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Association between hsCRP with urine albumin creatinine ratio in patients of type2 diabetes mellitus with and without nephropathy

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Abstract

Aim: To correlate hsCRP with urine albumin and urine creatinine ratio in patients of Type2 Diabetes Mellitus with and without Diabetic Nephropathy.

Material and Method: This prospective case control study was conducted among 200 patients (100 Patients of Diabetes without Nephropathy and 100 with nephropathy) in MMC Hospital, Muzaffarnagar. The clinical and demographic profile at the time of admission in the medicine ward including the age, sex, associated chronic illness like hypertension and hyperlipidemia was recorded for all study subjects. Venous blood samples were collected and sent to laboratory where hsCRP was measured by immunoturbidimetry method. A spot urine sample was taken and urine albumin creatinine ratio was calculated by Immunoturbidimetry and Spectrophotometry method in the biochemistry laboratory.

Results: Mean hsCRP in patients without nephropathy was 1.691 mg/L and Mean hsCRP in patients with nephropathy was 9.522 mg/L. Mean fasting blood sugar in patients with nephropathy was 185.22mg/dl. Mean hsCRP in patients with macroalbuminuria was significantly more as compared to subjects without macroalbuminuria.

Conclusion: In conclusion, Hs-CRP exerts an important diversity of actions implicated in diabetic nephropathy, from development of the initial stages of diabetes to progression to renal failure.

Keywords: hsCRP, diabetes, nephropathy

Introduction

Diabetes mellitus is a chronic condition that occurs when there are raised levels of glucose in the body because the body cannot produce any or enough of the hormone insulin or use insulin effectively. The lack of insulin or inability of the cells to respond to insulin or leads to high level of blood glucose, or hyperglycemia which is the hallmark of diabetes [1, 2].

Diabetic nephropathy remains major cause of morbidity & mortality for persons with either type l or type2 DM [3, 4]. Globally most patients with diabetes are in developing countries. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world". Patients with type 2 diabetes comprise the largest and fastest growing single disease group requiring renal replacement therapy (nearly 50-60% of diabetic subjects receiving renal replacement therapy. The overall prevalence of microalbuminuria & macroalbuminuria in patients with type 2 diabetes mellitus is 25% & 14 % (5-48) respectively. Studies based in southern India have estimated that the current prevalence of overt nephropathy is 2.2% and of microalbuminuria is 26.9%. [5].

An interaction of metabolic and hemodynamic factors has been considered as traditional aspect in the development of kidney lesions in patients with type 2 diabetes mellitus (DM) [6]. Despite improvement in the knowledge of diverse aspects related to DM, the pathogenesis and initial molecular events leading to diabetic nephropathy are still elusive. Several recent studies have also shown that patients with type 2 DM and overt nephropathy exhibit high levels of diverse acute phase markers of inflammation, including C-reactive protein (CRP), serum amyloid A, fibrinogen and IL-612-16It is well known that in the general population, as well as in diabetes, these acute-phase markers are associated with increased cardiovascular risk, because chronic inflammation is one of the pathogenic mechanisms of atherosclerosis [7]. In contrast, the relationships between low grade inflammation and diabetic microangiopathy are still unclear.

The coexistence of an inflammatory condition with diabetic nephropathy could explain its part in tremendously increased cardiovascular risk among these patients. This study was undertaken to investigate the role of subclinical inflammation in the pathogenesis of diabetic nephropathy by evaluating the association between the serum high-sensitivity CRP (hsCRP) (marker of inflammation) and urinary albumin excretion (UAE) in type2 diabetes mellitus.

Material and Method

This prospective case control study was conducted among 200 patients (100 Patients of Diabetes without Nephropathy and 100 with nephropathy) in MMC Hospital, Muzaffarnagar. Patients who qualified all inclusion and exclusion criteria were enlisted in the study after informed consent. Patients who are diagnosed cases of Type 2 Diabetes Mellitus with and without diabetic nephropathy aged above 35years were included in this study.

Exclusion criteria

Patients having a history of recent stroke (within last 6 months), recent myocardial infarction (within last 6

months), chronic liver disease, recent infection, rheumatoid arthritis, known case of cancer, recent surgery (within last 6 months) and major trauma (within last 6 months) were excluded.

Methods: The clinical and demographic profile at the time of admission in the medicine ward including the age, sex, associated chronic illness like hypertension and hyperlipidemia was recorded for all study subjects. A careful and detailed history was recorded according to Proforma to assess the onset and duration of clinical events and the probable risk factors for the same. A detailed general physical examination was performed including assessment of the nervous system, cardiovascular system, abdomen and respiratory system was done.

Laboratory Parameters

- Fasting Blood sugar level
- Post Prandial Blood sugar level
- HbA1c
- hsCRP
- Urine routine microscopy
- Blood Urea
- Serum Creatinine
- Serum electrolytes
- Liver function tests
- Viral markers (HBsAg, HCV, HIV)
- Chest X ray
- Ultrasound abdomen
- ECG
- UACR in spot Urine sample.
- Complete blood counts

Method to Assess hsCRP and Uacr Ratio

1. hsCRP – Venous blood samples were collected and sent to laboratory where hsCRP was measured by immunoturbidimetry method. hsCRP in mg/L <1 (Low), 1-3 (Average), 3-10 (High) and >10 (Persistent elevation may represent non-cardiovascular inflammation).
2. Urine Albumin Creatinine Ratio – a spot urine sample was taken and urine albumin creatinine ratio was calculated by Immunoturbidimetry and Spectrophotometry method in the biochemistry laboratory. Normal /Non diabetic was <30, Microalbuminuria 30-300 and Clinical albuminuria >300.
3. Glycosylated Hemoglobin (HbA1c) – Venous blood samples was taken and sent to the biochemistry laboratory where HbA1c is calculated by high performance liquid chromatography (HPLC).
4. Fasting and Postprandial Blood Sugar – Venous blood samples was send to biochemistry laboratory.

Statistical analysis

All the data were analysed using computer-based software SPSS version 24. Descriptive statistics were used to investigate the general characteristics of the patients. Measures of the central tendency including mean and standard deviation were used to ascertain the data regarding the different laboratory parameters. An independent t test was used to evaluate the difference in hsCRP between the type 2 diabetes patient with nephropathy and without nephropathy.

Results

The mean age of patients without nephropathy was 59.67 years and with nephropathy was 58.6 years. Amongst 100 patients without nephropathy there were 48 females and 52 males and with nephropathy there were 61 females and 39 males. Mean hsCRP in patients without nephropathy was 1.691 mg/L and Mean hsCRP in patients with nephropathy was 9.522 mg/L. This difference was found to be statistically significant. Mean fasting blood sugar in patients with nephropathy was 185.22mg/dl. This difference was found to be statistically significant (table 1).

Mean blood urea in patients without nephropathy was 33.529 mg/dl. Mean blood urea in patients with nephropathy was 67.2 mg/dl. This difference was found to be highly statistically significant (table 2). Mean hsCRP in patients with macroalbuminuria was significantly more as compared to subjects without macroalbuminuria (table 3).

Table 1: hsCRP, Fasting Blood Sugar (mg/dL), Post Prandial Blood Sugar (mg/dL) and HbA1c (%) in patients with and without Nephropathy

	Mean hsCRP (mg/L)
Patients without Nephropathy	1.69±0.83
Patients with Nephropathy	9.52±5.82
Fasting Blood Sugar (mg/dL)	
Patients without Nephropathy	174.04 ± 25.37
Patients with Nephropathy	185.22 ± 41.43
Post Prandial Blood Sugar (mg/dL)	
Patients without Nephropathy	282.74±36.69
Patients with Nephropathy	301.56±47.08
HbA1c (%)	
Patients without Nephropathy	9.08±1.37
Patients with Nephropathy	10.25±1.86

Table 2: Comparison of Renal Function Test with UACR and presence of Nephropathy

Group	**Mean Blood Urea (mg/dl)**	**Mean Serum Creatinine (mg/dl)**
No Nephropathy (UACR<3)	33.529	0.735
Nephropathy (UACR>3)	67.210	2.66

Table 3: hsCRP in patients with and without Macroalbuminuria

Group	**n**	**Mean hsCRP (mg/dl)**
Without Macro albuminuria	163	4.605 ±5.43
With Macro albuminuria	37	10.049 ±4.58

Discussion

Although there is now convincing evidence that Type 2 Diabetes Mellitus includes an inflammatory component that has been related to diabetic complications. There is limited data on Type 2 Diabetes Mellitus Nephropathy in Asia. In order to find an easier method for detection of diabetic nephropathy as a screening method of diabetic nephropathy we tried to find a relation between hsCRP as a marker of diabetic nephropathy.

In this study, the mean age of patients without nephropathy was 59.67 and mean age of patients with nephropathy was 58.6. In one study by Nikhil Choudhary, Ravinder S Ahlawat, the mean age was 55.05±7 and 57 ±4 in patients with micro and macro albuminuria respectively [8].

In our study we found that diabetic patients with nephropathy showed significantly higher levels of hsCRP. This result is in agreement with Picardi *et al.* [9] who reported that patients with recent onset of type 2 DM with

nephropathy had higher levels of hs-CRP as compared to patients without nephropathy. Also, Coulon *et al.* [10] proved that diabetic patients have higher levels of cytokines than normal individuals and this elevation might be related to activation of macrophages, increased oxidative stress, or induction of cytokines. So, type2 DM is now accepted to be a chronic immuno-inflammatory disorder. Prakash J *et al.* [11] in their study revealed a significant association was found between serum hsCRP levels and serum urea level. However, Yasuaki Hayashino *et al* did not observe a significant association between hsCRP level and the subsequent risk of diabetic nephropathy progression [12].

In our study we found that low-grade inflammation was already present in the early stage of microalbuminuria, and it was increased with progressive increase of urine albumin excretion. In agreement with our results, Litikesh A.B *et al* found that there was a statistically significant increase in serum hscrp levels in diabetics with microalbuminuria cases as compared to controls ($p<0.034$) [13]. Similarly, Sujesh kumar *et al* found that the mean hsCRP was higher in patient with microalbuminuria (7.28±3.46) comparing to diabetic patient without microalbuminuria (1.04 ±0.85) and was statistically significant ($p< 0.001$) [14].

We found that the level of HbA1c at baseline showed a significant positive correlation with Hs-CRP ($r = 0.750$, $p < 0.001$), in the diabetic group. These results are consistent with a cross sectional study with type 2 diabetes, in which they found that there is a significant correlation between Hs-CRP and glycemic control guided with FPG and HbA1c [15]. Also, Dogan *et al.* [16] found that there is a positive significant correlation between level of HbA1c and inflammatory markers, and hs-CRP. Another study was done by Hansen TK reported that patients with high HbA1c% showed a higher level of cytokines and presenting with micro-vascular complications which proceeds to nephropathy in type-2 diabetic patients earlier than people having controlled blood glucose level [17].

In addition, a study was done by Schalwijk CG [18] revealed that inflammatory markers especially CRP are more higher in diabetic hypertensive patients more than normotensive diabetic patients By doing step-wise multiple regression analysis to determine the independent association between potential predictor variables (age, duration of diabetes, waist circumference, CRP level, at baseline), the UAE was the dependent variable, after adjusting for the effect of other variables by partial correlation analysis. Association between UAE and the levels of inflammatory markers of Hs-CRP with $R^2 = 0.927$ ($p < 0.001$) was found. These results are consistent with Targer *et al.* [19] who conducted a study on sixty patients with type-2 diabetes mellitus who further divided into normoalbuminurics, microalbuminurics, and macroalbuminurics. They found that inflammatory markers in early type-2 diabetic nephropathy are elevated and are associated with urinary albumin excretion. It is possible to hypothesize on the participation of locally released cytokines in the development of kidney damage.

Also, we agree with Choudhary and Ahlawat [20] who found a high level of hs-CRP and IL-6 in patients with type 2 diabetes mellitus which were correlated to the albumin excretion in urine. These results are also consistent with a study done by Erbagci AB *et al.* [21] conducted on 212 type-2 diabetic patients with albuminuria, where they found that albuminuria in these patients was associated with elevation of the cytokines levels. In our study we found there was significant relationship between UAE and HbA1c levels. However, another study [22] proved that association between urine albumin excretion and HbA1c are independent, and these suggest that factors other than poor glycemic control may be involved in the pathogenesis of early diabetic nephropathy. On the other hand, Amine *et al.* [23] reported that urine albumin excretion had a significant association with HbA1c in a cross-sectional study of 39 patients with type 2 diabetes.

Conclusion

In conclusion, Hs-CRP exerts an important diversity of actions implicated in diabetic nephropathy, from development of the initial stages of diabetes to progression to renal failure.

References

1. Beaglehole R, Yach D: Globalisation and the prevention and control of non-communicable disease: The neglected chronic disease of adults. Lancet, 2003; 62:1763-1764.
2. Yach D, Hawkes C, Gould C, Hofman K. The global burden of chronic diseases: Overcoming impediments to prevention and control. JAMA, 2004; 291:261-262.
3. Ritz E, Rychlik I, Locatelli F, Halimi S. Endstage renal failure in type 2 diabetes: A medical catastrophe of worldwide dimensions. Am J Kidney Dis, 1999; 34:795-808.
4. Juan F. Navarro-Gonzalez and Carmen Mora-Femandez: The Role of Inflammatory Cytokines in Diabetic Nephropathy. J Am Soc Nephrol, 2008; 19:433442.
5. Ritz E, O1th SR. Nephtopathy in patients with type2diabetes mellitus. N Eng J Med, l999; 341:l127-1133.
6. Hans-Henrik Parving Michael Mauer Eberhard Ritz. Diabetic Nephropathy. The Kidney, Barry M. Brenner and Rector FC. Voll, 8th ed. W.B. Saunders, 2007, 1273-1275.
7. Dalla Vestra M, Mussap M, Gallina P, Doni A, van Hinsbergh VW, Stehouwer CD, *et al.* Acute-phase markers of inflammation and glomemlarstructure in patients with type 2 diabetes. J Am Soc Nephrol, 2005; 16:S78-82.
8. Nikhil Choudhary, Ravinder S Ahlawat. Interleukin-6 and C-Reactive Proteinin Pathogenesis of Diabetic Nephropathy. IJKD, 2008; 2:72-9
9. Picardi A, Valorani MG, Vespasiani Gentilucci U, Manfrini S, Ciofini O, Cappa M, *et al.* Raised C-reactive protein levels in patients with recent onset type 1 diabetes. Diabetes Metab Res Rev, 2007; 23:211-214.
10. Coulon J, Willems D, Dorchy H. Increase in C-reactive protein plasma levels during diabetes in infants and young adults. Presse Med, 2006; 34:89- 93.
11. Jay Prakash Sah, Chandra Kant Yadav, Dipendra Kumar Yadav. Assessment of hsCRP with serum urea in type 2 diabetic patients in Pokhra Nepal: American Journal of Drug Delivery and Therapeutics. 2015; 2(2):053-059.
12. Yasuaki Hayashino, Tsuyoshi Mashitani, Satoru Tsujii. Serum high sensitivity C –reactive protein levels are associated with high risk of development, not progression, of diabetic nephropathy among Japanese type 2 diabetic patient: A prospective cohort study:

Diabetes Care. 2014; 37(11):2947-2952.
13. Litikesh AB, Prabhakar K, Reddy Prasad K, Prassana Kumar. Estimation of high sensitivity c-reactive protein levels as a early marker of diabetic nephropathy: European Journal of Pharmaceutical and Medical Research. 2017; 4(4):315-318.
14. Sujesh Kumar N, Sajitha Krishnan. Association between the urine albumin creatinine ratio and high sensitivity C –reactive protein in patient with type 2 diabetes mellitus. International Journal of Clinical Biochemistry and Research. 2018; 5(3):386-391.
15. Karlsson Faresjo MG, Ernerudh J, Ludvigsson J. Cytokine profile in children during the first 3 months after the diagnosis of type 1 diabetes. Scand J Immunol, 2004; 59:517-526.
16. Dogan Y, Akarsu S, Ustundag B, Yilmaz E, Gurgoze MK. Serum IL-1β, IL-2, and IL-6 in insulin-dependent diabetic children. Mediat Inflamm, 2006; 2006:59206.
17. Hansen TK, Thiel S, Knudsen ST, Gravholt CH, Christiansen JS, Mogensen Ce, *et al*. Elevated levels of mannan-binding lectin in patients with type 1 diabetes. J Clin Endocrinol Metab, 2003; 88:4857-4861.
18. Schalwijk CG, Poland DCW, Van Dijk W. plasma concentration of C-reactive protein is increased in type 1 diabetic patients without macroangiopathy and correlates with markers of endothelial dysfunction: evidence for chronic inflammation. Diabetologia, 1999; 42:351-357.
19. Targer G, Zenari L, Bertolini L, Muggeo M, Zoppini G. Elevated levels of interleukin-6 in young adults with type 1 diabetes without clinical evidence of microvascular and macrovascular complications. Diabetes Care, 2001; 24:956-957.
20. Choudhary N, Ahlawat RS. Interleukin-6 and C - reactive protein in pathogenesis of diabetic nephropathy: new evidence linking inflammation, glycemic control, and microalbuminuria. Iranian J Kidney Dis, 2008; 2:72-79.
21. Erbagci AB, Tarakçioglu M, Cokun Y, Sivasli E, Sibel Namiduru E. Mediators of inflammation in children with type I diabetes mellitus: cytokines in type I diabetic children. Clin Biochem, 2001; 34:645-650.
22. Gomes MB, Yeo CK, Nazaimoon WM. Acute-phase proteins and microalbuminuria among patients with type 1 diabetes. Am J Kidney Dis Pract, 2004; 57:298.
23. Amine R, Turner C, Van Aken S, Bahu TK, Watts A, Lindsell DR, *et al*. The relationship between microalbuminuria and glomerular filtration rate in young type 1 diabetic subjects: The Oxford Regional Prospective Study. Kidney Int, 2005; 68:1740-1749.