anti-Rheumatic drugs (DMARDS) are used to suppress inflammation on the other hand these drugs mediate the CVD risk factors, as they enhance thrombotic effects<sup>14</sup>. RA and DM share several mechanisms that contribute to the increased risk of CVD and in the present of chronic inflammation implicated in this pathogenesis of RA. Diabetes and atherosclerosis appears to be the Key feature in such patients TNF- $\mu$  drugs are widely used to treat the inflammation are contra indicated in D.M patients because TNF- $\alpha$  decreases tyrosine kinase activity of insulin receptor,. Moreover TNF- $\alpha$  impedes insulin –mediated disposal of glucose of skeletal muscles these contradictory factors leads to the risk of cardio-vascular diseases. Hence in RA patients with DM have great clinical challenges to regulate hyperglycemia and treat the inflammation of RA.

### **Summary and Conclusion**

The present study of clearly indicates that, prevalence of CVD in RA has greater risk as compared to healthy individuals but same CVD problems are also with DM patients. Both RA and DM have same potential degree of CVD risk factors. Hence management of CVD in both RA and DM would be helpful to prolong morbidity and mortality of RA with DM patients. But this study further demands genetic, hormonal, Patho-physiological, pharmacological, nutritional studies because exact pathogeneses RA which mainly affects the CVS is still un-clear.

### **Limitation of Study**

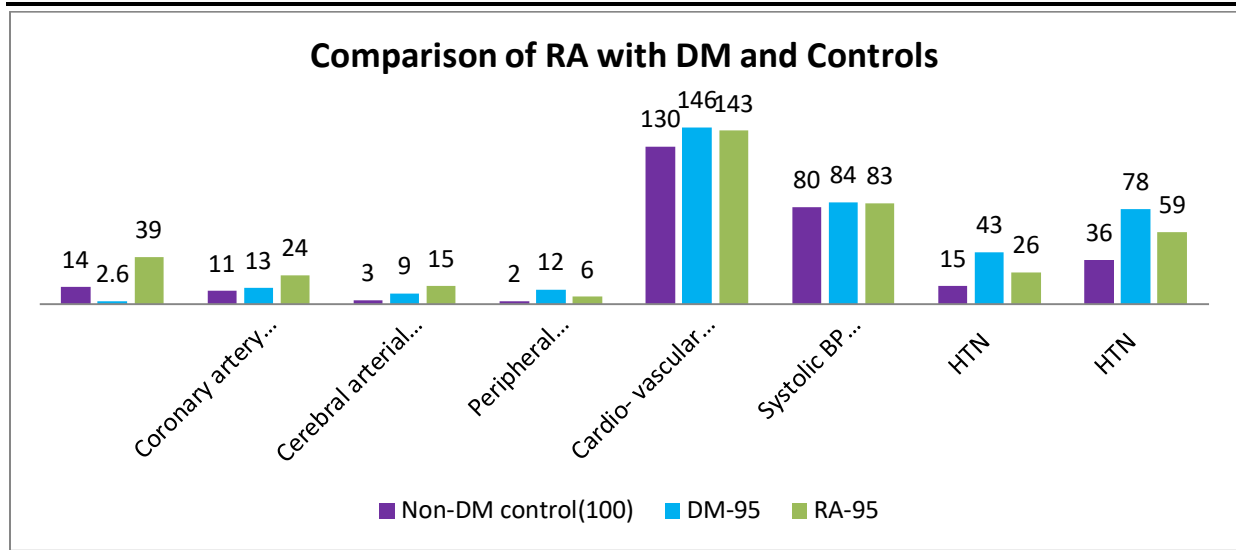
Owing to the Lack of funds and Non-availability of modern techniques we have limited findings

**Table-1**

(No of patients 95)

**Comparison of RA with DM and controls**

Particular	Hoorn study		CARRE Study
	Non-DM control(100)	DM-95	RA-95
Cardiovascular disease	14	2.6(27.6%)	39(41%)
Coronary artery disease	11	13(13.6%)	24(25.2%)
Cerebral arterial disease	03	9(9.47%)	15(15.7%)
Peripheral arterial disease	02	12(12.6%)	6(6.31%)
Cardio- vascular risk factors	130(±16)	146(±18)	143(±20)
Systolic BP diastolic Bp	80(±11)	84(±10)	83(±7)
HTN	15	43(45.2%)	26(27.3%)
HTN	36	78(82.1%)	59(62.1%)



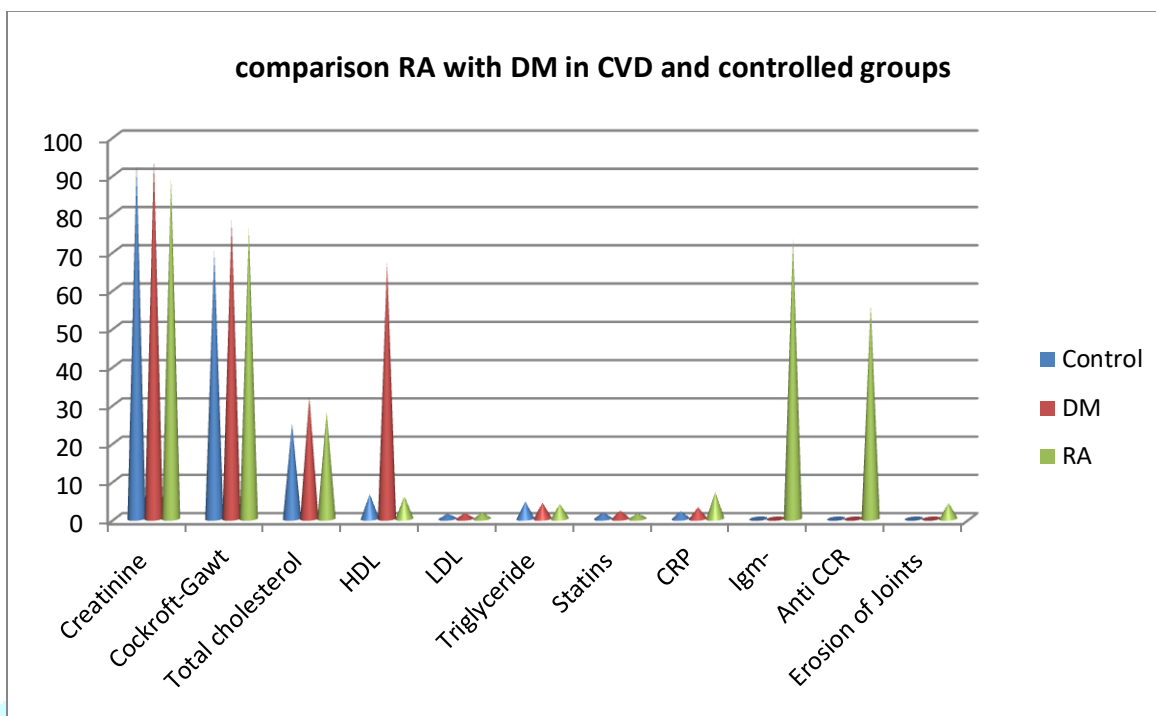
**Table-2**

**Laboratory findings in the comparison RA with DM in CVD and controlled groups**

(No of patients 95)

Particular Group	Hoorn study		CARRE Study
	Control(100)	DM	RA
Creatinine (mg/dL)	93	94(±1.3)	89(±1.2)
Cockroft-Gawt(ml/min)	70	78(±1-4)	76(±1.2)
Total cholesterol (mg/dL)	25	32(SD±1-4)	28(SD±11)
HDL (mg/dL)	6.5	67(±1-4)	5.9(±1.3)
LDL (mg/dL)	1.3(±1.3)	1.5(±0.4)	1.6(±0.7)
Triglyceride (mg/dL)	4.5(±1.2)	4.2(±1.3)	3.9(±11-1.2)
Statins (%)	1.7(±1.0-1-9)	2.1(±1.3-2.9)	1.4(±1.0-1.9)
CRP(mg/dl)	2(±1.4)	3(±1-5)	7(±3-17)
Igm-RFZIU/ml(%)	-	-	73
Anti CCR≥50AU/ml(%)	-	-	56
Erosion of Joints (Viewed Radiologically)	-	-	4.12(±1-4)

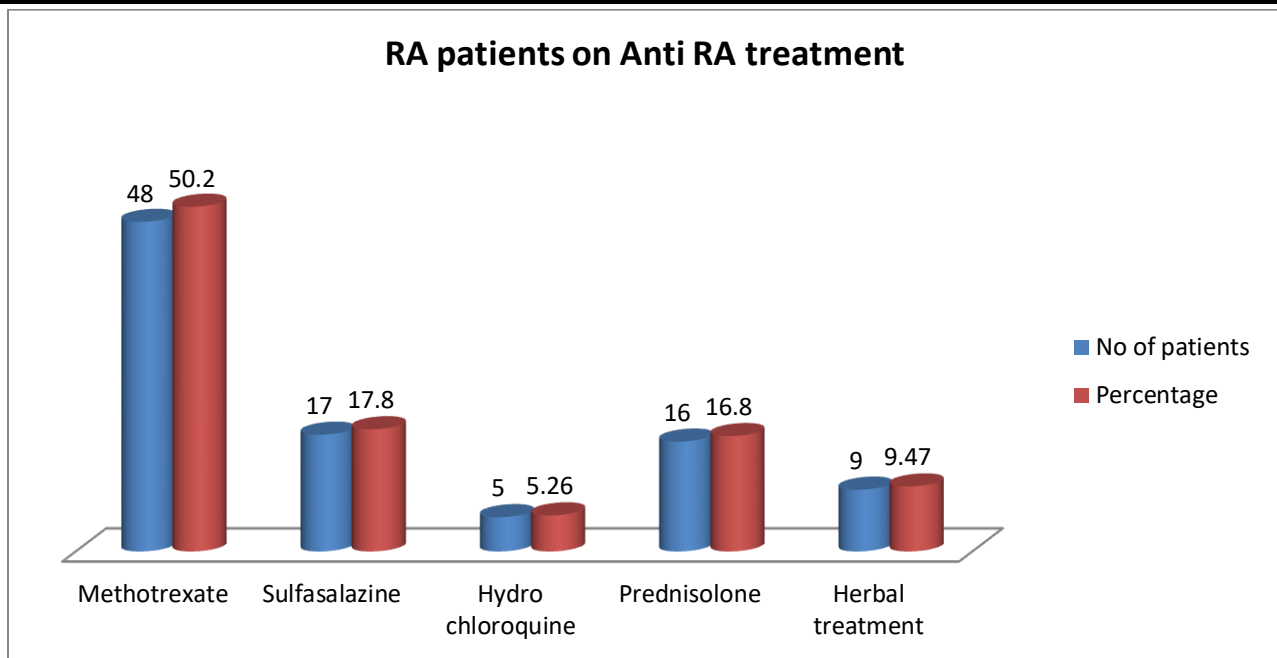




**Table-3**  
**Study of RA patients on Anti RA treatment**

(No of patients 95)

Drugs	No of patients	Percentage (%)
Methotrexate	48	50.2
Sulfasalazine	17	17.8
Hydro chloroquine	05	5.26
Prednisolone	16	16.8
Herbal treatment	09	9.47



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