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HbA_{1c} AND LIPID PROFILE IN NONDIABETIC END STAGE RENAL DISEASE PATIENTS ON MAINTENANCE HEMODIALYSIS

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ABSTRACT

BACKGROUND : Glycated Haemoglobin (HbA_{1c}) is a reliable marker of glycemic status over the preceding 2-3 months. Recent studies have shown impaired glycemic status in non diabetic End Stage Renal Disease (ESRD) patients who are on maintenance hemodialysis (MHD). Glycemic control, utilising serial measurement of HbA_{1c} is generally recommended to limit end organ damage including cardiovascular morbidity and mortality. Chronic Kidney Disease (CKD) is known to be associated with major changes in the composition of plasma lipoproteins. This alteration may worsen in patients on Maintenance Haemodialysis (MHD).

AIMS AND OBJECTIVES : The study was aimed to assess the level of HbA_{1c} and lipid profile in non diabetic ESRD patients on MHD and healthy controls.

MATERIALS AND METHODS : This was a case control study in which 40 non diabetic ESRD patients on maintenance hemodialysis were taken as cases and 40 apparently healthy individuals as controls. Fasting blood samples were analysed for glucose, HbA_{1c}, Triglyceride, Total cholesterol, LDL and HDL. Statistical analysis was carried out by student's t-test.

RESULT : HbA_{1c} level in ESRD patients on MHD was significantly higher when compared to healthy controls. (5.87 ± 0.46% versus 4.96 ± 0.3%; p<0.0001); Similar statistical difference were observed in the levels of: Triglyceride (162.22 ±14.13 mg/dl versus 119.65±29.89 mg/dl; p<0.0001); LDL (95.58 ± 19.42 mg/dl versus 80.02 ± 20.29 mg/dl; p<0.0008; HDL (29.35 ± 4.04 mg/dl versus 49.32 ± 7.47 mg/dl; p<0.0001).

CONCLUSION : The results indicate that non-diabetic ESRD patients undergoing MHD showed elevated HbA_{1c}, Triglyceride and low HDL level than controls. This altered lipid pattern and dysglycemia may accelerate the process of atherosclerosis, a risk for CVD and also increases the morbidity and mortality in patients.

INTRODUCTION

Chronic kidney disease (CKD) is a significant health problem. Cardiovascular disease is a major cause of morbidity and mortality among patients with chronic kidney disease (CKD) receiving haemodialysis (HD)[1]. In patients who finally advance to ESRD and especially those on hemodialysis patients, the prevalence of clinical coronary heart disease is 40% and CVD mortality is 10 to 30 times higher than in the general population of the same gender, age and race[2,3]. Lipid disorders are common among CKD patients and are recognized risk factors for CVD[4]. HbA_{1c}, a measure of chronic hyperglycemia, is a sensitive and reliable marker of impaired glucose metabolism. Recent reports suggest that the relationship between HbA_{1c} and cardiovascular disease (CVD) may extend below the limits currently defined as diabetes, since higher levels of HbA_{1c} were reported to be independent predictors of mortality in general population and non-diabetic CKD patients[5]. The present study was designed to assess and compare the level of HbA_{1c} and lipid profile in non-diabetic ESRD patients on MHD and healthy controls.

AIMS AND OBJECTIVES

1. To assess the level of HbA_{1c} and lipid profile in non diabetic ESRD patients on MHD and compare it with healthy controls.

MATERIALS AND METHODS

This was a case control study conducted at the Nephrology department, Vinayaka Mission's Hi-tech Hospital, Salem. 40 non-diabetic patients on end-stage

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renal disease undergoing maintenance hemodialysis aged 28-62 years, with age and sex matched 40 healthy controls were investigated. In ESRD patients the hemodialysis duration was 4 - 4.5 hours, once or twice a week. The study was granted Institutional ethical committee approval, and informed consent was obtained from both cases and control groups. Exclusion criteria included the following: diabetes mellitus, obesity, cigarette smoking, alcohol consumption and use of lipid lowering medication. Fasting blood sample was collected from the study groups for the analysis of lipid profile, glucose and HbA_{1c}. The serum total cholesterol and high density lipoprotein cholesterol (HDL) were analyzed using cholesterol-oxidase method, triglyceride by glycerol- kinase method while low density lipoprotein cholesterol (LDL) was calculated using Frieldwald formula, and glucose by glucose oxidase-peroxidase method. HbA_{1c} was measured by turbidimetric inhibition immunoassay (TINIA) method to avoid interference by carbamylated hemoglobin.

STATISTICAL ANALYSIS

- All analysis were performed with SPSS statistical package version 16.
- Data was expressed as mean ± SD for quantitative variables.
- Comparison between groups was done by student's t-test.
- P value <0.05 was considered statistically significant.

RESULTS

Table-1 shows the mean and standard deviation of HbA_{1c}, Glucose, Triglyceride, LDL, HDL and Total Cholesterol of controls and cases. HbA_{1c} was significantly higher (p<0.0001) in nondiabetic ESRD patients on MHD than in controls (5.87 ± 0.46% versus 4.96±0.3%). Also triglyceride (162.22±14.13mg/dl versus 119.65 ±29.89 mg/dl; p<0.0001) and LDL (95.58 ± 19.42 mg/dl versus 80.02 ± 20.29 mg/dl; p<0.0008) levels were significantly higher in patients. HDL level was significantly lower (p<0.0001) in ESRD patients than in controls (29.35 ± 4.04 mg/dl versus 49.32 ± 7.47 mg/dl). There was no statistical difference in Total Cholesterol and Fasting Glucose level between two groups.

Table 1: Lipid and carbohydrate metabolism biomarkers (M± SD)

Parameter	Cases (n=40)	Control (n=40)	P value
Age(yrs)	45.75±11.12	44.07 ±8.09	NS
HbA_{1c} %	5.87 ± 0.46	4.96 ±0.3	<0.0001
Fasting glucose(mg/dl)	100.35±13.94	97.67±10.53	NS
Triglyceride(mg/dl)	162.22±14.13	119.65 ±29.89	<0.0001
LDL(mg/dl)	95.58±19.42	80.02 ±20.29	<0.0008
HDL(mg/dl)	29.35 ±4.04	49.32 ±7.47	<0.0001
Total cholesterol(mg/dl)	157.37 ±18.06	153.27 ±20.84	NS

NS-Non-significant; P value <0.05 Significant

DISCUSSION

HbA_{1c} provides a more comprehensive picture of glycemic status and is more indicative of chronic hyperglycemia than a single plasma glucose measurement. The mean HbA_{1c} level of the non-diabetic ESRD subjects (5.87 ± 0.46%) was significantly higher than the controls. These results were consistent with the findings of Sangeeta et al[20] which also showed an elevated level of HbA_{1c} in ESRD patients on MHD than controls. Elevated value of HbA_{1c} in non-diabetic ESRD patients may reflect a true impairment of glycaemic control, as reported in uraemic patients[6]; and also partly caused by the transient stress with release of catecholamines and cortisol[7,8]. Insulin resistance exacerbated by effects of chronic inflammation, uremic toxin and chronic metabolic acidosis in CKD[24] may also be involved in increase of HbA_{1c} in ESRD patients. HbA_{1c} is a target for intracellular glycoxidation and peroxidation reactions that result in the formation of advanced glycation end products (AGE)[4,9]. These AGE have been implicated in the initiation and progression of atherosclerosis.

In the present study, we found increased levels of triglyceride in patients when compared to controls. This finding was supported by other studies[10,11,12] which also observed the elevation in triglyceride levels. This elevation was probably due to the following reasons: (1).

Impaired activity of lipoprotein lipase (LPL) and direct inhibitory effect of various uremic toxins on the enzymes involved in lipid metabolism. (2). The accumulation of triglycerides is the consequence of both a high production rate as possibly a consequence of impaired carbohydrate tolerance and enhanced VLDL synthesis; and a low fractional catabolic rate likely due to the decreased activity of endothelium-associated lipases, namely, LPL and hepatic triglyceride lipase, which have the primary physiologic function of cleaving triglycerides into free fatty acids (FFA) for energy production or storage[13]. In ESRD patients on MHD the repeated use of low molecular heparin for anticoagulation may also lead to a defective catabolism of triglyceride-rich lipoproteins as heparin releases lipoprotein lipase from the endothelial surface and thus its chronic use may result in lipoprotein lipase depletion[23].

In this study total cholesterol showed no statistical difference between patients on haemodialysis and controls .This was similar to the findings observed by Gómez Dumm et al[19].LDL levels were significantly higher compared to controls in this study. Reduced HDL fraction increases the LDL residence time in plasma which makes it more susceptible to oxidation, glycation and carbamylation[22], all of which reduce hepatic clearance. In earlier studies also, Irshad et al[14] observed that there were qualitative changes in LDL in patients with CKD and dialysis patients. There is a predominance of small dense particles ,LDL V a subtype of LDL that has high propensity to penetrate the vessel wall, becomes oxidized, and triggers the atherosclerotic process. However study carried out by Feingold K R et al.[15] had not found any increase in LDL in non-diabetic CKD.

HDL level was significantly lower in cases when compared with non-uremic individuals. In the context of uremic microinflammation, HDL also undergoes structural changes through the incorporation of serum amyloid A, resulting in the so-called acute phase or inflammatory HDL, which act not as protective particles, but as proatherogenic particles and hence, contribute to the reduction in plasma HDL cholesterol and impaired maturation of HDL[8]. The decreased ability of the HDL particles to carry cholesterol leads to an impairment in the reverse cholesterol transport from peripheral cells to the liver, thereby burdening the vasculature with cholesterol and promoting atherosclerosis[16]. Another important component of HDL is paraoxonase, an enzyme that inhibits the oxidation of LDL. Plasma paraoxonase activity is reduced in patients with CKD, thereby predisposing the LDL and possibly also HDL particles to oxidation[17,18] Furthermore, infection-associated or uremia-associated inflammation might convert HDL from an antioxidant into a prooxidant particle . All of these may contribute to atherogenesis.

CONCLUSION

In conclusion, non-diabetic ESRD patients exhibited a more atherogenic lipid profile and elevated HbA_{1c} than controls. These factors may influence the acceleration of atherosclerosis and cardiovascular diseases observed in hemodialysis patients and needs more attention. Our findings, may suggest the need for lowering of HbA_{1c} cutoff values for the earlier identification of persons at risk for, cardiovascular disease in non-diabetic ESRD patients on MHD.

LIMITATIONS.

- Studies with larger population and measurement of serum apolipoprotein in addition to lipid profile may be a better marker for atherogenecity.
- Serial monitoring of HbA_{1c} levels would be a better index of glycemic status than a single measurement which was performed in this study.

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