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Association of Albumin to Creatinine Ratio with Cardiovascular Risk Markers and Determination of Their Cut off Points in Type 2 Diabetic Nephropathy Patients

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Abstract: Urine albumin to creatinine ratio (ACR) is found to be the most promising indicator for confirmation of nephropathy in type 2 diabetes mellitus patients. It is also known that the increased excretion of urine microalbumin is associated with high risk of cardiovascular diseases. The present study was aimed to attain the association of BMI, FBG, HbA1c, cardiovascular markers, urine creatinine & urine microalbumin, and also to find out the cut off points of these markers for the prediction of cardiovascular disease in type 2 diabetic nephropathy patients. We included 110 type 2 diabetic nephropathy patients and 110 healthy age and gender matched healthy controls. The value of BMI, and levels of FBG, triglycerides, VLDL cholesterol, urine creatinine and urine microalbumin were found to be positively associated and HDL cholesterol was negatively associated with ACR in type 2 diabetic nephropathy patients. Further, ROC curve analysis of BMI, total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol and VLDL cholesterol gave the cut off values of >24.3, >187.2, >143.1, ≤42.7, >119.9 and >37.2, respectively with significant area under the ROC curve, highest sensitivity and highest specificity. From these results we conclude that the ACR apart from its function as an indicator of nephropathy can also serve as an indicator of cardiovascular risk in type 2 diabetic patients. These cut off values can be used for prediction of cardiovascular disease risk in type 2 diabetic nephropathy patients.

Keywords: Albumin to creatinine ratio, cardiovascular disease, triglycerides (TGs), type 2 diabetic nephropathy

I. Introduction

The incidence of diabetes mellitus is increasing globally, with its potential complications like heart disease, stroke, and kidney damage. [1] Diabetes is characterized by hyperglycemia, in most cases of diabetes; occurrence of hypertension is seen sooner or later, which is an established causal factor for diabetic nephropathy (DN). [2] DN is one of the most common clinical conditions leading to end stage renal disease (ESRD). [3] It is a life threatening complication resulting in a poor prognosis for patients as well as high medical costs. [4] The pathophysiological mechanisms of DN are attributed primarily to metabolic and hemodynamic derangements including hyperglycemia induced production of advanced glycation end products (AGEs), activation of polyol pathway, protein kinase C and rennin angiotensin system. [5, 6] The earliest demonstrable abnormalities include intrarenal hypertension, increased glomerular filtration rate, and microalbuminuria. [7] The characteristic increased albumin excretion of nephropathy, even microalbuminuria, is known to increase the risk of cardiovascular disease in diabetic as well as non-diabetic patients. The mechanism of this may be linked to the increased levels of atherogenic lipoproteins promoted by endothelial dysfunction. [8, 9] Albuminuria (>300 mg/24 hours) or microalbuminuria (≥30 mg/24 hours to 300 mg/24 hours), or albumin/creatinine ratio (≥30 mg/g), is used as a marker of renal damage and is used to define chronic kidney disease along with low estimated glomerular filtration rate (eGFR). [10]

Both cardiovascular disease and diabetes mellitus share many risk factors in common (the “common soil” hypothesis), [11] also lipid metabolism has been extensively investigated in diabetes; little information is available whether urine ACR is associated with lipids and lipoproteins. Therefore, we hypothesized that the cardiovascular markers are associated with ACR, cut off values of lipids and lipoproteins can be calculated for the prediction of cardiovascular disease.

II. Material And Methods

The present study consisted of, 110 T2DM patients with nephropathy within the age limit of 35-60 years. Patients visiting Medicine Department, BVDU Medical College and Hospital, Pune were included in the study. T2DM nephropathy patients, having cardiovascular, pulmonary diseases, with diabetic complications other than nephropathy, pregnant and lactating women and those on insulin therapy were excluded from the
Lipid Profile as a Marker of Cardiovascular Disease in Type 2 Diabetics with and without Nephropathy

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Abstract: Among the microvascular complications of type 2 diabetes mellitus, second most common complication is diabetic nephropathy (after retinopathy). Overt dyslipidemia may aggravate the condition, and it is also known to increase the risk of cardiovascular diseases (CVDs). The present study included 110 type 2 diabetic individuals each with and without nephropathy and 110 age and gender matched healthy non-diabetic individuals. The concentrations of FBG, HbA1c, TC, TGs, and high density lipoprotein cholesterol (HDL-C) were estimated from fasting blood samples. Significant increase was found in BMI, FBG, HbA1c, TC, TGs, LDL-C, VLDL-C, serum urea and creatinine in type 2 diabetic patients with as well as without nephropathy as compared to healthy individuals, while HDL-C was significantly decreased. The increased levels of urine creatinine and higher albumin/creatinine ratio were observed in type 2 diabetic nephropathy subjects as compared to healthy controls. Patients with proteinuria had significantly higher BMI, TC, TGs, LDL-C, VLDL-C, Serum urea, serum creatinine, urine creatinine, microalbumin, and albumin/creatinine ratio when compared to the patients with microalbuminuria. Hence, lipids and lipoproteins along with stage of nephropathy should be considered for prediction of CVDs in type 2 diabetic subjects with & without nephropathy.

Keywords: Cardiovascular diseases, diabetic nephropathy, total cholesterol (TC), triglycerides (TGs), type 2 diabetes mellitus (T2DM).

INTRODUCTION

From the rapid rise of diabetes incidence, the projected increase in the number of individuals is supposed to rise from 6.4% (285 million) in 2010 to 7.7% (439 million) in 2030 [1]. The important difficulty with this condition is its predisposition to suffer macro and/or microvascular complications as diabetes progresses, increasing the economic burden on the individuals and healthcare system as well [2].

One of the most serious life threatening and irreversible complication associated with diabetes mellitus is diabetic nephropathy [3, 4]. World Health Organization (WHO) projected, about 20-40% of both types of diabetes mellitus patients develop diabetic nephropathy within 20-30 years of the onset of diabetes [5]. It is characterized by continuous albuminuria, elevated blood pressure, declines glomerular filtration rate and high risk of CVDs [6].

The development and progression of diabetic nephropathy include various hyperglycemia-induced metabolic and hemodynamic derangements that involve increased formation of advanced glycation end products (AGEs), enhanced reactive oxygen species (ROS) generation and Protein Kinase C (PKC) activation, polyol pathway and Rennin Angiotensin System (RAS) [5, 7]. It represents the most common form of end-stage renal disease (ESRD) worldwide, accounting for increase in mortality rate in these patients [2, 8]. In developing countries like India, the high economic burden for treatment of ESRD, many of these patients are not getting optimal treatment [4].

According to estimates ever third individual with diabetes mellitus is affected and is related with substantial cardiovascular morbidity and mortality [7]. A number of risk factors have been identified from longitudinal and cross-sectional studies, in the development of diabetic nephropathy that includes race, genetic susceptibility, high blood pressure, hyperglycemia, hyperfiltration, smoking, male gender, age and dyslipidemia [5, 9]. The present study focused on lipid abnormalities in T2DM population with & without nephropathy and its comparison to normal healthy individuals.