DYSLIPIDAEMIA IN CKD PATIENTS AND ITS CORRELATION WITH SEVERITY OF RENAL DYSFUNCTION

Rina Mohanty[1], Ritesh Acharya[2], Pravat Kumar Thatoi[3], Hrudananda Bhuyan[4], Satarupa Mohapatra[5], Satyabrata Sahoo[6]

[1]Associate Professor, Department of Medicine, SCB Medical College, Cuttack, Odisha.
[2]Postgraduate Student, Department of Medicine, SCB Medical College, Cuttack, Odisha.
[3]Associate Professor, Department of Medicine, PRM Medical College, Baripada, Odisha.
[4]Postgraduate Student, Department of Medicine, SCB Medical College, Cuttack, Odisha.
[5]Postgraduate Student, Department of Medicine, SCB Medical College, Cuttack, Odisha.
[6]Postgraduate Student, Department of Medicine, SCB Medical College, Cuttack, Odisha.

ABSTRACT

BACKGROUND

Chronic kidney disease (CKD) is a significant global health problem with significant morbidity and mortality. Dyslipidaemia along with an abnormal apolipoprotein profile and composition is a common complication associated with the decline in eGFR in CKD. The association between abnormal lipid profile and severity of CKD has rarely been studied in a general population, especially in Indian setup and may have a future prognostic and management implication in patients with CKD.

Aims and Objectives- To study the pattern of lipid abnormalities in CKD patients and to correlate with severity of renal dysfunction.

MATERIALS AND METHODS

A descriptive comparative study was done using 50 cases of CKD of > 15 years age, along with 30 age and sex matched controls excluding confounding factors like diabetes, HTN, thyroid abnormalities, heart diseases, infection, inflammatory diseases, smoking, alcoholism etc. History, general and systemic examination, routine blood parameters, ECG, USG abdomen pelvis, serum total cholesterol, LDL, HDL, VLDL and triglycerides were done. The eGFR was calculated according to the CKD-EPI equation. Statistical analysis was done using student's t-test, ANOVA, Bonferroni test, Mann-Whitney U test, Chi-square test and Pearson's correlation. P value < 0.05 was considered as statistically significant.

RESULTS

The lipid profile in cases were TC: 184.96 ± 24.85 mg/dL; TGL: 148.10 ± 32.71 mg/dL; HDL: 32.38 ± 5.78 mg/dL; LDL: 122.82 ± 24.76 mg/dL; VLDL: 29.68 ± 6.54 mg/dL. Correlation between eGFR shows a significant negative correlation with TC (p= 0.007), TGL (p= 0.002), LDL (p= 0.000) and VLDL (p= 0.002) and positive correlation with HDL (p= 0.000). Comparison of lipid profile with grades of eGFR shows significant association with TGL (f= 3.804, p= 0.004), HDL (f= 18.099, p= 0.000), LDL (f= 3.793, p=0.004) and VLDL (f= 3.631, p= 0.005), but not with TC (f= 2.194, p= 0.064).

CONCLUSION

In CKD depending on severity there is a rise in TC, TGL, LDL, VLDL and a fall in HDL depending on severity.

KEYWORDS

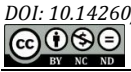
Chronic Kidney Disease, Total Cholesterol, Triglyceride, Low Density Lipoprotein, High Density Lipoprotein, Very High Density Lipoprotein, Disease Severity.

HOW TO CITE THIS ARTICLE: Mohanty R, Acharya R, Thatoi PK, et al. Dyslipidaemia in CKD patients and its correlation with severity of renal dysfunction. J. Evolution Med. Dent. Sci. 2018;7(11):1323-1327, DOI: 10.14260/jemds/2018/301

BACKGROUND

CKD encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in GFR.[1] CKD is a significant global health problem. About 6% adult population in US have CKD stage 1 and 2, and 4.5% have CKD stage 3 and 4.[1] Its prevalence is high in India with a study showing 229/million population suffering from ESRD.[2] Most common causes of CKD include diabetic nephropathy, glomerulonephritis, HTN associated CKD, ADPKD and cystic and tubulointerstitial nephropathy.[1]

'Financial or Other Competing Interest': None.
Submission 28-01-2018, Peer Review 20-02-2018,
Acceptance 27-02-2018, Published 12-03-2018.
Corresponding Author:
Dr. Ritesh Acharya,
Flat-404, Harihar Enclave, Goutam Nagar,
Bhubaneswar-751014,
Odisha, India.
E-mail: acharyaritesh1987@gmail.com
DOI: 10.14260/jemds/2018/301



Various complications of CKD include fluid electrolyte and acid base abnormalities, cardiovascular, neuromuscular, gastrointestinal, nutritional, endocrine and dermatological complications. Dyslipidaemia is a common complication of CKD and lipoprotein metabolism alteration and is associated with the decline in GFR; hence, lipid profile depends on the level of kidney function and the degree of proteinuria.[3,4] Disturbances in lipoprotein metabolism are evident even at the early stages of CKD and usually follow a downhill course that parallels the deterioration in renal function.[5] Severe lipid metabolism disorders arise in patients with kidney failure and the lipid metabolism disorder peculiar to this patient group is known as uraemic dyslipidaemia,[5] which may accelerate its progression.[6] Abnormal lipid profile in CKD includes hypertriglyceridaemia, increase in triglyceride remnant Lp (a), increase in VLDL, decrease in HDL, total cholesterol and LDL usually within normal limits except in nephrotic syndrome patients.[7] The association between lipid profile and severity of CKD has rarely been studied in a general population, especially in our part of the country and

may have a future prognostic and management implication in patients with CKD.

The present study evaluates the type of dyslipidaemia in CKD patients and correlates with severity of renal dysfunction in CKD patients.

MATERIALS AND METHODS

This study is a descriptive comparative study and conducted in Department of Medicine of SCB Medical College and Hospital, Cuttack, from December 2016 to November 2017. After clearance from Institutional Ethics Committee (IEC), we included 50 CKD patients admitted to medicine wards. Thirty age and sex matched controls were taken excluding confounding factors like diabetes, HTN, thyroid abnormalities, heart diseases, infection, inflammatory diseases, smoking, alcoholism etc. Written consent was obtained from each individual participating in the study.

Patient Selection Criteria: Males and females > 15 years of age who were diagnosed as chronic kidney disease patients, attending PG Department of Medicine of SCB Medical College and Hospital were taken as cases.

Exclusion Criteria: Patients with history of alcoholism, chronic smokers, liver disease, hypothyroidism, metabolic syndrome, diabetes mellitus, hypertension, malignancy, coronary artery disease, history of lipid lowering drug intake and connective tissue disorders were excluded.

Investigations

All patients had undergone thorough clinical examination and laboratory investigations like complete blood counts, serum urea and creatinine, serum sodium and potassium, serum calcium, liver function tests, serum protein and albumin, blood glucose, arterial blood gases, lipid profiles, thyroid function tests and urine analysis. Electrocardiography and ultrasonography of abdomen were done on every patient. All blood samples were collected after 12 hours of fasting.

The eGFR was calculated according to the CKD- EPI (Chronic Kidney Disease Epidemiology Collaboration) equation, 2009. EGFR was graded G1, G2, G3, G4 and G5 as per the KDIGO 2012 guidelines.[1] Urine albumin was graded on basis of heat coagulation test as 0, trace (T) +, ++, +++ and ++++.

Statistical Analysis

The statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 21.0. Univariate analysis was used in description of demographic characteristics of the study population. Continuous variables were presented as means and standard deviation for unskewed data and median and interquartile range for skewed data. Student t-test was used to compare mean values (for two groups) and F test for Analysis of Variance (ANOVA) for more than two groups with unskewed data. Post hoc analysis was done using the Bonferroni test. Mann-Whitney U test was used to compare skewed data. Discrete variables were presented as frequency and percentages. Chi-square test was used to determine the significant associations between categorical variables. Pearson's correlation was used to determine association between eGFR and other variables. P value < 0.05 was considered statistically significant and < 0.001 was considered as statistically highly significant.

RESULTS

Age (In Years)	Study Group		Chi-Square Tests
	Case	Control	
15-30	2 (4%)	3 (10%)	Chi-square: 2.048 df: 3 p: 0.562
31-45	17 (34%)	10 (33.3%)	
46-60	24 (48%)	11 (36.7%)	
>60	7 (14%)	6 (20%)	
Total	50 (100%)	30 (100%)	

Table 1. Age Distribution of Cases and Controls

Sex	Study Group		Chi-Square Tests
	Case	Control	
Male	29 (58%)	18 (60%)	Chi-Square: 0.031 df: 1 p: 0.860
Female	21 (42%)	12 (40%)	
Total	**50 (100%)**	**30 (100%)**	

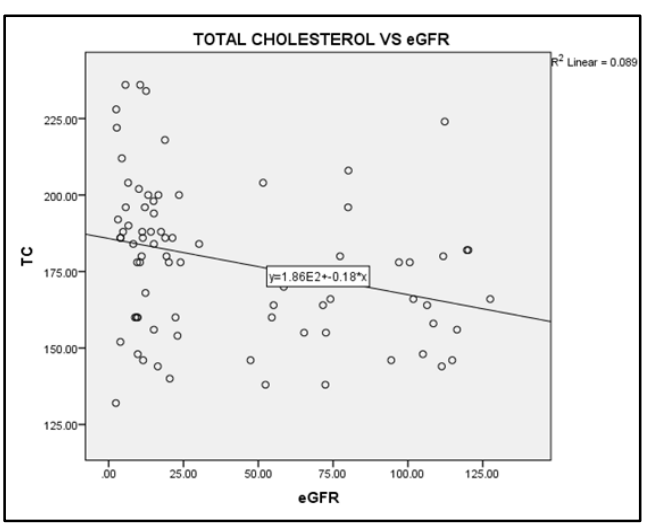
Table 2. Sex Distribution of Cases and Controls

The age and sex distribution of cases and controls shows both the study groups are age and sex matched.

eGFR (mL/ min./1.73 m²)	Cases (50)
≥90 (G1)	0 (0%)
60-89 (G2)	0 (0%)
45-59 (G3a)	1 (2%)
30-44 (G3b)	1 (2%)
15-29 (G4)	17 (34%)
<15 (G5)	31 (62%)

Table 3. Severity Grading of CKD Cases on Basis of eGFR

Grading the cases in terms of severity showed 62% of the cases were in grade 'g5' and 34% were in grade 'g4.'



Mean ± S.D.	Study Group		Significance
	Case (mg/dL)	Control (mg/dL)	
TC	184.96 ± 24.85	166.90 ± 19.81	p= 0.001
TGL	148.10 ± 32.71	124.33 ± 21.98	p= 0.001
HDL	32.38 ± 5.78	42.50 ± 4.25	p= 0.000
LDL	122.82 ± 24.76	100.33 ± 16.71	p= 0.000
VLDL	29.68 ± 6.54	25.06 ± 4.44	p= 0.001

Table 4. Comparison of Lipid Profile between Cases and Controls (Independent Samples T-Test)

The comparison between lipid profiles of cases and controls showed significant difference between total cholesterol (p= 0.001), triglyceride (p= 0.001), high density

lipoprotein (p= 0.000), low density lipoprotein (p= 0.000) and very low density lipoprotein (p= 0.001).

eGFR vs	Pearson's Correlation (r)	Significance (p)
TC	- 0.299	0.007
TGL	- 0.347	0.002
HDL	0.696	0.000
LDL	- 0.408	0.000
VLDL	- 0.336	0.002

Table 5. Correlation between eGFR and Lipid Profile

Correlation between eGFR and lipid profile shows a significant negative correlation of eGFR with total cholesterol (p= 0.007), triglycerides (p= 0.002), low density lipoproteins (p= 0.000) and very low density lipoproteins (p= 0.002) and positive correlation with high density lipoproteins (p= 0.000).

Lipid Profile	eGFR Grades	Mean ± S.D.	P value
TC	30-59	166.57 ± 22.38	0.043
	15-29	179.05±21.25	
	<15	187.61±26.85	
TGL	30-59	120.85±31.68	0.002
	15-29	134.84±34.73	
	<15	155.90±29.17	
HDL	30-59	39.14±3.84	0.000
	15-29	35.58±5.14	
	<15	30.38±5.42	
LDL	30-59	103.28±19.44	0.003
	15-29	116.17±20.58	
	<15	126.00±27.11	
VLDL	30-59	24.14±6.30	0.003
	15-29	27.05±6.95	
	<15	31.22±5.86	

Table 6. Comparison of Lipid Profile with various Grades of eGFR

There is a significant rise in total cholesterol (p= 0.043), triglycerides (p= 0.002), low density lipoproteins (p= 0.003) and very low density lipoproteins (p= 0.003) and fall in high density lipoproteins (p= 0.000) with decreasing eGFR grades.

	Cases (Mean ± S.D.)	Controls (Mean ± S.D.)	Significance (p)
Hb	8.782 ± 1.705	11.046 ± 1.617	0.000
S. Na^+	130.64 ± 11.82	140.36 ±6.49	0.000
S. K^+	3.98 ± 0.70	3.96 ± 0.50	0.871
S. Protein	6.53 ± 0.55	7.28 ± 0.45	0.000
S. Albumin	3.49 ± 0.46	4.29 ± 0.42	0.000
FBS	97.94 ± 15.89	91.70 ± 12.32	0.069
PPBS	127.14 ± 14.12	125.10 ± 11.43	0.505
HbA1C	5.56 ± 0.67	5.72 ± 0.52	0.255
BMI	19.97 ± 3.13	20.46 ± 3.48	0.513
Total Bilirubin	0.70 ± 0.24	0.63 ± 0.22	0.187
Direct Bilirubin	0.24 ± 0.11	0.19 ± 0.10	0.084
AST	24.8 ± 8.46	23.9 ± 8.84	0.652
ALT	24.32 ± 8.72	23.67 ± 8.83	0.748
ALP	74.12 ± 20.83	84 ± 23.17	0.053
TSH	2.53 ± 0.93	2.55 ± 0.94	0.956
FT3	4.87 ± 1.08	4.52 ± 1.10	0.172
FT4	17.19 ± 2.78	15.93 ± 3.33	0.073

Mann-Whitney U	Median	IQR	Significance (p)
Blood urea	75	38.00-128.25	0.000
Serum creatinine	3.25	1.025-5.725	0.000

Table 7. Comparison of various Parameters between Cases and Controls (Independent Samples T-Test)

On comparing various parameters between cases and controls, there is a significant decrease in Hb (p= 0.000), S. Na (p= 0.000), S. Protein (p= 0.000), S. Albumin (p= 0.000) and a rise in B. Urea (p= 0.000) and S. Creatinine (p= 0.000).

eGFR vs	Pearson Correlation (r)	Significance (p)
Hb	0.502	0.000
BMI	0.137	0.227
S. Na^+	0.414	0.000
S. K^+	0.052	0.647
B. Urea	-0.683	0.000
S. Creatinine	-0.682	0.000
S. Protein	0.526	0.000
S. Albumin	0.619	0.000
FBS	-0.192	0.088
PPBS	-0.156	0.167
HbA1C	0.057	0.617
Total Bilirubin	-0.082	0.470
Direct Bilirubin	-0.120	0.287
AST	-0.040	0.726
ALT	-0.041	0.716
ALP	0.181	0.108
TSH	-0.015	0.893
FT3	-0.105	0.356
FT4	-0.173	0.125

Table 8. Correlation between various Parameters and eGFR

On correlating eGFR with various parameters, statistical significance was observed with Hb (r= 0.502, p= 0.000), S. Na (r= 0.414, p= 0.000), B. Urea (r= -0.683, p= 0.000), S. Creatinine (r= -0.682, p= 0.000), S. Protein (r= 0.526, p= 0.000) and S. Albumin (r= 0.619, p= 0.000).

DISCUSSION

Fifty cases of CKD were taken in the study, eliminating those which fell under the exclusion criteria. Thirty age and sex category matched healthy individuals were taken as controls. The age of the study population ranged from 25 to 75 years. Mean age of cases was 49.06 ± 12.52 years and controls was 49.6 ± 12.07 years. This was similar to that of CKD Registry of India 2007,[8] where the mean age of cases was 48.3 ± 16.6 years and in the studies by Patel and Sirajwala[9] and by Adejumo, Okaka and Ojogwu.[10] As depicted in Table 1, the age group with maximum percentage of study population was 46-60 years' group with 48% of cases and 36.7% of controls in the same. In CKD Registry of India 2007[8], 71.2% of the cases belonged to age group 19 - 60 years. As depicted in Table 2, the sex distribution showed 58% of cases were males and 42% were females. Among controls, 60% were males and 40% were females. The majority of our patients belonged to male gender. In CKD Registry of India 2007[8], the percentages of male cases were 68.9 and female cases were 31.1. Similar results to current study were seen in studies by Abraham et al[11] and Ganta et al.[12] The mean eGFR calculated by the CKD-

EPI equation[1] was found to be 13.12 ± 8.67 in cases and 88.44 ± 23.9 in controls. There was a significant fall in eGFR in CKD cases. The mean eGFR of study by Sumanth and Shobharani[13] was 22.22 ± 8.70 and that by Adejumo et al[14] was 30.19 showing results similar to our study. On basis of severity grades 62% of cases were in G5 grade and 34% of cases were in G4 grade as shown in Table 3. Most CKD cases belonged to grade G5 followed by G4. In CKD Registry India 2007, 50.3% cases were in G5 and 24% were in G4. In study by Ganta et al,[12] 45.71% cases were in G5 and 37.14 % were in G4. These findings were similar to that in our study. As shown in Table 4, the study of various lipid parameters showed the Mean ± S.D. of serum total cholesterol to be 184.96 ± 24.85 in cases and 166.90 ± 19.81 in controls, and the difference was statistically significant with a 'p' value of 0.001. The Mean ± S.D. of serum triglycerides, high density lipoprotein, low density lipoprotein and very low density lipoprotein for cases were 148.10 ± 32.71, 32.38 ± 5.78, 122.82 ± 24.76 and 29.68 ± 6.54 and for controls were 124.33 ± 21.98, 42.50 ± 4.25, 100.33 ± 16.71 and 25.06 ± 4.44 respectively. The differences were statistically significant with 'p' values of 0.001, 0.000, 0.000 and 0.001 respectively for serum triglycerides, high density lipoprotein, low density lipoprotein and very low density lipoprotein. The correlation between eGFR and various lipid parameters depicted in Table 5 showed a statistically significant correlation between eGFR and serum total cholesterol (r= -0.299, p= 0.007), serum triglycerides (r= -0.347, p= 0.002), serum high density lipoprotein (r= 0.696, p= 0.000), low density lipoprotein (r= -0.408, p= 0.000) and serum very low density lipoprotein (r= -0.336, p= 0.002). As shown in Table 6 on comparing the various lipid parameters with grades of eGFR, serum triglycerides (F= 3.804, p= 0.004), high density lipoproteins (F= 18.099, p= 0.000), low density lipoproteins (F= 3.793, p= 0.004) and very low density lipoproteins (F= 3.631, p= 0.005) showed statistical significance, but no such significance was observed for serum total cholesterol (F= 2.194, p= 0.064). These findings indicate a rise in serum total cholesterol, triglycerides, low density lipoproteins, very low density lipoproteins and a fall in high density lipoproteins in CKD with fall in eGFR. Similar changes in lipid profile were seen by Machnur and Chandrashekar,[15] Patel and Sirajwala,[9] Ganta V et al,[12] Attman, Samuelsson and Alaupovic,[16] Mannangi et al and Wang et al,[17] Paul and Kurien[18] in separate studies showed significant inverse correlation between triglyceride and GFR and significant positive correlation between high density lipoprotein and GFR (p= < 0.001).

Table 7 depicted that comparing Mean ± S.D. of haemoglobin levels of case and controls showed a value of 8.782 ± 1.705 in cases and 11.046 ± 1.617 in controls with a 'p' value of 0.000. This shows a fall in haemoglobin with CKD. Similar reports have been given by studies of Chonchol et al[19] and Ortega et al.[20] For BMI, it was 19.97 ± 3.13 for cases and 20.46 ± 3.48 for controls. The values were not statistically significant with a 'p' value of 0.513. The CKD Registry of India 2007[8] had majority of patients between BMI range of 18.5 and 24.9. For serum sodium, the Mean ± S.D. of cases was 130.64 ± 11.82 and controls was 140.36 ± 6.49. The values were statistically significant with a 'p' value of 0.000. This indicates the presence of significant hyponatraemia in CKD patients. For potassium, it was found to be 3.98 ± 0.70 and 3.96 ± 0.50 for cases and controls respectively with no statistical significance (p= 0.871). The median of blood urea and serum creatinine were 75 (IQR= 38 - 128.25) and 3.25 (IQR= 1.025 - 5.725) respectively. The values were statistically significant with 'p' values of 0.000 for both. This indicates a significant rise in blood urea and serum creatinine in CKD patients. Similar results have been reported by Lakshmi, Subhashini and Swami.[21] The Mean ± S.D. of serum protein and serum albumin were 6.53 ± 0.55 and 3.49 ± 0.46 for cases, and 7.28 ± 0.45 and 4.29 ± 0.42 for controls respectively. The values were statistically significant with 'p' values of 0.000 for both. This indicates a fall in serum protein and albumin in CKD. Similar report has been submitted by the study of Adejumo et al.[10] As shown in Table 8, statistically significant correlation was found between eGFR and haemoglobin, serum sodium, serum protein, serum albumin, blood urea and serum creatinine with r= 0.502, 0.414, 0.526, 0.619, -0.683 and -0.682 respectively with 'p' value of 0.000 in all. Values of BMI and serum potassium did not show any statistical significance.

CONCLUSION

Our study revealed that there was significant dyslipidaemia in CKD patients. There was rise in total cholesterol, triglycerides, low density lipoproteins, very low density lipoproteins and a fall in high density lipoproteins in CKD. These changes in lipid profile varied significantly when correlated with fall in eGFR. There is significant change in all lipid parameters when compared with grades of eGFR.

REFERENCES

[1] Bargman JM, Skorecki K. Chronic kidney disease in Harrison's principles of internal medicine. Vol 2. 19th edn. McGraw-Hill Publication 2015;335:1811-21.
[2] Modi GK, Jha V. The Incidence of end-stage renal disease in India: a population-based study. Kidney Int 2006;70(12):2131-3.
[3] Cases A, Coll E. Dyslipidemia and the progression of renal disease in chronic renal failure patients. Kidney Int Suppl 2005;68(Suppl 99):S87-S93.
[4] Weiner DE, Sarnak MJ. Managing dyslipidemia in chronic kidney disease. J Gen Intern Med 2004;19(10):1045-52.
[5] Tsimihodimos V, Mitrogianni Z, Elisaf M. Dyslipidemia associated with chronic kidney disease. The Open Cardiovascular Medicine Journal 2011;5:41-8.
[6] Tudor MN, Mitrea A, Popa SG, et al. Apolipo proteins: Good markers for cardiovascular risk in patients with CKD and dyslipidemia. Romanian Journal of Diabetes, Nutrition and Metabolic Diseases 2014;21(3):185-91.
[7] Ulosoy S, Ozkan G. Lipid abnormalities in haemodialysis patients. Haemodialysis 2013;6:101-25.
[8] Dash ASC, Rana DS, Sharma RK, et al. 2nd Annual Report CKD Registry of India, Indian Society of Nephrology 2007.
[9] Patel L, Sirajwala H. Serum Apolipoprotein A-1, Apolipoprotein B and Apo B/Apo A-1 ratio as cardiovascular risk indicators in patients of chronic renal failure. International Journal of Biomedical and Advance Research 2014;5(5):234-6. DOI:10.7439/ijbar

[10] Adejumo OA, Okaka EI, Ojogwu LI. Lipid profile in pre-dialysis chronic kidney disease patients in southern Nigeria. Ghana Med J 2016;50(1):44-9.
[11] Abraham G, Sundaram V, Sundaram V, et al. C-reactive protein, a valuable predictive marker in chronic kidney disease. Saudi J Kidney Dis Transpl 2009;20(5):811-5.
[12] Ganta V, Yalamanchi RP, Mahanta KC, et al. A study of lipid profile in non-diabetic chronic kidney disease. Int J Adv Med 2016;3(4):965-70.
[13] Sumanth BK, Shobharani B. Comparative study of Hscrp in chronic kidney disease. IOSR Journal of Pharmacy 2015;5(7):8-12.
[14] Adejumo OA, Okaka EI, Okwuonu CG, et al. Serum C-reactive protein levels in pre-dialysis chronic kidney disease patients in southern Nigeria. Ghana Med Journal 2016;50(1):31-8.
[15] Machnur B, Chandrashekar. Lipid abnormality in chronic kidney disease: descriptive study. Int Journal of Med Research 2016;1(3):19-21.
[16] Attman PO, Samuelsson O, Alaupovic P. Lipoprotein metabolism and renal failure. Am J Kidney Dis 1993;21(6):573-92.
[17] Chu M, Wang AY, Chan IH, et al. Serum small-dense LDL abnormalities in chronic renal disease patients. British Journal of Biomedical Science 2012;69(3):99-102.
[18] Paul JK, Kurien SV. Study of lipid profile in chronic kidney disease patients of non-diabetic etiology and its relation to serum calcium. JMSCR 2017;5(9):28284-90.
[19] Chonchol M, Lippi G, Montagnana M, et al. Association of inflammation with anaemia in patients with chronic kidney disease not requiring chronic dialysis. Nephrol Dial Transplant 2008;23(9):2879-83.
[20] Ortega O, Rodriguez I, Gallar P, et al. Significance of high C-reactive protein levels in pre-dialysis patients. Nephrol Dial Transplant 2002;17(6):1105-9.
[21] Lakshmi MSR, Subhashini YR, Swami KSR. Study of lipid profile in chronic renal failure. J Evid Based Med Healthc 2016;3(32):1508-15.