ISSN 2515-8260 Volume 09, Issue 02, 2022

Detection of early nephropathy in type II diabetic patient by using kim-1 as a biomarker: A prospective study

[1]Dr. Khushant Jangid, [2]Dr. Archana Dubey, [3]Gunvi Ohari, [4]Dr. Ashok Kumar Kachhawah

[1]Assistant Professor, Department of Medicine, Dr. SNMC, Jodhpur, Rajasthan, India
[2]Senior Resident, Department of Medicine, GMC, Kota, Rajasthan, India
[3]Under Graduate Student, Dr. SNMC, Jodhpur, Rajasthan, India
[4]Senior Resident, Department of Medicine, Dr. SNMC, Jodhpur, Rajasthan, India

Corresponding Author:
Dr. Ashok Kumar Kachhawah

Abstract

Background: The present study aimed to investigate the clinical significance of urinary Kim-1 level in type II diabetic patients with and without nephropathy and to evaluate its relation to various clinical and laboratory parameters as an early predictor of diabetic nephropathy.
Methodology: The prospective study was conducted at Department of Medicine at Dr M.D.M. Hospital, Jodhpur. Attached to Dr. S.N. Medical College to study the detection of Kidney injury molecule-1 (Kim-1): An early biomarker for nephropathy in type II diabetic patients attending the Medicine Outdoor and Indoor at M.D.M. Hospital, Jodhpur. It includes 75 patients whose serum creatinine level was less than 1.5mg/dL. Diabetes was defined as fasting plasma glucose ≥126 mg/dL according to WHO criteria.
Results: Kim-1 is found raised in 68% patients and with normal albuminuria and microalbuminuria also significantly correlated with other variables i.e. fasting blood sugar, HbA1c p value is less than 0.001 for all these variables. So kim-1 can be used to diagnosis early nephropathy as a sensitive, rapid, noninvasive test in diabetes. With these we conclude KIM-1 is a good for early detection of Diabetic nephropathy and it is nicely correlating with urinary microalbumin level which is gold standard for detection of early nephropathy.

Keywords: Diabetes mellitus II, nephropathy, Kim-1

Introduction

Diabetes mellitus is a major health problem and a chronic metabolic disease. Diabetes mellitus (DM) is characterized by hyperglycaemia due to a total or relative lack of insulin secretion and insulin resistance or both. The metabolic abnormalities involve carbohydrate, protein, and fat metabolism. DM affects all age groups but is more common in adults [1]. Diabetic kidney disease is defined by characteristic structural and functional changes. The predominant structural changes include mesangial expansion, glomerular basement membrane thickening, podocyte injury, and, ultimately, glomerular sclerosis [2-4].
Pathologic abnormalities are noted in patients with long-standing diabetes mellitus before the onset of moderately increased albuminuria, formerly called "microalbuminuria" [5, 6, 7]. The last abnormality, which may have a nodular appearance (the Kimmelstiel-Wilson lesion), is

often associated with hyaline deposits in the glomerular arterioles (reflecting the insinuation of plasma proteins such as fibrin, albumin, immunoglobulins, and complement into the vascular wall) (picture 1A-C) [8]. These different histologic patterns appear to have similar prognostic significance [9].

Glycaemic control: Diabetic nephropathy is more likely to develop in patients with worse glycaemic control (higher HbA1c levels). Kidney injury molecule-1 (Kim-1) is a type I trans-membrane glycoprotein expressed on renal proximal tubule epithelial cells undergoing regeneration after toxic or ischemic injury. The extracellular domain of Kim-1 is composed of an immunoglobulin-link domain that points to a possible role in cell adhesion by homology to several known adhesion proteins [10]. Many studies indicate that Kim-1 is a sensitive and specific marker of kidney injury as well as a predictor of prognosis [11].
Thus, diagnosis of diabetic nephropathy (DN) in an earlier stage is critical and helps to reduce morbidity and mortality. The present study aimed to investigate the clinical significance of urinary Kim-1 level in type II diabetic patients with and without nephropathy and to evaluate its relation to various clinical and laboratory parameters as an early predictor of diabetic nephropathy.

Material and Methods

The study was conducted at Department of Medicine at Dr. M.D.M. Hospital, Jodhpur. Attached to Dr. S. N. Medical College.

Study Design

A prospective study was conducted to study the detection of Kidney injury molecule-1 (Kim-1): An early biomarker for nephropathy in type II diabetic patients attending the Medicine Outdoor and Indoor at M.D.M. Hospital, Jodhpur.

Sample size: 75 patients with type II diabetics.

Inclusion criteria

1. Patients admitted in MDMH with type II diabetic mellitus of any duration.
2. Patient attending medicine outdoor and patients admitted in Medicine unit at MDM Hospital Jodhpur.
3. Irrespective of treatment taken by patients for Diabetes mellitus oral hypoglycaemic agent or Insulin, Diabetes controlled or not were included in study.

Exclusion criteria

1. Type I diabetic patients.
2. End stage cardiac disease.
3. Cancer.
4. Autoimmune diseases.
5. Hypertension.
6. Serum creatinine above 1.5 mg/dl.

In this study detailed examination of Type 2 diabetic patient attending medical outdoor and Indoor, Internal Medicine Department of Dr. S. N. Medical College, Jodhpur. The study included 75 type 2 diabetes patients whose serum creatinine level was less than 1.5mg/dL.

ISSN 2515-8260 Volume 09, Issue 02, 2022

Diabetes was defined as fasting plasma glucose ≥126 mg/dL according to WHO criteria.

Observations and Results

Table 1: Age distribution of the patients in a study population with Type 2 Diabetes

Age (years)	No. of patients	Percentage
35-50	18	24.00
51-60	26	34.67
61-70	21	28.00
71-80	7	9.33
≥81	3	4.00
Total	75	100.00
Gender	**No. of patients**	**Percentage**
Male	44	58.67
Female	31	41.33
Total	75	100

A maximum number of patients were in between 51-60 years, which was 34.67% (n=26) of the total study population. 28% (n=21) patients were in age groups of 61-70 years. 24% (n=18) patients were of 35 to 50 years. 9% (n=7) patients were in age groups of 35-50 years.4% (n=3) patients were in age groups of>81 years. A maximum number of patients were male which was 58.67% (n=44) of the total study population.41.33% (n=31) were female patients of total study population.

Table 2: Kidney injury molecule -1 in study population

KIM-1(ng/ml)	No. of patients	Percentage
0.059-2.14	24	32.00
2.2-5	37	49.33
5.9.9	5	6.67
≥10	9	12.00

Above table Illustrate that (n=24) patients having normal kim-1 value. (n=37) patients with mild increased in kim-1 level, (n=5) patients with increased moderate level of kim-1. (n=9) patients with increased severe level of kim-1 in study population.

Table 3: Correlation of Hba1c with KIM-1 in Type 2 diabetics

Hba1c (%)	KIM-1				
	0.059-2.14	2.2-5	5.9.9	≥10	Total
5.7-6.4	1 (100%)	0	0	0	1 (1.33%)
≥6.5	23 (31.08%)	37 (50%)	5 (6.76%)	9 (12.16%)	74 (98.67%)

Kim-1 Normal Range 0.059-2.14 Ng/Ml

Above table illustrate that out of 75 patient's correlation between Hba1c and KIM-1. 1 patient with pre diabetic range with normal kim-1 leval, Hba1c with diabetes range with (n=23) normal range of kim-1, (n=37) with slightly increased level of kim-1, (n=5) moderately increased leval of kim-1, (n=9) severally increased leval of kim-1 in urinary sample.

Table 4: Correlation of Fasting blood sugar (FBS) with KIM-1 in study population

FBS (mg/dl)	KIM-1(ng/ml)			
	0.059-2.14	2.2-5	5.9.9	≥10
70-110	24	0	0	0
111-150	0	35	0	0
151-199	0	0	6	1
≥200	0	0	1	8

Above table Illustrate relation between fasting blood sugar and kim-1. (n=24) patients with normal kim-1 in the normal fasting sugar level. (n=35) with slightly increased level of kim-1 in mildly increased level of fasting blood sugar level, (n=6) patients with high level of kim-1 in the >150 mg level of fasting blood sugar only (n=1) with very high level of kim-1 in the same group. Only (n=1) patient with moderate level of increased kim-1and (n=8) patients with very high kim-1 level in higher level of fasting blood sugar

Discussion

In prospective study of 75 cases of diabetic with serum creatinine below 1.5mg/dl conducted in western Rajasthan. In our study 44 (58.67%) were male and 31(41.33%) were female.
In a study by EI-Zamarany *et al*. [12] has shown Urinary kim-1 levels were elevated significantly tenfold in type 2 diabetes microalbuminuric patients compared to normoalbuminuric patients. In present study Urinary kim-1 levels were positively correlated with microalbuminuria, serum creatinine, BUN, duration of diabetes, and BMI.
A Girish N. Nadkarni *et al*. [13] showed high consistency in the association between these biomarkers of inflammation and renal outcomes in DKD. Moreover, addition of these biomarkers kim-1 to clinical prognostic models significantly improved discrimination for the renal outcome. In present study KIM-1 also independently raised in 20 diabetes patients so addition of these marker useful in diagnosis early nephropathy in type 2 diabetes even before increased levels of urinary micro albumin level in type 2 diabetes patients.
Eun Jeong Lee *et al*. [14] suggest that tubular injury has a key role in pathogenesis of DKD and tubular injury marker KIM-1 were positive correlation in diabetic kidney disease. In our study KIM-1 had positively correlated for fasting blood sugar level, HbA1c and 24 hour urinary microalbumin level.
Joseph V *et al*. [15] study result show that kim-1 is early biomarker for diabetic nephropathy. In present study also kim-1 is raised in 68% of patients. So can be used in future early noninvasive marker for diagnosis of diabetes nephropathy.
We found that kim-1 is raised in diabetes even before urine microalbumin level in 26.66% patients kim-1 positively correlated for fasting blood sugar level, HbA1c.
This may be probably because the KIM-1 is a new marker, yet to be evaluated in larger number, expensive (above Rs 2000/-per test) hence not much studies are available. Still most of literature and our study showed that KIM-1 is a good marker for early detection of Diabetic nephropathy, even before urine microalbumin becomes positive and it can be a marker of Diabetic nephropathy in future.

Summary

A prospective study of 75 cases of diabetic with serum creatinine below 1.5mg/dl conducted during the period from February 2020 to June 2020, at SNMC Jodhpur. Among them (75 patients).
44 (58.67%) were male and 31 were female (41.33%). 69.33% patients of diabetic were taking treatment for more than 5 years. In our study 11.11% patients having fasting blood

sugar more than 200 mg/dl out of which 10.66% patients having very high level of kim-1 levels.

Kim-1 is found raised in 68% patients and with normal albuminuria and microalbuminuria also significantly correlated with other variables i.e. fasting blood sugar, HbA1c p value is less than 0.001 for all these variables.

So kim-1 can be used to diagnosis early nephropathy as a sensitive, rapid, noninvasive test in diabetes. With these we conclude KIM-1 is a good for early detection of Diabetic nephropathy and it is nicely correlating with urinary microalbumin level which is gold standard for detection of early nephropathy.

References

1. AL, Masklari AY, AL Maskari MY, AL-Sudairy S, *et al*. Oral manifestations and complications of diabetes mellitus. Sultan Qaboos Univ. Med. J. 2011;11(2);179-186.
2. Piwkowska A. Role of protein kinase G and Reactive oxygen species in the regulation of podocyte funcation in health and disease. J cell physiol. 2017 Apr;232(4):691-97.
3. Gnudil L, Coward RJ, Long DA, *et al*. Diabetic nephropathy: Perspective on novel molecular mechanisms. Trends Endocrinol Metab. 2016 Nov;27(11);820-30.
4. Haraldsson B, Nystrom J. The glomerular epithelium: new insight on function and structure. Curr. Opin. Nephrol Hypertens. 2012 May;21(3):258-63.
5. Rue TC, Cleary PA, De Boer IH, *et al*. Long-term renal outcomes of patients with type1 diabetes mellitus and microalbuminuria: an analysis of the Diabetes Control and Complication Trial/Epidemiology of Diabetes Intervention and Complication cohort. Arch intern Med. 2011;17(5);412-418.
6. Steffes MW, Fioretto P, Brown DM, *et al*. An overview of renal pathology in insulin dependent diabetes mellitus in relationship to altered glomerular hemodynamic. Am J kidney Dis. 1992;20(6);549-58.
7. Adler AUSSO. Diabetic nephropathy: Linking histology, cell biology. Kidney Int. 2004;66(5):2095-104, 60.
8. Mooyaart AL, Tervart TW, Amank, *et al*. Pathologic classification of diabetic nephropathy. J am Soc Nephrol. 2010;21(4):556-564.
9. D ‘Agathi VDSO, Nagr SH. Nodular glomerulosclerosis in the nondiabetic smoker. J am Soc Nephrol. 2007;18(7):2032-2038.
10. Veelken R, Hilgers KF. Type 2 diabetic nephropathy: never too early to treat? J am Soc Nephrol. 2005;16(3):574-5.
11. Yao L, AU Nagachi Y, Kohori H, *et al*. Temporary angiotensin 2 blockade at prediabetic stage attenuates the development of renal injury in type 2 diabetic rats. J am Soc nephrol. 2005;16(3):703-10.
12. Stefferes MW, Harris RD, Bilous RW, *et al*. Global glomerular sclerosis and glomerular hyalinosis in insulin dependent diabetes. Kidney Int. 1991;40(1):107.
13. Harris RD, Steffers MW, Bilous, *et al*. Global glomerular sclerosis and glomerular arteriolar hyalinosis in insulin dependent diabetes. Kidney Int. 199;40(1):107.
14. Emancipator SN, Mishar R, Kernt, *et al*. High glucose evokes an intrinsic proapoptotic signalling pathway in mesangial cells. Kidney Int. 2005;67(1):82.
15. Chenx, Ferry RJ Jr, Vasylyeva TL, *et al*. Insulin-like growth factor binding proyein-3 mediates cytokine-induced mesangial cell apoptosis. Growth horm IGF Rei. 2005 Mar 23;15(3):20.