Original Article

A Study on Correlation of High-Sensitivity C-Reactive Protein and renal function in Patients With Type 2 Diabetes Mellitus in a tertiary care centre

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Abstract

Background : Type 2 Diabetes mellitus can lead to many chronic complications, one of which is microvascular complications. In addition, approximately one in four patients with T2DM will have comorbid diabetic kidney disease (DKD) in the progression of T2DM. DKD is the most common cause of leading to end-stage renal disease worldwide and is a primary cause of mortality among patients with DM . Therefore, early intervention plays a vital role in preventing DKD development. To establish effective intervention strategies for DKD in clinical practice, identifying risk factors related to the presence of DKD is available.

Objectives : To study the Correlation of High-Sensitivity C-Reactive Protein and renal function in Patients with Type 2 Diabetes Mellitus.

Methodology : Cross sectional observational study done in General Medicine department of the Chettinad Health and Research Institute 2 months i.e December 2022 and January 2023. Patients who are known type 2 Diabetes Mellitus with Diabetic history of more than 5yrs were included.

Results : A total of 100 diabetic patients were included in the study during the study period. Figure 2 shows that the among the 100 study population 36% of the diabetics showed microalbuminuria and 64% did not showed microalbuminuria. Study showed different parameters among the patients with microalbuminuria and without microalbuminuria. Mean age of the study population among the two groups, duration of diabetes, FBS levels, BMI, SBP, DBP levels showed significant difference among the two groups i.e $p<0.05$. HbA1C levels were more among the microalbuminuria patients (6.66± 1.00 v/s 6.44± 1.06) but it was not statistically significant.

Among the serum proteins, serum albumin and total protein showed decreased levels among the microalbuminuria patients but the serum globulin levels were within the normal range among the two groups. The differences of serum albumin and total proteins were significant. Renal function tests showed blood urea levels were within the normal range among the two groups but the serum creatinine levels were significantly high among the microalbuminuria patients. 24 hours Urine albumin levels showed that higher value among the microalbuminuria patients compared to the other group. Urine casts were not present among the both groups. hsCRP levels were compared which showed significant differences among the two groups. The hsCRP levels also showed high levels of CRP with patients having diabetes for more than 10 years compared to patients with duration of diabetes between 5 to 10 years and the difference was statistically significant. the bio markers of the diabetes also showed significant increase in the group having the higher CRP levels.

Conclusion : It has been concluded that higher levels of hs CRP can be a prognostic element for the development of DM. It also has positive correlation with HbA1c, reflecting the glycemic status of the patient. The study shows that the early monitoring of the hsCRP can help managing and identifying the development of the diabetic kidney disease and thus can be managed appropriately and timely to prevent the development of the complications.

Keywords: Diabetes mellitus, High Sensitive C Reactive Protein, Diabetic kidney disease, Albuminuria, Creatinine.

INTRODUCTION

Diabetes mellitus (DM) has become a major and serious threat to global human health. In the population aged 20 to 79 years, approximately 536.6 million people were diagnosed with DM worldwide in 2021, and this number will rapidly grow to 783.2 million in 2045 worldwide (1). Type 2 DM (T2DM) has 90% proportion of DM, which is featured by insulin resistance and relatively insufficient insulin secretion (2). T2DM can lead to many chronic complications, one of which is microvascular complications. In addition, approximately one in four patients with T2DM will have comorbid diabetic kidney disease (DKD) in the progression of T2DM (3). DKD is the most common cause of leading to end-stage renal disease worldwide (4, 5) and is a primary cause of mortality among patients with DM (4). Therefore, early intervention plays a vital role in preventing DKD development. To establish effective intervention strategies for DKD in clinical practice, identifying risk factors related to the presence of DKD is available (6).

Chronic inflammation plays an important role in the development and progression of late complications of diabetes.(7,8) C-reactive protein (CRP), an acute phase reactant, is a highly sensitive marker of inflammation. Its level rises dramatically during an inflammatory processes.(9) 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.(10) CRP has been found to be associated with disorders like DM, cardiovascular disorders, metabolic syndrome, renal failure, etc.(11,12) 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.(13) It is also shown that the level of this marker of inflammation correlates with the levels of glycemic control, such as glycated hemoglobin A1c (HbA1c).(14)

Raised levels of CRP and poor glycemic control lead to macrovascular events and lead to raised diabetes risk in the future.(15) Although several studies have indicated that elevated CRP levels are found in DKD, the evidence of relationship between CRP and DKD is insufficient, and related studies are limited.

Therefore, we conducted this cross-sectional and observational study that aimed to identify the correlation between hs-CRP levels and DKD in patients with T2DM.

Study Objectives

To study the Correlation of High-Sensitivity C-Reactive Protein and renal function in Patients with Type 2 Diabetes Mellitus.

Study design: Cross sectional observational study

Study setting: General Medicine department of the Chettinad Health and Research Institute

Study period: 2 months i.e December 2022 and January 2023

Inclusion criteria

Patients who are known type 2 Diabetes Mellitus

Age 18 – 70 yrs

Diabetic history of more than 5yrs

Exclusion criteria

Age less than 18yrs

Diabetic history of less than 5 yrs

Who did not give consent

Patients who do not have emergency conditions like diabetic ketoacidosis.

Patients who are on ACE's, ARB'S and SGLT2 inhibitors

Sample size

After getting approval from the institutional ethics committee, patients who attended Medicine OPD for Diabetes screening on First week of January were recruited for the study. Convenient sampling Technique is used, 100 patients were enrolled. The data will be collected by pre tested semi structured questionnaire and biochemical tests will be done.

Variables studied based on concomitant diseases, laboratory results, and medical therapy. The study variables were as follows: age; sex (male or female); educational level (under high school/high school or above); hs-CRP ;body mass index (BMI); diastolic blood pressure (DBP); systolic blood pressure (SBP); glycated hemoglobin (HbA1c), blood urea, serum creatinine, Total cholesterol, serum Triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) levels, liver function tests and urine routine.

Microalbuminuria was defined as urine albumin excretion between 30 mg/d and 300 mg/d, and it was tested in 24-hour urine collection samples. High-sensitivity CRP (HS-CRP) CRP levels were measured by photometry method.

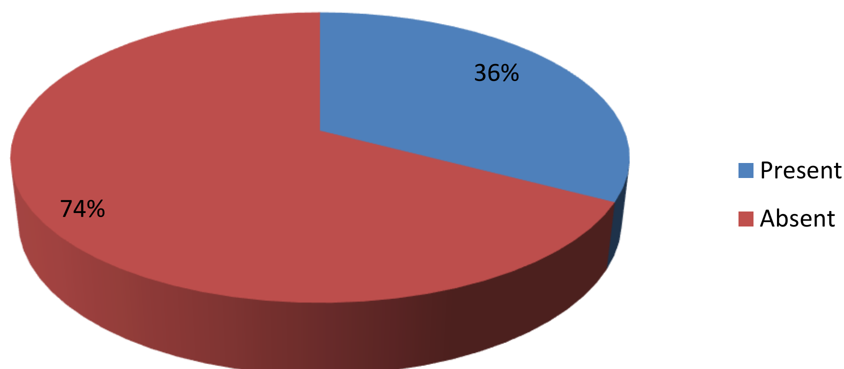
Lipid profile, blood glucose, and serum creatinine were also assessed and blood pressure was measured in a standard condition (sitting position, after 5 minutes of resting, and ceasing smoking, drinking tea or coffee, and overnight fasting).

Statistical analysis:

Continuous variables will be analyzed using student T test, and categorical variables were evaluated using the chi square test to identify intergroup differences. Data will be entered and analyzed using SPSS software version 26.

RESULTS:

Distribution of the study population based on the presence or absence of microalbuminuria



Characteristics of diabetic patients with and without microalbuminuria

	Microalbuminuria		
Parameter	**Positive(n=36)**	**Negative(n=64)**	**P value**
Age , years	55.17 ± 10.58	45.61±6.54	**0.0001**
Male/Female	24/12	39/25	0.324*
Duration of diabetes , years	9.60 ± 6.62	7.95 ± 2.97	**0.0003**
HbA1C	6.66± 1.00	6.44± 1.06	0.303
FBS, mg/dl	190.86±4.05	89.25±2.36	**0.001**
BMI, Kg/m^2	26.33±2.43	25.32±2.55	0.0561
SBP, mmHg	145.56±20.3	123.33±13.4	**0.0001**
DBP, mmHg	87.11 ± 13.46	75.95 ± 11.54	**0.0001**
hsCRP levels, mg/dl	5.21±1.3	2.53 ± 0.64	**0.0001**
Total Cholesterol, mg/dL	200.38±32.62	155.3±33.10	**0.0001**
Triglycerides, mg/dL	176.22±29.29	119.17±36.2	**0.0001**
HDL, mg/dL	40.77±9.9	46.59±10.94	**0.005**
LDL, mg/dL	108.02±20.97	82.34±16.64	**0.0001**
VLDL, mg/dL	31.66±9.63	21.69±6.45	**0.0001**
Serum albumin, g/dl	2.62±0.51	3.85±0.45	**0.0001**
Serum globulin, g/dl	2.43±0.43	2.54±0.39	0.1951
Total protein, g/dl	5.50±1.35	7.24±1.26	**0.0001**
Blood urea, mg/dl	21.93±12.19	20.32±9.93	0.4756
S. creatinine, mg/dl	1.93±0.40	0.70±0.26	**0.0001**
24 hrs Urine albumin, mg/dl	247.13±34.32	27.32±9.64	**0.0001**
Urine casts	NIL	NIL	

*Represents the p value calculated using chi square test

Others was calculated using student T test.

	hsCRP		
Parameter	**Positive(n=27)**	**Negative(n=73)**	**P value**
Age , years	56.8 ± 10.7	48.6 ± 8.0	**0.0001**
Duration of diabetes , years	11.21 ± 6.62	6.99 ± 4.57	**0.0005**
HbA1C	10.50±7.18	6.0±5.22	0.0009
FBS, mg/dl	210.83±33.05	97.45±34.36	**0.0001**

Comparison of the hsCRP levels with duration of diabetes

	Duration of diabetes		
	>10 years	**5-10 years**	**P value**
hsCRP	7.13±1.93	4.47±1.72	**0.0001**

A total of 100 diabetic patients were included in the study during the study period. Figure 2 shows that the among the 100 study population 36% of the diabetics showed microalbuminuria and 64% did not showed microalbuminuria.

Table 1 of the study showed different parameters among the patients with microalbuminuria and without microalbuminuria. Mean age of the study population among the two groups, duration of diabetes, FBS levels, BMI, SBP, DBP levels showed significant difference among the two groups i.e $p<0.05$. HbA1C levels were more among the microalbuminuria patients (6.66± 1.00 v/s 6.44± 1.06) but it was not statistically significant.

Lipid profile the study population showed that the all the patameters showed significant difference among the two groups i.e Total Cholesterol(200.38±32.62 v/s 155.3±33.10), Triglycerides(176.22±29.29 v/s 119.17±36.2), HDL(40.77±9.9 v/s 46.59±10.94) , LDL(108.02±20.97 v/s 82.34±16.64) and VLDL(31.66±9.63 v/s 21.69±6.45).

Among the serum proteins, serum albumin and total protein showed decreased levels among the microalbuminuria patients but the serum globulin levels were within the normal range among the two groups. The differences of serum albumin and total proteins were significant.

Renal function tests showed blood urea levels were within the normal range among the two groups but the serum creatinine levels were significantly high among the microalbuminuria patients. 24 hours Urine albumin levels showed that higher value among the microalbuminuria patients compared to the other group. Urine casts were not present among the both groups.

hsCRP levels were compared which showed significant differences among the two groups.

Based on the manufacturer's instructions, serum HS-CRP levels higher than 4 mg/L were considered positive, and accordingly, the patients were classified as HS-CRP positives and HS-CRP negatives. The mean age, serum triglyceride, and duration of DM were significantly different in patients with a positive HS-CRP (Table 2).The hsCRP levels also showed high levels of CRP with patients having diabetes for more than 10 years compared to patients with duration of diabetes between 5 to 10 years and the difference was statistically significant. the bio markers of the diabetes also showed significant increase in the group having the higher CRP levels. (Table 2)

DISCUSSION

In several studies, it has been reported that there is a correlation between serum CRP levels and microalbumiuia in diabetic patients and even in the general population. (16) These observations suggest that low-grade inflammation, reflected by high serum HS-CRP levels, may play a role in the induction of microalbuminuria. (17)

It is reported that prevalence of microalbuminuria is about 12.6% to 25.3% in patients with type 2 DM.(18,19) There is limited data on type 2 DM nephropathy in Asia and also in Iran.(19)

In this study, there was a rise in BMI in diabetic patients as matched to the control and this is in covenant with the study of Pan et al., 2017.(20)

Raised blood pressure (BP) is an additional vital liberated risk influence for nephropathy. Lower BP was related with decreased risk for development from moderate to severe albuminuria or ESRD. Furthermore, in patients with T2DM, lower BP was connected with deterioration from moderate albumin to normoalbuminuria.(21)

The patients had greater HbA1c levels corresponded with the controls, and adjustment for the Hb1Ac levels would be problematic due to its striking variance between patients and controls.(22) It has been shown that diabetic patients tend to have a higher BMI and tend to be dyslipidemic, with high serum TAG and low HDL C concentrations, which were in agreement with the earlier studies.(23,24) which was similar to our study findings.

hsCRP levels were compared which showed significant differences among the two groups. The hsCRP levels also showed high levels of CRP with patients having diabetes for more than 10 years compared to patients with duration of diabetes between 5 to 10 years and the difference was statistically significant.The stronger association between hs CRP levels and glycemia in Iraqi females compared to males may be clarified by the larger accumulation of subcutaneous fat in females than in males, which is paralleled with earlier study.(25) Furthermore, serum hs CRP levels elevate with BMI in adults and are greater in females than males at all higher levels of BMI.(26)

CONCLUSION:

It has been concluded that higher levels of hs CRP can be a prognostic element for the development of DM. It also has positive correlation with HbA1c, reflecting the glycemic status of the patient. The study shows that the early monitoring of the hsCRP can help managing and identifying the development of the diabetic kidney disease and thus can be managed appropriately and timely to prevent the development of the complications.

Limitations:

Sample size of the study is low the sampling method is convenient sampling. So the generaliszability of the results are questionable. Need a prolong follow-up to know how fast it is progressing to CKD.

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