International Journal of Research in Medical Sciences
Vaishya GP et al. Int J Res Med Sci. 2019 Jul;7(7):2754-2757
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20192913

Original Research Article

Correlational study of interleukin-6 with albuminuria in type 2 diabetes mellitus

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Received: 07 May 2019
Accepted: 31 May 2019

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ABSTRACT

Background: Individuals with type 2 diabetes mellitus display features of low-grade inflammation. Mediators of inflammation such as IL-6 have been proposed to be involved in the events causing as well as progression of diabetes Mellitus. Diabetic nephropathy is one of the commonest causes of chronic kidney failure throughout the world. Although Diabetic nephropathy is traditionally considered a non-immune disease, accumulating evidence now indicates that immunologic and inflammatory mechanisms play a significant role in its development and progression.
Methods: This cross-sectional study was conducted in the department of medicine, UPUMS, Saifai, Etawah, Uttar Pradesh, India. The study was conducted from June 2018 to February 2019. A total of 80 type 2 diabetes patients were included in the study. After informed consent, patients were recruited. FBS, PPBS, HbA1C, 24 Hours Urinary protein and interleukin-6 levels were measured. The data was analysed using SPSS 23. Pearson co relation coefficient was determined between IL -6, HbA1c and Urinary protein.
Result: A total of 80 type 2 Diabetes Mellitus patients were studied. The study subjects were divided into 3 groups based on the urinary protein level into normo-albuminuria, Micro- albuminuria and macro- albuminuria. FBS, PPBS, HBA1c, 24 Hours Urinary protein and Interleukin – 6 were significantly associated with proteinuria ($p<0.001$). Urinary protein was positively correlated with IL-6 ($R2=0.57$, $p<0.01$). The blood glucose was positively correlated with IL-6 ($R^2=0.413$, p-0.01).
Conclusion: Raised IL-6 levels in Diabetes Mellitus revealed the presence of inflammation. Our study showed positive correlation between IL-6, HBA1c and Urinary protein.

Keywords: Albuminuria, Diabetes, Interleukin-6

INTRODUCTION

Individuals with Type 2 Diabetes Mellitus display features of low-grade inflammation. This low-grade inflammation has been proposed to be involved in the pathogenitic processes causing Type 2 Diabetes Mellitus. Inflammatory mechanisms play an important role in the pathogenesis of Type 2 Diabetes Mellitus. Mediators of inflammation such as Interleukin-6 (IL-6) have been proposed to be involved in the events causing as well as progression of Diabetes Mellitus. IL-6 has been proposed to affect glucose homeostasis directly and indirectly by action on skeletal muscle cells, adipocytes, hepatocytes, pancreatic cells, and neuroendocrine cells.[1]A vast number of studies have investigated the role of action/lack of action of IL-6 in the pathogeneses underlying obesity, insulin resistance, beta-cell destruction, Type 1 Diabetes Mellitus, and Type 2 Diabetes Mellitus. Interleukin (IL)-6 is a pleiotropic cytokine with a key role in both immunoregulation and non-immune events in most cell

types and tissues outside the immune system.[2] Interleukin-6 (IL-6) are cytokines with metabolic and/or weight regulating effects. The role IL-6 plays in obesity and insulin resistance remains controversial even after many years of research. Circulating levels of IL-6 are increased in obesity and it has been proposed that IL-6 contributes to the pathogenesis of insulin resistance in different disease states.[3,4,5] Diabetic nephropathy is one of the commonest causes of chronic kidney failure throughout the world.[6] It is one of the commonest complications of diabetes mellitus (DM); which silently follow the DM patients for years and induce the morbidity and mortality in DM patients.[7] Various hemodynamic and metabolic factors may be involved in the developments of renal disorders among DM patients.[7,8] Although diabetic nephropathy is traditionally considered a non-immune disease, accumulating evidence now indicates that immunologic and inflammatory mechanisms play a significant role in its development and progression.[9,10]

METHODS

This cross-sectional study was conducted in the department of medicine, UPUMS, Saifai, Etawah, Uttar Pradesh, India. The study was conducted from June 2018 to February 2019. A total of 80 Type 2 Diabetes Mellitus patients were included in the study. Any patients with acute illnesses including infectious diseases within the past 1 month, malignancy, and active immunological diseases were excluded. Confounding factors for proteinuria such as uncontrolled hypertension (> 160/100 mm Hg) or renal insufficiency (serum creatinine > 1.5 mg/dL) and urinary tract infection were excluded from the study.

After informed consent, patients were recruited. History and physical examination were done. Fasting blood sugar (FBS), Post prandial blood sugar (PPBS) , HbA1C, 24 Hours Urinary protein and interleukin-6 levels were measured. The data was analysed using SPSS 23. The results were expressed in terms of tables and graphs. Student t-Test was used to study association between urinary protein and study variables. Pearson co relation coefficient was determined between IL -6, HbA1c and Urinary protein.

RESULTS

A total of 80 Type 2 Diabetes Mellitus patients were studied. The study subjects were divided into 3 groups based on the urinary protein level into normo-albuminuria, Micro- albuminuria and macro-albuminuria. The mean age of the study population was 52.34±5.85 years. Males were 56.3% and females were 43.7%.

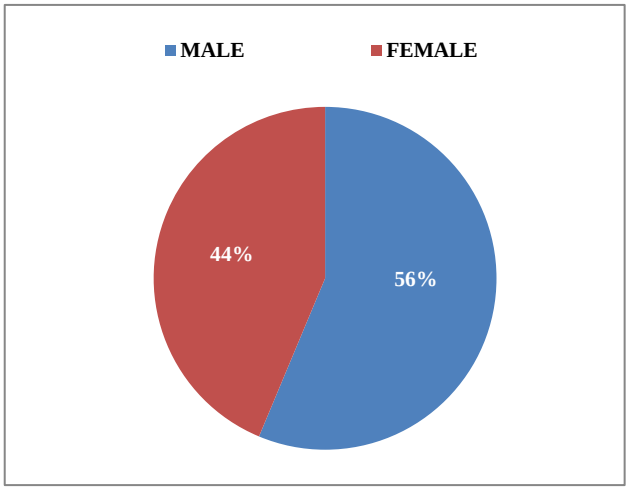

Figure 1: Gender distribution of the study population (N=80).

Table 1: Comparison of variables in diabetes mellitus patients in relation to albuminuria.

	Normo-Albuminuria	Micro-Albuminuria	Macro-Albuminuria	P-value
Age (Years)	51.8±6.2	53.3±5.4	53.6±5.2	0.2
FBS (mg/dl)	121.2±22.3	164.9±37.5	169.6±42	<0.001
PPBS (mg/dl)	192.2±38.4	231.1±53.1	211.8±42.8	<0.001
HBA1C (%)	7.05±0.5	8.2±0.8	8.2±0.6	<0.001
24 HRS urinary protein (mg/d)	8.07±4.8	171.3±62.6	617.4±179	<0.001
IL-6 (pg/ml)	5.6±2.5	16.2±0.8	17.9±0.6	<0.001

The mean age with standard deviation in the groups was 51.8±6.2, 53.3±5.4 and 53.6 ±5.2 respectively. It was not statistically significant between groups and the groups were comparable. Glycaemic control parameters like FBS and PPBS were statistically significant between groups. The mean value of HBA1c was 7.05±0.5 in normo albuminuria group, 8.2±0.8 and 8.2±0.6 in micro and macro albuminuria groups respectively. The differences were statistically significant (P<0.001). Interleukin – 6 levels were 5.6±2.5 in normoalbumiuria group, 16.2±0.8 in microalbuminuria and 17.9±0.6 in macroalbuminuria group. It was significantly associated with proteinuria (p <0.001).

Table 2. Comparison of variables in diabetes mellitus patients in relation to gender.

	Age (years)	FBS (mg/dl)	PPBS (mg/dl)	HBA1C%	24 Urinary Protein(mg/d)
Male	52.3±5.5	140.5±39.3	203.5±40.9	7.6±0.8	187.8±271
Female	52.37±6.3	149±39.4	211±52	7.7±0.8	218.4±265
P-value	0.9	0.3	0.4	0.6	0.6

Various parameters were compared in male and females of the study population. The mean Interleukin-6 level was 10.9±6.2 in males and 11.9±5.9 in females. There was no statistical significance in difference (P=0.4). There was no significant difference between Male and Female in glycaemic control parameters i.e. FBS, PPBS and HBA1c. The mean 24 Hours urinary protein was 187.8±271 in male and 218.4±265 in females. The difference was not statistically significant (P=0.6).

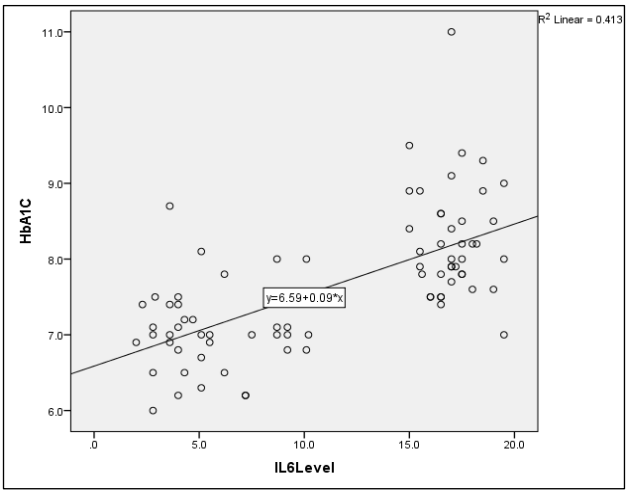

Figure 2. Scatter plot showing Correlation between HBA1c and IL-6 (P value <0.01).

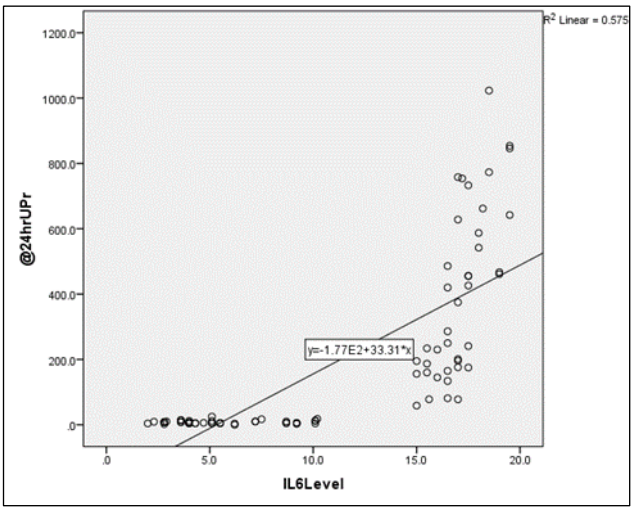

Figure 3. Scatter plot showing Correlation between 24 Hours urinary protein and IL-6 (P <0.01).

It is evident from the Figure 2. that the level of HbA1c has a significant positive correlation with Interleukin-6 level. The P value is < 0.01 and r2 value is 0.413. This signifies the degree of inflammation in diabetes increase with poor glycaemic control, as Interleukin -6 levels linearly increase with poorly controlled Diabetes Mellitus.

The level of 24 Hours Urinary protein was positively correlated Figure 3 with Interleukin-6 level. The P value is <0.01 and r^2 is 0.57. The positive correlation suggests the presence of inflammation in diabetic nephropathy. As the proteinuria increases the interleukin -6 levels were also increased, suggesting a role in progression of diabetic nephropathy.

DISCUSSION

Raised IL-6 levels in Diabetes Mellitus revealed the presence of inflammation. Our study showed positive correlation between IL-6, HBA1c and Urinary protein. Similar studies conducted by Soni S et al.[11] studied 150 diabetic patients in Moradabad. They found that IL-6 was significantly high in microalbuminuria diabetic nephropathy patients compare to normoalbumiuria and IL-6 was significantly high in macroalbuminuria diabetic nephropathy patients compare to microalbuminuria patients. Various studies confirmed the role of inflammation in nephropathy in Diabetes Mellitus patients.[12,13]

Various data suggest that IL-6 causes increase infiltration of macrophages. Interleukin-6 interferes with metabolism of glycosaminoglycan an important component of glomerular basement as well as vascular endothelium.[14] The relationship between insulin resistance and circulating IL-6 levels is well established, there is little information on an independent association between plasma IL-6 levels and insulin secretion.[15]

Conflicting results have also been reported from in vitro studies.[16,17,18] Joshi S.V. et al.[19] showed that there is no direct relationship between fasting blood sugar and IL6 however, raised IL-6 was observed in 66.66% diabetic and in 50% with diabetic neuropathy.

In this study it was observed that though patients with diabetes were within glycaemic control raised IL-6 levels revealed the presence of inflammation.

CONCLUSION

Present study showed positive correlation between IL-6, HBA1c and Urinary protein. Various studies assessed the co relation between interleukin-6 and various variables in Diabetes, but results are variable. Diagnostics and Therapeutic importance of measuring interleukin-6 in diabetes patient is still questionable.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Vaishya GP, Kumar G, Vijayavarman V, Pandey SK, Kumar A, Kiran K. Correlational study of interleukin-6 with albuminuria in type 2 diabetes mellitus. Int J Res Med Sci 2019;7:2754-7.