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RETROSPECTIVE ANALYSIS OF THE CORRELATION BETWEEN THE INCIDENCE OF CHRONIC KIDNEY DISEASE AND DYSLIPIDEMIA IN INDIAN SUBJECTS

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ABSTRACT

Background: Globally, extensive research is being conducted for assessing the hyperlipidemia role in subjects of chronic kidney disease including in India according to the lipid nephrotoxicity hypothesis.

Aim: The present retrospective clinical study was conducted to assess the correlation between the incidence of chronic kidney disease and dyslipidemia in Indian subjects.

Methods: The present retrospective clinical study collected and assessed clinical data from medical records of subjects with no overt kidney disease. The included study subjects were divided into 4 groups based on low-density lipoprotein and total cholesterol levels. The collected data were subjected to statistical evaluation to assess the correlation between chronic kidney disease and blood lipid profile.

Results: Lowest HDL-C value and highest HDL-C values were seen for the highest cholesterol group with a value of >5.40mmol/l ($p<0.001$). BUN and FPG values were lowest for cholesterol value of ≤4.20 mmol/l and highest for cholesterol range of >5.40mmol/l with $p<0.001$. SUA and hypertension values were significantly highest for high cholesterol values compared to low cholesterol values with $p<0.001$. Incidence of new chronic kidney disease (CKD) was highest in the age of >60 years with 8.08% (n=24) subjects followed by 3.93% (n=21) for >40-≤60 years, and least in 1.93% (n=9) subjects in ≤40 years. Incidence of new chronic kidney disease events was higher in the high cholesterol group with an incidence of 8.07% (n=26) subjects compared to the low cholesterol group with 1.82% (n=6) subjects

Conclusion: 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.

Keywords: chronic kidney disease, eGFR, epidemiology, Lipid profiles, renal disease

INTRODUCTION

Recently, the prevalence of chronic kidney disease (CKD) is increasing globally including in India. With increased prevalence globally and in India, chronic kidney disease poses a high burden on the health care sector in India. Chronic kidney disease increase mortality and leads to various complications along with its progression to ESRD (end-stage renal disease). Hence, it is desirable to detect, control, and manage the risk factors associated with chronic kidney disease, which, in turn, can help in the prevention of chronic kidney disease (CKD).[1]

Owing to the regular alterations in diet habits, lifestyle, and living standards, a significant increase is seen in dyslipidemia incidence every year worldwide as well as in India. Dyslipidemia includes mixed hyperlipidemia, lower high-density lipoproteinemia, hypercholesterolemia, and hypertriglyceridemia. Various previous literature data depict that dyslipidemia increases the risk for the development of cardiovascular diseases.[2]

After the proposal of the Lipid Nephrotoxicity Hypothesis in 1982, an association between dyslipidemia and chronic kidney disease was postulated. In the recent past, this hypothesis and postulation is being researched and assessed continuously. Studies conducted in the 1990s including a large sample size concluded that in subjects with dyslipidemia, proteinuria also increase in subjects with chronic kidney disease after a follow-up of 10 years. Another study that evaluated the risk for chronic kidney diseases and the dietary patterns for a follow-up period of 6 years showed that the incidence of chronic kidney disease is increased in high sugar diets and high-fat diet groups compared to vegetarian diets where the risk of chronic kidney disease was lower. Similarly, one other study has shown a positive correlation between a decreased renal function with high sweet and fat intake.[3]

The data that exist are controversial regarding the role of LDL (low-density lipoprotein), TC (total cholesterol), and TG (triglycerides) on the development of chronic kidney disease, and if any influence exists, the extent is still unclear. The data in the literature is scarce concerning the raised blood lipid levels as an independent risk factor for chronic kidney disease development or whether reduction of eGFR (estimated glomerular filtration rate) annually will result in the development of CKD (chronic kidney disease). Also, limited data in the literature is available concerning which blood lipids type has a great impact on the development of CKD.[4]

The present retrospective clinical study was conducted to assess the correlation between incidence and progression of chronic kidney disease and dyslipidemia in Indian subjects. The study was based on the annual assessment of eGFR ≥60 mL/min/1.73m2 and no kidney disease on the baseline. The study also analyzed different groups of blood lipid types.

MATERIALS AND METHODS

The present retrospective clinical study was conducted to assess the correlation between incidence and progression of chronic kidney disease and dyslipidemia in Indian subjects. The study was based on the annual assessment of eGFR ≥60 mL/min/1.73m2 and no kidney disease on the baseline. The study also analyzed different groups of blood lipid types. The study was conducted at Department of medicine after obtaining clearance from the concerned Ethical committee. The study population was comprised of the subjects visiting the Outpatient Department of the Institute.

The present study screened a total of 2843 subjects with available baseline data. Study subjects were excluded based on incomplete data, life-threatening illness, renal surgery, malignancy, severe infections, liver damage, baseline eGFR of <60ml/min/173m2, cerebrovascular diseases, and cardiovascular diseases leaving the final sample size of 1296 subjects with complete medical records and follow-up.

After the final inclusion of the study subjects, detailed history was recorded for all the subjects followed by a clinical examination. For all the subjects, characteristics noted at baseline were medical history, biochemical assessments gender, and age. Also, height and weight were measured to assess BMI in kg/m2. The blood pressure was noted for all the subjects after 15 minutes of rest in a sitting position where 2 readings were noted and the mean value was taken.

To perform the biochemical tests, fasting blood samples were taken from all the subjects after 12 hours of overnight fasting. Using a biochemical automatic enzyme analyzer, biochemical parameters were assessed including 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).

All the parameters were assessed at baseline as well as a follow-up. eGFR formula was used to assess the kidney function: eGFR (ml / min / 1.73m2) = 186 × S. Cr - 1.154×age - 0.203 (in females X0.742) was used. This formula is taken from the MDRD (Modification of Diet in Renal Disease) for Chinese people.

Following the 2012 clinical practice guidelines of the kidney disease: Improving Global Outcomes, CKD (chronic kidney disease) event was considered for eGFR <60ml/min/1.73 m2. In subjects having more than one event of chronic kidney disease during the follow-up, the first event was only considered for study purposes.

RESULTS

The present retrospective clinical study was conducted to assess the correlation between incidence and progression of chronic kidney disease and dyslipidemia in Indian subjects. The study included 1296 subjects of both genders. The baseline characteristics of the study subjects with or without CKD are described in Table 1. The mean age of the study subjects with and without CKD was 68.42±24.46 and 47.64±21.28 years respectively which was significantly higher in subjects with CKD ($p<0.001$). The gender difference was statistically non-significant with $p=0.969$. BMI of the study subjects with and without CKD was 24.34±2.76 and 23.16±3.03 kg/m2 respectively. TG, TC, LDL, HDL-C, FBG, BUN, and serum uric acid was significantly higher for subjects with CKD with respective values of 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 compared to subjects without CKD where the respective values were 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. All these parameters were statistically significant with $p<0.001$. eGFR at baseline at ending point was significantly lower in subjects with CKD with values at baseline and ending was 68.73±7.64 and 48.73±8.74 ml/min/1.73m2, whereas, in subjects without CKD, eGFR at baseline and ending was 87.03±15.14 and 72.36±10.97 ml/min/1.73m2 ($p<0.001$). Also, Hypertension and diabetes were significantly higher in subjects with CKD ($p<0.001$) (Table 1).

On comparing the characteristics of the study subjects based on the age groups, it was seen that there were significantly more males for all the ages of ≤40 years, >40-≤60 years, and >60 years compared to females with p<0.001. The age was significantly higher in the age of >60 years followed by >40-≤60 years, and ≤40 years with a mean age of 72±6.83, 51±8.24, and 34±4.66 years respectively (p<0.001). BMI was also highest in the age of >60 years followed by >40-≤60 years, and ≤40 years with the mean value of 23.83±2.96, 23.57±2.87, and 22.46±3.07 kg/m2 (p<0.001). Cholesterol and HDL-C levels were also significantly higher at>60 years followed by >40-≤60 years, and ≤40 years with a p-value of 0.001 and <0.001 respectively. HDL-C, BUN, and FPG were also significantly higher for the age of >60 years followed by >40-≤60 years, and ≤40 years with the p-values of 0.002, <0.001, and <0.001 respectively. S. creatinine showed a non-significant difference between the three age groups with p=0.07. Serum uric acid, diabetes, and hypertension were statistically significant between the three age groups with p<0.001. eGFR was significantly lower in the age of >60 years followed by >40-≤60 years, and ≤40 years with the mean value of 86.84±11.75, 87.77±14.02, and 93.85±14.92 respectively with p<0.001. Incidence of new chronic kidney disease (CKD) was highest in the age of >60 years with 8.08% (n=24) subjects followed by 3.93% (n=21) for >40-≤60 years, and least in 1.93% (n=9) subjects in ≤40 years (Table 2).

Concerning the comparison characteristics of the study subjects based on the total cholesterol, the subjects were divided into 4 groups ≤4.20mmol/l, >4.20 -≤4.80 mmol/l, >4.80-≤5.40 mmol/l, and >5.40 mmol/l. There were significantly higher males in all 4 age groups with p<0.001. Higher BMI was for a cholesterol level of >5.40 kg/m2 and reduced with decreased cholesterol levels with p<0.001. Higher triglyceride values were seen for cholesterol levels of >5.40 mmol/l and decreased with lesser cholesterol levels (p<0.001). The lowest HDL-C value and highest HDL-C values were seen for the highest cholesterol group with a value of >5.40mmol/l (p<0.001). BUN and FPG values were lowest for cholesterol value of ≤4.20 mmol/l and highest for cholesterol range of >5.40mmol/l with p<0.001. SUA and hypertension values were significantly highest for high cholesterol values compared to low cholesterol values with p<0.001, whereas diabetes percentage and serum creatinine showed non-significant differences with higher values in the high cholesterol group and respective p-values of 0.373 and 0.08. eGFR showed a significant reduction with increased cholesterol values with p<0.001. Incidence of new chronic kidney disease events was higher in the high cholesterol group with an incidence of 8.07% (n=26) subjects compared to the low cholesterol group with 1.82% (n=6) subjects (Table 3).

DISCUSSION

The present retrospective clinical study was conducted to assess the correlation between incidence and progression of chronic kidney disease and dyslipidemia in Indian subjects. The study included 1296 subjects of both genders. The mean age of the study subjects with and without CKD was 68.42±24.46 and 47.64±21. TG, TC, LDL, HDL-C, FBG, BUN, and serum uric acid was significantly higher for subjects with CKD with respective values of 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 compared to subjects without CKD where the respective values were 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. All these parameters were statistically significant with p<0.001. eGFR at

baseline at ending point was significantly lower in subjects with CKD with values at baseline and ending was 68.73±7.64 and 48.73±8.74 ml/min/1.73m2, whereas, in subjects without CKD, eGFR at baseline and ending was 87.03±15.14 and 72.36±10.97 ml/min/1.73m2 ($p<0.001$). Also, Hypertension and diabetes were significantly higher in subjects with CKD ($p<0.001$). These demographics were comparable to the studies by Li LC et al[5] in 2018 and Yokoi H et al[6] in 2016 where authors assessed subjects with comparable demographics as to the present study.

For the comparison of the characteristics of the study subjects based on the age groups, it was seen that there were significantly more males for all the ages of ≤40 years, >40-≤60 years, and >60 years compared to females with $p<0.001$. The age was significantly higher in the age of >60 years followed by >40-≤60 years, and ≤40 years with a mean age of 72±6.83, 51±8.24, and 34±4.66 years respectively ($p<0.001$). BMI was also highest in the age of >60 years followed by >40-≤60 years, and ≤40 years with the mean value of 23.83±2.96, 23.57±2.87, and 22.46±3.07 kg/m2 ($p<0.001$). Cholesterol and HDL-C levels were also significantly higher at>60 years followed by >40-≤60 years, and ≤40 years with a p-value of 0.001 and <0.001 respectively. HDL-C, BUN, and FPG were also significantly higher for the age of >60 years followed by >40-≤60 years, and ≤40 years with the p-values of 0.002, <0.001, and <0.001 respectively. S. creatinine showed a non-significant difference between the three age groups with $p=0.07$. Serum uric acid, diabetes, and hypertension were statistically significant between the three age groups with $p<0.001$. eGFR was significantly lower in the age of >60 years followed by >40-≤60 years, and ≤40 years with the mean value of 86.84±11.75, 87.77±14.02, and 93.85±14.92 respectively with $p<0.001$. Incidence of new chronic kidney disease (CKD) was highest in the age of >60 years with 8.08% (n=24) subjects followed by 3.93% (n=21) for >40-≤60 years, and least in 1.93% (n=9) subjects in ≤40 years. These results were consistent with the findings of Gai Z et al[7] 2019 and Adeosun SO et al[8] in 2018 where authors showed that poor parameters for chronic kidney disease were associated with a higher age group.

In comparing the characteristics of the study subjects based on the total cholesterol, the subjects were divided into 4 groups ≤4.20mmol/l, >4.20 -≤4.80 mmol/l, >4.80-≤5.40 mmol/l, and >5.40 mmol/l. There were significantly higher males in all 4 age groups with $p<0.001$. Higher BMI was for a cholesterol level of >5.40 kg/m2 and reduced with decreased cholesterol levels with $p<0.001$. Higher triglyceride values were seen for cholesterol levels of >5.40 mmol/l and decreased with lesser cholesterol levels ($p<0.001$). The lowest HDL-C value and highest HDL-C values were seen for the highest cholesterol group with a value of >5.40mmol/l ($p<0.001$). BUN and FPG values were lowest for cholesterol value of ≤4.20 mmol/l and highest for cholesterol range of >5.40mmol/l with $p<0.001$. SUA and hypertension values were significantly highest for high cholesterol values compared to low cholesterol values with $p<0.001$, whereas diabetes percentage and serum creatinine showed non-significant differences with higher values in the high cholesterol group and respective p-values of 0.373 and 0.08. eGFR showed a significant reduction with increased cholesterol values with $p<0.001$. Incidence of new chronic kidney disease events was higher in the high cholesterol group with an incidence of 8.07% (n=26) subjects compared to the low cholesterol group with 1.82% (n=6) subjects. These results were in agreement with the

studies of Asghari G et al[9] in 2018 and Chang YC et al[10] in 2019 where higher cholesterol values are associated with degraded parameters of chronic kidney disease.

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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TABLES

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