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EVALUATION OF CARDIOMETABOLIC RISK FACTORS IN CHRONIC KIDNEY DISEASE

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ABSTRACT

Introduction: Chronic kidney disease (CKD) is defined as the persistent kidney damage confirmed by renal biopsy or markers of kidney damage and/or glomerular filtration rate (GFR) < 60ml/min/1.73m^2 for greater than 3 months. Cardiovascular disease is the leading cause of death in patients with CKD rather than ESRD. Metabolic and cardiovascular complications of renal disease may be consequence of abnormal insulin action and obesity. Hence in the present study waist to height ratio, insulin resistance, TAG: HDL ratio and proteinuria were studied as cardiometabolic risk factors in CKD. **Materials and Methods**: 60 patients newly diagnosed as CKD in the age group between 20-60 years were selected for the study. Patients taking ACE inhibitors, lipid lowering drugs, antioxidants, hormonal therapy and in End stage renal disease were excluded from the study. **Statistics**: One sample `t` test was done to know the significance of all parameters in CKD. PEARSON`S correlation was done to know association between study parameters with creatinine and P<0.05 was taken as statistically significant. **Result:** Statistically significant increase in waist to height ratio, TAG: HDL ratio, HOMA-IR and urine albumin was found in CKD patients after doing one sample t test. Statistically significant correlation was not found between serum creatinine, insulin resistance, TAG: HDL ratio and urine albumin. **Conclusion:** Cardiometabolic risk factors waist to height ratio, TAG: HDL ratio, HOMA-IR and urine albumin were significantly elevated in CKD patients but longitudinal studies have to be undertaken to establish the significant correlation between study parameters. The present study enlightens the significance of anthropometric and biochemical markers as cardiovascular risk factors in CKD.

KEYWORDS: Chronic kidney disease, cardiometabolic risk factors, TAG: HDL, HOMA-IR, waist to height ratio, creatinine.

INTRODUCTION

Chronic kidney disease (CKD) is a major public health problem due to high prevalence in general population, reduction in life expectancy, quality of life and enormous cost spent on treatment. A combination of multiple environmental, genetic, traditional and novel risk factors predisposes CKD patients to cardiovascular risk. Premature cardiovascular disorders like stroke, peripheral vascular disorders, congestive heart failure and coronary artery disease are frequently seen in CKD patients.[1] CKD is an independent risk factor for cardiovascular disorders.

CKD is defined as the persistent kidney damage confirmed by renal biopsy or markers of kidney damage and/or glomerular filtration rate (GFR) < 60ml/min/1.73m^2 for greater than 3 months.[2] As GFR declines below 60ml/min/1.73m^2 the risk for cardiovascular disorders increases. This is attributed to the prevalence of traditional risk factors like hypertension, diabetes mellitus and hyperlipidaemia along with novel risk factors like oxidative stress, endothelial dysfunction and persistent inflammation predisposing to cardiovascular risk in CKD. As the renal function declines the accumulation of uremic toxins and metabolic alterations further increases the risk for cardiovascular diseases. Metabolic syndrome is a cluster of cardiac and metabolic risk factors. Insulin resistance is one of the consequences of metabolic syndrome, seen in early stages of CKD. Insulin resistance in CKD is because of the elevated uremic toxins, metabolic acidosis, vitamin D deficiency and due to post receptor defect in skeletal muscles.[3] Cardiovascular complications in CKD may be because of abnormal

insulin action so insulin resistance may be one of the therapeutic targets to reduce the cardiovascular mortality.

Obesity is a risk factor for CKD and cardiovascular diseases (CVD). The association between different indexes of obesity and CKD is unknown. Waist-to-height ratio (WHtR) correlates well with CT assessment of intra-abdominal fat and is more strongly associated with CVD risk than waist to hip ratio (WHR), waist circumference (WC) or body mass index (BMI)[4]

Albuminuria measurement for CKD detection is already recommended for individuals with diabetes mellitus. In individuals who do not have diabetes, it is not yet established whether testing for albuminuria or proteinuria is superior for detection of CKD or for determining risk of progression. Microalbuminuria seen in the early stages of CKD progresses to massive albuminuria and may be a marker of generalised endothelial dysfunction and permeability.[5]

Dyslipidemia in the form of high triacyglycerol and low HDL levels is commonly observed in CKD. Previous studies have established that TAG: HDL ratio predicts cardiovascular risk in diabetes but limited studies have been done in CKD. This ratio predicts the size of small and dense LDL particle which easily penetrates the vascular endothelium and gets deposited in the vasculature.[6]

Hence in the present study insulin resistance, TAG: HDL ratio, albuminuria and waist to height ratio were evaluated as cardio metabolic risk factors in CKD.

MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry in collaboration with Department of Nephrology at Mahatma Gandhi Medical College and Research Institute, Pondicherry. Sixty clinically diagnosed chronic kidney disease patients in the age group between 20-60 years were included in the study. Patients on ACE inhibitors, hypolipidemic drugs and patients suffering from autoimmune disorders were excluded. Ethical committee clearance was obtained. After taking an informed consent from the patients, 5ml of fasting venous blood was collected from anticubital vein. After centrifugation all serum samples were stored in deep freezer until analysis. Fasting blood glucose and lipid profile parameters and urine albumin were estimated by IFCC (International federation of clinical chemistry) recommended kit method in Hitachi 902 autoanalyser. Fasting insulin was estimated by Chemiluminescence technology by Cobas e411. HOMA-IR was calculated using formula HOMA-IR= GLUCOSE (mg/dl) X INSULIN (mIU/L)/405. TAG: HDL ratio was calculated. Waist circumference was measured at the highest point of iliac crest and height in upright position in centimetres was measured and waist to height ratio was calculated.

Statistical analysis

Descriptive statistical analysis was carried out. Results on continuous measurements were presented as Mean +/- SD (Min-Max) and results on categorical measurements were presented in Number (%). SPSS 20.0 software was used for statistical analysis. One sample `t ` test was done to know the significance of all parameters with reference to their normal reference range in CKD. PEARSON`S correlation analysis was done to know the association of study parameters with serum creatinine and P value <0.05 was taken as statistically significant.

RESULTS

In the present study mean values of all the parameters were significantly elevated when compared to their reference range (table:1). HOMA-IR cut off value was taken as >2, TAG: HDL ratio>3, waist to height ratio>0.5 and urine microprotein 17mg/dl.

Pearson`s correlation analysis (table:2) was done in this study to know the association of serum creatinine with TAG:HDL ratio, Waist: height ratio, HOMA-IR and urine microprotein. Statistically significant association was not found between parameters.

Table 1 :shows mean values of the study parameters in CKD

Parameters	Mean+/-SD	P-Value
Waist-Height Ratio	0.538 +/- 0 .052	.000*
HOMA-IR	4.25 +/- 3.78	.000*
Insulin(mIU/L)	14.32 +/- 12.76	.000*
TAG-HDL Ratio	3.93 +/- 1.35	.005*
Microprotein(mg/dl)	75.23 +/- 38.31	.000*

Table 2: Pearson`s correlation analysis between study parameters in CKD

Parameters	Waist-Height Ratio	HOMA-IR	Insulin	TAG-HDL Ratio
Waist to Height ratio	-	0.057	0.086	0.882
HOMA-IR	.057	-	0.000	0.107
Insulin(mIU/L)	0.086	0.000	-	0.105
TAG:HDL	0.882	0.107	0.105	-
Serum Creatinine(mg/dl)	0.746	0.753	0.637	0.632
Urine microprotein	0.485	0.538	0.403	0.945

DISCUSSION

Despite of recent advances in the management of CKD it remains the major public health problem. Metabolic syndrome and its components are associated with chronic kidney disease (CKD) development. Insulin resistance (IR) plays a central role in the metabolic syndrome and is associated with increased risk for CKD in nondiabetic patients. IR is common in patients with mild-to-moderate stage CKD, even when the glomerular filtration rate is within the normal range. In the present study insulin resistance estimated by HOMA-IR is increased in CKD patients and is statistically significant ($p<0.05$). IR estimated by HOMA not only depends on fasting glucose and insulin levels but also on the oxidative stress,

vitamin D levels and serum adipokines.[7] Low grade inflammation in CKD promotes insulin resistance as observed in the study done by Min-Tser Liao et.al.[8] IR along with other metabolic risk factors predicts the cardiovascular risk in CKD as hypothesised by Johns BR et al.[9] In the present study there was no significant association between insulin resistance and TAG: HDL ratio and waist to height ratio. This could be attributed to the low body mass index observed in chronic debilitating diseases like CKD. A study done by Knight MG et.al[10] proposed that TAG: HDL ratio doesn`t predicts the insulin resistance and it depends on ethnicity of the population. Sophia SK et.al[11] proposed that racial differences should be taken into consideration for the dyslipidaemia of insulin resistance. Because of all these factors and limited number of samples statistical significance was not found. Hsieh and Yoshinaga[12] demonstrated that individuals with similar waist circumference (WC) values and lower height presented a worse metabolic and cardiovascular profile, demonstrated by greater hyperglycaemia prevalence, hepatic steatosis and hypertension, compared with individuals with greater height, even after adjustment for age, smoking and lipid profile. This suggested that WHtR would be a more accurate tool in screening for the metabolic consequences of visceral deposits of adipose tissue. Chronic kidney disease is one of the complications of obesity induced diabetes mellitus. Obesity is subclinical inflammation characterized by the secretion of cytokines that influence the formation of atherosclerotic plaque and endothelial dysfunction. Waist-to-height ratio (WHtR) has emerged as new option and is better than other anthropometric indices. WHtR is easier to obtain, does not require reference tables, less influenced by sexual maturity, suitable for population and epidemiologic studies and can be used on a large scale in screening for metabolic risk in both adults and children.[13]

CONCLUSION

Cardiovascular disease is the primary cause of morbidity and premature mortality in chronic kidney disease. In the previous studies, it is well established that patients in renal failure are at a higher risk of cardiovascular disease, but patients in the early stages of CKD also experience a fatal or nonfatal cardiovascular events. Metabolic syndrome is a risk factor for cardiovascular morbidity and mortality. There is a close correlation between metabolic syndrome components and kidney diseases. Hence in the present study insulin resistance, TAG: HDL ratio, waist to height ratio and urine albumin were studied as cardiometabolic risk factors and Statistical analysis showed a significantly high levels of these parameters in CKD but correlation was not significant which may due to limited number of sample size in short duration of study. So, longitudinal studies have to be undertaken to establish the significant correlation. The present study enlightens the significance of anthropometric indices and biochemical markers as cardiovascular risk factors in CKD.

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