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CHRONIC KIDNEY DISEASE AND DYSLIPIDEMIA- A CORRELATION STUDY

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ABSTRACT

Background: Based on the lipid nephrotoxicity hypothesis, a great deal of research is being done worldwide to evaluate the impact that hyperlipidemia plays in patients with chronic renal disease, particularly in India.

Aim: The purpose of this retrospective clinical investigation was to evaluate the relationship between dyslipidemia and the prevalence of chronic renal disease in Indian participants.

Methods: Clinical data from patients' medical records who did not have overt kidney illness were gathered and evaluated for this retrospective clinical investigation. Based on their levels of total cholesterol and low-density lipoprotein, the study participants were split into four groups. A statistical analysis was performed on the gathered data to see whether chronic renal disease and blood lipid profile were correlated.

Results: For the group with the highest cholesterol, the lowest HDL-C value and highest HDL-C values were seen, with values of >5.40 mmol/l ($p<0.001$). With $p<0.001$, BUN and FPG values were highest for cholesterol ranges >5.40 mmol/l and lowest for cholesterol values ≤ 4.20 mmol/l. When comparing high cholesterol to low cholesterol levels, SUA and hypertension values were significantly higher ($p<0.001$) for high cholesterol values. The age group of >60 years old had the highest incidence of new chronic kidney disease (CKD) at 8.08% (n=24) individuals, followed by >40-≤60 years old at 3.93% (n=21) subjects, and ≤40 years old at 1.93% (n=9) subjects. The high cholesterol group had an incidence of 8.07% (n=26) new chronic kidney disease events, while the low cholesterol group had an incidence of 1.82% (n=6) patients.

Conclusion: The current study's findings indicate that elevated levels of total cholesterol, low-density lipoprotein (LDL), and triglycerides are independently associated with a higher risk of declining eGFR (estimated glomerular filtration rate) and developing chronic kidney disease.

Keywords: eGFR, epidemiology, lipid profiles, chronic kidney disease, and renal disease

INTRODUCTION

Chronic kidney disease (CKD) is becoming more commonplace worldwide, particularly in India. Chronic kidney illness is becoming more common both internationally and in India, which places a significant strain on the country's healthcare system. Chronic kidney disease (CKD) increases mortality and progresses to end-stage renal disease (ESRD) with a host of problems. Therefore, it is important to identify, manage, and control the risk factors linked to chronic kidney disease (CKD), as doing so can aid in the illness's prevention.1

Due to the frequent changes in lifestyle, eating patterns, and living standards, dyslipidemia prevalence is rising significantly both globally and in India. Mixed hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, and decreased high-density lipoproteinemia are all considered forms of dyslipidemia. Data from earlier studies show that dyslipidemia raises the risk of developing cardiovascular illnesses.2

There was a hypothesis that linked dyslipidemia to chronic kidney disease after the Lipid Nephrotoxicity Hypothesis was proposed in 1982. This hypothesis and postulation have been the subject of ongoing investigation and evaluation in

the recent past. Research was out in the 1990s with a sizable sample size found that, after a ten-year follow-up, people with chronic renal disease also had higher levels of proteinuria if they had dyslipidemia.

The incidence of chronic kidney disease is higher in high-sugar and high-fat diet groups than in vegetarian diets, where the risk of chronic kidney disease was lower, according to a different study that assessed the risk for chronic kidney diseases and dietary patterns over a 6-year follow-up period. In a similar vein, another study found a significant link between excessive intake of fat and sugar and a decline in renal function.3.

The available information on the impact of TG (triglycerides), TC (total cholesterol), and LDL (low-density lipoprotein) on the onset of chronic kidney disease is debatable, and if it does, it's not obvious to what degree.

There is a dearth of information in the literature about the relationship between reduced eGFR (estimated glomerular filtration rate) annually and the development of chronic kidney disease (CKD) or elevated blood lipid levels as an independent risk factor for the development of CKD. Furthermore, there is no information in the literature on the blood lipid type that most strongly influences the onset of chronic kidney disease.4

The current retrospective clinical investigation was carried out to evaluate the relationship between dyslipidemia and the occurrence and progression of chronic renal disease in Indian participants. The annual evaluation of eGFR ≥60 mL/min/1.73 m2 and the absence of renal disease at baseline served as the foundation for the investigation. The study also examined various blood lipid types in groups.

MATERIALS AND METHODS

The current retrospective clinical investigation was carried out to evaluate the relationship between dyslipidemia and the occurrence and progression of chronic renal disease in Indian participants. The annual evaluation of eGFR ≥60 mL/min/1.73 m2 and the absence of renal disease at baseline served as the foundation for the investigation. The study also examined various blood lipid types in groups. The study was carried out at the Department of Medicine following approval from the relevant Ethical committee. The subjects who visited the Institute's outpatient department made up the study population.

2843 participants in total who had baseline data available were screened for the current investigation.The final sample size consisted of 1296 subjects with complete medical records and follow-up. Study subjects were excluded due to incomplete data, life-threatening illness, renal surgery, malignancy, severe infections, liver damage, baseline eGFR of <60ml/min/173m2, cerebrovascular diseases, and cardiovascular diseases.

Following each subject's final participation in the study, a thorough history was taken and a clinical examination was conducted. At baseline, age, gender, biochemical tests, and medical history were recorded for each individual. To calculate BMI in kg/m2, measurements of height and weight were also taken. After a 15-minute break, all individuals' blood pressure was measured while seated. Two measurements were recorded, and the mean value was calculated.

Following a 12-hour overnight fast, fasting blood samples were obtained from each individual in order to conduct the biochemical testing. Biochemical parameters, such as serum uric acid (SUA), LDL (low-density lipoprotein), HDL (high-density lipoprotein), TG (triglycerides), TC (total cholesterol), FBG (fasting blood glucose), and BUN (blood urea nitrogen), were measured using a biochemical automatic enzyme analyzer.

Every parameter was evaluated both at the baseline and during the follow-up. The kidney function was evaluated using the eGFR formula, which is as follows: eGFR (ml / min / 1.73m2) = 186 × S. Cr - 1.154×age - 0.203 (in females, X0.742). This formula is adapted from the Chinese version of the MDRD (Modification of Diet in Renal Disease).

According to the kidney disease: Improving Global Outcomes clinical practice recommendations from 2012, an incident of chronic kidney disease (CKD) was defined as having an eGFR of less than 60 ml/min/1.73 m2. Only the initial occurrence of chronic renal disease was taken into consideration for research purposes in participants who experienced several events during the follow-up.

RESULTS

The current retrospective clinical investigation was carried out to evaluate the relationship between dyslipidemia and the occurrence and progression of chronic renal disease in Indian participants. There were 1296 people in the study, both male and female. Table 1 lists the baseline characteristics of the research participants with and without CKD. The study individuals with and without CKD had mean ages of 68.42±24.46 and 47.64±21.28 years, respectively. The subjects with CKD had a substantially higher mean age ($p<0.001$).

With $p=0.969$, the gender difference was statistically not significant. The study participants' BMIs were 24.34±2.76 kg/m2 for those without CKD and 23.16±3.03 kg/m2 for those with. Subjects with CKD had significantly higher levels

of TG, TC, LDL, HDL-C, FBG, BUN, and serum uric acid (1.73±1.27, 5.14±1.04, 2.96±0.84, 1.33±0.26, 5.44±1.03, 5.66±1.19 mmol/l, and 6.22±1.43 mg/dl, respectively) than subjects without CKD (1.44±1.13, 4.85±0.93, 2.84±0.75, 1.32±0.33, 5.22±0.84, 4.94±1.16 mmol/l, and 5.57±1.35 mg/dl, respectively).

With p<0.001, each of these values was statistically significant. Subjects with CKD had eGFR values at baseline and ending points of 68.73±7.64 and 48.73±8.74 ml/min/1.73m2, significantly lower than subjects without CKD, whose values were 87.03±15.14 and 72.36±10.97 ml/min/1.73m2 (p<0.001).

Additionally, Table 1 shows that participants with CKD had considerably higher levels of diabetes and hypertension (p<0.001).

When the characteristics of the study subjects were analyzed according to age groups, it was found that there were considerably more males than females for all age categories: ≤40, >40-≤60, and >60 (p<0.001). With mean ages of 72±6.83, 51±8.24, and 34±4.66 years, respectively, the age group >60 years was substantially older than the age groups >40–≤60 years and ≤40 years (p<0.001). The age groups with the greatest BMI were also those over 60, >40–≤60, and ≤40, with mean values of 23.83±2.96, 23.57±2.87, and 22.46±3.07 kg/m2 (p<0.001).

With a p-value of 0.001 for cholesterol and <0.001 for HDL-C, the values were likewise considerably higher at >60 years, >40-≤60 years, and ≤40 years, respectively. With p-values of 0.002, <0.001, and <0.001, respectively, HDL-C, BUN, and FPG were likewise considerably higher for those over 60, followed by those between 40 and 60 years old, and those under 40. With p=0.07, S. creatinine did not significantly differ among the three age groups. Between the three age groups, there was a statistically significant difference (p<0.001) in serum uric acid, diabetes, and hypertension. The age groups of >60, >40-≤60, and ≤40 years had significantly lower eGFR mean values (p<0.001), with 86.84±11.75, 87.77±14.02, and 93.85±14.92, respectively. According to Table 2, the incidence of new chronic kidney disease (CKD) was highest in participants aged >60 (8.08%; n = 24), followed by >40–60 (3.93%; n = 21) and ≤40 (1.93%; n = 9).

The study individuals were categorized into four groups based on their total cholesterol levels: ≤4.20 mmol/l, >4.20 - ≤4.80 mmol/l, >4.80-≤5.40 mmol/l, and >5.40 mmol/l.In all four age categories, the proportion of males was significantly higher (p<0.001). When the cholesterol level was greater than 5.40 kg/m2, the BMI increased and decreased (p<0.001).

Triglyceride levels were higher when cholesterol was greater than 5.40 mmol/l and decreased when cholesterol was lower (p<0.001).The group with the greatest cholesterol had the lowest HDL-C value and the highest HDL-C value, with a value of >5.40mmol/l (p<0.001).

With p<0.001, BUN and FPG values were highest for cholesterol ranges >5.40 mmol/l and lowest for cholesterol values ≤ 4.20 mmol/l. While serum creatinine and diabetes percentage showed non-significant differences with higher values in the high cholesterol group and respective p-values of 0.373 and 0.08, SUA and hypertension values were significantly highest for high cholesterol values compared to low cholesterol values with p<0.001. A substantial decrease in eGFR was observed with elevated cholesterol levels (p<0.001). The high cholesterol group had an incidence of 8.07% (n=26) new chronic kidney disease events, whereas the low cholesterol group had an incidence of 1.82% (n=6) patients (Table 3).

DISCUSSION

The current retrospective clinical investigation was carried out to evaluate the relationship between dyslipidemia and the occurrence and progression of chronic renal disease in Indian participants. There were 1296 people in the study, both male and female. The mean age of the research participants with and without CKD was 47.64±21 and 68.42±24.46, respectively.

Subjects with CKD had significantly higher levels of TG, TC, LDL, HDL-C, FBG, BUN, and serum uric acid (1.73±1.27, 5.14±1.04, 2.96±0.84, 1.33±0.26, 5.44±1.03, 5.66±1.19 mmol/l, and 6.22±1.43 mg/dl, respectively) than subjects without CKD (1.44±1.13, 4.85±0.93, 2.84±0.75, 1.32±0.33, 5.22±0.84, 4.94±1.16 mmol/l, and 5.57±1.35 mg/dl, respectively). With p<0.001, each of these values was statistically significant.

Subjects with CKD had eGFR values at baseline and ending points of 68.73±7.64 and 48.73±8.74 ml/min/1.73m2, significantly lower than subjects without CKD, whose values were 87.03±15.14 and 72.36±10.97 ml/min/1.73m2 (p<0.001). Moreover, individuals with CKD had considerably higher levels of diabetes and hypertension (p<0.001).

These demographics were similar to those of the investigations conducted in 2018 by Li LC et al. and in 2016 by Yokoi H et al., where the authors evaluated patients who shared similar demographics with the current study.

When the characteristics of the study subjects were examined based on age groupings, it was found that there were considerably more males than females for all age categories: ≤40 years, >40-≤60 years, and >60 years (p<0.001).

The age group >60 years old had a substantially higher mean age of 72±6.83, 51±8.24, and ≤40 years old, respectively (p<0.001). These groups were followed by >40-≤60 years and ≤40 years. The age groups with the greatest BMI were also those over 60, >40–≤60, and ≤40, with mean values of 23.83±2.96, 23.57±2.87, and 22.46±3.07 kg/m2 (p<0.001).

With a p-value of 0.001 for cholesterol and <0.001 for HDL-C, the values were likewise considerably higher at >60 years, >40-≤60 years, and ≤40 years, respectively. With p-values of 0.002, <0.001, and <0.001, respectively, HDL-C, BUN, and FPG were likewise considerably higher for those over 60, followed by those between 40 and 60 years old, and those under 40. With p=0.07, S. creatinine did not significantly differ among the three age groups.

Between the three age groups, there was a statistically significant difference (p<0.001) in serum uric acid, diabetes, and hypertension. The age groups of >60 years, >40-≤60 years, and ≤40 years had eGFR values that were considerably lower, with mean values of 86.84±11.75, 87.77±14.02, and 93.85±14.92, respectively, and p<0.001. The age group of >60 years old had the highest incidence of new chronic kidney disease (CKD) at 8.08% (n=24) individuals, followed by >40-≤60 years old at 3.93% (n=21) subjects, and ≤40 years old at 1.93% (n=9) subjects. These outcomes supported the findings of Adeosun SO et al. (2018) and Gai Z et al. (2019), who demonstrated that worse parameters for chronic kidney disease were linked to an older age group.

The study participants were classified into four groups according to their total cholesterol levels: ≤4.20 mmol/l, >4.20 - ≤4.80 mmol/l, >4.80-≤5.40 mmol/l, and >5.40 mmol/l. This allowed for a comparison of their features. In all four age categories, the proportion of males was significantly higher (p<0.001). When the cholesterol level was greater than 5.40 kg/m2, the BMI increased; when the cholesterol level fell, the BMI decreased (p<0.001). Triglyceride levels were higher when cholesterol was greater than 5.40 mmol/l and decreased when cholesterol was lower (p<0.001). With a value of >5.40mmol/l (p<0.001), the highest cholesterol group had the lowest and highest HDL-C levels. With p<0.001, BUN and FPG values were highest for cholesterol ranges >5.40 mmol/l and lowest for cholesterol values ≤ 4.20 mmol/l.

While serum creatinine and diabetes percentage showed non-significant differences with higher values in the high cholesterol group and respective p-values of 0.373 and 0.08, SUA and hypertension values were significantly highest for high cholesterol values compared to low cholesterol values with p<0.001. A substantial decrease in eGFR was observed with elevated cholesterol levels (p<0.001). The high cholesterol group had an incidence of 8.07% (n=26) new chronic kidney disease events, while the low cholesterol group had an incidence of 1.82% (n=6). These findings corroborated those of research by Chang YC et al. (2019) and Asghari G et al. (2018), which found a correlation between worsening chronic kidney disease parameters and elevated cholesterol levels.

CONCLUSION

Within its limitations, the present study concludes that high total cholesterol, LDL, and triglyceride levels have an independent association with increased chances of declined eGFR (estimated glomerular filtration) rate and chronic kidney disease development. The present study had a few limitations including small sample size, shorter monitoring period, and geographical area biases. Hence, more longitudinal studies with larger sample size and longer monitoring period will help reach a definitive conclusion.

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Characteristics	CKD (n=57)	Without CKD (n=1239)	p-value
Gender			
Males	34	759	0.969
Females	22	480	
Age (years)	68.42±24.46	47.64±21.28	<0.001
BMI (kg/m2)	24.34±2.76	23.16±3.03	<0.001
Triglycerides	1.73±1.27	1.44±1.13	0.001
Total Cholesterol	5.14±1.04	4.85±0.93	<0.001
LDL	2.96±0.84	2.84±0.75	<0.001
HDL-C	1.33±0.26	1.32±0.33	0.04
FBG	5.44±1.03	5.22±0.84	<0.001
BUN	5.66±1.19	4.94±1.16	<0.001
S. Uric acid	6.22±1.43	5.57±1.35	<0.001
Hypertension (%)	26 (45.61)	187 (15.09)	<0.001
Diabetes (%)	7 (12.28)	44 (3.55)	<0.001
eGFR (ml/min/1.73m2)			
Baseline	68.73±7.64	87.03±15.14	<0.001
Ending	48.73±8.74	72.36±10.97	<0.001

Table 1: Demographic characteristics of the study subjects at baseline

Age range (years)	≤40 (n=465)	>40-≤60 (n=534)	>60 (n=297)	p-value
Gender				
Males	302	320	178	<0.001
Females	163	214	119	
Age (years)	34±4.66	51±8.24	72±6.83	<0.001
BMI (kg/m2)	22.46±3.07	23.57±2.87	23.83±2.96	<0.001
Triglycerides	1.16±0.93	1.55±1.31	1.63±1.04	<0.001
Total Cholesterol	4.47±0.83	4.91±0.87	5.14±0.91	0.001
LDL	2.56±0.73	2.86±0.72	3.03±0.76	<0.001
HDL-C	1.32±0.27	1.26±0.33	1.33±0.34	0.002
BUN	4.74±1.04	4.97±1.14	5.36±1.17	<0.001
FPG	4.92±0.38	5.22±0.81	5.72±1.06	<0.001
S. Creatinine	82.55±13.82	82.51±13.93	83.62±13.22	0.07
SUA	5.46±1.34	5.56±1.36	5.72±1.34	<0.001
Hypertension (%)	9 (0.43)	72 (13.48)	136 (45.79)	<0.001
Diabetes (%)	1 (0.21)	15 (2.80)	37 (12.45)	<0.001
eGFR (ml/min/1.73m2)	93.85±14.92	87.77±14.02	86.84±11.75	<0.001
New CKD incidence	9 (1.93)	21 (3.93)	24 (8.08)	<0.001

Table 2: Comparison of characteristics of the study subjects based on the age groups

Age range (years)	≤4.20 (n=329)	>4.20 -≤4.80 (n=322)	>4.80-≤5.40 (n=323)	>5.40 (n=322)	p-value
Gender					

Males	207	203	200	183	<0.001
Females	122	119	123	139	
Age (years)	38±4.48	46±6.24	50±2.96	55±3.64	<0.001
BMI (kg/m2)	22.52±2.97	22.14±2.92	23.46±2.93	23.82±3.13	<0.001
Triglycerides	1.06±0.78	1.26±0.87	1.47±0.98	1.85±1.29	<0.001
HDL-C	1.35±0.36	1.30±0.32	1.27±0.31	1.230.23	<0.001
LDL-C	2.05±0.36	2.57±0.32	2.96±0.39	3.65±0.69	<0.001
BUN	4.77±1.09	4.96±1.15	5.05±1.17	5.13±1.15	<0.001
FPG	5.06±0.67	5.18±0.83	5.24±0.82	5.43±0.97	<0.001
S. Creatinine	82.24±13.46	82.73±13.93	83.01±13.63	83.11±13.86	0.373
SUA	5.42±1.26	5.54±1.34	5.63±1.34	5.81±1.37	<0.001
Hypertension (%)	33 (10.03)	48 (14.90)	58 (17.95)	74 (22.98)	<0.001
Diabetes (%)	10 (3.03)	13 (4.03)	9 (2.78)	16 (4.96)	0.08
eGFR (ml/min/1.73m2)	90.83±15.65	87.62±16.07	84.82±14.33	81.54±13.42	<0.001
New CKD incidence	6 (1.82)	13 (4.03)	10 (3.09)	26 (8.07)	<0.001

Table 3: Comparison of characteristics of the study subjects based on the total cholesterol