IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 3 Ver. I (Mar. 2016), PP 47-51
www.iosrjournals.org

Correlation of Myeloperoxidase with Urea, Creatinine and Lipid Profile in Type 2 Diabetes Mellitus

Dr. Preethi M Shenoy[1], Dr.Anusha A.M[2], Dr.P.T.Annamala[3]
[1]*Associate Professor, Dept of Biochemistry, Jubilee Mission Medical College, Thrissur, Kerala*
[2]*Assistant Professor, Dept of Pathology, PKDAS Institute of Medical Sciences, Palakkad, Kerala*
[3]*Professor, Dept of Biochemistry, Jubilee Mission Medical College, Thrissur, Kerala*

Abstract: *Diabetes mellitus type 2 (T2DM) is a leading cause of morbidity and mortality worldwide. With approximately 10% of people affected, it is one of the major diseases causing socio-economic challenges to the society. Type 2 DM is emerging as the leading cause for End Stage Renal Disease (ESRD) across nations. Even though the course of the diabetic nephropathy has been clarified to a certain extent, specific early marker to detect the disease has yet to be identified. This case-control study was undertaken to elucidate the role of myeloperoxidase enzyme (MPO) in the development of nephropathy. Myeloperoxidase levels were compared with urea, creatinine and lipid profile levels in serum. The myeloperoxidase levels showed a positive but insignificant correlation with blood urea whereas a negative correlation was observed with creatinine. LDL-C levels correlated positively with MPO levels. The study points to different pathogenic roles for MPO in macrovascular and microvascular complications in DM.*
Keywords: *Myeloperoxidase, Diabetes mellitus, nephropathy*

I. Introduction

In 2014, worldwide prevalence of diabetes mellitus (DM) was approximately 9% among adults aged 18+ years. In 2012, an estimated 1.5 million deaths were directly caused by DM worldwide. More than 80% of DM deaths occur in low- and middle-income countries. According to WHO, by 2030 DM will be 7th leading cause for death[1]. Increased food consumption, decreased physical activity and a substantial genetic component are contributors to the growing Indian type 2 diabetes mellitus (T2DM) epidemic[2].

As per U.S. National diabetes statistics report for the year 2014, DM was listed as the primary cause of kidney failure in 44% of all new cases in 2011[3]. As a result of its long-term complications, end-stage renal disease (ESRD) resulting from DM has become very common in the U.S. and Europe[4]. Diabetic nephropathy occurs in 20-40% of patients with diabetes[5]. A population-based study from South India reported the prevalence of overt nephropathy as 2.2% and microalbuminuria in 26.9%. Glycated haemoglobin, duration of diabetes and systolic blood pressure were independently associated with diabetic nephropathy[6].Diabetic nephropathy has a well-outline course, first starting with microalbuminuria followed by proteinuria, azotemia and culminating in ESRD[7].

Microalbuminuria is said to predict the risk for progression to overt albuminuria in both type1 (T1DM) and type 2 DM (T2DM). In T2DM, the predictive value of microalbuminuria is less[8]. Even though 90% of cases show morphological lesions, only 20-40% show clinical nephropathy[9]. At present, there are no early morphological appearances which will distinguish those patients who are at risk from those who are not. Identification of patients prone to develop the clinical disease is primarily based on functional parameters. It has been indicated that the course and onset of diabetic nephropathy can be alleviated to significant extent if early interventions are introduced[10]. It is therefore important to describe the early abnormalities, recognize its origins and determinants, examine its relationship to diabetes and its control and analyze the prognostic significance[8].

A subgroup of patients have normal range of albumin in urine, even though they have pathological changes and declining renal function, therefore urinary albumin levels cannot be taken as perfect marker for the early detection of nephropathy. Hence, biomarkers of renal damage, inflammation, and oxidative damage may be useful tools for detection of nephropathy at an early stage or prediction of diabetic nephropathy[11].

Myeloperoxidase (MPO) is a heme enzyme in the azurophilic granules of nucleated leukocytes. Oxidative products characteristic of MPO have been observed in diseased tissue. The main pathways through which MPO damages biological targets, all require H_2O_2 and nitrite, tyrosine or chloride (low molecular intermediate)[12].

In view of the ambiguity regarding biomarkers of renal damage, we decided to study the correlation of the enzyme myeloperoxidase with serum urea, creatinine and lipid levels. We hypothesize that MPO has a role in initiation of renal damage in T2DM patients, either due to changes in glomerular basement membrane protein or oxidative damage to membrane lipids.

II. Aims And Objectives

The aims of the study are to:

1. Estimate the serum levels of MPO in T2DM.
2. Compare the serum MPO levels of T2DM patients with controls.
3. Correlate MPO levels of T2DM patients with their lipid profile.
4. Correlate MPO levels of T2DM patients with serum creatinine and urea levels.

III. Methodology

A prospective case-control study was performed with 20 cases and controls each. The cases were selected from consecutive out-patients. Controls were age-matched subjects without diabetes. Blood samples were collected in fasting state and were analysed for the following parameters - glycated Hb (HbA1c), serum creatinine, urea, serum lipid profile. Glycated Hb (HbA1c) was estimated using ion-selective high performance liquid chromatography. Serum creatinine, urea and lipid profile were analyzed using standard methods. Myeloperoxidase was determined by indirect non-competitive enzyme-linked immune assay using MPO ANCA method.

IV. Statistical Analysis

The values were analyzed using SPSS version 22. Correlation between variables was assessed by correlation coefficient Pearson 'r'. We used student *t*-test to examine dependent variables and independent variables. (p value <0.05 was taken as significant)

V. Results And Discussion

It is well-established by previous studies that poor metabolic control is critical in the etiology of diabetic nephropathy. Nephropathy is uncommon in patients with HbA1c consistently <7.5 - 8%. Glucose is a meaningful and clinically relevant marker, as shown in the DCCT and other treatment trials that demonstrated decreased nephropathy with lowered serum glucose[13]. In the present study, the mean value for glycated hemoglobin (HbA1c) is 8.73% which signifies the environment of glucose toxicity in cases, which is a harbinger for development of nephropathy.

The mean value of MPO for controls was 4.41, whereas, it was higher (8.97) for the cases. The Pearson 'r' value indicates a positive correlation between MPO and LDL-Cholesterol (LDL-C), HDL-Cholesterol (HDL-C) and total Cholesterol (TC) in the cases, whereas a negative correlation was found for triglycerides (TG). This could mean that MPO levels are increased in cases when LDL-C is high, indicating the role of MPO in oxidative damage to membrane lipids. This finding is consistent with a study which found that increasing MPO levels were associated with greater progression of atherosclerosis in diabetic patients using intravascular ultrasound in coronary vessels[14].

The mean value of urea among cases is 28.47mg/dl whereas for the controls, it is 23.08mg/dl. The correlation coefficient 'r' between urea versus MPO was found to be 0.08 for the cases. This indicates a slight positive correlation (p value = 0.73). The high mean value for urea in cases compared to controls maybe due to increased protein catabolism in patients with uncontrolled DM (Mean HbA1c – 8.73%)[15].

The serum creatinine showed negative correlation with MPO, Pearson 'r' being -0.112 (p value = 0.63) in cases, but positively correlated with controls (0.329). The decrease in MPO with increase in creatinine may indicate that failing kidneys lead to excretion of proteins in urine including enzyme proteins. Previous studies have shown increased urinary enzyme protein excretion in DM[16]. Still other studies have demonstrated a decreased activity of MPO in chronic kidney failure[17]. Thus, a decrease in MPO from baseline levels in patients of T2DM may indicate a progressive decrease in renal function. Further studies comparing MPO with estimated GFR (e-GFR) and cystatin C are required for establishing that decreasing MPO levels indicate reduction in renal function in T2DM.

VI. Conclusion

The present study shows that in contrast to the correlation of MPO as a cardiovascular risk factor, whereby the enzyme levels increase with significant coronary artery disease, in assessing the renal complications of T2DM, there is a progressive decrease in MPO levels. The stage at which the MPO levels start decreasing has to be clarified with comparative studies using e-GFR and cystatin C.

Table 1: Comparison of cases and controls based on gender

Gender	Cases	Controls
M	7	9
F	13	11

Table 2: Biochemical Parameters and myeloperoxidase of diabetic cases and controls

Group		Age (yrs)	HbA1c (%)	MPO (U/ml)	FBS (mg/dl)	PPBS (mg/dl)	S. Urea (mg/dl)	S. Creatinine (mg/dl)
Type 2 DM (Cases) (N=20)	Mean	56.40	8.73	8.97	166.75	259.80	28.47	1.11
	SD	9.46	1.20	1.22	54.67	71.43	2.81	0.12
Control (N=20)	Mean	52.70	5.56	4.41	91.80	122.40	23.08	0.96
	SD	14.63	0.28	1.22	7.21	5.88	2.76	0.30

MPO = Myeloperoxide

Table 3: Lipid profiles of diabetic cases and controls

Group		T. Cholesterol(mg%)	Triacyl glycerol(mg%)	HDL – C(mg%)	LDL – C(mg%)
Type2 DM (Cases)(N=20)	Mean	210.50	168.40	43.16	200.22
	SD	16.12	28.08	2.85	17.81
Control(N=20)	Mean	180.20	126.55	43.76	162.50
	SD	12.12	21.14	2.59	14.53

Table 4: Correlation of MPO with various parameters

Variable	Pearson 'r' for Cases	Pearson 'r' for Controls
Urea*MPO	0.080	0.328
Creatinine*MPO	-0.112	0.329
TC*MPO	0.129	0.021
LDL-C*MPO	0.193	-0.038
HDL-C*MPO	0.025	0.009
TG*MPO	-0.129	-0.285

MPO= Myeloperxidase TC = Total Cholesterol, TG = Triacyl glycerol

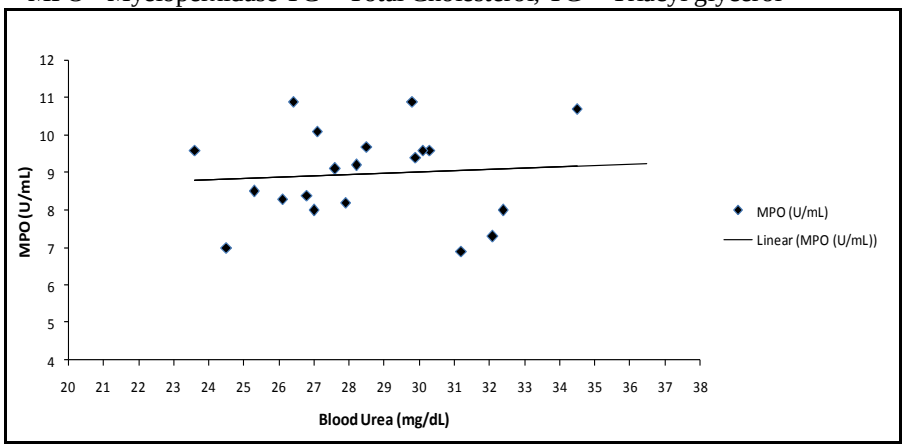

Fig 1: Scatter diagram showing correlation between Serum Urea and MPO values in cases

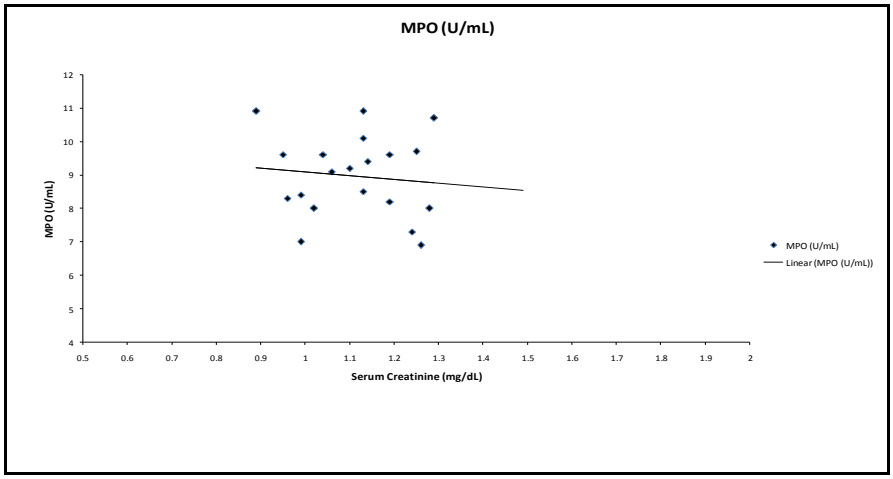

Fig 2: Scatter diagram showing correlation between Serum Creatinine and MPO values in cases

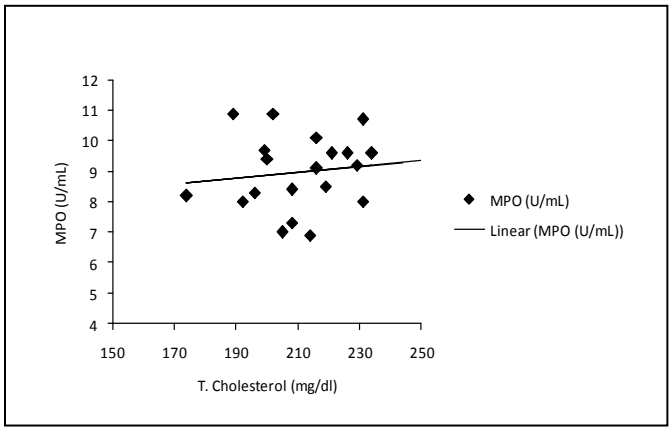

Fig 3: Scatter diagram showing correlation between Total Cholesterol and MPO values in cases

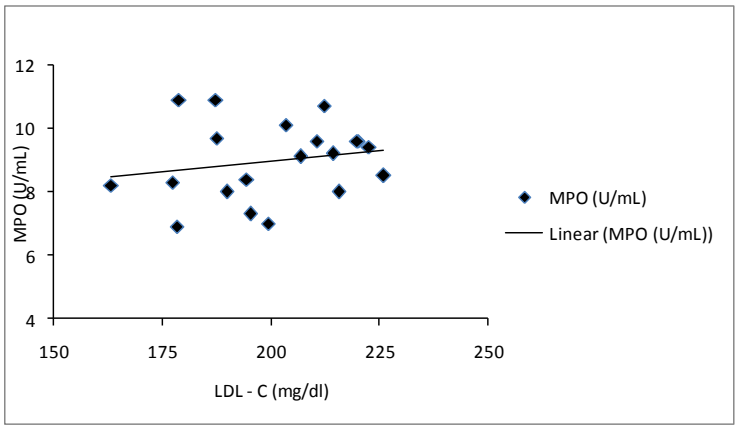

Fig 4: Scatter diagram showing correlation between LDL- Cholesterol and MPO values in cases

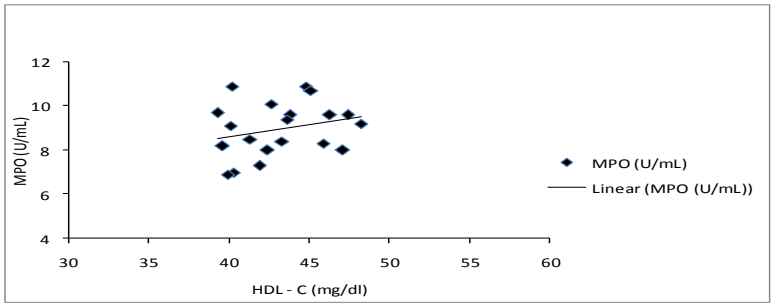

Figure 5: Scatter diagram showing correlation between HDL- Cholesterol and MPO values in cases

References

[1]. World Health Organization. Global Health Estimates: Deaths by Cause, Age, Sex and Country, 2000-2012. Geneva, WHO, 2014.
[2]. Holliday E. Hints of Unique Genetic Effects for Type 2 Diabetes in India. Diabetes. 2013;62(5):1369-1370.
[3]. Centers for Disease Control and Prevention. National Diabetes Statistics Report: estimates of diabetes and its burden in the United States, 2014. Atlanta, GA: US Department of Health and Human Services, 2014.
[4]. Diabetic Nephropathy. Diabetes Care. 2002;25(Suppl 1):S85-S89.
[5]. Microvascular Complications and Foot Care. Diabetes Care. 2014;38(Suppl 1):S58-S66.
[6]. Unnikrishnan R, Rema M, Pradeepa R, Deepa M, Shanthirani C, Deepa R et al. Prevalence and Risk Factors of Diabetic Nephropathy in an Urban South Indian Population: The Chennai Urban Rural Epidemiology Study (CURES 45). Diabetes Care. 2007;30(8):2019-2024.
[7]. Raptis A, Viberti G. Pathogenesis of diabetic nephropathy. Experimental and Clinical Endocrinology & Diabetes. 2001;109(Suppl 2):S424-S437.
[8]. Parchwani D, Upadhyah A. Diabetic nephropathy: Progression and pathophysiology. Int J Med Sci Public Health. 2012;1(2):59.
[9]. Dronavalli S, Duka I, Bakris GL. The pathogenesis of diabetic nephropathy. Nature Reviews Endocrinology. 2008;4:444-452.
[10]. American Diabetic Association: Nephropathy in diabetes - 2004. Diabetes care.2004;27(Suppl 1):s79-83.

[11]. Moresco R, Sangoi M, De Carvalho J, Tatsch E, Bochi G. Diabetic nephropathy: Traditional to proteomic markers. Clinica Chimica Acta. 2013;421:17-30.
[12]. Brennan M, Anderson M, Shih D, Qu X, Wang X, Mehta A et al. Increased atherosclerosis in myeloperoxidase-deficient mice. Journal of Clinical Investigation. 2001;107(4):419-430.
[13]. Evans TC, Capell P. Diabetic nephropathy. Clinical diabetes, Winter 2000; 18(1):7-10.
[14]. Kataoka Y, Shao M, Wolski K, Uno K, Puri R, Murat Tuzcu E et al. Myeloperoxidase levels predict accelerated progression of coronary atherosclerosis in diabetic patients: Insights from intravascular ultrasound. Atherosclerosis. 2014;232(2):377-383.
[15]. Pupim L, Flakoll P, Majchrzak K, Aftab Guy D, Stenvinkel P, Alp Ikizler T. Increased muscle protein breakdown in chronic hemodialysis patients with type 2 diabetes mellitus. Kidney International. 2005;68(4):1857-1865.
[16]. Ahmed A, Elhassan K, Abdallah H, Elabid B. Evaluation of Myeloperoxidase in Saudi Patients with Chronic Renal Failure. International Journal of Health Sciences and Research. 2013; 3(12): 69-74.
[17]. Madhusudhana Rao A, Anand U, Anand C. Myeloperoxidase in Chronic Kidney Disease. Indian Journal of Clinical Biochemistry. 2010;26(1):28-31.