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Original Research Article

A Hospital-Based Assessment of High-Sensitivity C-Reactive Protein, Malondialdehyde and Their Association with Glycated Hemoglobin in Type II Diabetes Patients: Prospective Observational Study

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Abstract

Aim: The aim of the present study was to assess high-sensitivity C-reactive protein, malondialdehyde and their association with glycated hemoglobin in type II diabetes patients.

Methods: A prospective evaluation study was carried out in the Department of Biochemistry, Netaji Subhas Medical College and Hospital, Patna, Bihar India for 10 months and 100 type 2 diabetic patients of both sexes aged between 35-45 years on oral hypoglycemic drugs, attending Department of General Medicine were selected for present study.

Results: In the present study, there were 60 male and 40 females. 55% patients belonged to 40-50 years of age group. The BMI and waist/hip ratio showed significant difference. The mean serum hs-CRP and MDA levels were significantly high in type 2 diabetic patients compared with healthy patients. Hs-CRP and MDA levels we are shown significant positive correlation with glycocylated hemoglobin (HbA1C), insulin resistance, triglycerides and negative correlation with HDL cholesterol.

Conclusion: Elevated hs - CRP, MDA levels are potentially important diagnostic markers for the assessment of endothelial dysfunction in type 2 diabetic patients. Tight blood glucose control, regular monitoring of hs-CRP, MDA levels within normal range might be useful for reduction of vascular complications in type 2 diabetic patients.

Keywords: Glycated Hemoglobin, Malondialdehyde, Diabetes Mellitus.

Introduction

Diabetes mellitus (DM) considered as a widespread global disease. Conferring to recent reports, about 171 million persons in the world with DM in the year 2000 and this number expected to increase to 366 million through 2030. This disease is correlated with reducing life expectancy and significant other illnesses due to its relationship with microvascular complications (ischaemic heart disease, stroke and peripheral vascular disease), as a result led to lessen life quality. [1] Glycated hemoglobin (HbA1c) represents the blood glucose average level within the past 3 months.

Therefore, HbA1c is a very important biochemical parameter that provide long term status of blood glucose levels and

monitoring tool for measuring glycemic control in Type – 2 diabetic patients. [2] HbA1c in general, developed when the hemoglobin joined with glucose in the blood and become glycated. [3] According to many studies, HbA1c levels could be used as an independent risk factor for stroke and Cardiovascular disease (CVD) in both healthy and diabetics persons. It has been found that a (0.2%) decrease of HbA1c level can lower the risk of CVD development by 10%. [4] Furthermore, many studies have revealed, newborns moms with high HbA1c levels are more likely suffering from development of CVD in the future. [5]

Chronic hyperglycemia and oxidative stress increases the pro-inflammatory proteins with infiltrated macrophages secreting inflammatory cytokines which leads to systemic inflammation. [6] Hs C-reactive protein is an acute phase reactant protein produced by liver response to several cytokines and sensitive marker of low grade systemic inflammation. [7,8] Studies reported that hs -CRP directly binds to oxidized low-density lipoprotein cholesterol (LDLC), induces plasminogen activator inhibitor-1 expression, endothelial dysfunction by which leads to cardiovascular disease (CVD). [9–11] Hyperglycemia induced oxidative stress induces pro inflammatory reactants with infiltrated macrophages secreting inflammatory cytokines which leads to local and systemic inflammation. [12] It has been recognized high levels of free radicals or reactive oxygen species (ROS), reactive nitrogen species (RNS) directly damage to the lipids which leads to formation of aldehydes such as malondialdehyde (MDA), propanal, hexanal, and 4-hydroxynonenal (4- HNE). [13,14]

The aim of the present study was to assess high-sensitivity C-reactive protein, malondialdehyde and their association with glycated hemoglobin in type II diabetes patients.

Materials and Methods

A prospective evaluation study was carried out in the Department of Biochemistry, Netaji Subhas Medical College and Hospital, Patna, Bihar India for 10 months and 100 type 2 diabetic patients of both sexes aged between 35-45 years on oral hypoglycemic drugs, attending Department of General Medicine were selected for present study.

We excluded the patients on insulin, smokers, alcoholics, tobacco chewers, renal disease, inflammatory disorders, neoplastic disorders, thyroid disorders, liver dysfunction, history of acute myocardial infarction, stroke, and occlusive peripheral vascular disease. Fifty healthy age and sex matched subjects were selected as controls. The informed consent was obtained from all the study subjects and the study was approved by the Institutional Human Ethics Committee (IHEC). Experiments were done in accordance with Helsinki declaration of 1975.

Biochemical analysis

Fasting venous blood samples were collected from the study subjects and centrifuged at 3000 rpm for 15 min. Routine laboratory investigations were carried out by standardized protocols with ERBA EM-360 fully automated analyzer. Serum insulin estimated by Enzyme Linked Immuno Sorbe nt Assay (ELISA), HbA1c estimated by (Ion Exchange Resin method) hs- CRP was assessed by (latex turbidimetric immunoassay), malondialdehyde (MDA) estimated by Thiobarbituric Acid Reactive Substances (TBARS) method.[15] Post prandial venous blood sample collected for plasma glucose (PPG) analysis. Homeostasis model assessment for Insulin Resistance (HOMA-IR) HOMA- IR calculated by using fasting glucose and insulin values: HOMA – IR= fasting insulin X fasting glucose (m M/L)/22.5[16]

Statistical analysis

Statistical analysis carried out with SPSS 25.0 software and values were expressed as mean ±standard deviation, p value < 0.05 was considered as statistical significant. Pearson correlation test performed for correlation analysis.

Results

Table 1: Gender and age distribution of patients

Variables	N=100	Percentage %
Gender		
Male	60	60
Female	40	40
Age		
30-40 years	45	45
40-50 years	55	55

In the present study, there were 60 male and 40 females. 55% patients belonged to 40-50 years of age group.

Table 2: Comparison of baseline parameters in controls, type 2 diabetic patients

Parameters	Controls(N=50)	T2DM(N=50)	p-value
Age	36.4±3.16	40.5±6.4	0.60
Body mass index (BMI) kg/m^2	25.5±1.7	27.3±2.8	0.010
Waist/Hip ratio	0.90±0.01	0.93±0.07	0.020
Systolic BP(mmHg	115.5±5.3	118.2±9.1	0.20
Diastolic BP (mm Hg)	78.2±5 .3	81.01±7.3	0.24

The BMI and waist/hip ratio showed significant difference.

Table 3: Comparison of FPG, PPG, HbA1C, HOMA-IR, Lipid profile, Liver profile, Renal profile hs-CRP and MDA levels in control and type 2 diabetic subjects

Parameters	Controls (N=50)	T2DM(N=50)	p-value
FPG(mg/dl)	82.8± 8.2	132.0±12.8	0.017
PPG(mg/dl)	102.2±8.2	184±22.8	0.030
HbA1C	5.6±0.5	8.2±0.4	0.020
Serum Triglycerides (mg/dl)	96.4±10.2	134.4±14.6	0.032
Serum cholesterol (mg/dl)	176.84±8.2	206.4±20.8	0.040
HOMA-IR	1.2±0.2	3.8±0.2	0.038
HDLcholesterol (mg/dl	42.0±1.6	40.2±3.4	0.025
LDLcholesterol (mg/dl)	110±12.2	136.0±12.2	0.012
Total Bilirubin(mg/dl	0.76±0.04	0.77±0.03	0.75
Direct Bilirubin(mg/dl)	0.2±0.05	0.18±0.02	0.45
Serum urea(mg/dl)	22.9±4.6	27.2±6.9	0.26
Serum creatinine(mg/dl)	0.68±0.2	0.75±0.6	0.340
Hs-CRP(mg/L)	1.6±0.4	4.2±1.6	0.017
MDA(µmol/L	1.8±0.2	5.2±1.8	0.022

The mean serum hs-CRP and MDA levels were significantly high in type 2 diabetic patients compared with healthy patients.

Table 4: Correlation between hs-CRP &measured parameters in type 2 diabetic patients

Parameters	Correlation Coefficient(r)
BMI	0.600
W/H ratio	0.212
FBS	0.320
PPBS	0.199
HbA1C	0.520
HOMA-IR	0.478
Cholesterol	0.240
TGL	0.309
HDL	-0.333
LDL	0.156
MDA	0.640

Table 5: Correlation between MDA &measured parameters in type 2 diabetic patient

Parameters	Correlation Coefficient(r)
BMI	0.375
W/H ratio	0.270
FBS	0.606
PPBS	0.190
HbA1C	0.420
HOMA-IR	0.555
Cholesterol	0.220
TGL	0.312
HDL	-0.280
LDL	0.118

Hs-CRP and MDA levels we are shown significant positive correlation with glycocylated hemoglobin (HbA1C), insulin resistance, triglycerides and negative correlation with HDL cholesterol.

Discussion

Type 2 diabetes mellitus is a major public health problem worldwide and accompanied by enduring vascular complications, which leads to morbidity and mortality. Inflammation plays a pivotal role in the development of type 2 diabetes and vascular complications. [17] Impaired insulin secretion and sensitivity leads to oxidative stress, endoplasmic reticulum stress, amyloid deposition in the pancreas, lipotoxicity and glucotoxicity. [18] Type 2 diabetes mellitus is a major public health problem worldwide and accompanied by enduring vascular complications, which leads to morbidity and mortality. Inflammation plays a pivotal role in the development of type II diabetes and vascular complications. [19] Impaired insulin secretion and sensitivity leads to oxidative stress, endoplasmic reticulum stress, amyloid deposition in the pancreas, lipotoxicity and glucotoxicity. [20,21] Studies reported that insulin resistance, inflammatory biomarkers, metabolic syndrome, dyslipidaemia, hypertension are predictive markers of cardiovascular disease (CVD) in type 2 diabetes mellitus. [22,23]

In the present study, there were 60 male and 40 females. 55% patients belonged to 40-50 years of age group. The BMI and waist/hip ratio showed significant difference. Tang et al [24] recruited 927 patients. The median age of the recruited patients was 55 years, and there were 346 female patients and 581 male patients. The

hs-CRP levels were evidently higher in patients with DKD than those without DKD. After adjusting for age, sex, diastolic blood pressure, systolic blood pressure, body mass index, neck circumference, waist circumference, hypertension, duration of diabetes, common carotid artery plaque, fasting plasma glucose, glycated hemoglobin, hemoglobin, erythrocyte, leukocyte, γ-glutamyl transferase, albumin, urea nitrogen, uric acid and triglyceride, a significant increase in the odds ratios for DKD in the fourth hs-CRP quartile compared with the first quartile was observed and the ORs in the fourth quartile of hs-CRP were 1.968 for DKD compared to the first quartile. Moreover, the RCS curves presented a positive association between hs-CRP and DKD in total subjects, male subjects and female subjects, respectively.

We have observed significantly increased total cholesterol, triglycerides, LDL- C and decreased HDL-C in T2DM patients compared with healthy individuals and also hs -CRP, MDA levels were positively correlated triglycerides and negatively correlated with HDLcholesterol In the present study we observed hs - CRP levels showed significant positive correlation with MDA, HbA1c and HOMA-IR. Chronic inflammation is potentially unifying mechanistic cause, accompanied by activation of major inflammatory pathways such as JunN-terminal kinases and the transcription factor NF-kappaB along with decreased HDL-cholesterol, with impairment in reverse cholesterol transport mechanism and parallel changes in apolipoproteins, enzymes, decreased anti- oxidant capacity. [25-27]

The mean serum hs-CRP and MDA levels were significantly high in type 2 diabetic patients compared with healthy patients. Oxidative stress plays a crucial role in pathogenesis of diabetic vascular complications. [28] Chronic hyperglycemia in diabetic patients can increase production of free radicals through Amadori re arrangement. [29] In general, the ROS and RNS are continuously generated in physiological conditions and are eliminated by several antioxidant enzymes. C o-existence of inflammation, increased lipid peroxidation, dyslipidemia along with hyperglycemia conditions could pathologically increase the effect of oxidative stress. [30,31] However, the decreased efficiency of cellular antioxidant mechanisms with simultaneously enhanced lipid peroxidation along with increased insulin resistance and HbA1c may contribute factors of provoking inflammatory pathways and vascular complications in type 2 diabetes mellitus.

Conclusion

Elevated hs - CRP, MDA levels are potentially important diagnostic markers for the assessment of endothelial dysfunction in type 2 diabetic patients. Tight blood glucose control, regular monitoring of hs-CRP, MDA levels within normal range might be useful for reduction of vascular complications in type 2 diabetic patients.

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