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CORRELATION BETWEEN CRP AND GLYCEMIC CONTROL IN ADULTS WITHTYPE 2 DIABETIES MELLITUS

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ABSTRACT

Aims and Objectives: To correlate C - reactive protein (CRP) with glycosylated haemoglobin (HbA1c) in patients with poorly controlled Type 2 diabetes mellitus; To determine if better control of HbA1c reduces CRP levels.

Methods: A hospital based longitudinal study, was done in cohort of outpatients and inpatients diagnosed with Type2 DM attending to Department of General Medicine of MNR Medical College and Research Hospital from January 2021 to July 2022.

Results: CRP is well correlated with HbA1c and the elevation in HbA1c levels are significantly correlated with elevation in CRP (P<0.05). Better glycaemic control leading to the reduction in HbA1c also resulted in decrease in CRP levels (P=0.000). CRP also showed significant positive correlation with other atherosclerotic risk factors-like age (P<0.05), duration of type 2 DM (P<0.05) total cholesterol (P<0.05), triglycerides (P<0.05) and also creatinine (P<0.05), which are seen in Diabetic patients. It also showed a negative correlation with HDL-C. CRP level was not significantly correlated with BMI (P= 0.88).

Conclusion: This study therefore, reveals that CRP is an additional marker of better glycaemic control and also correlates with the dyslipidaemic profile, seen in T2DM.

Keywords: Type 2 Diabeties Mellitus, glycaemic, CRP, HbA1c.

INTRODUCTION

Diabetes is one of the rapidly growing global health emergencies in 21st century. It is one of the commonest major risk factors for death. It is a progressive disorder with innumerable both fatal and nonfatal complications that will impose a tremendous burden to the patients, their families, and the health care system.[1] Uncontrolled diabetes leads to increased risk of vascular disease. The macrovascular complications include cardiovascular, cerebrovascular, and peripheral artery disease and microvascular complications include diabetic retinopathy, nephropathy, and neuropathy. [2,3]

As per recent evidence more than half a billion people are living with diabetes worldwide. In the year 2021, it is estimated that 537 million people have diabetes, which is projected to reach 643 million by 2030, and 783 million by 2045. Also, 541 million people are estimated to have had impaired glucose tolerance in 2021. Also annually there is a marked increase in the number of children and adolescents (i.e. up to 19 years old) living with diabetes. In the year 2021, over 1.2 million children and adolescents have had type 1 diabetes mellitus. Direct health expenditures contributed by diabetes mellitus are already close to one trillion USD and will still raise this figure by 2030.[4,5] As per WHO top 10 causes of death globally diabetes mellitus is the 9th cause of death. [6]

This rising trend predicts a significant health burden due to diabetes especially in developing countries like India.[7,8] Among developing economies, the highest increase in number of people with diabetes is in China followed by India. There is also evidence that Asian Indians progress more rapidly through the prediabetes stage as compared to people of other ethnic groups.

MATERIALS AND METHODS

A hospital based longitudinal study, was done in cohort of outpatients and inpatients diagnosed with Type2DM attending to Department of General Medicine of MNR Medical College and Research Hospital from January 2021 to July 2022.

SAMPLING TECHNIQUE:

Patients were selected by purposive sampling method.

Inclusion criteria:

Patients belonging to 30 – 70yrs with fasting venous blood glucose value equal or more than 126mg/dl and postprandial glucose >200mg/dl were included in the study.

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Exclusion criteria:

- Patients on statins, thiazolidinediones (TZDs), and anti-inflammatory drugs which are knownto reduce CRP levels were excluded from the study.
- Patients with heart failure, acute febrile illness, renal, hepatic & malignant disorders, chronic illnesses, asymptomatic infections and smokers were also excluded from the study.
- Patients who were not willing to participate in the study

Method of collection of data

After obtaining institutional ethical committee clearance and written informed consent from the patients attending MNR Medical College and Hospital to General Medicine OPD data was collected. A semi-structured questionnaire was used which consists of socio- demographic data, detailed history on presenting illness, physical examination, and anthropometric measurements (like height,weight, waist circumference, waist hip ratio, body mass index). Fasting blood sample (after 8 hours of fasting) of about 20 ml and midstream urine was collected from the patient under aseptic precautions for biochemical analysis. Investigations like haemoglobin estimaton (Hb), total count (TC), differential count (DC), erythrocyte sedimentation rate (ESR), blood urea (BU), serum creatinine (SC), urine examination (CUE), c-reactive protein (CRP), fasting blood sugar (FBS), post prandial blood sugar (PPBS), glycated haemoglobin (HbA1c), serum total cholesterol, serum triglycerides (TG), high-density lipoprotein (HDL), low density lipoprotein (LDL) were done. CRP was correlated with HbA1c statistically.

METHODS

All the investigations were done at entry and at subsequent follow up with a minimum gap of 3 months. All samples were collected on the same day. Patients were prescribed with OHA/ insulin, for control of blood sugar along with advice on diet and physical activity. The patients who were prescribed with statins and TZDs were excluded for follow up.

Statistical Analysis

Data was entered in Microsoft excel 2007. Statistical analysis was done using SPSS 20 package. Risk factors of CAD were studied among the 150 Type 2 diabetic patients. Correlation of CRP was done with Pearson correlation and P values were calculated. P values < 0.05 was considered to be significant. Student's 't' test, Anova test and Pearson correlation was done with $P<0.05$ was considered to bestatistically significant.

RESULTS

Out of the 150 patients in the study, there were 105(70%) male and 45(30%) female patients. Age ranges from 32-75 years with mean ± Standard deviation (SD) of age being 53.74 ± 9.82, with majority belonging to 50-60(44%) years age group. With respect toduration of Type 2 DM, mean was 4.44±3.41. About 46% were suffering from Type 2 DM formore than 5 years. (Shown in table 1)

TABLE 1: DISTRIBUTION OF STUDY PATIENTS BY AGE, SEX AND DURATIONOF TYPE2 DM

Socio-demographic detail	Category	Frequency (n=150)	Percentage
Age	30-40	18	12%
	41-50	33	22%
	51-60	66	44%
	61-70	27	18%
	>70	6	4%
Sex	Male	105	70%
	Female	45	30%
Duration Of Type 2 DM	< 5 year	81	54%
	≥ 5 year	69	46%

Range, Mean and SD of various parameters of 150 patients were studied. The range for BMI was 17 - 32 with mean 23.77 ± 2.62, range for FBS was 106- 421 with mean of 232.20 ± 84.14, range for PPBS was 143 - 524 with mean 305 ± 96.75, range for HbA1c was 7.0 - 14.0 with mean 9.65 ± 1.87. Total cholesterol of 150 study patients ranges from 97 to 432 with a mean of 196 ± 69.31, LDL cholesterol ranges from 0 - 202 with mean 92.72 ± 36.98, HDL ranges from 12-82 with mean 39.32 ± 10.70, Triglyceride ranges from 100-759 with mean 233 ± 199.4, urea ranges from 11 - 33 with mean 23.28± 4.09, creatinine ranges from 0.60 - 1.20 with mean 0.94 ± 0.14, CRP ranges from 0 - 5.6 with mean 1.38 ± 1.41. Haemoglobin ranges from 9.8gm/dl - 15.3 gm/dl, with mean 12.01±1.31. With respect to WBC count the range was 4800-13500 cells/dl and mean 7532±1653.36. (Shown in the table 2).

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TABLE 2: MINIMUM, MAXIMUM MEAN AND STANDARD DEVIATION OFPARAMETERS STUDIED.

Parameters (n=50)	Minimum	Maximum	Mean	SD
Body mass index	17.00	32.00	23.77	2.62
FBS	106	421	232.20	84.14
PPBS	143	524	305	96.75
HbA1c	7.0	14.0	9.65	1.87
Total cholesterol	97.00	432	196	69.31
Ldl-cholesterol	0	202	92.72	36.98
Hdl-cholesterol	12.00	82.00	39.32	10.70
Triglyceride	100.00	759.00	233.3	119.40
Creatinine	0.60	1.20	0.94	0.14
Urea	11	33	23.28	4.09
CRP	0.00	5.6	1.38	1.41
Hemoglobin	9.8	15.3	12.02	1.31
WBC count	4800	13500	7532	1653.36
ESR	5	82	21.98	12.00

CRP AND HBA1C IN DIFFERENT AGE GROUPS

Mean CRP and mean HbA1c was high in patients with 41-50 years age compared with otherage groups. shown in table 3.

TABLE 3: DISTRIBUTION OF CRP AND HBA1C VERSUS VARIOUS AGEGROUPS

Age group(n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
31 – 40 (6)	0-2.9	1.48±1.20	7-12.8	9.30±2.52
41 – 50 (11)	0-5.6	2.25±1.74	9-14	11.25±1.82
51 – 60 (22)	0-5.4	1.34±1.28	7-12	9.23±1.46
61 – 70 (9)	0-2.4	0.53±0.84	7-10.6	8.96±1.23
71+ (2)	0-1.2	0.60±0.66	8-11.4	9.70±1.87
ANOVA test P value	6.971/0.000		9.831/0.00	

CRP AND HBA1C IN MALE AND FEMALE

In male patients, the range of CRP was 0-5.6. In female patients, the range of CRP was 0-5.4. Though females show slightly higher mean CRP (1.4 ± 1.43) compared to males (1.37 ± 1.41), it was not statistically significant (P>0.05). With respect to HbA1c, it ranges from 7-14 in males with mean 9.77± 1.99, where as in females it was slightly lower with mean 9.37±1.54 which was not significant (p>0.05). These values are shown in the table 4.

TABLE 4: DISTRIBUTION OF CRP AND HBA1C IN MALE AND FEMALE

Sex(n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
Female (45)	0-5.4	1.40±1.43	7-12	9.37±1.54
Male (105)	0-5.6	1.37±1.41	7-14	9.77± 1.99
Anova test/ P value	0.013/0.910		1.482/0.225	

Patients with type 2 DM for ≤ 5 years have more mean CRP and mean HbA1C. (shown intable 5)

TABLE 5: DISTRIBUTION OF PATIENTS BY CRP AND HBA1C VERSUSDURATION OF TYPE 2 DM

Duration of Type 2 DM	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
≤ 5 years (102)	0-5.6	1.64±1.55	7-14	10.07±1.93
6-10years(42)	0-2.4	0.77±0.87	7-11.4	8.79±1.33
≥ 10 years(6)	1.2-1.2	1.20±0.00	7-10	8.50±1.64
ANOVA test P value	6.066/0.003		9.010/0.000	

In patients with BMI 23-24.9 has mean CRP 1.64±1.67 which was higher than patients who were overweight, obese and

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non obese patients which was not significant. Mean HbA1c was higher in patients with BMI ≥ 30. HbA1c increased with increasing BMI but was notsignificant (table 6).

TABLE 6: DISTRIBUTION OF STUDY PATIENTS BY CRP AND HBA1C VERSUSBMI

BMI (n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
<18 (3)	1.2-1.2	1.20±0	9-9	9.00±0
18-22.9 (33)	0-4.6	1.18±1.52	7-14	9.35±2.55
23-24.9 (63)	0-5.6	1.64±1.67	7-13.3	9.59±1.74
25-29.9 (48)	0-2.4	1.20±0.96	7-12.8	9.89±1.54
≥ 30 (3)	1.2-1.2	1.20±0	11-11	11.00±0
ANOVA and P value	0.903/0.464		0.895/0.468	

CRP AND HBA1C VERSUS FASTING BLOOD SUGAR

Patients with FBS >300 had mean CRP and mean HbA1c 2.34 and 11.330 respectively. Mean HbA1c and mean CRP increased with increase in FBS which was significant satistically. Shown in table 7.

TABLE 7: CRP AND HBA1C VERSUS FASTING BLOOD SUGAR

Fasting blood sugar in mg/dl (n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
100-200 (69)	0-2.4	0.57±0.86	7-10.6	8.24±1.19
200-300 (51)	0-5.6	1.91±1.71	9-12.8	10.57±1.30
>300 (30)	1.2-3.7	2.34±0.70	9-14	11.33±1.61
	30.126/0.000		75.573/0.000	

PPBS with HbA1c and CRP

Patients with PPBS 400-500 had highest mean CRP and patients with PPBS >500 had highestmean HbA1c which was statistically significant. Shown in table 8.

TABLE 8: DISTRIBUTION OF CRP AND HBA1C VERSUS POST PRANDIALBLOOD SUGAR

Post Prandial Blood Sugar in mg/dl (n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
140-200 (24)	0-0	0±0	7-9	7.75±0.85
200-300 (51)	0-2.4	0.71±0.85	7-10.6	8.85±1.06
300-400 (45)	0-5.4	1.95±1.38	7-12.4	10.15±1.56
400-500 (24)	1.2-5.6	2.88±1.24	9-13.3	11.36±1.52
>500 (6)	2.4-2.4	2.4±0	12.8-14	13.4±0.66
P value	43.946/0.000		33.575/0.000	

CRP AND HBA1C VERSUS TOTAL CHOLESTEROL

Mean CRP and mean HbA1c of the patients was highest in the patients with total cholesterol in the non desirable range (>240mg/dl) and was statistically significant. (shown in table 9).

TABLE 9: DISTRIBUTION OF CRP AND HBA1C VERSUS TOTALCHOLESTEROL

Total cholesterol in mg/dl (n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
Desirable <200 (114)	0-4.6	0.91± 1.07	7-13	9.09± 1.51
Optimal 200-239mg/dl (18)	1.2-5.4	2.50±1.44	7-14	10.90±2.19
Non desirable >240mg/dl (18)	2.4-5.6	3.23±1.19	9.8-13.3	11.92±1.22
P value	31.39/0.000		42.75/0.000	

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CRP AND LDL CHOLESTEROL

Highest mean CRP and mean HbA1c was found in patients with LDL cholesterol >190 and 130-160mg/dl respectively, which was significant statistically (P>0.05).Values are shown in table 10.

TABLE 10: DISTRIBUTION OF CRP AND HBA1C VERSUS LDL

LDL cholesterol range in mg/Dl	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
< 100 (optimal) (90)	0-5.6	1.48±1.45	7-14	9.53±2.13
101-129 (near optimal) (39)	0-5.4	0.88±1.52	7-12	9.19±1.13
130-159 (Borderline high) (12)	1.2-2.4	2.1±0.54	10.4-12.8	11.25±1.03
160-189 (high)(6)	1.2-1.2	1.2±0	9.6-11.6	10.6±1.09
>190 mg/dl (very high) (3)	2.4-2.4	2.4±0	11-11	11±0
P value	3.95/0.004		2.65/0.036	

CRP AND HDL CHOLESTEROL

Highest mean CRP and mean HbA1c was found in patients with HDL cholesterol in the undesirable range (<40mg/dl). This was not significant statistically (P>0.05). Values are shown in table 11.

TABLE 11: DISTRIBUTION OF CRP AND HBA1C VERSUS HDL

HDL range (n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
Desirable ≥60mg/dl (6)	0-2.4	1.2± 1.31	7-9.5	8.25±1.37
Optimal- 40-59mg/dl (66)	0-5.6	1.31±1.66	7-13.3	9.55±1.97
Undesirable <40mg/dl (6)	0- 5.4	1.45±1.19	7-14	9.84±1.78
P value	2.227/0.111		0.236/0.790	

CRP AND TRIGLYCERIDE

Highest mean CRP and mean HbA1c was found in patients with borderline (150- 199mg/dl) and very high triglyceride (>500 mg/dl) respectively. This was not significant statistically (P>0.05). Values are shown in table 12.

TABLE 12: DISTRIBUTION OF STUDY PATIENTS BY CRP AND HBA1C VERSUSTRIGLYCERIDE

Triglyceride (n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
Desirable <150mg/dl (18)	0-2.9	1.08±1.23	7-13	9.58±2.34
Borderline 150-199mg/dl (57)	0-5.6	1.36±1.70	7-14	9.81±2.08
High 200-499mg/dl (66)	0-5.4	1.34±1.24	7-12	9.47±1.40
Very high (9)	2.4-2.4	2.4±0	7-12.8	10.07±2.52
P value		1.882/0.135		0.490/0.690

HBA1C AND CRP

Mean CRP was higher in patients with HbA1c >11 and was statistically significant. (P<0.05).Also Mean CRP increased with increasing HbA1c (shown in table 13).

TABLE 13: DISTRIBUTION OF STUDY PATIENTS BY CRP VERSUS HBA1C

HbA1c (n)	CRP		Anova test/ P value
	Range	Mean±SD	

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≤7 (27)	0-2.4	0.40±0.81	53.621/ 0.000
7.1-9 (42)	0-2.4	0.51±0.77	
9.1-11 (51)	0-2.4	1.55±0.81	
>11 (30)	1.2-5.6	3.18±1.54	

Mean CRP and mean HbA1c was high in patients with creatinine 1-1.2 this was notstatistically significant. (Shown in table 14)

TABLE 14: DISTRIBUTION OF STUDY PATIENTS BY CRP AND HBA1C VERSUSCREATININE

Creatinine (n)	CRP		HbA1c	
	Range	Mean±SD	Range	Mean±SD
0.6-0.9 (84)	0-4.6	1.19±1.19	7-14	9.58±1.83
1-1.2 (66)	0-5.6	1.62±1.674	7-13.3	9.74±1.92
P value	3.399/0.067		0.277/0.599	

CRP AND RISK FACTORS FOR CAD

Age, duration of type 2 DM, HbA1c, Total Cholesterol, creatinine and Triglyceride showed highly significant correlation with CRP. Other risk factors like BMI and LDL cholesterol alsohad positive correlation but were of lesser significance, Whereas HDL showed a negative correlation. Values are shown in Table 15.

TABLE 15: CRP AND RISK FACTORS FOR CAD

	Correlation of CRP versus risk factors for CAD										
Pearsons	Age	ration of T2DM	Weight	BMI	ESR	HbA1c	Total Cholesterol	Tryglyceride	LDL	HDL	Creatinine
	-0.29	-0.23	-0.05	0.01	0.07	0.69	0.53	0.28	0.07	-0.07	0.22
p Value	0.000	0.004	0.545	0.879	0.365	0.000	0.00	0.0001	0.378	0.358	0.006

Among all the risk factors which were assessed, Age, duration of type 2 DM, HbA1c, Total cholesterol, creatinine and Triglyceride showed significant correlation with CRP. According to Pearson correlation, values obtained for age was -0.29 with P value <0.04, duration of type 2 DM was -0.23 with P value 0.004, HbA1c was 0.69 with P <0.05, for total cholesterol was 0.53 with P<0.05, and for triglyceride was 0.28 with P<0.05 which were significant.

Comparison of initial and followup HbA1C and CRP

Of the 150 initial patients, only 60 patients who were on antidiabetic treatment but not put on statin therapy came for follow up. Therefore, comparison between these 60 patients was done for HbA1c and CRP. Comparison was done between initial HbA1c and HbA1c on follow up and betweeninitial CRP and CRP on follow up. The initial mean HbA1c of those 60 patients was 9.28 ± 1.88. The mean HbA1c on follow-up was 7.38 ± 1.325. The initial mean CRP of those 60 patients was 0.78 ± 0.96. The mean CRP of those 60 patients on follow-up was 0.30 ± 0.524. HbA1c has significantly reduced in patients, after being put on treatment (P<0.05) and lower the HbA1c, the CRP levels also reduced (P<0.05). (Shown in table 16)

TABLE 16: 60 INITIAL AND 60 FOLLOW-UPS

	1c1 Initial (n=20)	c2 Follow up (n=20)	P1 Initial(n=20)	Follow up (n=20)
Mean	9.285	7.385	0.78	0.300
SD	1.88	1.325	0.959	0.524
P value	39.782/0.000		4.037/0.049	

DISCUSSION

Diabetes mellitus is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiency of insulin secretion and/or insulin action.[9] The major risk factors associated with diabetes are positive family history, age, obesity, especially upper body adiposity, physical

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inactivity and insulin resistance. A close link exists between DM and cardiovascular disease (CVD). CVD is the most prevalent cause of mortality and morbidity in diabetic populations. [10] CVD death rates in the world are 1.7 times higher among adults (>18 years) with DM than those without diagnosed DM, largely due to an increased risk of stroke and myocardial infarction (MI) CV risk factors including obesity, hypertension and dyslipidemia are common in patients with DM, particularly those with T2DM. oxidative stress, increased coagulability, endothelial dysfunction and autonomic neuropathy.[11,12] C-reactive protein is an acute phase reactant and nonspecific marker of inflammation, produced predominantly in hepatocytes as a pentamer of identical subunits in response to several cytokines.[13] Serum CRP levels are elevated in response to acute infection, inflammatory condition and trauma. In this situation, the serum CRP levels rise rapidly generally. Aim of this present study was to assess the association Between CRP and HbA1c in Type-2DM.

The current study was done in 150 patients with type 2 DM of which 105(70%) were male and 45(30%) were female patients. Age ranges from 32-75 years with mean ± Standard deviation (SD) of age being 53.74 ± 9.82, with majority belonging to 50-60(44%) years age group. With respect to duration of Type 2 DM, mean was 4.44±3.41. In the current study males were slightly more this could be due to higher prevalence of DM in adult asian males compared to females and also in younger age group.[14]

CRP AND HBA1C IN DIFFERENT AGE GROUPS

In the current study Mean CRP (2.25±1.74) and mean HbA1c (11.25±1.82) was high in patients with 41-50 years age compared with other age groups which was significant statistically ($p<0.05$). In study by Vijay Lal et,al Patients between age 35-45 years were 29 with mean HbA1C and CRP of 10.67 and 2.1, respectively. There was no significancebetween different age groups in this study ($p>0.05$).[15]

CRP AND GENDER:

In the current studythough females show slightly higher mean CRP (1.4 ± 1.43) compared to males (1.37 ± 1.41), it was not statistically significant ($P>0.05$). Unlike in study by Vijay Lal *et al*, done in 120 patients, 85 patients were males, and 35 were females with mean CRP levels of 1.26±1.37 and 1.24±0.90, respectively. There was no significant difference between male and female patients ($p>0.05$) which was similar to current study.[15]

Hu and others studied the hazard ratios of T2DM for different levels of serumCRP. The multivariable adjusted hazard ratios of diabetes at three different levelsof CRP (0.05–0.99, 1.0–2.99, and ≥3.0 mg/litre) were1.00, 1.87, and 2.51(P for trend<0.001) in men and 1.00, 5.46, and 14.9 (P for trend<0.001) in women,respectively.There were significant interactions between sex and CPR as a continuous variable with the risk of diabetes in multivariable analyses. Their results indicated that the association between CRP and the risk of diabeteswas stronger in women than men.[16]

Study by Lakoski *et al* shows that women had substantially higher median CRP levelscompared with men (2.56 vs 1.43 mg/L, $P < .0001$).C-reactive protein levels were higher in women compared with men despite accounting for BMI and other common confounding variables. This gender difference was maintained across all ethnic subgroups. These results suggest that evaluation of gender-specific CRP cut points to determine cardiovascular risk should be considered.[17]

CRP and BMI, WHR & WC

In the current study In patients with BMI 23-24.9 has mean CRP 1.64±1.67 which was higher than patients who were overweight, obese and non obese patients which was not significant. Mean HbA1c was higher in patients with BMI ≥ 30. HbA1c increased with increasing BMI but was not significant. As this study was done in rural south Indian population who are generally not obese.

In study by Vijay Lal *et, al.* patients with BMI 25-30 have mean CRP 1.62 which was higher than obese and non obese patients.[15]

In study by MottaghiT *et al*, shows that BMI was associated with increase in ESR and CRP levels (β-ESR = 4.67, $P < 0.001$ and β-CRP = 0.71, $P < 0.001$). Also, this association remained after adjustment for other different variables. These findings indicate that higher BMI is related to increase inflammatory markers including CRP and ESR in Diabetic patients.[18] In study by Firdous *et al*, CRP level increased with body mass index. There was an intermediate positive correlation between CRP and BMI. If BMI increases by 1 unit on the average, CRP rises by 0.239 times and this unit rise was significant.[19]

Study by Sudhakar M *et al* shows that serum levels of leptin, CRP, showed that CRP levels were significantly elevated ($p < 0.0001$) in non-morbid obese subjects ($n = 42$) compared to lean subjects ($n = 32$) and correlated positively with body mass index (BMI) ($r = 0.74$, $p < 0.0001$) and leptin ($r = 0.8$, $p < 0.0001$).[20]

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In another study done by Williams and others, multiple regression analysis showed that obesity was independently related to CRP with an increase in ratio CRPof 1.03 (95% CI 1.01, 1.05) for men and 1.07 (1.05, 1.09) for women associated witha 1 kg/m^2 increase in BMI.[21] But, on excluding two groups of patients with BMI <18 and >30, where there was only 3 patients in each group, CRP shows a positive correlation with BMI as in other studies.

Meta analysis done by Choi J *et al* done by data from 51 cross-sectional studies that usedbody mass index (BMI), as measure of obesity shows that the Pearson correlation (r) for BMIand CRP was 0.36 (95% confidence interval [CI], 0.30-0.42) in adults and 0.37 (CI, 0.31-0.43) in children. In adults, r for BMI and CRP was greater in women than men by 0.24 (CI, 0.09- 0.37), the sex difference in r for BMI and CRP was 0.01 (CI, -0.08 to 0.06).Obesity is associated with elevated levels of CRP and the association is stronger in women and North Americans/Europeans. The sex difference only emerges in adulthood.[22]

CRP AND HBA1C VERSUS FASTING BLOOD SUGAR

In the current study Patients with FBS >300 had mean CRP and mean HbA1c 2.34 and 11.330 respectively. Mean HbA1c and mean CRP increased with increase in FBS which was significant satistically. Which was similar to study by Vijat et,al where Patients with FBS >300 had mean CRP and mean HbA1c 2.23 and 11.59 respectively. FBS and HbA1C weredirectly correlated.[15]

PPBS WITH HBA1C AND CRP

In the current study patients with PPBS 400-500 had highest mean CRP (2.88±1.24) and patients with PPBS >500 had highest mean HbA1c (13.4±0.66) which was statisticallysignificant. Where as in study by Vijay *et al*, patients with PPBS >500 had highest mean CRP(2.98) an mean HbA1c (13.79).[15]

CRP AND TOTAL CHOLESTEROL

In the current study mean CRP of the patients was highest in the patients with total cholesterol in the non desirable range (>240mg/dl) and was statistically significant. Unlike In study by Vijay *et, al.* where highest mean CRP was found in patients with TC <100mg/dl.[15]

In another study by Johnsson H *et, al.* A total of 11 437 blood samples was included. They identified a significant ($p<0.001$) biphasic relationship between Total Cholesterol and CRP: Total Cholesterol increased within the healthy CRP range of less than 5 mg/l, but decreased with CRP levels above 10 mg/l. The two effects approximately cancelled each other out inthe intermediate CRP range of 5-10 mg/l. There was an inverse relationship between HDL- cholesterol and CRP. Lipid levels change significantly during inflammatory illness in apopulation with both acute and chronic conditions. These results provide a strong epidemiological basis for the better understanding of lipid changes in inflammatory conditions and with anti-inflammatory therapies.[23]

CRP and LDL cholesterol: In the current study highest mean CRP was found in patients with LDL cholesterol >190 and 130-160mg/dl respectively, which was significant statistically (P>0.05). In study by Vijay *et, al.* mean CRP was highest in patients with LDL cholesterol >140mg/dl. [15]

In study by Kitagawa K et, al found that Patients with LDL cholesterol ＜120 mg/dL showed 29% reduction in recurrent stroke and TIA than those with LDL cholesterol ≥ 120 mg/dL (event rate 2.20 vs. 3.11 per 100 person-years, hazard ratio [HR] 0.71, 95% confidence interval (CI) 0.50-0.99, p＝0.048). Patients with CRP ＜1 mg/L had 32% reduction compared with that of patients with CRP ≥ 1 mg/L (event rate 2.26 vs. 3.40 per 100person-years; HR 0.68, 95% CI 0.48-0.96, p＝0.031). Although LDL cholesterol and CRP levels were not correlated in individual patients, those who achieved both LDL cholesterol ＜120 mg/dL and CRP ＜1 mg/L showed 51% reduction in complications compared with that of patients with LDL cholesterol ≥ 120 mg/dL and CRP ≥ 1 mg/L (event rate 2.02 vs. 4.19 per 100 person-years; HR 0.49, 95% CI 0.31- 0.79). Also concluded that, the control of both LDL cholesterol and CRP levels appears to be effective for preventing recurrent stroke and TIA in patients with non-cardiogenic ischemic stroke.[24]

CRP AND HDL CHOLESTEROL

In this study Highest mean CRP (1.45±1.19) was found in patients with HDL cholesterol in the undesirable range (<40mg/dl). This was not significant statistically (P>0.05). In study by Vijay *et al* Patients with HDL cholesterol between 0-20 has the highest mean CRP (2.12).[15]

CRP AND TRIGLYCERIDES

In the current study highest mean CRP was found in patients with borderline (150- 199mg/dl)and very high triglyceride (>500 mg/dl) respectively. This was not significant statistically (P>0.05). In study by Vijay et, al highest mean CRP was found in patients with very high triglyceride (>500 mg/dl) which was 2.43.[15]

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In study by Lee HR the mean values of most cardiometabolic variables including body mass index, blood pressure, fasting plasma glucose levels, leukocyte count, median CRP levels, and Framingham 10-year CVD risk scores increased gradually with TG/HDL ratio quartiles. The OR (95% CI) of the highest TG/HDL ratio quartile and TG quartile as compared with thelowest TG/HDL ratio quartile and TG quartile for high Framingham 10 -year CVD risk was 9.27 (6.68-12.86) and 0.97 (0.69-1.36) after adjusting for confounding variables, respectively. They concluded that compared to TG, the TG/HDL ratio was found to be positively and independently associated with Framingham 10-year CVD risk in a large Korean cohort.[25]

In study by Firdous *et al*, fund that there was an intermediate positive correlation between CRP and triglycerides 1 unit rise increase in triglycerides on the average cause CRP to decrease -0.006 times but this value was insignificant, no such trend was observed fortriglycerides.[26] Also concluded that **r**aised CRP and high fasting TG were major findings in all age groups especially among young and middle aged people. Obesity, hypertriglyceridemia and raised CRP are interrelated suggesting that obesity is not only linked to hypertriglyceridemia but vascular inflammation among pre-obese and obese withoutovert diabetes mellitus causes high CRP as well and this can be used as a marker to predict the future risk of CAD. However, in the absence of dyslipidaemia, raised CRP can still be considered as a strong predictor of CAD and stroke. [26]

CRP AND HBA1C

In the current study Mean CRP (3.18±1.54) was higher in patients with HbA1c >11 and was statistically significant. (P<0.05). Also Mean CRP increased with increasing HbA1c. Whereas in study by Vijay et, al Mean CRP (2.36) was higher in patients with HbA1c >10.[15] Similar findings were seen in study by Son YE *et al*, shows a significant relationship betweenHbA1c levels and serum ferritin and CRP levels, suggesting that serum ferritin and CRP levels can be used as a routine screening tool for the early diagnosis of DM.[26]

In study by Demirkol ME *et al* shows that The CRP and CAR (CRP to albumin ratio) levels were significantly higher in the DM and prediabetes group than in the control group ($p < 0.05$, for both). Albumin levels were significantly lower in the DM group than in both the prediabetes and control groups ($p < 0.05$, for both). In the uncontrolled DM group, CRP and CAR values were found to be significantly higher than the control and controlled DM groups, while albumin values were significantly lower than the control group, prediabetes group, and controlled DM group ($p < 0.05$, for all).[27] Also concluded that CAR, a liver related inflammatory marker, can be applied as an inflammation marker in both prediabetes, determined by HbA1c, and patients diagnosed with DM. Further prospective studies will better demonstrate the utility of CAR values as an inflammatory marker in DM and prediabetes.

In the current study Age, duration of type 2 DM, HbA1c, Total Cholesterol, creatinine and Triglyceride showed highly significant correlation with CRP. Other risk factors like waist hipratio, body weight, BMI and LDL cholesterol also had positive correlation but were of lesser significance, Whereas HDL showed a negative correlation. In study by Vijay *et al*. There wassignificant correlation between CRP and HbA1C (p<0.05).[15]

CRP AND HBA1C IN 'FOLLOW –UP' SUBJECTS

Of the 150 initial patients, only 60 patients who were on antidiabetic treatment but not put on statin therapy were enrolled for follow up. Therefore, comparison between these60 patients was done for HbA1c and CRP. Comparison was done between initial HbA1c and HbA1c on follow up and between initial CRP and CRP on follow up. The initial mean HbA1c of those 60 patients was 9.28 ± 1.88. The mean HbA1c on follow-up was 7.38 ± 1.325. The initial mean CRP of those 60 patients was 0.78 ± 0.96. The mean CRP of those 60 patients on follow-up was 0.30± 0.524. HbA1c has significantly reduced in patients, after being put on treatment (P<0.05) and lower the HbA1c, the CRP levels also reduced (P<0.05).

In study by Vijay *et, al.* found that the mean HbA1C of 120 patients initially was 9.87±1.92, and the mean CRP was 1.142±0.9684. A follow-up of 60 cases was done on patients who were not on statin therapy. On follow-up, the mean HbA1C of 60 cases had reduced to 7.53±1.36 (p<0.05) and mean CRP of those 60 patients reduced to 0.29±0.51 (p<0.05). A comparison was made between initial HbA1C, CRP levels with HbA1C, CRP levels of follow up cases among 60 cases. The initial mean HbA1C of 60 patients was 9.54±1.677, and the mean HbA1C on follow up was 7.62±1.36. The initial mean CRP of 60 patients was 0.92±0.915 and mean CRP on follow up was 0.34±0.45. HbA1C has significantly reduced in patients, after being put on treatment (p<0.05).[15]

The results of this study therefore, goes a step further with the finding that among people with established diabetes, at successively higher levels of HbA1c the number of patients with CRP positive is significantly higher. The main implication of these findings is that inflammation may not only be implicated in the development of diabetes, but also in ongoing levels of hyperglycemia once diabetes is established.

This study has found that there exists a positive correlation between CRP and Glycemic control. It has also revealed

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positive correlations between cholesterol and triglycerides andthe Waist –Hip ratio, markers of increased CAD risk, a major complication of T2DM. The negative correlation between CRP and HDL was a finding similar to other studies and is probably related to the fact that, in thin diabetics, inflammation as a potential mechanism T2DM may be independent of obesity.

The findings were similar to study by Vijay *et al*, and Meriga RK *et al* where, a positive correlation between CRP and HbA1C was found. Further, it was found that there exists a positive correlation between CRP and other risk factors of coronary artery disease like total cholesterol, triglycerides. At the same time, HDL showed a negative correlation with CRP. Their studies concluded that Follow-up studies revealed that better glycaemic control resulted in the lowering of CRP, which was significant.[15,27]

CONCLUSION

In this study of 150 type 2 diabetes mellitus patients, attending tertiary care hospital a positive correlation between serum CRP and HbA1c was found. Further, it was also found that there exists a positive correlation between CRP and other risk factors of coronary artery disease, like age, duration of type 2 diabetes mellitus, total cholesterol, triglyceride and creatinine. HDL showed a negative correlation with CRP, which was also significant. The strongest association of CRP was found with age, duration of type 2 DM, HbA1c, total cholesterol and triglyceride levels. The finding regarding BMI in this study, contrary to others, suggest that CRP level was not significantly associated with BMI and that inflammation as a potential mechanism in T2DM may be independent of obesity and may independently lead to an increased risk of cardiovascular events. Follow up studies revealed that better glycaemic control resulted in lowering of CRP, which was significant. This study therefore, reveals that CRP is an additional marker of better glycaemic control and also correlates with the dyslipidaemic profile, seen in T2DM.

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