ORIGINAL ARTICLE

Role of Serum Triglycerides in Development and Progression of Diabetic Nephropathy

IMRAN ALI ZAIDI¹, HALEEMA SAJID², SOBIA NIAZ³, SHAMAILA DOGGAR⁴, FAROUK QAMAR MALIK⁵, SANA HAFEEZ⁶

¹Assistant Professor of Biochemistry, Fatima Memorial College of medicine and dentistry Lahore.

Correspondence to Dr. Imran Ali Zaidi, Email: imranalisir@hotmail.com, Cell: 0331-5408383

ABSTRACT

Background: Hypercoagulation is hallmark complication of Diabetes mellitus where increased coagulability of blood manifests in the form of more clot formation. Type 2 Diabetes Mellitus is a longstanding metabolic abnormality indicated by elevated sugar values in blood and insulin resistance.

Aim: To evaluate role and association of serum triglycerides levels in onset and progression of diabetic nephropathy.

Materials: 120 patients are included in our study and cases are managed into 02 groups(60 patients each group).

A Group: included diabetic cases without nephropathy

B Group: included 60 diabetes patients with nephropathy

The study data was then analyzed by software SPSS 21 number version. The Probability (P statistical Value) value of ≤ 0.05 was decided as convincing number statistically.

Results. The serum triglycerides levels were 159± 13 in A group and 210± 13 in the B group. The unpaired(independent) samples T- statistical test was utilized Using a two-tailed 0.05 criterion, the test showed remarkable difference between the two groups statistically (p value was < 0.05) in relation to serum triglycerides. Based on the inferences of the unpaired (independent sample) t- statistical test (p value was less than 0.05), we repudiated the null statistical hypothesis.

Conclusion: Hypertriglyceridemia plays significant part in onset, development and progression of nephro-pathy in diabetic patients.

Keywords: Hypertriglyceridemia, Diabetic Nephropathy, Diabetes Mellitus

INTRODUCTION

Hypercoagulation is hallmark complication of Diabetes mellitus where increased coagulability of blood manifests in the form of more clot formation^{1,2,3}.

Type 2 Diabetes Mellitus is a longstanding metabolic abnormality indicated with elevated sugar levels in blood and insulin resistance. Major complications of diabetes include dysfunctioning of major body organs or systems like kidneys, cardiovascular system, eye retina, liver or body neurons^{4,5,6}.

Diabetic nephropathy is a type of diabetic renal disease and is considered as one of the topmost etiological factor of end stage renal disease. It is classified as a micro-vascular complication of diabetes and is seen in both types of diabetes mellitus I and II. The disorder is diagnosed with persistent albuminuria and a gradual reduction in the glomerular filtration rate (GFR)^{7,8}.

Many factors including abnormal triglycerides level play significant role in onset and progression of diabetic nephropathy⁹.

nephropathy is diagnosed by microalbuminuria which is defined as urine albumin excretion of 30-300mg/24 hours 10.

Diabetic nephropathy is screened by either 24 hour urine collection (gold-standard) or measurement of spot urine for microalbuminuria evaluation¹¹.

Hypertriglyceridemia is considered as frequent serum lipid disorder in diabetes patients. Serum Triglycerides levels are increased alongwith the hyperglycemia in diabetics, but hyperinsulinemia joined by insulin resistance is also linked with abnormal Triglyceride levels. Chemical structure of Triglycerides shows three fatty acid molecules, moreover, the circulating plasma free fatty acids plays an important role in Triglyceride synthesis in hepatocytes^{12,13}.

Diabetic nephropathy definition under the broad term of Chronic renal(kidney) disease (abbreviated as CKD) is coined as occurrence of renal functions deterioration and the estimated rate (eGFR) of glomerular filtration < 60 ml per min per 1.73 meter square of body surface area, present for a period of 3 months or

Received on 09-03-2022 Accepted on 17-07-2022 more¹⁴. In the past few years, elevation of serum triglyceride has been related to onset and progression of nephropathy in diabetics¹⁵.

Through this research process we are evaluating an association of serum triglyceride levels with onset and progression of diabetic nephropathy in diabetic patients.

METHODS & MATERIAL

This cross sectional statistical model was conducted in Medical unit 2 Services Hospital Lahore from 1st January 2022- 30th June 2022. Total 120 cases are arranged into two groups (60 patients per group) were included in our study. Purposive sampling method with Non Probability technique was used.

A Group: included diabetes cases not having nephropathy B Group: included diabetes patients having nephropathy **Included samples criteria:**

- Patients of Type II Diabetes (DM) with and without diabetic nephropathy.
- Age range 18-75.
- Both genders.

Excluded samples criteria:

- Patients with kidney disease due to some other causes like infections, drugs, idiopathic.
- Patients with familial hypercholesterolemia and related lipid abnormalities.
- 3. Severe hepatic or cardiac failure or malignancy patients.
- 4. Patients in multi-organ failure.

Statistical analysis of data: The assessment of research data was completed with SPSS soft-ware on model 21 with windows of the computers. Descriptive statistics/inferences are calculated by the formula mean ± Standard deviation (SD). The un-paired (independent) samples t statistical test was projected for calculating variables means. The Probability value of statistics (P-statistical values < 0.05 are thought to be remarkable values statistically.

Biochemical analysis: Serum triglycerides values are checked by the help of chemistry analysis machine 902 numbered Hitachi from Roche group of Germany.

²Assistant Professor of Biochemistry, Lahore Medical and Dental College, Lahore.

³Associate Professor of Physiology, Gujranwala Medical College Gujranwala.

⁴Assistant Professor of Physiology, FMH College of Medicine & Dentistry, Lahore.

⁵Medical Director, Genesis Healthcare consultants, 96-Shadman, Jail Road Lahore

⁶PhD Scholar, Department of Zoology, University of the Punjab Lahore

RESULTS

Table 1: A Group diabetic patients without diabetic nephropathy (n=60)

Variables	Units	(Mean + SD)	P value
Serum Triglyceride	mg / dl	159± 13	< 0.05

Table 2: B Group cases having diabetic nephro-pathy (n=60)

Variables	Units	(Mean <u>+</u> SD)	P value
Serum Triglyceride	mg/dl	210± 13	< 0.05

The serum triglycerides levels were 159± 13 in A group and 210± 13 in B group. The unpaired (independent) samples t-statistical test was put in order for checking that is there any remarkable difference between diabetic patients not having nephropathy (A Group) and diabetes patients having nephropathy (B Group) in relation to serum triglycerides. Using a two-tailed 0.05 criterion, the difference between two groups was numerically remarkable in statistics. Relying on the results of the unpaired (independent) t-statistics test (probability value of less than 0.05), we repudiated the null statistical hypothesis.

Table 3: The unpaired(independent) samples t statistical test comparing Serum Triglycerides in A group and B group

Study Variable	A Group (mean±SD)	B Group (mean±SD	P value
Serum Triglyceride (mg/dl)	159± 13	210± 13	< 0.05

DISCUSSION

Deranged lipid profile plays crucial part in onset, development and progression of nephro-pathy in diabetes type 2(DM TYPE II) and ultimately leads to poor prognosis and early mortality^{16,17}.

In a study done in the United Kingdom, 50 % of cases with type II DM(diabetes mellitus) had elevated serum levels of Triglycerides. ¹⁸ Diabetic nephro-pathy is considered as most prevalent and imminent diabetes complications, characterized by excessive excretion of urinary proteins and kidney insufficiency. ¹⁹

Our study showed that high serum triglycerides levels were significantly associated with renal diseases in diabetics.

Various studies have established relationship between triglycerides abnormalities with more fast progression of renal nephropathy in diabetics.

Zaman et al conducted a work on plasma triglycerides link and association with chronic diseases of the kidneys in DM patients of type 2 and concluded that higher serum triglycerides were significantly associated with establishment and propagation of chronic renal disorder in diabetic patients which is the same finding given in our study²⁰.

In another research paper floated publically by Penno et al, it is concluded that hypertriglyceridemia is independently linked and attached with nephro-pathy in DM patients of type 2 which is in consensus with our work project. Moreover they suggested aggressive statin therapy alongwith fibrates is beneficial for patients to avoid nephropathy in chronic diabetes²¹.

In another publication by Palazhy et al, high serum triglycerides were found to be 160.14±84.7 in diabetic subjects without nephropathy and 189.64±114.71 in diabetics with nephropathy. This is in agreement with our findings that uncontrolled hypertriglyceridemia leads to overt nephropathy in diabetic patients²².

In research program of Toth et al, more hospitalization was observed in diabetic patients with new onset kidney disease with elevated triglyceride levels (≥150 mg/dL) identifying hypertriglyceridemia as potential risk factor of diabetic nephropathy onset and progression. This is also in agreement with our study results²³

Omega 3 fatty acid supplementation may be beneficial in reducing albuminuria and maintaining renal function in patients of diabetic nephropathy^{24,25}.

Our study suggests an important role of serum triglycerides in onset, development and progression of diabetic nephropathy in DM patients of type II.

Study constraints: This research model has certain constrainsts. The number of cases selected for research were small numbered. Other risk factors were not included in this researchmodel. Henceforth It is presumed that in future studies, based upon large population numbers, we can get minute details, explanations and implications of this linkage and association diabetes with nephropathy in DM type II diabetics with risk factors better elucidated...

CONCLUSION

Our research model proposed that high serum triglycerides contribute significantly in development and progression of nephropathy in diabetic patients.

Recommendations: It is recommended based on this study that early drug therapy like statins and fibrates and early management may be initiated to lower serum triglyceride levels in order to prevent onset and progression of diabetic nephropathy in diabetic patients. Moreover omega 3 fatty acid supplementation should be given to patient of diabetic nephropathy for reducing albuminuria and to slow down the process of renal damage.

Contribution by Authors: IAZ: Corresponding Author and Main Researcher, HS: Literature search and Referencing, SN: Statistical Analysis,SD: Data collection and manuscript writing, FQM: Manuscript editing and proofreading., SH: Biochmeical Analysis Acknowledgments: The authors acknowledge Department of Medicine Services Hospital Lahore for sampling, data collection and working facilities for this study project.

REFERENCES

- Pretorius L, Thomson GJA, Adams RCM, Nell TA, Laubscher WA, Pretorius E. Platelet activity and hypercoagulation in type 2 diabetes. Cardiovasc Diabetol. 2018;17(1):141
- Ephraim RK, Awuku YA, Adu P, Ampomah LT, Adoba P, Panford S, et al. High risk of coagulopathy among Type-2 Diabetes Mellitus clients at a municipal hospital in Ghana. Ghana Med J. 2017; 51(3):101-107.
- 3. Vinik AI, Erbas T, Park TS, Nolan R, Pittenger GL. Platelet dysfunction in type 2 diabetes. Diabetes Care. 2001; 24(8):1476-85
- Demir S, Nawroth PP, Herzig S, Ekim Ustunel B. Emerging Targets in Type 2 Diabetes and Diabetic Complications. Adv Sci (Weinh). 2021; 8(18)
- Daryabor G, Atashzar MR, Kabelitz D, Meri S, Kalantar K. The Effects of Type 2 Diabetes Mellitus on Organ Metabolism and the Immune System. Front Immunol. 2020; 11:1582.
- Lorenzo C, Okoloise M, Williams K, Stern MP, Haffner SM. The metabolic syndrome as predictor of type 2 diabetes: the San Antonio heart study. Diabetes Care. 2003; 26:3153–9
- McFarlane P, Cherney D, Gilbert RE, Senior P. Chronic Kidney Disease in Diabetes. Diabetes Canada Clinical Practice Guidelines Expert Committee. Can J Diabetes. 2018; 42 Suppl 1:S201-S209.
- Sulaiman MK. Diabetic nephropathy: recent advances in pathophysiology and challenges in dietary management. Diabetol Metab Syndr. 2019; 11:7.
- Russo G, Piscitelli P, Giandalia A, Viazzi F, Pontremoli R, Fioretto P et al. Atherogenic dyslipidemia and diabetic nephropathy. J Nephrol. 2020; 33(5):1001-1008.
- LambersHeerspink HJ, Gansevoort RT, Brenner BM, Cooper ME, Parving HH, Shahinfar S et al. Comparison of different measures of urinary protein excretion for prediction of renal events. J Am Soc Nephrol. 2010;21(8):1355–60
- Witte EC, LambersHeerspink HJ, de Zeeuw D, Bakker SJ, de Jong PE, Gansevoort R. First morning voids are more reliable than spot urine samples to assess microalbuminuria. J Am Soc Nephrol. 2009; 20(2): 436-43.
- Reaven GM: Compensatory hyperinsulinemia and the development of an atherogenic lipoprotein profile: the price paid to maintain glucose homeostasis in insulin resistant individuals. Endocrinol Metab Clin North Am. 2005; 34: 49-62.
- Lewis GF, Uffelman KD, Szeto LW, Weller B, Steiner G: Interaction between free fatty acids and insulin in the acute control of very low density lipoprotein production in humans. J Clin Invest. 1995; 95: 158-166.
- 14. Vaidya SR, Aeddula NR. Chronic Renal Failure. 2021.
- Hirano T, Satoh N, Kodera R, Hirashima T, Suzuki N, Aoki E et al. Dyslipidemia in diabetic kidney disease classified by proteinuria and renal dysfunction: A cross-sectional study from a regional diabetes cohort. J Diabetes Investig. 2022; 13(4):657-667

- Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney Int. 2003; 63(1):225–32.
- Rutledge JC, Ng KF, Aung HH, Wilson DW. Role of triglyceride-rich lipoproteins in diabetic nephropathy. Nat Rev Nephrol. 2010;6(6):361– 70.
- U.K. Prospective Diabetes Study 27. Plasma lipids and lipoproteins at diagnosis of NIDDM by age and sex. Diabetes Care. 1997;20(11):1683–7
- Parving HH, Persson F, Rossing P. Microalbuminuria: a parameter that has changed diabetes care. Diabetes Res Clin Pract. 2015;107:1–
- Zaman SB, Karim MA, Hossain N, Al Kibria GM, Islam SMS. Plasma triglycerides as a risk factor for chronic kidney disease in type 2 diabetes mellitus: Evidence from northeastern Thailand. Diabetes Res Clin Pract. 2018; 138:238-245
- Penno G, Solini A, Zoppini G, Fondelli C, Trevisan R, Vedovato M et al. Renal Insufficiency And Cardiovascular Events (RIACE) Study Group. Hypertriglyceridemia Is Independently Associated with Renal,

- but Not Retinal Complications in Subjects with Type 2 Diabetes: A Cross-Sectional Analysis of the Renal Insufficiency And Cardiovascular Events (RIACE) Italian Multicenter Study. PLoS One. 2015: 10(5)
- Palazhy S, Viswanathan V. Lipid Abnormalities in Type 2 Diabetes Mellitus Patients with Overt Nephropathy. Diabetes Metab J. 2017; 41(2):128-134.
- Toth PP, Philip S, Hull M, Granowitz C. Elevated Triglycerides (≥150 mg/dL) and High Triglycerides (200-499 mg/dL) Are Significant Predictors of Hospitalization for New-Onset Kidney Disease: A Real-World Analysis of High-Risk Statin-Treated Patients. Cardiorenal Med. 2019;9(6):400-407.
- 24. Han E, Yun Y, Kim G, Lee YH, Wang HJ, Lee BW et al. Effects of Omega-3 Fatty Acid Supplementation on Diabetic Nephropathy Progression in Patients with Diabetes and Hypertriglyceridemia.
- de Boer IH, Zelnick LR, Ruzinski J, et al. Effect of Vitamin D and Omega-3 Fatty Acid Supplementation on Kidney Function in Patients With Type 2 Diabetes: A Randomized Clinical Trial. *JAMA*. 2019;322(19):1899–1909