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Original Research Article

A Study on Evaluation of HDL Cholesterol as a Predictor of Diabetic Nephropathy in Type II Diabetes Mellitus

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Conflict of interest: Nil

Abstract:

Objective: To measure the levels of HDL Cholesterol in blood and correlate its levels with the development of diabetic nephropathy in Type II Diabetes Mellitus Patients

Material and methods: This is a prospective case control Study in which 50 Clinically diagnosed type 2 Diabetic patients with albuminuria were selected as cases and age and sex matched type 2 Diabetic 50 patients with normoalbuminuria were selected as controls. The study was done in a tertiary care hospital attached to NRIIMS medical college, Visakhapatnam from December 2022 to January 2023.

Results: In the present study there was a significant (P=0.02) association between the study population cases and controls in relation to the age factor, whereas there was an insignificant (P=0.15) association between the cases and controls with regard to gender. There was a marked rise in BMI, FBS, eGFR and TC for the case group than the control group. After performing a Pearson's correlation analysis HDL-Cholesterol and urine albumin creatinine ratio(UACR) were negatively which indicates that with decreasing value of HDL-Cholesterol, UACR value increases(r value= -0.457) and HDL-Cholesterol and eGFR were positively correlated indicating eGFR value raises with increase in HDL-Cholesterol value.

Conclusion: It is therefore proposed that we can use HDL-Cholesterol as an adjunct biochemical parameter to UACR(urine albumin creatinine ratio) measurement in type 2 diabetes mellitus patients to improve predictive precision of diabetic nephropathy risk.

Keywords: Diabetic nephropathy, Dyslipidaemia, HDL Cholesterol

Introduction

One of the vital reasons for mortality and morbidity in today's health scenario is Diabetes Mellitus. Among different types of Diabetes Mellitus type 2 DM is the most common. It constitutes about 85% to 95% of the total number of diabetes mellitus cases.

Both microvascular and microvascular complications have been reported in type 2 DM cases and more than one-third of DM patients develop microangiopathic complications like retinopathy, neuropathy and nephropathy. [1,2]. Diabetic Nephropathy in one of the harmful complications of type 2 DM and is the leading cause of ESRD (End Stage renal disease), it is calculable that 20 % of Diabetic patients reach ESRD during their lifetime [3]. In addition to the renal vasoactive factors like renin-angiotensin aldosterone system and other vasoconstrictors [4,5] the characteristic dyslipidaemia pattern in Diabetics (high TG, LOW HDL, high LDL) have a synergistic effect on renal damage [6]. Diabetic Nephropathy is Characterised by urine albumin excretion and increased blood pressure leading to reduction of glomerular filtration rate. Though measuring micro albuminuria serves as a gold standard for detection and prediction of Diabetic nephropathy, its prognostic powers are less as it has been reported that a decline in the renal function of individuals with diabetes is not always accompanied by increased urine albumin creatinine ratio (UACR) and in other cases, one may have micro albuminuria that is not related to the decline of renal function. Therefore, markers that offer greater predictability and sensitivity to development of DN need to be identified to overcome the problems inherent in measurement of UACR. The studies on other modifiable risk factors in addition to persistent hyperglycemia and raised blood pressure in the causation of Diabetic Nephropathy are limited. The role of dyslipidemia in microvascular complications

has not been studied extensively. This study, therefore, aimed to check whether or not measuring of HDL-Cholesterol levels will add additional predictive value in predicting development of Diabetic nephropathy among type 2 diabetic patients. It is envisaged that information generated by this study will improve our knowledge on the predictors of diabetic nephropathy.

Materials and Methods:

The study was done in a tertiary care hospital attached to NRIIMS medical college, Visakhapatnam from December 2022 to January 2023.

This Study has been done in the Department Of Biochemistry and was approved by institutional ethics committee .Total number of 100 subjects participated in the study after informed consent. This is a prospective case control Study in which 50 Clinically diagnosed type 2 Diabetic patients with albuminuria were selected as cases and age and sex matched type 2 Diabetic 50 patients with normoalbuminuria were selected as controls.

Inclusion Criteria

1. All subjects are type 2 Diabetes Mellitus diagnosed patients.
2. Patients of age 30 and above.
3. Patients who were not using lipid lowering drugs.
4. Patients attending out patient department regularly for last six months.
5. Signed and informed consent to participate in study.

Exclusion Criteria

1. All non diabetic cases with kidney damage.
2. Patients on lipid lowering drugs.
3. Patients with symptoms of urinary tract infections.
4. Those who denied to give consent

Blood sample collection

Fasting venous blood samples (5mL) will be collected under aseptic conditions from the study group. Serum was separated by using centrifugation and is used for analysis of the following parameters in Fully automated clinical chemistry analyzer (Beckman) using standard reagents/ kits(Beckman)

- Fasting blood sugar by GOD-POD method,
- Total cholesterol by CHOD-POD method,
- High Density Lipoprotein by Enzymatic End point method,
- Serum creatinine by Jaffe's end point method for estimation of eGFR,.
- Low density lipoprotein cholesterol and very low density lipoprotein were determined using the Friedewald's formula as follows:
- VLDL = TG ÷ 5, LDL-c = (TC) – (VLDL +HDL)

Method for collection of urine sample

Urine samples were collected from the subjects in urine collection bottles on the spot ad at random during their visit to the hospital, and then was examined microscopically for evidence of any urinary tract infection and hematuria and analysed for following parameter

- Urine albumin by Turbidimetric Immunoassay
- Urine creatinine by Jaffe's End point method
- Urinary albumin creatinine ratio was calculated

Statistical analysis: Statistical analyses was done using the SPSS version 24.0. For comparison of variables between the cases and controls, Mean and SD was calculated for all the parameters in cases and controls. An unpaired t-test was used to compare the mean and SD Vain of all parameters in cases and controls. Pearson's correlation was used to assess the relationship between parameters. A $p \leq 0.05$ was considered statistically significant.

Results:

The demographic variables like age and gender wise distribution of case and controls were explained in Table.1 There was a significant (P=0.02) association between the study population cases and controls in relation to the age factor, whereas there was an insignificant (P=0.15) association between the cases and controls with regard to gender. More females were reported than males in the current study (Table 1).

Table 2 represented the Body mass index (BMI), systolic blood pressure (SBP), Diastolic Blood Pressure (DBP), FBS, eGFR and Total cholesterol (TC) values of both cases and controls. There was a marked rise in BMI, FBS, eGFR and TC for the case group than the control group. After performing a Pearson's correlation analysis HDL-C and UACR were negatively which indicates that with decreasing value of HDL-C, UACR value increases(r value= -0.457) and HDL-C and eGFR were positively correlated indicating eGFR value raises with increase in HDL-C value. (Table-3)

Table 1: Demographic Characteristics of Study Population

Study variable		**Case Mean** ± SD	**Control Mean** ± SD	**p-value**
Age		48.6±9.13	47.9±10.2	P=0.02
Gender		**Case (%)**	**Control (%)**	**p-value**
	Male	48	36	P=0.15
	Female	52	64	

p<0.05 (Significant). p>0.05 (Insignificant)

Table 2: BMI, SBP, DBP, FBS, eGFR & TC among cases & controls

Study Variables	Case/Control	Mean	Standard deviation (SD)	p-value
BMI	Case	29.3	2.0	< 0.001
	Control	24.9	1.86	
SBP	Case	154.2	8.75	< 0.001**
	Control	133.7	7.39	
DBP	Case	93.04	6.47	< 0.001**
	Control	82.9	4.02	
FBS	Case	205	68.9	< 0.0001**
	Control	145.6	21.9	
eGFR	Case	99.46	22.9	< 0.001**
	Control	112.52	23.0	
TC	Case	189.06	50.8	< 0.009*
	Control	157.8	38.2	

***p<0.05 (Significant)**
****p<0.001 (Highly Significant)**
p>0.05 (Insignificant)

Table 3: Pearson's Coefficient of Determination of HDL-C with UACR & eGFR

Blood glucose, Lipid profiles and ratios	Correlation Coefficient	Significance
HDL-C and UACR	-0.457	Negative correlation
HDL-C and eGFR	0.197	Positive correlation

Discussion

Altered glucose metabolism and dyslipidemia are characteristic abnormalities in Diabetes Mellitus. This persistent increased blood sugar levels of diabetes can lead to long term damage, dysfunction and multi organ failure and symptoms of retinopthy, nephropathy, neuropathy and diseases of heart and blood vessels [7]. Insulin resistance, particularly in Type 2 Diabetes mellitus is associated with a cluster of metabolic abnormalities including glucose intolerance, hypertension, a unique dyslipidemia (increased serum triglyceride, increased LDL cholesterol and decreased HDL cholesterol) and a procoagulant state causing an increase in micro and macro vascular diseases [8]. It is estimated that 20% of type 2 diabetic patients during their life time reach ESRD and the leading cause of end stage renal disease is diabetic nephropathy. Diabetic Nephropathy is mainly characterized by progressive rise in urine albumin excretion, increasing blood pressure leading to reduction of glomerular filtration rate. The residual risk of DN remains high in the patients even after control of modifiable risk factors like hyperglycemia and raised blood pressure. The role of dyslipidemia in microvascular complications is not very well established when compared to that in macrovascular complications.

In the present study the authors aimed to evaluate the role of HDL-C as an alternative early predictor of diabetic nephropathy in the type 2 diabetes mellitus patients, by correlating HDL-C with the analytes for kidney function like Urine Albumin Creatinine Ratio (UACR) and estimated glomerular filtration rate (eGFR) levels as predictors or markers of Diabetic Nephropathy. In the present study majority of the patients (80%) were aged 40-69 years, the finding which is similar with the worldwide estimates of diabetes where the majority of diabetic patients in developing countries aged between 40 and 60 years [9]. Agarwal et al [10] conducted study on 300 newly diagnosed patients having type 2 diabetes and observed that men with advanced age had more risk of developing nephropathy.

.In this study the mean BMI level was 29.3±2.0 in subjects and 24.9±1.86 in the control group. The rise in the mean concentrations of body mass index in the cases group is statistically significant when compared to control group (p< 0.001). This findings are similar to Agarwal et al. [10] who conducted study in 300 newly diagnosed patients with type 2 diabetes and observed high BMI elevates the risk of diabetic nephropathy.

The rise in the mean concentrations of Fasting Blood Sugar values in the cases group in this study is statistically significant, when compared to control group (p< 0.0001). By this we can say that persistent hyperglycaemia is an important risk factor for development of Diabetic nephropathy. Impaired insulin signalling as well as reductions in glucose transport within insulin-sensitive tissues are the biochemical defects that provoke insulin resistance. [11]

In this present study there were significant high levels of mean of both systolic and diastolic blood pressure in albuminuric subjects compared to the normoalbuminuric group. This was according to the findings of Ahmedani et al. [12].Statistically significant association was found between high blood pressure and incidence of diabetic nephropathy.

In this study patients with eGFR values greater than 90.1 ml/min/1.73 m^2 were classified as normal while those ≤ 90 ml/min/1.73 m2 were in the abnormal region. Albuminuria group has mean eGFR level of 99.46±22.9 and normoalbuminuric group have mean eGFR 112.52±23.0 (p-value<0.001).

The mean concentrations of serum Total Cholesterol in the cases group in this study is significantly higher, when compared to control group (p< 0.009). This was in accordance with El-wakf et al [13] study characterized by increased serum Total cholesterol which was significantly increased in albuminuric group, than normoalbuminuric group.

UACR and HDL-C were found to be inversely proportional,i.e, as the HDL-C levels reduced, UACR levels increased and vice versa. El-wakf et al (2011) [13] showed that patients with decreased HDL-C levels, were associated with higher chances of having albuminuria.

There was a, positive relationship between eGFR, and HDL-C Kong et al. [14], significant association was found between HDL-C and reduced eGFR. [15]

Conclusion:

It is therefore proposed that the use of HDL-Cholesterol as an adjunct biochemical parameter to UACR(urine albumin creatinine ratio) measurement in type 2 diabetes mellitus patients to improve predictive precision of diabetic nephropathy risk.

Limitations of the Study: As the study was done in a small group limited to a particular area the results cannot be generalised to the whole population.

Ethics Approval: taken from the institute ethics approval committee

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