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Effect of Hypertriglycridemia on the Frequency of Albuminuria in Saudi Populaion with Type 2 Diabetes Mellitus

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Abstract

Background: *Diabetes is one of the most common chronic diseases. The development of albuminuria in type 2 diabetes (T2DM) might be induced by hypertriglycridemia.*

Methods: *The study was retrospective conducted at the Primary Health Care Clinics at King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia. A total of 1590 Saudi with T2DM were randomly selected.*

Results: *Total of 1590 patients with T2DM included in this study; 642 (40.4%) male and 948 (59.6%) female with mean age 55.7 ± 12.1 years. Hypertension was present in 899 (56.5%). Mean BMI 31.8 ± 6.8, HbA1c was 8.2± 2.2, mean TG was 2.3 ± 1.7 mmol/l and mean albumin excretion rate was 73.3 ± 226.6. Albuminuria was present in 525 (33.0%) and was significantly more prevalent in female (50.7%) with female predominance (sex ratio male: female) 1:1.1. Cases with albuminuria have significantly higher HbA1c compared to normalbuminuria, 8.7±2.2 vs. 8.0±2.2 respectively, p<0.0001. HTN with albuminuria was more frequent in 355(67.6%) of albuminuria group with odd ratio 2.0 (1.6-2.6), p<0.0001. The mean triglycerie is higher in age groups 30-39 and 40-49 years with significant male predominant across age groups.*

Conclusion: *We conclude that hypertriglyceridemia should be considered as a potential risk factor and as a diagnostic biomarker to be used in conjunction with other biochemical markers for early diagnosis, assessment, and follow-up of albuminuria.in diabetic patients by using a continuing, comprehensive and coordinated ap-proach.*

Keywords: *Type 2 diabetes, albuminuria and hypertriglycridemia*

1. INTRODUCTION

Diabetes mellitus remains a challenge to public health worldwide. Diabetic nephropathy is the leading cause of end stage renal disease.[1] Moderately increased albuminuria formerly known as microalbuminuria is the first clinical sign of involvement of kidneys in patients with Type 2 diabetes (T2DM). It is also responsible for about third of all patients requiring renal replacement therapy. The development of diabetic nephropathy is characterized by progressive increase in the excretion of protein particularly albumin. Urinary albumin leakage is a manifestation of generalized vascular damage.[2] The estimation of the burden of albuminuria and its strength of association with cardiovascular disease would guide the management of public health programs for prevention and management of chronic disease. Such targeted strategies could be particularly useful in population shown to be at high risk of cardiovascular disease, diabetes or micro albuminuria.[2]

Diabetic dyslipidemia is common in T2DM and is characterized by high levels of fasting triglycerides (TG), low high density lipoprotein cholesterol levels, and predominance of small, dense low density lipoprotein cholesterol particles.[3] Moreover, the majority of patients with T2DM show high and prolonged postprandial lipemia after meals.[4] Hyperlipidemia has been found to be a risk factor for albuminuria in patients with diabetes.[5] Specifically, TG levels have been indicated as a strong independent determinant of micro albuminuria and macro albuminuria in diabetes and have been reported to be an important contributing factor in the progression of diabetic

nephropathy.[6,7] Elevated triglyceride-rich lipoproteins, a key factor of altered lipid profile in diabetic nephropathy, is present even in the earlier stages of renal disease.

Although T2DM is more common in Saudi Arabia than in Europe, very little is known about complications and their risk factors in Saudi Arabia. There have been few studies on the influence of hypertriglyceridemia on albuminuria in Saudi populations. In this study we report on the frequency of albuminuria in patients with T2DM and hypertriglyceridemia attending a primary care clinics in Saudi Arabia.

2. METHODS

The study is a retrospective conducted at the Primary Health Care Clinics at King Fahad Armed Forces Hospital. A total of 1590 Saudi with T2DM were randomly selected. The demographic data and medical history were documented. Blood Pressure readings were within a gap of 15 minutes using a mercury sphygmomanometer by palpation and auscultation method in right arm in sitting position. Two readings, 15 min apart, were taken and the average of both the readings was taken for analysis. Hypertension (HTN) was also diagnosed based on anti HTN medications or having a prescription of antihypertensive drugs and were classified as Hypertensive irrespective of their current blood pressure reading or if the blood pressure was greater than 140/90 mmHg i.e. systolic BP more than 140 and diastolic BP more than 90 mm of Hg – Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines.[8] HbA1c was expressed as percentage. High performance liquid chromatography was used. Albuminuria was assessed by measurement of mean albumin excretion rate (AER) on timed, overnight urine collections. We use a polyclonal radioimmunoassay for albumin measurement. Albuminuria was defined as AER ≥30 g/min in overnight urine collections (equivalent to ≥30 mg/g creatinine in a random spot sample).[9] The method used for determining TG levels in the laboratory was the Enzmatic method.

3. STATISTICAL ANALYSIS

Univariate analysis of baseline demography and clinical laboratory were accomplished using unpaired t-test. Chi square(X^2) test were used for categorical data comparison. The independent relationship between risk factors and the odds ratio of having albuminuria were analyzed using logistic regression. All statistical analyses were performed using SPSS Version 22.0. All P values were based on two-sided tests. $P<0.05$ was considered to be significant.

4. RESULTS

Total of 1590 patients with T2DM included in this study; 642 (40.4%) male and 948 (59.6%) female with mean age 55.7 ± 12.1 years, table 1. Hypertension was present in 899 (56.5%). Mean BMI 31.8 ± 6.8, HbA1c was 8.2± 2.2, mean TG was 2.3 ± 1.7mmol/l and mean albumin excretion rate was 73.3 ± 226.6. Albuminuria was present in 525 (33.0%) and was significantly more prevalent in female (50.7%) with female predominance (sex ratio male: female) 1:1.1, table 2. Cases with albuminuria have significantly higher HbA1c compared to normalbuminuria, 8.7±2.2 vs. 8.0±2.2 respectively, $p<0.0001$. HTN with albuminuria was more frequent in 355(67.6%) of albuminuria group with odd ratio 2.0 (1.6-2.6), $p<0.0001$, table 2 and 3. Figure for the mean TG according to age groups stratified by gender in patients with albuminuria showed the mean TG is higher in age group 30-39 and 40-49 years with significant male predominant across age groups.

Table1: *Demographic patients parameters (mean ± standard deviation or number (%))*

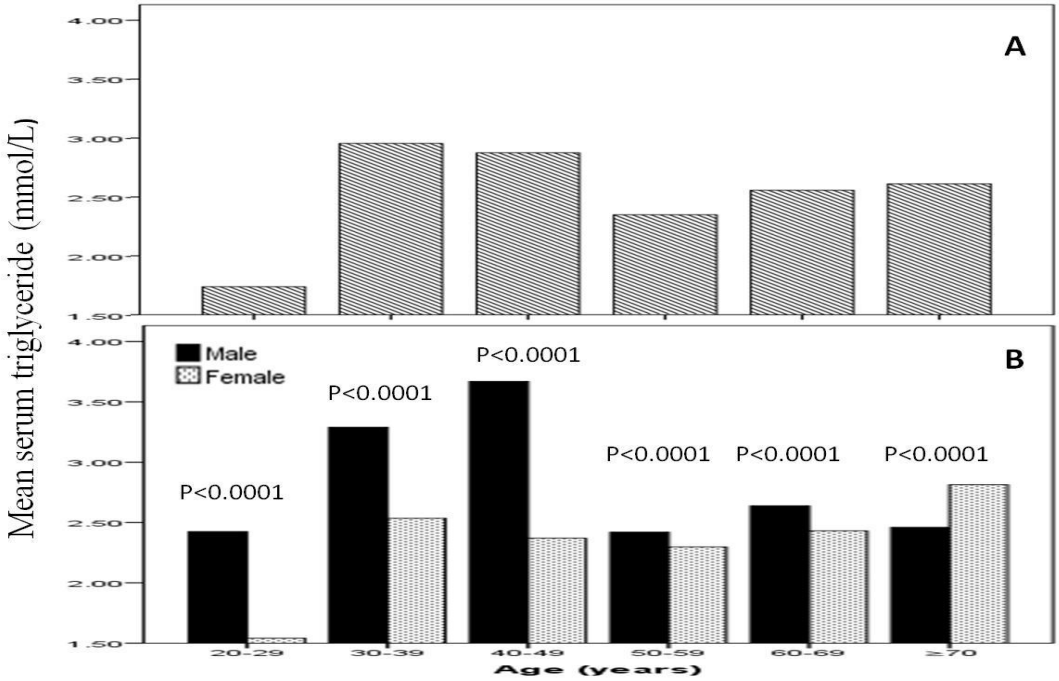
Parameters		Total
n (%)		1590
Age (years)		55.7 ± 12.1
Gender	Male	642 (40.4)
	Female	948 (59.6)
Body mass index (kg/m²)		31.8 ± 6.8
Hypertension		899 (56.5)
HbA1c		8.2 ± 2.2
Serum triglyceride (mmol/L)		2.3 ± 1.7
Serum creatinine (μmol/L)		72.9 ± 23.0
Urine albumin (g/min)		73.3 ± 226.6

Table2: *Comparison of features between albuminuria groups (mean±standard deviation or number (%))*

Parameters		Albuminuria 525(33.0)	Normoalbuminuria 1065(67.0)	P value
Gender	Male	259(49.3)	383(36.0)	<0.0001
	Female	266(50.7)	682(64.0)	
Age(years)		57.1±12.3	55.0±11.9	0.001
Body mass index(kg/m²)		32.0±6.8	31.6±6.8	0.4
Hypertension		355(67.6)	544(51.1)	<0.0001
HbA1c		8.7±2.2	8.0±2.2	<0.0001
Serum triglyceride (mmol/L)		2.6±2.2	2.2±1.5	<0.0001
Serum creatinine (µmol/L)		81.4±35.7	68.8±20.2	<0.0001
Urine microalbumin (g/min)		201.4±362.0	10.2±7.3	<0.0001

Table3: *Frequency of albuminuria in Saudi adults based on regression analysis*

Parameters	Odd ratio (95% CI)	P value
Age(years)	1.0 (1.0-1.02)	0.2
Gender	1.8 (1.4-2.3)	0.001
Body mass index (kg/m²)	1.02 (1.0-1.04)	0.04
Hypertension	2.0 (1.6-2.6)	<0.0001
HbA1c	1.1 (1.1-1.2)	<0.0001
Serum triglyceride (mmol/L)	1.1 (1.0-1.2)	0.045



Mean serum triglyceride according to age groups (years) stratified by gender (A and B) in patients with type 2 diabetes and albuminuria

5. DISCUSSION

Proteinuria is a well-known marker for renal disease.[10] The association of heavy proteinuria with edema, hypoalbuminemia, hyperlipidemia is also well recognized. [11] Over the past two decades, evidence for a direct adverse impact by proteinuria on the progression of chronic kidney disease to end-stage renal failure has accumulated. [12] However, these findings were obtained at stages with extensive renal injury and may have represented secondary effects. Proteinuria is also associated with increased risk of atherosclerotic cardiovascular disease. [13] Hyperlipidemia is a metabolic abnormality frequently associated with diabetes mellitus. Its prevalence is variable, depending on the type and severity of diabetes, glycemic control, nutritional status, age and other factors. The most characteristic lipid abnormality in diabetics is hypertriglyceridemia.[14]

This study based on the data collected from 1590 patients in the department of primary care

at a tertiary care Hospital at Jeddah, Saudi Arabia showed significant increased albuminuria with 33% in Type 2 diabetic patients. Dyslipidemia is common among T2DM patients. Raised serum TG levels often precede the onset of T2DM for many years.[15] Hypertriglyceridemia and hyperglycemia are associated with an increased risk of future moderately increased albuminuria. Experimental and clinical studies have shown a strong association between hypertriglyceridemia and diabetic nephropathy.[16] Lipids may induce renal injury by stimulating Transforming growth factor-beta, thereby inducing the production of reactive oxygen species and causing damage to the glomeruli and glomerular glycocalyx.[17] In experimental animals fed a high fat diet which suggested that lipotoxicity might represent a major mechanism in renal disease by inducing glomerulosclerosis and tubulo-interstitial injury, associated with renal lipid accumulation.[18] Insulin affects the liver Apo lipoprotein production. It regulates the enzymatic activity of lipoprotein lipase and Cholesterol ester transport protein. All these factors are likely cause of dyslipidaemia in Diabetes mellitus with albuminuria. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active lipoprotein lipase may be altered in Diabetes mellitus.[19] In our study, fasting serum TG were significantly associated with increased albuminuria as shown present in mean fasting serum TG level of 2.6±2.2 mmol/l and absent among those with 2.2±1.5 mmol/l, p<0.0001. Increased TG have been associated with microalbuminuria, although associations with lipid abnormalities were found to be more marked in patients with macroalbuminuria.[20] With respect to the pediatric populations with diabetes, data from the Oxford Regional Prospective Study showed that the prevalence of microalbuminuria increased across tertiles of total cholesterol, and a German study has shown a predictive value of TG on the development of persistent microalbuminuria.[21,22] A time of exposure to elevated triglyceride levels >1.7 mmol/l (150mg/dL) predicts incident moderately increased albuminuria. In a study carried out by Gomes where total of fifty patients were enrolled. Moderately increased albuminuria was present in 10% of the patients. No difference concerning serum lipids were found in comparison between normalbuminuria and moderately increased albuminuria patients. A total of 4% of all patients had elevated triglyceride levels.[23] Another study showed out of total 184 cases, seventy six subjects, 41.3% had moderately increased albuminuria. There was no significant difference between subjects with and without moderately increased albuminuria with regards to triglyceride concentrations.[24] This was in contradiction to our study.

In our study more females 50.7% had MA as compared to males 49.3%.It was contradictory to study done by Hussain S that showed male dominance.

A metaanalysis of epidemiological data has shown that TG is an independent cardiovascular risk factors and evidence has accumulated over the past 10 years showing the importance of TG as an independent risk factor for coronary artery disease.[25-27] In Asian populations, nonfasting TG levels predict the incidence of coronary heart disease.[28] Also in Asian populations, TG appears to be more important than low density lipoprotein and high density lipoprotein as the major lipid parameters related to atherogenesis in the presence of hypertension. [29] TG levels increase with HTN. [30] This relationship persists in patients across patients with HTN, which indicates a biological interrelation between HTN and TG.[31] In our study, we identified a significant interaction between TG and HTN on albuminuria demonstrating a role for therapy targeting TG and HTN in early renal impairment in hypertensive diabetic patients.

A clinic based study introduces referral bias, is one of the limitations of this study. This could have introduced some degree of referral bias. However the prevalence of albuminuria is similar to that reported in other studies. A single urine spot collection with semi quantitative dipstick determinations was used to detect albuminuria. The American Diabetes Association guidelines stated that this technique has acceptable sensitivity and specificity, but recommend that several collections should be done in a 3 to 6 month period before diagnosing a patient as having albuminuria.[32]

6. CONCLUSION

We conclude that hypertriglyceridemia should be considered as a potential risk factor and as a diagnostic biomarker to be used in conjunction with other biochemical markers for early diagnosis, assessment, and follow-up of albuminuria.

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