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International Journal of Current Research
Vol. 7, Issue, 12, pp.24266-24273, December, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

THE STUDY OF hsCRP IN TYPE 2 DIABETIC MELLTUS & ITS COMPLICATIONS

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ARTICLE INFO

Article History:
Received 15th September, 2015
Received in revised form
22nd October, 2015
Accepted 27th November, 2015
Published online 30th December, 2015

Key words:
Atherothrombotic,
Diabetes,
Inflammation,
Characterized,
Microalbunuria,
Creatinine.

ABSTRACT

Background and objectives: Diabetes Mellitus (DM) is an inflammatory atherothrombotic metabolic disease. In patients with type 2 diabetes, low grade inflammation is characterized by increased plasma levels of several biomarkers of inflammation such as high sensitivity C-reactive protein (hsCRP). This prospective observational study was designed to assess serum levels of hsCRP in type 2 diabetes and determine correlation between hsCRP and complications associated with diabetes.
Methods: A total of 60 subjects were enrolled in the study as per the inclusion and exclusion criteria.
Results: Hypertension (36.7%), duration of diabetes (14 years), urine microalbunuria (46.7%), serum creatinine, hsCRP and diabetic retinopathy (40%) were higher in DM patients with complications. Intermediate and high risk levels of hsCRP were higher in patients with diabetic complications. Correlation of hsCRP levels and other findings suggest that there was no significant correlation whereas the propensity of having abnormal ECG increases with rise in hsCRP levels. Rise in hsCRP levels were significantly associated with increase in serum creatinine, microalbuminuria and abnormal ECG.
Interpretation and Conclusion: The results of this study revealed that there is a significant association between hsCRP and complications of DM. Abnormal ECG findings suggest the linkage amongst DM, cardiovascular complications and hsCRP. The role of hsCRP in metabolic abnormalities cannot be neglected as it may be very essential biomarker to detect associated complications.

Citation: Dr. Anaz Bin Azeez, Dr. Manish Pendse and Dr. Smita Patil, 2015. "The study of hsCRP in type 2 diabetic melltus & its complications", *International Journal of Current Research*, 7, (12), 24266-24273.

INTRODUCTION

Diabetes is the fifth leading cause of death in the United States, and it is also a major cause of significant morbidity. Epidemiological data suggest that nine of 10 cases of type 2DM could be attributed to habits and forms of modifiablebehavior (WHO, 2015). The incidence of type 2 diabetes mellitus (type 2DM) is increasing at an alarming rate both nationally and worldwide, with more than 1 million new cases per year diagnosed in the United States alone (Hall *et al.,* 2014). The disease is characterized by metabolic alterations that correlate hyperglycaemia to other risk factors that contribute to complications in the circulatory system, such as high blood pressure (HBP) (Gomez *et al.,* 2006). Diabetes mellitus is characterized by absolute or relative deficiency of Insulin leading to progressive worsening of glycaemic control and it is well-recognized independent traditional risk factor for cardiovascular disease. CRP is a liver derived protein from Pentraxin family composed of five 23 KDa subunits with plasma half-life about 18 hours.

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It is an acute phase reactant protein now understood to be a mediator and marker of atherothrombotic disease (Mark *et al.,* 1999). C-reactive protein (CRP) is a highly sensitive marker of inflammation. During inflammatory processes, its level rises dramatically (Ejerblad *et al.,* 2006). CRP has a long half- life, affordability of estimation, and stability of its levels with no circadian variation, and therefore is one of the best markers of vascular inflammation (Kotsis *et al.,* 2010). CRP has been found to be associated with disorders like DM, cardiovascular disorders, metabolic syndrome, renal failure, etc (Re, 2009; Abrass, 2004).

Serum high sensitivity CRP (hsCRP) level is higher in patients with Type 2 diabetes than in normal subjects and plays an important role in the development and progression of Type 2 DM (Hall *et al.,* 2004). Also the mild elevation of high – sensitivity C – reactive protein (hs-CRP) associated with future cardiovascular risk. Chronic low grade systemic inflammation plays a major role in pathophysiology of both T2DM as well as atherosclerosis (Stuveling *et al.,* 2005). Diabetes mellitus (DM) comprises a group of common metabolic disorders that share common phenotype of hyperglycaemia (Praga *et al.,* 2000). Hyperlipidemia is a disorder of increased lipid or

lipoprotein levels and is the most common form of dyslipidemia. For the purpose of adhering strictly to the human body and the phenomenon of hyperlipidemia, lipids are classified into 6 types. They are: High density lipids (HDL), low density lipids (LDL), Intermediate density lipids (IDL), very low density lipids (VLDL), triglycerides and cholesterol. If any one or more of these types become abnormally elevated in the blood, it is known as hyperlipidemia or it is characterized by elevated concentrations of circulating lipids, increasing the risk of atherosclerosis and other serious conditions. Hyperlipidemia often results from delayed or defective clearance, or overproduction of VLDL by the liver, which is subsequently transformed into LDL. The liver's production of VLDL and triglycerides were increased by the excess intake of saturated fats via a molecular Mechanism involving protein activators (Wolz *et al.,* 2000).

Hyperglycaemia not only defines the disease but is the cause of its most characteristic symptoms and long-term complications. Understanding the pathogenesis and preventing long-term complicationshave have been major goals of research in diabetes mellitus. Diabetes is undoubtedly one of the most challenging health problems in 21st century (Qureshi *et al.,* 2013). Research in the past few years has linked oxidative stress and inflammationton, β-cell dysfunction resulting from chronic exposure to hyperglycaemia. A growing body of data reinforces the concept that inflammation plays an important role in the pathogenesis of type 2 DM and links DM with concomitant conditions with inflammatory components (The World Health Report, 2002).

A wealth of epidemiologic data show that the prevalence of Type 2 Diabetes Mellitus (T2DM) is rising at an alarming rate virtually in each and every developed and developing country. This explosive rise in the prevalence of T2DM and its complications represent the greatest health care challenge facing the world today (Krishna, 2011). T2DM, a worldwide health crisis emerged as a major growing health problem imposing socioeconomic burden is an important cause of mortality and morbidity from cardiovascular disease (CVD) accounting for 65-80% of deaths in them CVD is in part an inflammatory process; C reactive protein (CRP) has been widely investigated in context of atherosclerosis and subsequent vascular events (Sachidananda, 1998). So we designed this prospective randomized study and the aim of study was to investigate the predictive value of Hs-CRP (High Sensitivity C-reactive protein) in coronary heart disease (CHD). Hs-CRP is marker of inflammation in coronary heart disease. The level of CRP in the serum samples was estimated by a high sensitivity immunoturbidometric assay. Master chart was prepared and statistical analysis was done find out dyslipidaemia in type 2 Diabetic and correlation with coronary risk factor.

Aims and Objectives of the study

The current study was planned with the following aims and objectives:

- To assess the serum levels of hsCRP in type 2 diabetes
- To correlate hsCRP with blood sugar levels
- To study and correlate hsCRP with complication of diabetes

MATERIALS AND METHODS

The study was initiated after obtaining permission from the Institutional Ethics Committee of D.Y. Patil Hospital, Navi Mumbai. All ethical principles laid out by ICH GCP and ICMR guidelines were strict adhered to during the entire conduct of the study.

Study design: It was a prospective, single-centre observational study.

Study Site: The study was conducted at General Medicine Department of D.Y. Patil Hospital, Navi Mumbai, Maharashtra.

Study period: It is planned to complete this thesis during the duration of post-graduation for the degree of M.D. General Medicine from September 2014 to August 2015 and/or after the date of approval by institutional Human Research Ethic Committee.

Study Group: The study groups comprised a total of 100 subjects which were divided into the following 2 groups

Group 1: Comprised of 30 patients of DM with complications
Group 2: Comprised of 30 patients of DM without complications

Study selection Criteria

Inclusion Criteria

- Consenting 60 subjects of 30-60 years of age.
- History of Type-2DM

Exclusion Criteria

- Women on Hormone replacement therapy.
- Pregnant females
- Critical ill patients
- Trauma /Surgery/burns
- Pancreatitis
- Liver diseases / alcoholism
- Acute respiratory infection.
- Chronic Inflammation eg: arthritis.
- Drugs – pioglitazone, NSAIDS

Method

30 Type-2 Diabetics without any complications and 30 diabetic individuals with known/proven complications of age group above 30 from outdoor and indoor departments of D.Y. Patil hospital were selected. Diabetic patients were selected as per the criteria laid down after taking an informed consent and proper history. Each subject was instructed to visit the cardio respiratory clinic in specific date with Nine hours of fasting. Blood samples would be drawn to estimate FBS, HbA1c, Total cholesterol, Triglycerides, LDL, HDL, VLDL, Non HDL and Hs CRP The subject were asked to take breakfast and blood would be drawn two hours later for estimation of PPBS.

Patient would be further investigated for glycosylated haemoglobin, creatinine levels, creatinine clearance, urinary microalbumin, Fundoscopy, carotid intima thickness and arterial Doppler to rule out complications. Correlation with risk factor such as age, sex, anthropometry, duration of diabetes, duration of hypertension, history of ischemic heart disease, history of cerebro-vascular accidents, history of intermittent claudication pain, obesity, would be recorded in respective proforma. Master chart would be prepared and statistical analysis would be done using following method.

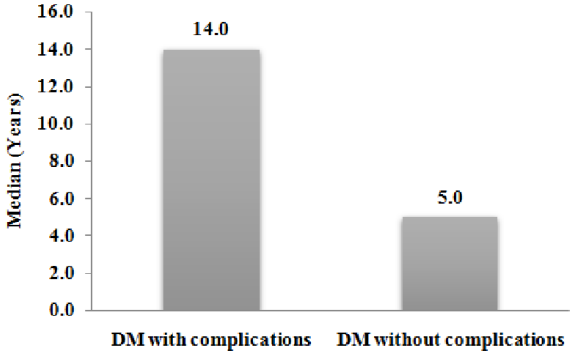
Statistical methods

Baseline study participant characteristics will be described using descriptive statistics. Parametric data if it passes the tests of normality will be analyzed using parametric tests or else non-parametric tests will be used for its analysis. Categorical data will be analyzed using Chi-square test. Parametric correlation analysis will be done using Pearson correlation test while non parametric correlation analysis will be done using Spearman correlation test. Regression analysis will be done using linear regression model

RESULTS

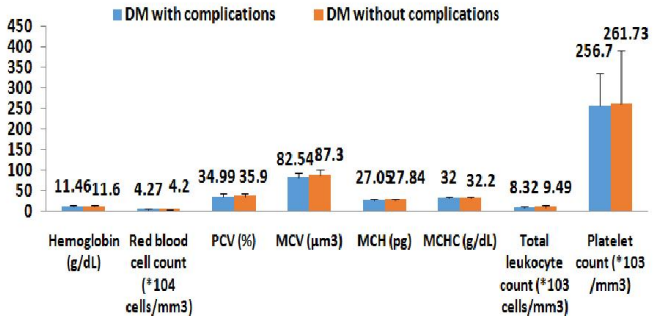
Duration of diabetes was observed in 46.7% and 16.7% subject of DM with and without complications respectively. P value <0.0001 by using Mann-Whitney test, indicating that the duration of diabetes in patients with complications is significantly more than in patients without complications.

Duration of Diabetes		
Duration of Diabetes	DM with complications Number of Patients(N=30)	DM without complications Number of Patients(N=30)
Median	14	5
Range	5-35	1-12



Duration of Diabetes

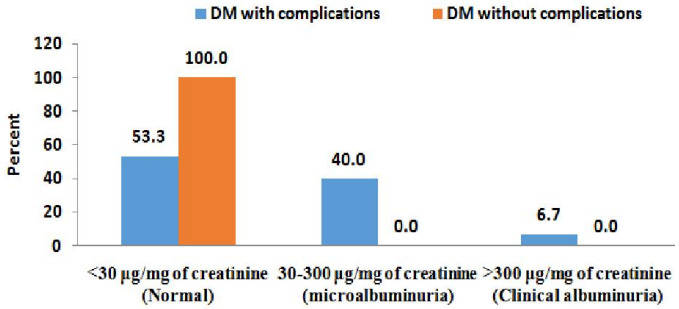
Haematology			
Parameter	DM with complications	DM without complications	P-Value
Haemoglobin (g/dL)	11.46 ± 2.46	11.6 ± 2.73	0.8354
Red blood cell count (RBC) (*104 cells/mm3)	4.27 ± 0.9	4.16 ± 0.83	
PCV (%)	34.99 ± 7.56	35.94 ± 7.27	0.6217
MCV (µm3)	82.54 ± 10.03	87.32 ± 13.06	0.1173
MCH (pg)	27.05 ± 3.74	27.84 ± 3.41	0.3961
MCHC (g/dL)	32 ± 4.18	32.20 ± 3.33	0.8383
Total leukocyte count (TLC) (*103 cells/mm3)	8.32 ± 3.46	9.49 ± 5.06	0.3002
Platelet count (*103 /mm3)	256.7 ± 78.16	261.73 ± 130.25	0.8567



Haematology

Haematological estimations revealed that Haemoglobin (Hb) levels, RBC count and TLC was 11.46 ± 2.46 g/dL, 4.27 ± 0.9(*104 cells/mm3) and 8.32 ± 3.46 (*104 cells/mm3) respectively in DM with complications group. In DM without complication group Hb, RBC and TLC was 11.46 ± 2.46 g/dL, 4.27 ± 0.9 (*104 cells/mm3) and 8.32 ± 3.46 (*104 cells/mm3) respectively.

Urine microalbuminuria				
Urine microalbuminuria	DM with complications		DM without complications	
	Number of Patients(N)	Percent	Number of Patients(N)	Percent
<30 µg/mg of creatinine (Normal)	16	53.3	30	100.0
30-300 µg/mg of creatinine (microalbuminuria)	12	40.0	0	0.0
>300 µg/mg of creatinine (Clinical albuminuria)	2	6.7	0	0.0
Total	30	100.0	30	100.0

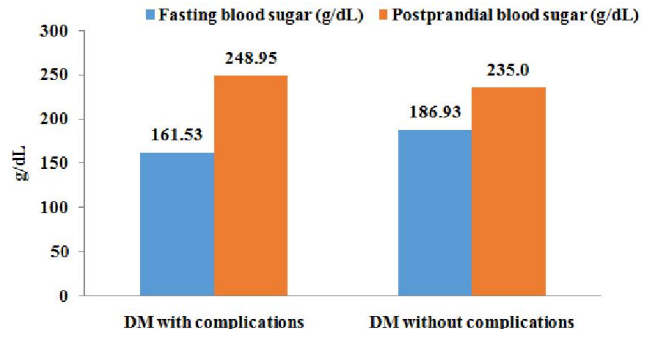


Urine microalbuminuria

Urine microalminuria levels were normal in 53.3% and 100% subjects of DM with and without complications respectively. Microalbuminuria and clinical albuminuria were observed in 40% and 6.7% patients respectively of DM with complications group.

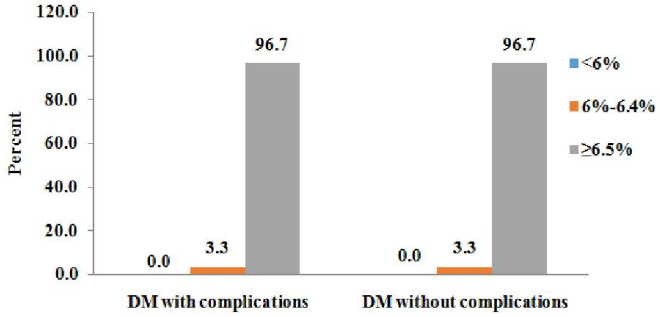
Blood Sugar			
Parameter	DM with complications	DM without complications	P-value
Fasting blood sugar (g/dL)	161.53 ± 97.19	186.93 ± 83.40	0.2818
Postprandial blood sugar (g/dL)	248.95 ± 117.80	234.98 ± 85.81	0.6016

Average fasting Blood sugar was found 161.53 ± 97.19 g/dL and 186.93 ± 83.40 g/dL of DM with and without complications respectively. Mean postprandial blood sugar levels of diabetics with and without complications were 248.95 ± 117.80 g/dL and 234.98 ± 85.81 g/dL respectively.



Blood Sugar

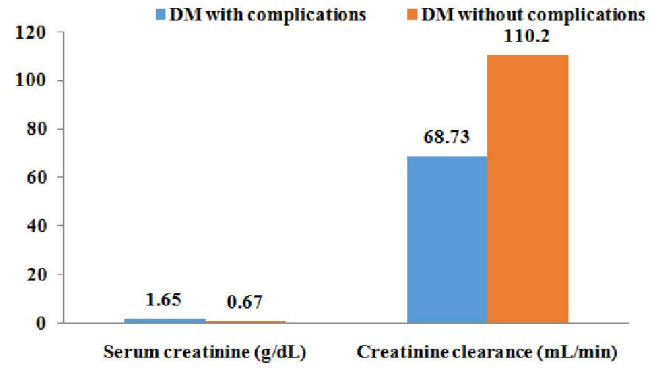
HbA1C				
HbA1C(%)	DM with complications		DM without complications	
	Number of Patients(N)	Percent	Number of Patients(N)	Percent
<6%	0	0.0	0	0.0
6%-6.4%	1	3.3	1	3.3
≥6.5%	29	96.7	29	96.7
Total	30	100.0	30	100.0



HbA1C

HbA1C levels were found similar in both groups. The 96.7% and 3.3% patients from each group had ≥6.5% and 6%-6.4% HbA1C levels respectively. The mean ± SD HbA1C levels were 8.96 ± 1.98% (8.91 ± 2.04 in patients with complications and 9.00 ± 1.95 in patients without complications of diabetes).

Renal Function Test			
Parameter	DM with complications	DM without complications	P-value
Serum creatinine (g/dL)	1.65 ± 1.32	0.67 ± 0.15	0.0002
Creatinine clearance (mL/min)	68.73 ± 40.76	110.2 ± 16.12	<0.0001

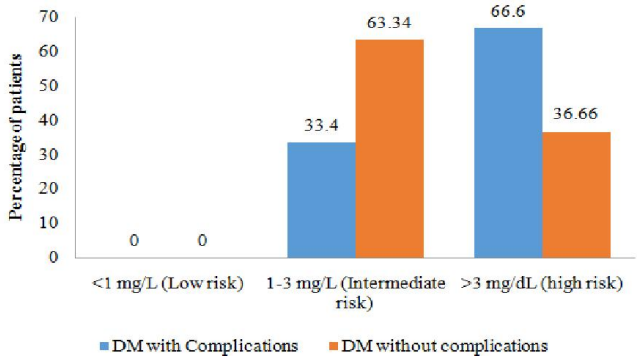


Renal Function Test

Serum Creatinine levels were higher in DM with complications (1.65 ± 1.32 g/dL) than without complication (0.67 ± 0.15 g/dL) whereas Creatinine clearance was more in DM without complications group (110.2 ± 16.12 mL/min) than DM with complications group (68.73 ± 40.76 mL/min).

hsCRP						
hsCRP	DM with complications		DM without complications		Total	
	Number of Patients(N)	Percent	Number of Patients(N)	Percent	Number of Patients(N)	Percent
<1 mg/L (Low risk)	0	0.0	0	0.0	0	0.0
1-3 mg/L (Intermediate risk)	10	33.4	19	63.34	29	48.33
>3 mg/dL (high risk)	20	66.6	11	36.66	31	51.67
Total	30	100.0	30	100.0	60	100

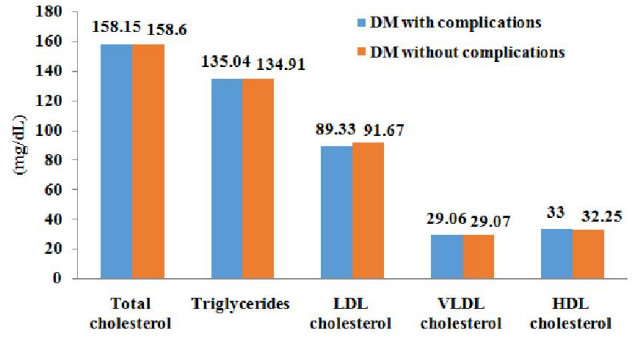
P value=0.1927 by using chi-square test,



hsCRP

The 0%, 33.4% and 66.6% diabetics with complications showed low, intermediate risk and high risk elevation of hsCRP respectively whereas 63.34% and 36.66% subjects suffering from DM without complications associated with intermediate and high risk respectively. None of the patient of this study was found at low risk. The mean ± SD hsCRP levels were 3.87 ± 1.50 mg/L in patients without complications, and 6.73 ± 6.89 mg/L with complications (p=0.0302, indicating that patients without diabetic complications had significantly lower hsCRP as compared to those with complications)

Fasting Lipid Profile			
Parameter	DM with complications	DM without complications	p-value
Total cholesterol (mg/dL)	158.15 ± 57.81	158.60 ± 49.45	0.9743
Triglycerides (mg/dL)	135.04 ± 86.07	134.91 ± 80.32	0.9952
LDL cholesterol (mg/dL)	89.33 ± 45.19	91.67 ± 40.05	0.8327
VLDL cholesterol (mg/dL)	29.06 ± 16.54	29.07 ± 16.19	0.9981
HDL cholesterol (mg/dL)	33.00 ± 9.33	32.25 ± 9.40	0.7575



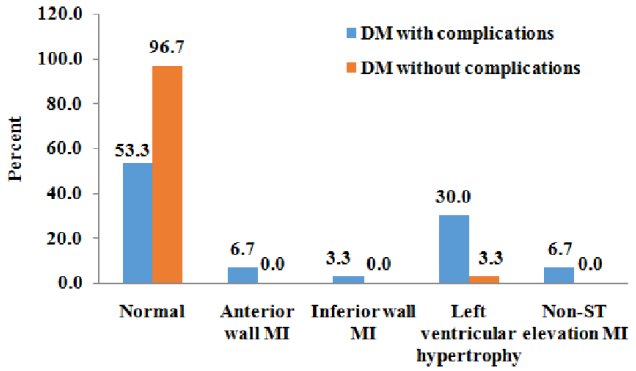
Fasting Lipid Profile

Total cholesterol levels of DM with and without complication were 158.15 ± 57.81 mg/dL and 158.60 ± 49.45 mg/dL respectively. In DM with complications group, LDL and HDL cholesterol levels were 89.33 ± 45.19 mg/dL and 91.67 ± 40.05 mg/dL respectively.

Electrocardiogram (ECG):

ECG Parameter	DM with complications		DM without complications	
	Number of Patients(N)	Percent	Number of Patients(N)	Percent
Normal	16	53.3	29	96.7
Anterior wall myocardial infarction (MI)	2	6.7	0	0.0
Inferior wall MI	1	3.3	0	0.0
Left ventricular hypertrophy	9	30.0	1	3.3
Non-ST elevation MI	2	6.7	0	0.0
Total	30	100.0	30	100.0

P value=0.0002 using Fisher's exact test



ECG

ECG findings were normal in 53.3% and 96.7 % subjects of DM with and without complications respectively. Left ventricular hypertrophy was observed in 30% patients of DM with complications group and 3.3% of diabetics without complications. Non-ST elevation MI was seen in 6.7% patients of DM with complication. P value=0.0002, using Fisher's exact test, indicating that significantly greater proportion of patients without DM complications had normal ECG.

Correlation between hsCRP and fasting blood sugar

After correlating the values, P-value for correlation was 0.001 and Pearson's correlation coefficient= 0.90 indicating that hsCRP correlate significantly with FBS.

Correlation between hsCRP and post lunch blood sugar

After correlating the values, P-value for correlation was 0.01 and Pearson's correlation coefficient= 0.82 indicating that hsCRP correlate significantly with PLBS.

Correlation between hsCRP and HbA1C

After correlating the values, P-value for correlation was 0.8657 and Pearson's correlation coefficient= 0.0322 indicating that hsCRP does not correlate significantly with HbA1c.

Correlation between hsCRP and presence of hypertension

After correlating the values, P-value for correlation was 0.9596 and Spearman's correlation coefficient= 0.0006673 indicating that hsCRP does not correlate significantly with presence of hypertension.

Correlation between hsCRP and abnormal ECG

After correlating the values, P-value for correlation was 0.0120 and Spearman's correlation coefficient= 0.3223 indicating that as hsCRP levels increase, the propensity of having abnormal ECG increases.

DISCUSSION

Diabetes mellitus (DM) is a complex heterogeneous syndrome, consequence of genetic or acquired defects in the insulin secretion and/or insulin resistance of peripheral tissues leading to deep modifications in protein, carbohydrate, lipid, ionic and mineral metabolisms. Due to the raise in number of obesity and longevity worldwide the count of diabetics will be doubled in next 20 years. As DM is considered as a risk factor for heart disease, now it has become an epidemic and high public health concern, especially in older people (Dietz *et al.,* 1985; Chagnon *et al.,* 2003). Type 2 diabetes is the majority of the diabetes burden, comprising some 85% of cases. Peripheral insulin resistance and compensatory hypersecretion of insulin from the pancreatic islets may precede the decline in islet secretory function observed in DM. The reduction in insulin sensitivity to skeletal muscle, liver, and adipose tissue showed association with the particular requirements for glucose uptake and metabolism at these sites (Schousboe *et al.,* 2003). Pick up *et al*. suggested an increasing interest in the involvement of low-grade inflammation in the pathogenesis of type-2 diabetes. CRP is an inflammatory marker produced and released by the liver under the stimulation of cytokines such as tumor necrosis factor and interleukins 1 and 6. Yeh et al., has shown that hs-CRP emerged as a powerful risk marker for cardiovascular disease. Inflammation has also been postulated to play a role in the pathogenesis of type 2 diabetes (Stunkard *et al.,* 1986; Allison *et al.,* 1996).

The present study was conducted to evaluate serum levels of high sensitivity C- reactive protein (hsCRP) in type-2 diabetes. Moreover, this study aimed to correlate hs-CRP with blood sugar levels and complications associated with diabetes. After clinical diagnosis, 30 patients of DM with complications (Group 1) and 30 patients of DM without complications (Group 2) were included in present study. This was a prospective observational Study conducted in the General Medicine Department of D.Y.Patil University School of Medicine for 12 months after obtaining Ethics Committee approval. Present study comprised of 30 subjects in each group. The subjects were suffering from DM and with age between 61-70 years were 40% and 13.3% with and without complications respectively. A 33.3% of study population had age between 51-60 years were suffering from DM with or without complications whereas 3.3% from each group of 81-90 years of age. The mean age of both groups was62.63 ± 10.33 years and 58.93 ± 13.45 years respectively. The studies that are already published have shown similar age group. A study done by Dambal et al in 2012 showed that patients with DM and associated complications have mean age of 65±9.9 years. So it is observed that complications are common in elderly DM

patients.[25]For hypertension as a complication the mean age was 56.2 ± 6.5 years (Martorell *et al.,* 2001).

In the group 1, 76.7% were male and 23.3% were female subjects whereas 70% males and 30% females were included in group 2. In similar study the male patients' comprised of 54% of all and females were 46% (Bogardus *et al.,* 1986). So our study has shown increased age for having DM related complications. Diabetic patients with complications showed height, weight, BMI and waist-hip ratio was 159.37 ± 9.90 cm, 67.07 ± 9.28 kg, 26.51 ± 3.94 kg/ m^2 and 1.14 ± 0.12 respectively. In case of subjects with DM without complications had height (162.53 ± 9.74 cm), weight (68.3 ± 8.39 kg), BMI (25.87 ± 2.74 kg/m^2) and waist-hip ratio (1.16 ± 0.09). General examination diabetic patients with complications showed mean temperature, mean Pulse, mean RR, mean SBP and mean DBP was 98.00 ± 0.00 °C, 91.4 ± 7.59 bps, 17.63 ± 0.89 breaths per minute, 139.53 ± 13.59 mm Hg and 89.06 ± 8.61 mm Hg respectively. Few studies have compared the outcome as a complication of DM. Ina study by Soinio et al in 2006 have observed that the mean BMI was found to be 29.2±5.2 kg/ m^2. But they studied death as complications. So it was higher than our study findings.[26] In another study with hypertension as a complication, the BMI was slightly lower as 28.1 ± 3.5 kg/ m^2 (Bray, 1985).

In case of subjects with DM without complications had temperature (198.00 ± 0.00 °C), pulse (88.4 ± 7.49 bps), RR (17.13 ± 1.04 breaths per minute), SBP (138 ± 9.1 mm Hg) and DBP (86.2 ± 6.48 mm Hg). Average fasting Blood sugar (FBS) was found 161.53 ± 97.19 g/dL and 186.93 ± 83.40 g/dL of DM with and without complications respectively. Mean postprandial blood sugar (PPBS) levels of diabetics with and without complications were 248.95 ± 117.80 g/dL and 234.98 ± 85.81 g/dL respectively. The mean ± SD HbA1C levels were 8.96 ± 1.98% (8.91 ± 2.04 in patients with complications and 9.00 ± 1.95 in patients without complications of diabetes). Other studies with hard endpoints like mortality have found higher blood sugar levels. In one study the HbA1C was 9.9 ± 1.9 gm% and was associated patient mortality in DM patients (Bray, 1984). A study performed by Amanullah compared various parameters in diabetic and non-diabetic individuals. The mean age of diabetic patients was 51 ± 10 years. Average BMI, SBP and DBP of diabetic individuals was 24.8 ± 4.2 kg/m^2, 129.7 ± 21 mm Hg and 75.7 ± 11 mm Hg. Fasting Plasma glucose and HbA1C of patients with type 2 diabetes was 163 ± 72 (mg/dL) and 8.7 ± 2.3 % respectively. Even though the values were found to be slightly higher, these were comparable (Bogardus *et al.,* 1986).

Additionally, we also performed haematological estimations which revealed that Haemoglobin (Hb) levels, RBC count and TLC was 11.46 ± 2.46 g/dL, 4.27 ± 0.9(x10^4 cells/mm3) and 8.32 ± 3.46 (x10^4cells/mm3) respectively in DM with complications group. In DM without complication group Hb, RBC and TLC was 11.46 ± 2.46 g/dL, 4.27 ± 0.9 (x10^4 cells/mm3) and 8.32 ± 3.46 (x10^4 cells/mm3) respectively. No difference in both groups was observed. Urine microalbuminuria levels were normal in 53.3% and 100% subjects of DM with and without complications respectively. Serum creatinine levels were higher in DM with complications (1.65 ± 1.32 g/dL) than without complication (0.67 ± 0.15 g/dL) whereas Creatinine clearance was more in DM without complications group (110.2 ± 16.12 mL/min) than DM with complications group (68.73 ± 40.76 mL/min). Since the DM itself can cause reduction in creatinine clearance. It is well known fact that duration of DM affects creatinine clearance. The raise in creatinine levels from 0.8 to 1.3 has been observed when the clearance is reduced by about one third. Our study showed similar findings (Turkbey *et al.,* 2010).

Lipid profile of our study revealed that both groups showed similar levels. Total cholesterol levels of DM with and without complication were 158.15 ± 57.81 mg/dL and 158.60 ± 49.45 mg/dL respectively. In DM with complications group, LDL and HDL cholesterol levels were 89.33 ± 45.19 mg/dL and 91.67 ± 40.05 mg/dL respectively. Other studies have also shown that higher levels of Total cholesterol and lowered HDL cholesterol were found to be associated with higher mortality as a complication of DM. 243.61 ± 56.32 mg/dL and HDL levels of 40.22± 10.2 mg/dL are associated with higher mortality as complications (Bray, 1984). The 33.3%, 43.3% and 23.3% diabetics with complications showed intermediate risk, high risk and unspecified elevation of hs-CRP respectively whereas 53.3% and 46.7% subjects suffering from DM without complications associated with intermediate and high risk respectively. None of the patient of this study was found at low risk. The mean ± SD hs-CRP levels were 3.87 ± 1.50 mg/L in patients without complications, and 6.73 ± 6.89 mg/L with complications.

Baig et al performed study to evaluate serum hsCRP levels, lipid profile, blood sugar levels in diabetics with and without complications. FBS and PPBS of DM with complications were 187± 29.89mg/dL and 317 ± 48.32mg/dL respectively whereas 142.97 ± 12.48mg/dL and 230.70± 26.84mg/dL were FBS and PPBS of DM without complications group. Lipid profile of the same study demonstrated that Total cholesterol was higher in DM with complication (267.07± 31.89 mg/dL). HDL and LDL of DM with complications were 28.97± 6.72 mg/dL and 187.60± 28.96 mg/dL respectively. Mean hsCRP of DM with and without complications was 3.35± 0.86 mg/dL and 2.27 ± 1.14mg/L respectively. Higher levels of hsCRP were associated with the complications of diabetes. Author had compared findings amongst control, diabetes with and without complications groups. The results of this study are similar to our findings (Rogers, 2003). In this study we tried to find out the correlation between hsCRP levels and complications of DM. We found a significant correlation in between levels of hsCRP and coronary artery disease suggested by ECG, microalbuminuria, serum creatinine and presence of xanthomas.

Another study designed by LIMA, Luciana M. et alet al to assess active inflammatory status in DM and high blood Pressure (HBP) patients by determining hsCRP levels. The results revealed that median hsCRP levels of DM and DM+HBP group was 3.20g/dL and 3.50 g/dL respectively whereas median hsCRP of control group was 1.70g/dL. The 41% of DM+HBP and 46% of DM group showed hsCRP levels >3.0 g/dL while more than 3g/dL of hsCRP was seen 59% and 41% patients of DM+HBP and DM group respectively. In our study, history of hypertension was observed in 36.7% and 13.3% diabetic patients with and

without complications respectively. The results of both studies demonstrated that diabetes mellitus with hypertension might be responsible for incidence of inflammation (Martorell *et al.,* 2001). In prospective cohort study performed in a highrisk population of Aboriginal Australians by Wang et al, observed a significant positive association between elevated CRP levels and incident diabetes. Higher CRP levels were strongly associated with BMI. However, the association remained statistically significant even after adjusting for age, sex, BMI, impaired glucose regulation, systolic blood pressure, total cholesterol, urine albumin to creatinine ratio, smoking and drinking. They found a 75% increased risk for those with upper tertile CRP values relative to the bottom two tertiles. In our study, hsCRP values were found in higher tertile in diabetic patients with complications than without complications. Results of the studies are compatible with other (Peeters *et al.,* 2003). As per prior literature hsCRP levels and hypertension has strong linkage with diabetes. In present study, ECG findings were abnormal in 46.7% and 3.3 % subjects of DM with and without complications respectively. The fundoscopy also showed statistically significant difference between patients of DM with complication and without complication. Only 1 (3.3%) patient from group1 was diagnosed with infarct of right middle cerebral artery whereas all patients from another group were normal as per CT scan of brain.

Additionally we evaluated patients who have hsCRP levels between1-3 and >3 mg/L. We observed that there was a significant difference in both study groups in terms of presence of xanthoma, microalbuminuria, creatinine and ECG. Not many studies have evaluated patients in terms of values of hsCRP as up to 3 or >3 mg/L. It can be assumed that even rise in hsCRP up to 1-3 can be a good predictor for developing of cardiovascular or renal abnormality in patients of DM with complications. In this study, we initially assessed history, performed general examination and laboratory investigations of diabetic patients with or without complications. Hypertension, duration of diabetes, urine microalbunuria, serum creatinine, hsCRP, diabetic retinopathy was higher in DM patients with complications. Correlation of hsCRP levels and other findings suggest that there was no significant correlation whereas the propensity of having abnormal ECG increases with rise in hsCRP levels.

This study suggests that high hscrp levels were present in patients of type 2 diabetic. The hscrp showed positive correlation with high blood sugar levels. hsCRP level were higher in diabetic with complications. This association of high hscrp in diabetic patients justifies measurements of hscrp apart from other routine lipids. The incidence of coronary risk factor was more in patients with high hscrp indicating hscrp as a stong predictor of coronary artery disease.

Summary and Conclusion

- The 0%, 33.4% and 66.6% diabetics with complications showed low, intermediate risk and highrisk elevation of hsCRP respectively. 63.34% and 36.66% subjects suffering from DM without complications associated with intermediate and high risk respectively. None of the patient of this study was found at low risk. This indicate that patients without diabetic complications had significantly lower hsCRP as compared to those with complications
- hsCRP does not correlate significantly with Xanthoma.
- hsCRP does not correlate significantly with Xanthelesma.
- hsCRP correlate significantly with FBS.
- hsCRP correlate significantly with PLBS.
- hsCRP does not correlate significantly with HbA1c.
- hsCRP does not correlate significantly with presence of hypertension.
- hsCRP does not correlate significantly with level of microalbuminuria.
- hsCRP does not correlate significantly with serum creatinine.
- hsCRP does not correlate significantly with creatinine clearance.
- In our study the diabetic patient with high hscrp had ischemic changes in the ECG
- hsCRP does not correlate significantly with abnormal findings on fundus
- In those patients who had hscrp between 1-3 mg/L there was no statsticial significance with FBS PLBS and HBA1C
- In patient who had hscrp between 1-3 mg/L there was had stastitical significance with ECG

We found that significant number of patients with diabetic complications showed higher levels of serum creatinine, microalbuminuria and creatinine clearance. The intermediate and higher risk of hsCRP levels was high in patients with diabetic complications. In conclusion, the results of this study revealed that there is a significant association between hsCRP and diabetics with and without complication. Abnormal ECG findings suggest the linkage amongst DM, cardiovascular complications and hsCRP. The role of hsCRP in metabolic abnormalities cannot be neglected, as it may be a very essential biomarker to detect associated complications. An aggressive and early screening for high hscrp and diabetics may prevent onset and complication of coronary artery disease. More such studies under larger scale should be undertaken to help people with diabetics.

REFERENCES

Abrass, C. K. 2004. Overview: obesity: what does it have to do with kidney disease? *J Am Soc Nephrol*., Nov; 15(11):2768-72.

Allison, D. B., Kaprio, J., Korkeila, M., Koskenvuo, M., Neale, M. C., Hayakawa, K. 1996. The heritability of body mass index among an international sample of monozygotic twins reared apart. *Int J Obes Relat Metab Disord*, 20:501-06.

Bogardus, C., Lillioja, S., Ravussin, E., et al. 1986. Familial dependence of the resting metabolic rate. *N Eng J Med.,* 315:96–100.

Bray, G. A. 1985. Complications of obesity. Ann Intern Med. Dec;103(6 (Pt 2)):1052-62.

Bray, G. A. 1984. Syndromes of hypothalamic obesity in man. Ped Annals, 13:525-36.

Chagnon, Y. C., Rankinen, T., Snyder, E. E., Weisnagel, S. J., Perusse, L., Bouchard, C. 2003. The human obesity gene map: the 2002 update. Obes Res., 11:313-67.

Dietz, W. H. Jr, Gortmaker, S. L. 1985. Do we fatten our children at the television set? Obesity and television viewing in children and adolescents. Pediatrics, May; 75(5):807-12.

Ejerblad, E., Fored, C. M., Lindblad, P., Fryzek, J., McLaughlin, J K., Nyrén, O. 2006. Obesity and risk for chronic renal failure. *J Am Soc Nephrol*, Jun; 17(6):1695-702.

Gomez, P. *et al*., 2006. FATH Study Group. Prevalence of renal insufficiency in individuals with hypertension and obesity/overweight: the FATH study. *J Am Soc Nephrol*., Dec;17(12 Suppl 3):S194-200.

Hall, J. E., Henegar, J. R., Dwyer, T. M., Liu, J., Da Silva, A. A., Kuo, J. J., Tallam, L. 2004. Is obesity a major cause of chronic kidney disease? Adv Ren Replace Ther., Jan;11(1):41-54.

Hall, M. E., do Carmo, J. M., da Silva, A. A., Juncos, L. A., Wang, Z., Hall, J. E. 2014. Obesity, hypertension, and chronic kidney disease. *International Journal of Nephrology and Renovascular Disease*., 7 :75-88.

Kotsis, V., Stabouli, S., Papakatsika, S., Rizos, Z., Parati, G. 2010. Mechanisms of obesity-induced hypertension. Hypertens Res., May;33(5):386-93.

Krishna, V. 2011. Indigenous Communities and Climate Change Policy: An Inclusive Approach. In: Walter heal Filho. The Economic, Social and Political elements of Climate Change. New York. Springer- Verlag.

Mark, A. L., Correia, M., Morgan, D. A., Shaffer, R. A., Haynes, W. G. 1999. State-of-the-art-lecture: Obesity induced hypertension: new concepts from the emerging biology of obesity. Hypertension, 33:537-41.

Martorell, R., Stein, A. D., Schroeder, D. G. 2001. Early nutrition and later adiposity. *J Nutr*., 131:874S–880S.

Peeters, A., Barendregt, J. J., Willekens, F., Mackenbach, J. P., Al Mamun, A. , Bonneux, L. 2003. NEDCOM, the Netherlands Epidemiology and Demography Compression of Morbidity Research Group. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. Ann Intern Med., 138:24–32.

Praga, M., Hernandez, E., Herrero, J. C. *et al*. 2000. Influence of obesity on the appearance of proteinuria and renal insufficiency after unilateral nephrectomy. Kidney Int., 58: 2111-8.

Qureshi, A. I., Suri, M. F., Kirmani, J. F., Divani, A. A. 2005 Prevalence and trends of prehypertension and hypertension in United States: National Health and Nutrition Examination Surveys 1976 to 2000. Med Sci Monit., Sep. 11(9):CR403-9.

Re, R. N. 2009. Obesity-Related Hypertension. *The Ochsner Journal,* 9(3):133-6.

Rogers, I. 2003. EURO-BLCS Study Group. The influence of birthweight and intrauterine environment on adiposity and fat distribution in later life. *Int J Obes Relat Metab Disord*., 27:755-77.

Sachidananda, Prasad, R. R., 1998. editors. Encyclopaedic profile of Indian Tribes. Vol III. New Delhi: Discovery Publishing House.

Schousboe, K., Willemsen, G., Kyvik, K. O., et al. 2003. Sex differences in heritability of BMI: a comparative study of results from twin studies in 8 countries. Twin Res 6: 409-21.

Stunkard, A., Sorensen, T. I. A., Hanis, C., et al. 1986. An adoption study of human obesity. *N Engl J Med* 314:193-98.

Stuveling, E. M., Bakker, S. J., Hillege, H. L., de Jong, P. E., Gans, R. O., de Zeeuw, D. 2005. Biochemical risk markers: a novel area for better prediction of renal risk? Nephrol Dial Transplant, Mar;20(3):497-508.

The World Health Report 2002 Reducing Risks, Promoting Healthy Life. Geneva, Switzerland: World Health Organization; 2002. Available at http://www.who.int/ whr/2002 /en/ \n _blank.

Turkbey, E. B., McClelland, R. L., Kronmal, R. A., et al. 2010. The impact of obesity on the left ventricle: the Multi-Ethnic Study of Atherosclerosis (MESA). JACC Cardiovasc Imaging, 3: 266-74.

WHO, 2015. Obesity and overweight, Accessed on: [24th September 2015] Accessed from: [http://www.who.int/mediacentre/factsheets/fs311/en/]

Wolz, M., Cutler, J., Roccella, E. J., Rohde, F., Thom, T., Burt, V. 2000. Statement from the National High Blood Pressure Education Program: prevalence of hypertension. *Am J Hypertens*, Jan. 13(1 Pt 1):10-34.

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