

## A Cross Sectional Study of Plasma Lipid Profile and Cardiac Risk Markers in Diabetic Nephropathy

Dr. Sridhar Reddy Konuganti<sup>1\*</sup>, Dr. Venkatesh Pabbiseti<sup>2</sup>, Dr. Naresh Tolichuka<sup>3</sup>, Dr. Vijay Kumar Perla<sup>4</sup>

<sup>1\*</sup>Civil Assistant Surgeon, Area Hospital, Zaheerabad.

<sup>2</sup>Associate Consultant, Department of Gastroenterology, Yashodha Hospital, Somajiguda, Hyderabad.

<sup>3</sup>GDMO, DGJAUNTI, Under CDMO Northwest location, Delhi.

<sup>4</sup>Senior Resident, Osmania Medical College, Hyderabad.

Corresponding Author: Dr. Sridhar Reddy Konuganti

### Abstract

**Introduction:** Nephropathy is one of the serious diabetic complications and hemodialysis the common modality employed generally aimed to correct the altered crystalloids as well as to remove accumulated nitrogenous waste products. But it rarely corrects the vascular lipid levels, hence increasing the thrust of dyslipidemia and dyslipidemia induced cardiovascular complications in these patients. A study was planned to assess the cardiovascular risk factors, Cardiac Risk Ratio, Atherogenic Index of plasma and Atherogenic Coefficient in these patients to evaluate the cardiovascular risk.

**Materials and Methods:** Patients of type 2 diabetes suffering from diabetic nephropathy undergoing hemodialysis at Area Hospital, Zaheerabad in the age group of 30-60 years were randomly selected. A heparinised blood sample was collected after obtaining a written consent. Plasma lipid profile, Cardiac Risk Ratio, Atherogenic index of plasma and Atherogenic Coefficient were estimated. Aged matched non-diabetic subjects and type 2 diabetic patients without renal complications served as normal controls and diabetic controls respectively.

**Results:** Levels of FPG, TC, TAG, HDLC, LDLC, VLDLC, CRR, AIP and AC were significantly elevated in patients of diabetic nephropathy.

**Conclusion:** Patients of diabetic nephropathy undergoing regular hemodialysis must be screened frequently for cardiovascular complications.

**Key Words:** Diabetic Nephropathy, Hemodialysis, Cardiac Risk Markers.

Date of Submission: 24-09-2020

Date of Acceptance: 07-10-2020

### I. Introduction

Diabetes Mellitus (DM) is a chronic metabolic complication involving nutrient metabolism in general and glucose metabolism in particular resulting in persistent hyperglycemia and glucosuria.<sup>1</sup> Further this disease involves derangement in lipid turnover leading to dyslipidemia.<sup>2</sup> The persistent hyperglycemia and the DM induced dyslipidemia are the root cause for many life threatening diabetic complications including micro and macro vascular complications.<sup>3</sup>

Nephropathy is one of the serious diabetic complication which makes the life miserable for a diabetic patient whose kidneys normal function is much affected and the patient needs frequent hemodialysis to maintain vascular fluid normalcy as well as to thrive-on.<sup>4</sup>

Hemodialysis is generally aimed to correct the altered blood crystalloid substances as well as to remove the accumulated metabolic nitrogenous waste products, but it rarely corrects the vascular lipid levels which tends to alter in a diabetic patient due to underlying dyslipidemia, thus driving the diabetic nephropathic (DN) patients to dyslipidemia induced cardio-vascular complications.<sup>5</sup> Though raised levels of VLDL, LDL and triacylglycerols have been agreed as the risk factors of CVD but the significance of cardiac risk markers - Cardiac Risk Ratio (CRR), Atherogenic Index of Plasma (AIP) and Atherogenic Coefficient (AC) in DN patients have not been established.

Hence a study was undertaken to assess the plasma lipid profile parameters as well as the cardiovascular risk factor in DN patients undergoing Hemodialysis.<sup>6</sup>

## II. Materials And Methods

The present analytical cross-sectional study was carried-out during January-April 2019 by Department of General Medicine, Area Hospital, Zaheerabad. A total number of 150 subjects including normal control subjects (n=50), control diabetic subjects (n=50) and diabetic with renal complications (n=50) were included in the present study. The type-2 diabetes mellitus patients, in the age group of 30-60 years and are without any diagnosed diabetic complications (as screened by expert clinical examination) attending medical outpatient department of Area Hospital, Zaheerabad were randomly selected for the present study and were employed as control diabetic subjects (group-2). The diabetic subjects in the age group of 30-60 years with diagnosed renal complications and are undergoing routine hemodialysis (biweekly) at Area Hospital, Zaheerabad taken as DN patients (Group-3). The age- matched normal control subjects were taken from the employees of Area Hospital, Zaheerabad (group-1). A fasting heparinised blood sample (4-6 ml) was collected from normal control subjects (group-1), control diabetic subjects (group-2) and from the DN patients (Group-3) after obtaining an informed consent from each one of them.

The blood samples were centrifuged at 3000 rpm for 6-8 mins and the separated clear plasma was employed for the estimation of glucose, total cholesterol, triacylglycerols (TAG), and HDL-cholesterol levels. Using the data VLDL cholesterol (VLDLC), LDL-cholesterol (LDLC) levels as well as the cardio-vascular risk indicators Atherogenic Coefficient (AC), Atherogenic Index of Plasma (AIP) and Cardiac Risk Ratio (CRR) were evaluated using the following standard relations.

- $VLDLC = (TAG/5)$
- $LDLC = (TC - HDLC - VLDLC)$
- $CRR = (TC/HDLC)$
- $AIP = \log (TAG/HDLC)$
- $AC = (TC-HDLC/HDLC)$

## III. Results

A total number of 150 subjects were involved in the present study including 50 in group-1, 50 in group-2 and 50 in group-3 subjects. Results obtained in the present study are depicted in table-1 and table-2. Table-1 narrates the plasma levels of glucose (Fasting plasma glucose), total cholesterol (TC), triacylglycerol (TAG), HDL-cholesterol (HDLC), LDL-cholesterol (LDLC) and VLDL-cholesterol (VLDLC) in group-1, group-2 and group-3. It is evident from the table that the levels of FPG, TC, TAG, HDLC, LDLC and VLDLC are significantly elevated in group-2 patients as compared to group-1, whereas except FPG all other parameters are significantly increased in group-3 as compared to group-2 patients.

	FPG (mg/dl)	TC (mg/dl)	TAG (mg/dl)	HDLC (mg/dl)	LDLC (mg/dl)	VLDLC (mg/dl)
<b>Group 1 (50)</b>	88.27±13.30	168.38±22.25	98.60±10.25	59.92±9.50	91.31±46.39	20.92±6.30
<b>Group 2(50)</b>	152.31±21.80***	216.20±26.50***	218.80±36.60***	39.90±16.92***	98.62±39.25**	44.06±11.38***
<b>Group 3 (50)</b>	216.0±27.0	132.62±18.50***	132.71±18.30***	24.94±11.50***	83.25±9.30**	27.54±8.98***

*Table 1. Plasma Levels of Fasting Plasma Glucose (FPG), Total Cholesterol (TC), Triacylglycerols (TAG), HDL-Cholesterol (HDLC), VLDL Cholesterol (VLDLC), and LDL-Cholesterol (LDLC)*

**Note**

1. The values expressed as their Mean±SD.
2. The number in parentheses indicates the number of subjects.
3. Probability \* p>0.05, \*\*p>0.01 and \*\*\*p>0.001.

	CRR	AIP	AC
<b>Group 1 (50)</b>	2.81±0.72	1.66±0.15	1.82±0.18
<b>Group 2 (50)</b>	6.27±1.98***	6.21±1.65***	5.27±1.98**
<b>Group 3 (50)</b>	6.32±2.02	6.47±1.98	5.32±1.95

*Table 2. Cardiac Risk Ratio (CRR), Atherogenic Index of Plasma (AIP) and Atherogenic Coefficient (AC) in Group 1, Group 2 as Well as in Group 3*

**Note**

1. The values expressed as their Mean ± SD.
2. The number in parentheses indicates the number of subjects.
3. Probability \* p>0.05, \*\*p>0.01 and \*\*\*p>0.001.

Table-2 gives the levels of CRR, AIP and AC in group-1, group-2 and group-3. It is clear from the table that all the three calculated parameters are significantly elevated in group-2 and group-3 as compared to group-1 suggesting both group-2 and group-3 patients are prone to cardio-vascular risk threat though they are undergoing regular hemodialysis (constant clinical supervision).

#### IV. Discussion

DM is a multi-systemic abnormality characterized by increased blood glucose levels (hyperglycemia), increased blood lipid levels (hyperlipidemia) with a prevalence to develop micro and macro vascular complications,<sup>7</sup> hence the diabetic patients are more prone to cardiovascular diseases. The more relevant predisposing factor of DM induced vascular complications is dyslipidemia, an alteration in the composition and concentrations of lipid levels in the body.<sup>8</sup> The basic components of body lipids apart from free fatty acids are TAG, cholesterol and phospholipids. As the metabolism of triacylglycerols and cholesterol is much affected in diabetic condition, due to insufficient amount or insufficient functioning of hormone insulin and also due to more availability of precursor substances like acetyl CoA, fatty acids and glycerol-phosphate. Resulting in elevated formation of these basic lipid components leading to dyslipidemia, which further results in cardio vascular complications.<sup>9</sup>

Further DM is considered as a chronic inflammatory disease and normally inflammatory conditions trigger the release of cell signaling compounds like cytokines, interleukins, tissue necrotic factors and others causing alterations in systemic lipid metabolism and lipid turnover through stimulating SREBP target genes as well as by of-regulation HMG CoA educates gene. This leads to an increase in the systemic synthesis of lipids including cholesterol which is need of inflammatory state for the extra lipid requirement. The elevation observed in cardiovascular risk indicators in group-2 and group-3 patients as observed in the present study (table 3) indicates these patients are more vulnerable group for the development of cardiovascular complications. Though there is significance of decreased HDLC in predicting the cardiovascular risk, the importance of raised plasma TAG levels as cardiovascular risk marker cannot be ignored. The development of cardiovascular complications, including atherosclerosis, is a multi-factorial process and the raised plasma lipid levels as well as dyslipidemia are the major key factors.<sup>10</sup>

The two principle lipid constituents, triacylglycerols and cholesterol make up the lipoproteins salient lipid transporting particles in humans. The very low density lipoproteins (VLDL) mainly transport endogenous or liver synthesized TAG whereas the cholesterol is being transported by low density lipoproteins (LDL) and High density lipoproteins (HDL).<sup>11</sup> The development of cardiovascular disease is generally predicted by cardiovascular risk indicators and the principally employed risk indicators are cardiac risk ratio (CRR), atherogenic index of plasma (AIP) and atherogenic coefficient (AC). The results obtained in the present study in group-2 and group-3 patients (Table 3 and 5) indicates that risk indicators CRR, AIP and AC are significantly elevated in these patients proving that these patients are more susceptible for cardiovascular complications and specific remedial steps are necessary in considering their treatment.<sup>12</sup>

It is further clear by the results depicted in table-1 that the plasma lipid parameters are significantly lowered in group-3 patients as compared to group-2 patients falsely suggesting that the diabetes induced dyslipidemia in under control, but this may be due to regular hemodialysis which might have cleared many of the lipogenic precursors from the system. It is clear by the results of the present study shown in table-3 that the DN patients (group-3) are under great cardiovascular risk as indicated by the significant elevations seen in all the cardiac risk indicators (refer table-3).<sup>13</sup>

#### V. Conclusion

In DN patients, plasma lipid profile parameters do not throw much light on the prediction of cardiovascular complications. In these patients, cardiac risk markers are better predictors of cardiac risk. Hence, the DN patients undergoing regular hemodialysis must be screened frequently for their plasma cardiac risk indicators in order to control the development of cardiovascular complications

#### References

- [1]. Johansen JS, Jensen BV, Roslind A, Nielsen D, Price PA: Serum YKL-40, a new prognostic biomarker in cancer patients? *Cancer Epidemiol Biomarkers Prev.*2006;15:194 –202.
- [2]. Recklies AD, White C, Ling H: The chitinase 3-like protein human cartilage glycoprotein 39 (HC-gp39) stimulates proliferation of human connective tissue cells and activates both extracellular signal-regulated kinase-and protein kinase B-mediated signalling pathways. *Biochem J.*2002;365:119 –126.
- [3]. Jun Ho Le, Sang Soo Kim , In Joo Kim, Sang Heon Song. Clinical implication of plasma and urine YKL-40, as a proinflammatory biomarker, on early stage of nephropathy in type 2 diabetic patients. *Journal of Diabetes and Its Complications.*2012;26:308-312.
- [4]. Anders R. Nielsen, Christian Erikstrup, Julia S. Johansen, Rikke Krogh-Madsen, Sarah Taudorf et al. Plasma YKL-40 .A BMI-Independent Marker of Type 2 Diabetes. *Diabetes .*2008;57: 3078-3082.
- [5]. A. K., Omerovic, E., & Vestergaard, H. YKL-40 levels are independently associated with albuminuria in type 2 diabetes. *Cardiovascular Diabetology.*2011; 10 (54):1-6.
- [6]. Zachary T. Bloomgarden. Blood pressure and diabetic nephropathy. *Diabetes care.* 2010; 33(3):e30-e35.

*A Cross Sectional Study of Plasma Lipid Profile And Cardiac Risk Markers In Diabetic Nephropathy*

- [7]. Matheson, A., Willcox, M. D., Flanagan, J., & Walsh, B. J. Urinary biomarkers involved in type 2 diabetes: a review. *Diabetes/Metabolism Research and Reviews*.2010;26:150–171.
- [8]. Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, Kofoed Enevoldsen A: Albuminuria reflects widespread vascular damage. The Steno hypothesis. *Diabetologia*.1989;32:219-226.
- [9]. Rathcke CN, Vestergaard H: YKL-40, a new inflammatory marker with relation to insulin resistance and with a role in endothelial dysfunction and atherosclerosis. *Inflamm Res*.2006;55:221-227.
- [10]. Thomsen SB, Rathcke CN, Zerahn B, Vestergaard H: Increased levels of the calcification marker matrix Gla Protein and the inflammatory markers YKL-40 and CRP in patients with type 2 diabetes and ischemic heart disease. *CardiovascDiabetol*.2010;9:81-86.
- [11]. Yasuda T, Kaneto H, Katakami N, Kuroda A, Matsuoka TA, Yamasaki Y, Matsuhisa M, Shimomura I: YKL-40, a new biomarker of endothelial dysfunction, is independently associated with albuminuria in type 2 diabetic patients. *Diabetes Res Clin Pract*.2011;91:e50-e52.
- [12]. Eknoyan G, Hostetter T, Bakris GL, et al. Proteinuria and other markers of chronic kidney disease: a position statement of the National Kidney Foundation and the National Institute of Diabetes and Digestive and Kidney Diseases. *Am J Kidney Dis*.2003; 42:617-622.
- [13]. Rathcke, C. N., Raymond, I., Kistorp, C., Hildebrandt, P., Faber, J., & Vestergaard. Low grade inflammation as measured by levels of YKL-40: association with an increased overall and cardiovascular mortality rate in an elderly population. *International Journal of Cardiology*.2010;143:35-42.

Dr. Sridhar Reddy Konuganti, et. al. "A Cross Sectional Study of Plasma Lipid Profile and Cardiac Risk Markers in Diabetic Nephropathy." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(10), 2020, pp. 38-41.