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RESEARCH ARTICLE
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A STUDY OF LIPID PROFILE AND THYROID HORMONE STATUS IN CHRONIC KIDNEY DISEASE PATIENTS ATTENDING THE DEPTARTMENT OF GENERAL MEDICINE, BANKURA SAMMILANI MEDICAL COLLEGE AND HOSPITAL, BANKURA

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INTRODUCTION

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologycal processes associated with abnormal kidney function and progressive decline in glomerular filtration rate. Now the recently updated classification in which stages of CKD are stratified by estimated GFR and the degree of Albuminuria in order to predict the risk of progression of CKD. Previously CKD has been staged solely by the GFR. However the risk of worsening of the kidney function is closely linked to the amount of albuminuria and so it has been incorporated into the classification[1].

The National Kidney Foundation (NKF) sponsored the Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines in 2002, which described the conceptual model, definition, and classification of CKD (Kidney Disease Outcomes Quality Initiative (K/DOQI), 2002). These guidelines were subsequently adopted with minor modifications by the international guideline group Kidney Disease Improving Global Outcomes (KDIGO) in 2004 (Levey et al., 2005)[2,3].

In 2009, KDIGO held a controversies conference to re-examine the CKD definition and classification. Participants at this conference reached a consensus to retain the 2002 KDOQI definition of CKD, but recommended including the cause of CKD and the level of albuminuria in the revised classification system (Levey et al., 2011)[2,4]. Based on these recommendations, KDIGO recently updated the 2002 KDOQI guidelines in 2012 (Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work

Group, 2013). CKD is defined as the presence of kidney damage or GFR < 60 mL/min/1.73 m2 (GFR in mL/min/1.73 m2 may be converted to mL/s/1.73 m^2 by multiplying by 0.01667) for ≥ 3 months, irrespective of cause (Kidney Disease Outcomes Quality Initiative (K/DOQI), 2002; Levey et al., 2005).[2]

CKD is classified based on Cause, GFR category (G1-G5) and Albuminuria category (A1-A3), abbreviated as CGA.[5]

GFR categories (ml/min/ 1.73 m^2). Description and range[5]

G1	Normal or high	≥90
G2	Mildly decreased	60-89
G3a	Mild to moderately decreased	45-59
G3 b	Moderate to severely decreased	30-44
G4	Severely decreased	15-29
G5	Kidney failure	<15

Persistent albuminuria categories. Description and range (By albumin-creatinine ratio – ACR)[5]

A1	**A2**	**A3**
Normal to mildly increased	Moderately increased	Severely increased
<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol

Chronic kidney disease (CKD) is becoming a serious health problem. The number of people with impaired renal function is rapidly rising, especially in industrialized countries[6]**.** The crude and age adjusted end stage renal disease (ESRD) incidences in India have been estimated to be 151 and 232 per million population, respectively.[7]

In India, Mani[8,9]reported a prevalence of CKD of 1.1% among a rural population of 25,000 who were subjects of a universal screening program in which serum creatinine level was measured only in those with hypertension or proteinuria. Agarwaland colleagues[8,10]screened 4700 adults in an urban community and found a point prevalence of 7852 per million individuals with a serum creatinine level greater than 1.8 mg/dL. These figures must be interpreted with caution because of the wide variations in the definition of CKD, methodology, and sampled population.[8]

Reports suggest that progression of CKD is associated with having a number of complications, including dyslipidemia, thyroid dysfunction and CVD.[11,12] Of the multiple lipid abnormalities in patients on maintenance HD, low high-density lipoprotein (HDL) and elevated lipoprotein (a) [Lp(a)] are key predictors of cardiovascular disease.[8] Lipid abnormalities are common in patients with CKD. In several studies, dyslipidemia has been identified as both a susceptibility risk factor and a progression risk factor for CKD. Dyslipidaemia is a major risk factor for coronary heart disease. Several factors contribute to the development of dyslipidemia associated with chronic renal impairment. Patients with CKD have a reduction in the activity of lipoprotein lipase and hepatic triglyceride lipase. This interferes with uptake of triglyceride rich, apolipoprotein B containing lipoproteins by the liver and in peripheral tissue, yielding increased circulation of these atherogenic lipoproteins[11]. Progression of CKD is accompanied by the development of specific alterations of the lipoprotein metabolism[12]. Reports show that mortality due to CVD was 10–30 times higher in dialysis patients than in the general population[13]. Abnormalities in lipid metabolism occur in all stages of CKD. In CKD beyond stage 3, the characteristic lipid profile is accumulation of very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), elevated triglyceride (TG), low high density lipoproteins (HDL)[13,14]and elevated LDL/HDL ratio[15,16]

The pattern of dyslipidaemia depends on the stage of CKD, dialysis and transplantation, proteinuria, drug therapy, and primary disease (e.g. diabetes). It is simplest, therefore, to refer to dyslipidaemia, rather than hyperlipidaemia, as cholesterol concentrations may not be raised.[2]

The characteristic features of dyslipidaemia associated with CKD are elevated triglycerides (TGs), reduced high-density lipoprotein cholesterol (HDL-C), and increased intermediate-density lipoprotein cholesterol (IDL-C) (Kidney Disease Outcomes Quality Initiative (K/DOQI) Group 2003; Prichard, 2003; Jardine et al., 2008. These are associated with qualitative changes in lipoproteins, including an excess of TG-rich, immature, atherogenic lipoproteins (Vaziri, 2006).[17,18,18,19,20]

All these defects contribute to the overall pattern of dyslipidaemia—the pattern reflecting the effects of low GFR and proteinuria. The key features are an increase in TG-rich, immature particles; with elevated TGs, reduced HDL-C and increased IDL-C rather than the increase in LDL-C that is associated with increased risk of CVD in other populations.[16,17,20]

It is also seen that Moorhead and colleagues advanced the hypothesis that abnormalities in lipid metabolism may contribute to the progression of CKD.[8,21,22] They proposed that urinary losses of albumin and lipoprotein lipase activators result in an increase in circulating LDLs, which in turn bind to the glomerular basement membrane further impairing its permeability; filtered lipoproteins accumulate in the mesangium, stimulating extracellular matrix synthesis and mesangial cell proliferation; filtered LDL is taken up and metabolized by the tubules, leading to cell injury and interstitial disease. Several lines of experimental evidence confirm the association between dyslipidemia and renal injury.[21.22]

Several epidemiological studies found a strong association between CKD progression and dyslipidemia. In the MDRD study, low serum HDL cholesterol was found to be an independent predictor of more rapid rates of decline in GFR.[21,23]Elevated total cholesterol, LDL-cholesterol, and apolipoprotein B have been found to correlate strongly with GFR decline in CKD patients.[21,24] Hypercholesterolemia was shown to be a predictor of loss of renal function in type 1 and type 2 diabetics.[21,25]Among non-diabetic patients CKD advanced more rapidly in patients with hypercholesterolemia and hypertriglyceridemia, independent of blood pressure control.[21,26]

Most endocrine systems are tightly regulated in a multiple-level feedback loop to attain circulating hormone levels to maintain adequate amount of hormone level. Reduced renal function and ureamia can interfere with this feedback system and cause significant derangement of circulating hormonal level[26,27].
Thyroid hormones and renal systems are interlinked in a very complex manner.[28,29]The kidney normally plays an important role in the metabolism, degradation and excretion of thyroid hormones. CKD affects the hypothalamus pituitary thyroid axis, including low circulating thyroid hormone levels, altered peripheral hormone metabolism, insufficient binding to carrier proteins, reduced tissue thyroid hormone content and altered iodine storage in the thyroid gland. Thus in CKD thyroid hormone metabolism is impaired [29,30].It also alters the 'Milieu interior' that affects every system in the body. One such system in the body is thyroid hormonal system. Kidney is closely related to thyroid in the fact that it is the only other organ that competes with iodide clearance[31,32]. Thus, in CKD, thyroid hormone metabolism is impaired.Thyroid hormones (TH) are necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis. On the other hand, kidney is involved in the metabolism and elimination of TH. Both hypothyroidism and hyperthyroidism are accompanied by remarkable alterations in the metabolism of water and electrolyte, as well as in cardiovascular function. All these effects generate changes in water and electrolyte kidney management[32].Thyroid dysfunction acquires special characteristics in those patients with advanced kidney disease[31,33,34]. On the other hand, the different treatments used in the

management of patients with kidney and thyroid diseases may be accompanied by changes or adverse events that affect thyroid and kidney function respectively. Epidemiological data showed that CKD has increased risk of hypothyroidism. In CKD, hypothyroidism causes increased cardiac morbidity[32,34].

AIMS AND OBJECTIVES

AIMS

To find out the prevalence of lipid and thyroid disorders in patients of chronic kidney disease.

OBJECTIVES

1) To assess lipid profile in chronic kidney disease patients.
2) To find out serum levels of different hormones related to thyroid function (T_3, T_4, TSH) in chronic kidney patients.
3) To study the correlation of thyroid hormone status with derangement of kidney function.
4) To study the correlation of lipid profile with derangement kidney function.

MATERIALS AND METHODS

Study area:Department of General Medicine, BSMCH, Bankura
Study period:One year
Study population:Patients admitted (indoor) and attending outpatient department of BSMC&H.
Inclusion Criteria
All patient with age > 18 yr with proved chronic kidney disease according to NKF-KDOQI guidelines. CKD will be defined on the basis of National Kidney Foundation guidelines of having an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.732 m2 for more than 3 months. The Modification of Diet in Renal Disease study (MDRD) equation will be used to calculate eGFR.

Exclusion Criteria
• Hypopituiterism
• Secondary hypothyroidism due to ICSOL and radiation therapy
• Patient on thyroid or antithyroid medication and anti lipid medications.
• Previously undergone thyroid surgery
• Acute on chronic kidney disease
• Any febrile episode during the evaluation

Sample size:$N= (Z^2pq)/L^2$, where Z=1.96 at 5% precision, p=prevalence of thyroid dysfunction, q= (100-p), L= allowable error.
Now, $N= (3.84\times9\times91)/5^2$ ..... [Assuming p=9% & L=5 (absolute)]
=125.79=126 (Approx.).
Revised sample size, Ns = N×FPC (Finite population correction)
$Ns=N\times FPC=N\times\sqrt{\{(Np-N)/(Np-1)\}}= 126\times0.79= 99.5 \approx100$ ..... [where, Np = target finite population; here it will be 600].

Sampling design: Systemic Random Sample will be taken. There will be minimum 28 (7x4) weeks for data collection. Number of patients will have to selected per clinic day=100/28=3.57=4. These four patients will be selected from the 20 patients attending daily. Systemic Random Sampling technique will be undertaken for selecting study subjects. So, every 20/4=5th patient will be approached. The starting will be done unbiasedly, using simple random sampling method involving those who will be present at the time of starting sampling

Study Type: Descriptive hospital based study.
Study Design:Cross sectional study.

Study Variables:
Socio-demographic variables:
Age, Sex, Residence, Occupation, Marital status, Family income, Co-morbidity
Biochemical parameter
- Serum creatinine, urea, sodium , potassium
- Serum T_3, T_4, TSH
- Lipid profile- Total Cholesterol, Low density lipoprotein, High density lipoprotein, Triglyceride, Very low density lipoprotein

Radiological study
-Ultrasonography of kidney, ureter, bladder system

Study tools:
1. Predesigned & pretested Questionnaire.
2. Equipments for clinical examination including anthropometry (weighing machine, sphygmomanometer, measuring tape).
3. Materials needed for withdrawal blood from patients: cotton & spirit, disposable syringe with needle, hub-cutter, gloves, tourniquet, vials (clotted, fluoride), eppendorfs.
4. Sterile container for collection of urine.
5. Laboratory instruments: The machines are already existed in the laboratory & will be used for the present study-

a. Semi automated clinical chemistry analyzer.
b. ELISA reader.
c. Centrifuge machine.
d. Micropipettes, beaker, centrifuge tubes, funnel, measuring cylinder, test tubes, test tube rack, dispensing bottle.

6. USG machine available in Radiology department.
7. Reagents and kits for estimation of serum T_3, T_4, TSH, urea, creatinine and lipid profile.

Study technique:Patient attending outdoor and admitted in BSMC&H Medicine dept are randomly selected according to inclusion and exclusion criteria and subjected to detailed history taking , clinical, haematological, biochemical and radiological examination.
Procedure of data collection: Subjects will be selected according to the exclusion & inclusion criteria. The patients will be taken from the outpatient department as well as the Inpatient department of General Medicine.
Method of data analysis: Data will be codified, compiled & tabulated in MS Excel spread sheet and summarised using mean, median, proportions, standard deviation, range etc. Tables, charts, diagrams etc will be prepared for describing data. Different statistical tests like Chi-square, Independent t-test, ANOVA, Pearson's/Spearman's correlation coefficients etc. will be done as per necessity. Statistical software [Statistical Package for Social Sciences (SPSS)- free version] will be utilised, if required
Ethical consideration: This study will be conducted only after obtaining proper written ethical permission. From the Ethics Committee of BSMC&H and approval from West Bengal University of Health Sciences. Written informed consent will be taken from every study subject or from their legal representative.

Additional Resources
- Human resources:
- Financial support: No additional financial support is required as the procedures will be done in the respective departments in the Institute

Table 1: Distribution of patients according to Age and Sex (n=100)

Age (years)	Male		Female		Total	
	No	%	No	%	No	%
≤ 30	12	75.0	4	25.0	16	100.0
31 – 60	41	66.1	21	33.9	62	100.0
> 60	18	82.8	4	18.2	22	100.0
Total	71	71.0	29	29.0	100	100.0
Mean age 50.56, SD 13.72						

It is observed from the above table that the maximum number of study subjects were male(71%) and 29% were female. Highest proportion of participants found in age group of 31-60 years of age, of which 66.1% were male (41 patients) and rest were female (34%, 21 patients).Total 62 patients in this age group.

Among the patients less than or equal to 30 years of age male patients were 12 in number (75%) and female patients were 4 in number (25%).

Above 60 years of age 82% (18 in number) were male and 18% (4 in number) were female. Mean age is 50.56 and SD 13.72

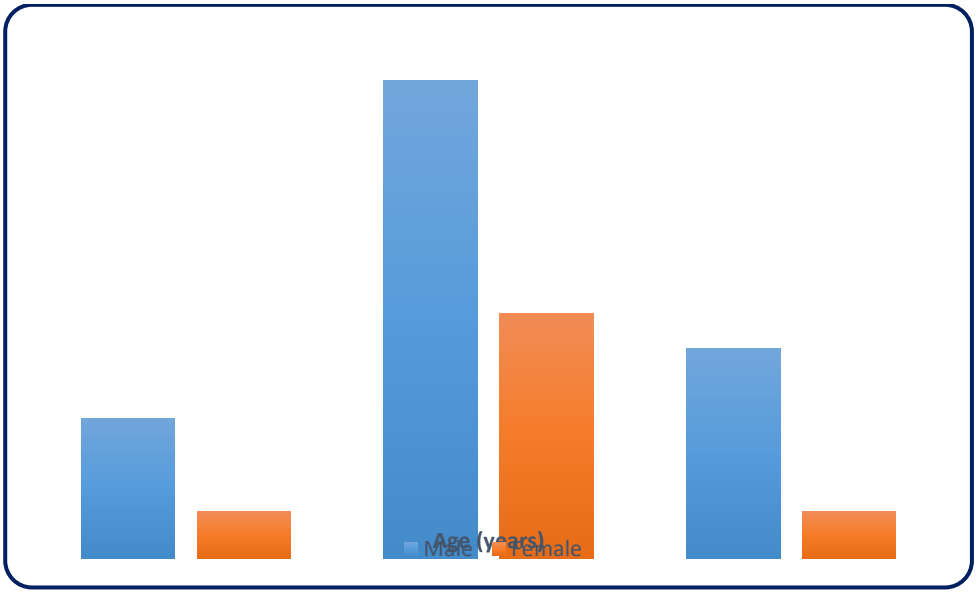

Fig …….: Bar diagram showing age and sex distribution of study participants (n = 100)

Table 2: Distribution of patients according to staging of CKD (n=100)

	Range of eGFR (ml/min)	No	%	Mean of eGFR (ml/min)	SD of eGFR (ml/min)
CKD- III	30-59	9	9.0	35.54	3.49
CKD- IV	15-29	25	25.0	19.35	3.55
CKD- V	<15	66	66.0	8.12	3.79

In this table it has been showed that maximum number of participants were within CKD stage V (66%). Minimum number of patients were in CKD III (9%). CKD-IV stage had only 25% of participants. Mean eGFR and SD of CKD stage III,IV,V are 35.54±3.49, 19.35±3.55, 8.12±3.79

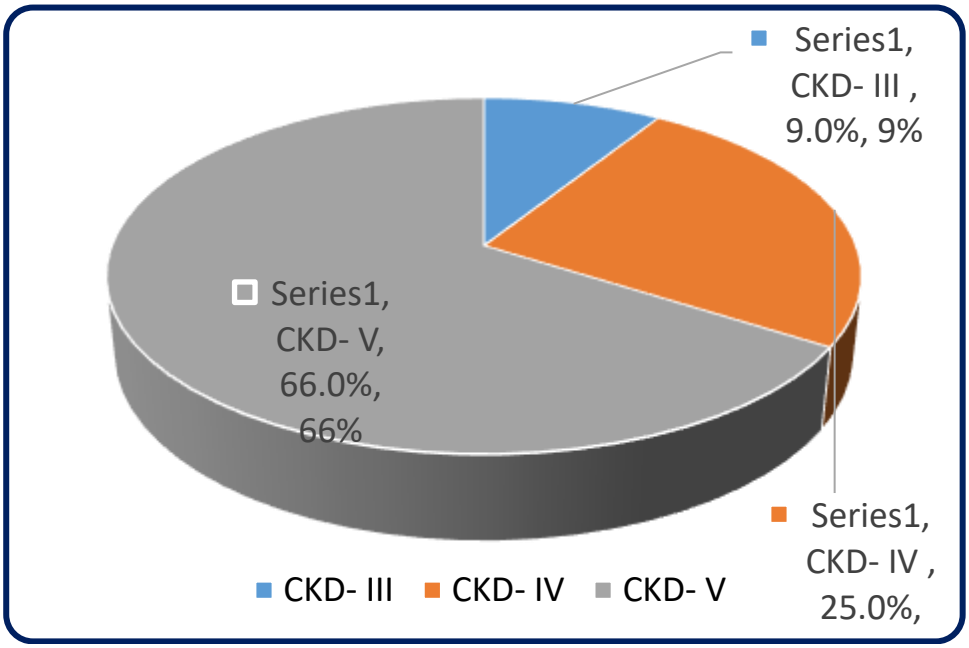

Fig …….: Pie diagram showing stages of CKD among study participants (n = 100)

Table 3 : Mean and SD of urea and creatinine levels in study subjects (n = 100)

	Mean	SD
Urea (mg/dl)	107.34	28.69
Creatinine (mg/dl)	6.68	4.03

It is observed from above table Mean and SD of urea and creatinine are 107.34±28.69 , 6.68±4.03

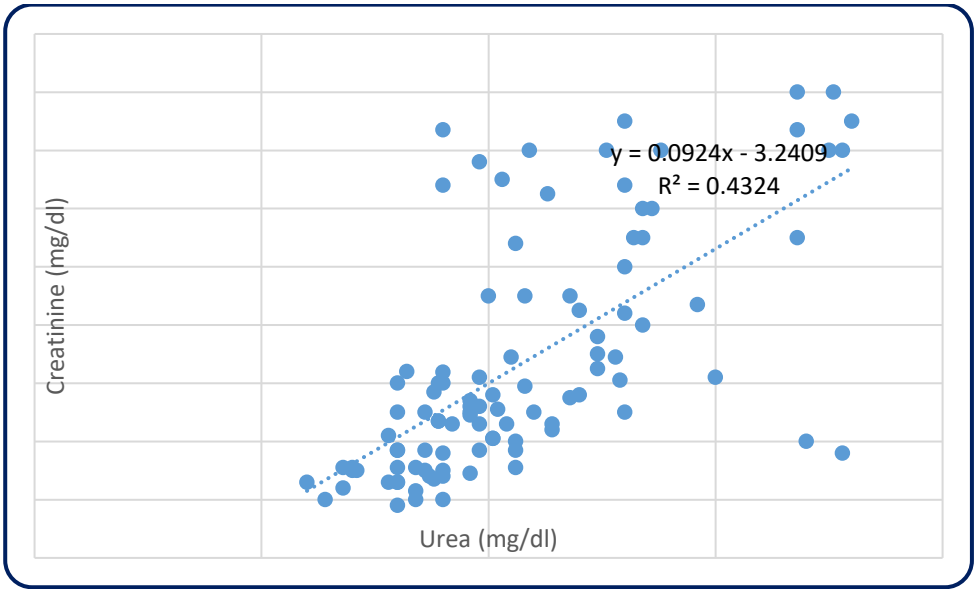

Fig …….: Scatter plot and trendline showing urea and creatinine values among study participants (n = 100)

Table 4: Distribution of patients according to Sonographic finding and level of urea (n=100)

	No	%	Level of urea (mg%)		
			Mean	SD	
BLCK (Bilateral Contracted Kidney)	84	84.0	110.7	29.1	t = 2.78 DF = 98 p = 0.007
CMDL (Cortico-Medullary Differentiation Lost)	16	16.0	89.7	18.6	
Total	100	100.0			

From the above table highest number of patients were found to have bilateral contracted kidney disease (BLCK) that was 84% and rest was 16 %. Mean and SD of urea is 110.7±29.1in case of BLCK and 89.7±18.6 in case of CMDL . p=0.007 and it is significant.

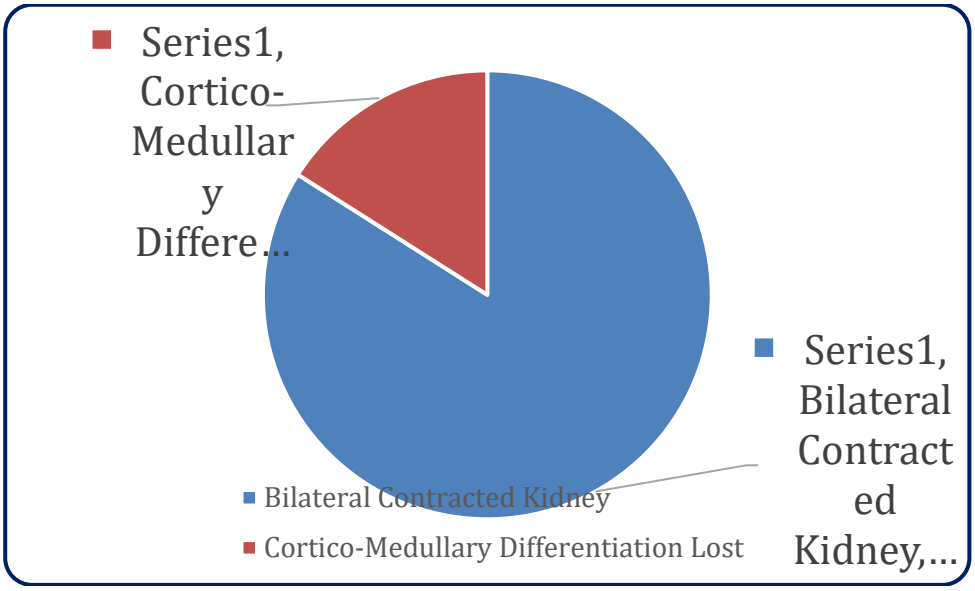

Fig …….: Pie diagram showing sonographic findings of CKD among study participants (n = 100)

Table 5: Distribution of patients according to Sonographic finding and level of creatinine (n=100)

	No	%	Level of creatinine		
			Mean (mg%)	SD (mg%)	
BLCK (Bilateral Contracted Kidney)	84	84.0	6.95	3.92	t = 1.59 DF = 98 p = 0.115
CMDL (Cortico-Medullary Differentiation Lost)	16	16.0	5.22	4.39	
Total	100	100.0			

From the above table it has been shown mean and SD of creatinine in BLCK is6.95± 3.92 , and in CMDL it is 5.22 ± 4.39. p=0.115 it is not significant.

Table 6: Distribution of patients according to CKD stageand level of total cholesterol(n=100)

	High total cholesterol		Normal total cholesterol		
	No	%	No	%	Chi square 0.1112 df 2 p 0.946
CKD III	4	44.44%	5	55.56%	
CKD IV	12	48.00%	13	52.00%	
CKD V	33	50.00%	33	50.00%	

It has been shown for the table maximum number of patients in CKD-V stage (50%), followed by in CKD stage IV (48%) and in CKD III (44%).

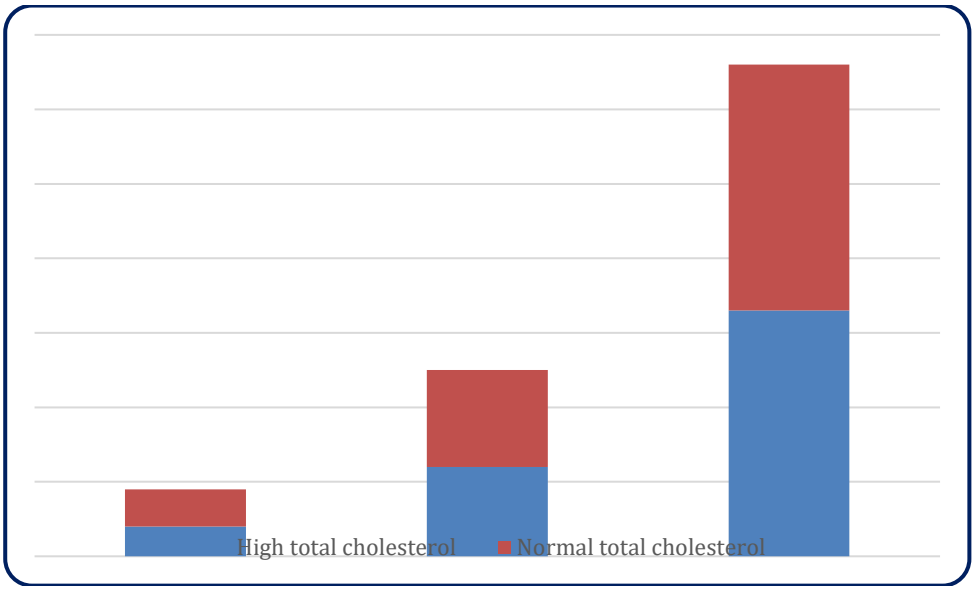

Fig …….:Compound Bar diagram showing stages of CKD and level of cholesterol among study participants (n = 100)

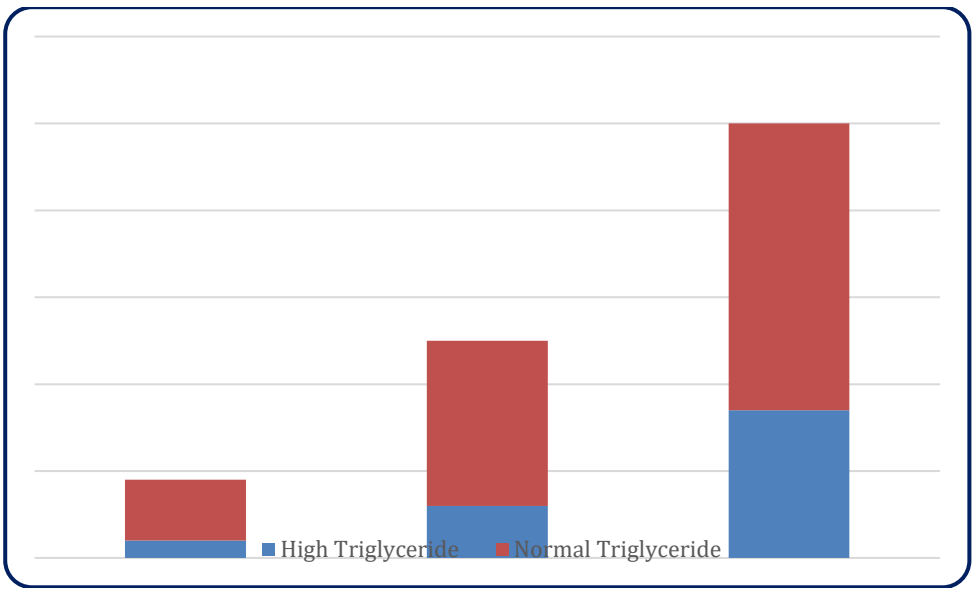

Fig …….:Compound Bar diagram showing stages of CKD and level of Triglyceride among study participants (n = 100)

Table 7 : Level of Cholesterol according to sex (n=100)

	No	%	Level of Cholesterol		
			Mean (mg%)	SD (mg%)	t =-.08 DF =98 p =0.437
Male	71	71	197.88	77.11	
Female	29	29	184.42	81.03	
Total					

This table shows mean and SD of cholesterol in male and female patients are 197.88± 77.11 and 184.42±81.03.p =0.437

Table 8 :Level of Triglyceride according to sex (n=100)

	No	%	Level of TG		
			Mean (mg%)	SD (mg%)	t = -0.50 DF = 98 p = 0.619
Male	71		122.02	45.9	
Female	29		117.05	43.55	
Total	100	100.0			

Mean and SD of triglyceride are 122.02±45.9 for male and 117.05±43.55 in case of female.p=0.619

Table 9: Distribution of patients according to CKD staging and Triglyceride level (n=100)

	High Triglyceride		Normal Triglyceride		
	No	%	No	%	Chi square 0.07 DF 2 P value 0.9653
CKD III	2	22.2	7	78.8	
CKD IV	6	24.0	19	76.0	
CKD V	17	25.8	49	74.2	
TOTAL	25	25.0	75	75.0	

From the above table it has been found that total 25% of patients had high Triglyceride (TG) level. Proportion of high TG level were 22.2%, 24.0% and 25.8% among patients in stage III, stage IV and stage V respectively. However this difference was not significant as p = 0.965

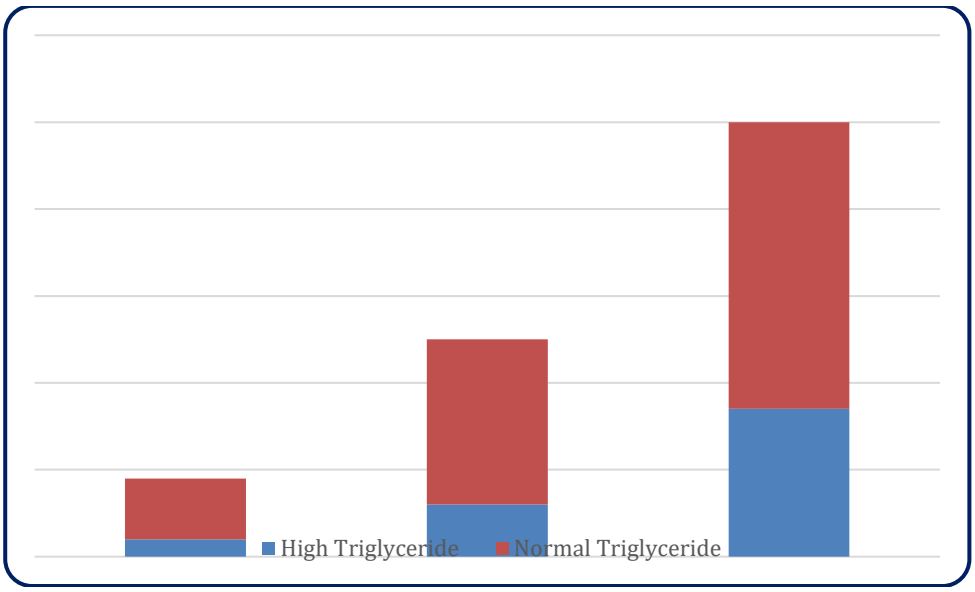

Fig …….:Compound Bar diagram showing stages of CKD and level of Triglyceride among study participants (n = 100)

Table 10: Distribution of patients according to CKD staging and HDL (n=100)

	Low HDL		Normal HDL		
	No	%	No	%	Chi square 2.345 DF 2 P value 0.3096
CKD III	6	54.6	5	45.6	
CKD IV	22	88.0	3	12.0	
CKD V	56	84.8	10	15.2	
TOTAL	84	84.0	18	18.0	

It has been shown that among all 84 patients having low HDL cholesterol , maximum percentage of patients are in stage CKD-IV (88%), then in stage CKD-V (84.8%), and 6 patients are in CKD-III staging (54.6%).
Rest of the patients (18%) out of 100 total had normal HDL cholesterol. However this difference was not significant as p = 0.309

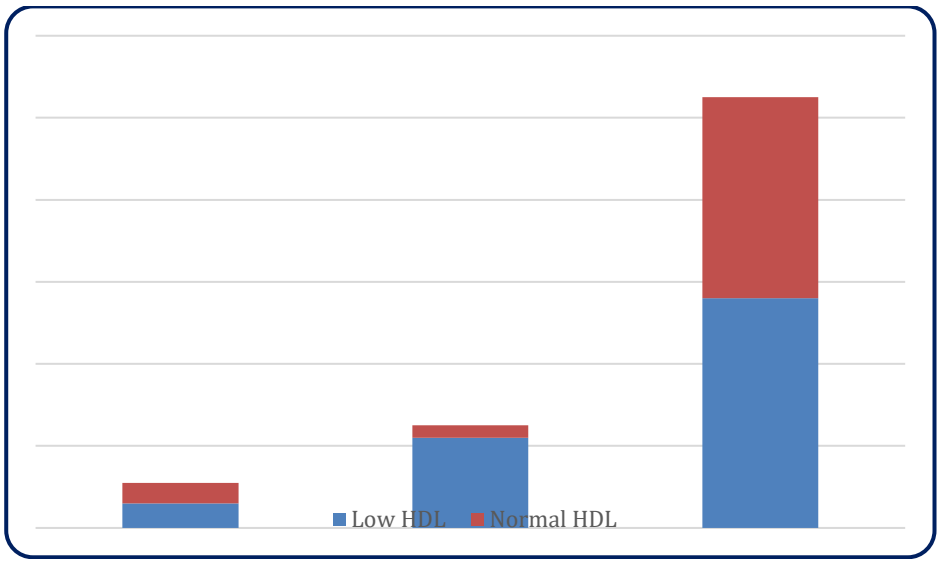

Fig …….:Compound Bar diagram showing stages of CKD and level of HDL among study participants (n = 100)

Table 11 : Level of HDL according to sex (n=100)

	No	%	Level of HDL		
			Mean (mg%)	SD (mg%)	t = -0.53 DF = 98 p = 0.596
Male	71		34.14	7.04	
Female	29		33.34	5.93	
Total	100	100.0			

Mean and SD of HDL cholesterol is 34.14±7.04 in male and 33.34±5.93 in female. p= 0.596

Table 12 : Distribution of patients according to CKD staging and LDL (n=100)

	High LDL		Normal LDL		Total	
	No	%	No	%		Chi square 1.15 DF 2 P value 0.562591
CKD III	4	44.4	5	55.6	9	
CKD IV	7	28.0	18	72.0	25	
CKD V	18	27.3	48	72.7	66	
TOTAL	29	29.0	75	29.0	100	

From the above table it has been found that total 29% of patients had high LDL level. Proportion of high LDL level were 44.4%, 28.0% and 27.3% among patients in stage III, stage IV and stage V respectively. However this difference was not significant as p = 0.562

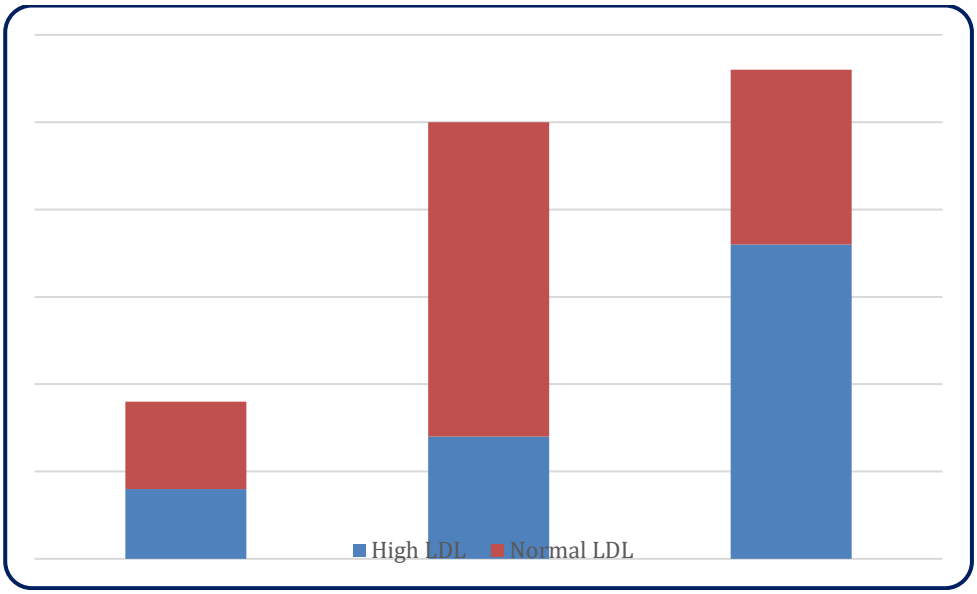

Fig …….:Compound Bar diagram showing stages of CKD and level of LDL among study participants (n = 100)

Table 13 : Level of LDL according to sex (n=100)

	No	%	Level of LDL		
			Mean (mg%)	SD (mg%)	t = 1.2 DF = 98 p = 0.234
Male	71		81.09	24.79	
Female	29		88.34	33.23	
Total	100	100.0			

Mean and SD of LDL cholesterol is 81.09±24.79 in male and 88.34±33.23 in female patients. P = 0.234 is not significant.

Table 14: Distribution of patients according to CKD staging and VLDL (n=100)

	High VLDL		Normal VLDL		Total	
	No	%	No	%		Chi square 0.38 DF 2 p value 0.827
CKD III	4	44.4	5	55.56	9	
CKD IV	14	56.0	11	44	25	
CKD V	36	54.6	30	30	66	
TOTAL	54	54.0	46	46.0	100	

It has been shown that among all 54 patients having high VLDL cholesterol , maximum 14 patients are in stage CKD-IV (56%), then in stage CKD-V 36 patients (54.6%), and 4 patients are in CKD-III staging (44.4%).

Rest of the patients (46%) out of 100 total had normal VLDL cholesterol. However this difference was not significant as p = 0.827

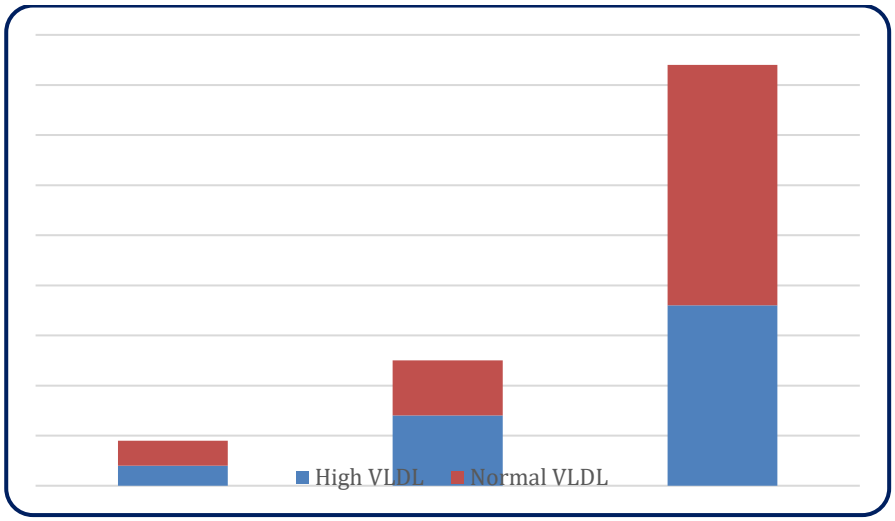

Fig …….:Compound Bar diagram showing stages of CKD and level of VLDL among study participants (n = 100)

Table 15 : Level of VLDL according to sex (n=100)

	No	%	Level of VLDL		
			Mean (mg%)	SD (mg%)	t = 1.57 DF = 98 p = 0.119
Male	71		30.44	6.8	
Female	29		34.67	20.1	
Total	100	100.0			

Mean and SD of VLDL is 30.44±6.8 in male and 34.67±20.1 in female patients. P== 0.119 is not significant.

Table 16 :Mean and SD of the lipid profile of study subjects

	Mean (mg/dl)	SD
Cholesterol	193.97	78.1
Triglyceride	120.58	45.07
HDL	33.91	6.72
LDL	83.20	27.52
VLDL	31.67	12.27

From the above table it was found that out of 100 patients studied mean value of cholesterol, triglyceride, HDL, LDL, VLDL were 193.97(mg/dl), 120.58(mg/dl), 33.9(mg/dl)1, 83.20(mg/dl), 31.67(mg/dl) respectively.
Standard deviation were 78.1, 45.0, 6.72, 27.52, 12.27 for cholesterol, triglyceride, HDL, LDL, VLDL respectively.

Table 17 : Distribution of patients according to Thyroid abnormalities (n = 100)

	No	%
Low T_3 syndrome	13	13.0
Low T_4syndrome	4	4.0
Low T_3& T_4 syndrome	5	5.0
Subclinical hypothyroid	15	15.0
Overt hypothyroid	9	9.0
Euthyroid	59	59.0
Total	100	100.0

It has been found that 41% of patients showed some or other thyroid abnormalities and among them highest number of patients hadsub-clinical hypothyroidism (15%). Second highest was CKD with low T_3 syndrome. Low T_3 &low $T_4$was found amongst 5% of all participants. Lowest number of patients had CKD with low T_4 and 9% of the patients were suffering from overt hypothyroidism.

Table 18 : Distribution of patients according to CKD staging and T_3 status (n=100)

	Low T_3		Normal T_3		Total	
	No	%	No	%		Chi square 3.30 df 2 p =0.1916
CKD III	5	55.56	4	44.44	9	
CKD IV	6	24.00	19	76.00	25	
CKD V	26	39.39	40	60.61	66	
TOTAL	37	37.0	63	63.0		

Proportion of Low T_3level was highest in patients of CKD-III stage (55.6%), followed by CKD-IV patients (39.4%)..Only 6 patients of CKD-IV staging had low T_3status (24.0%).
This apparent difference was not found to be significant as p = 0.192.

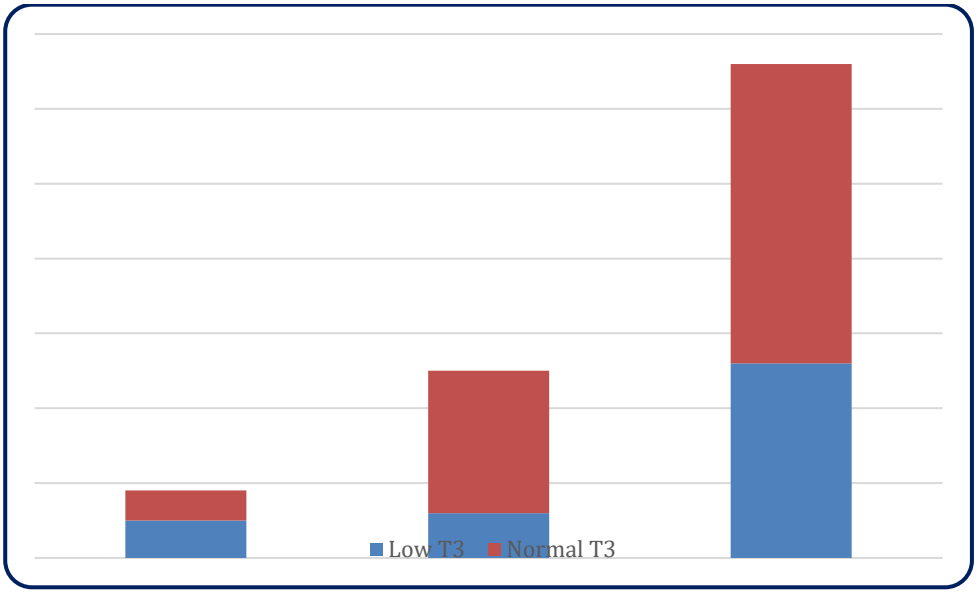

Fig …….:Compound Bar diagram showing stages of CKD and level of T_3 among study participants (n = 100)

Table 19 : Distribution of patients according to CKD staging and T_4 status (n=100)

	Low T_4		Normal T_4		
	No	%	No	%	
CKD III	2	22.2	7	77.8	Chi square 0.08 df 2 p 0.961
CKD IV	5	20.0	20	80.0	
CKD V	15	22.7	51	77.3	
TOTAL	22	22.0	78	78.0	

From the above table it had been found that proportion of Low T_4 status is highest in CKD-V stage (22.73%). 22.2% of all CKD-III patients and 20% of all CKD-IV patients showed low T_4status.
So total 22 patients out of 100 patients had CKD with low T_4 hormone level and rest 78 participants had only CKD with normal thyroid hormone status. There was no statistically significant difference (p = 0.961).

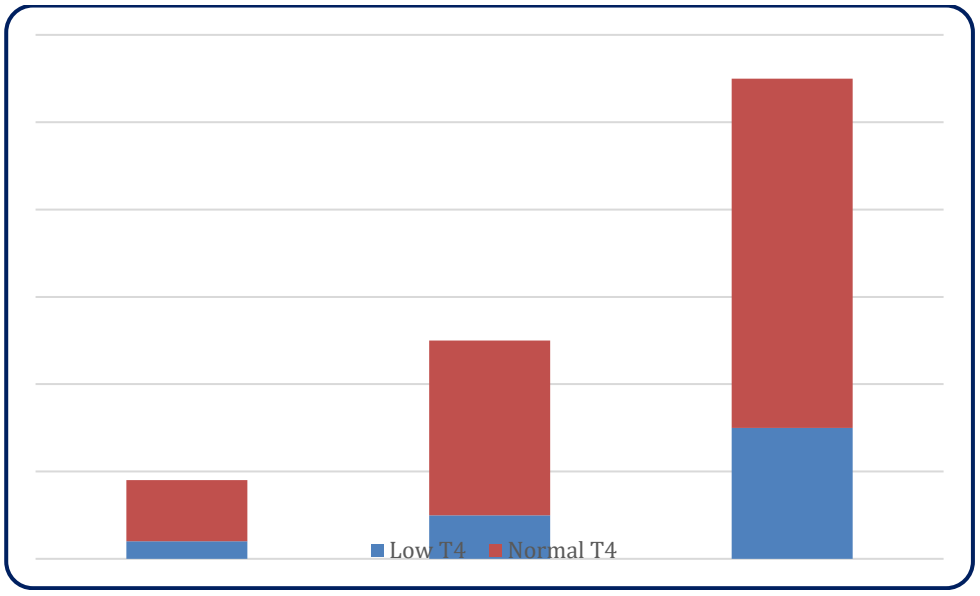

Fig …….:Compound Bar diagram showing stages of CKD and level of T4 among study participants (n = 100)

Table 20 : Distribution of patients according to CKD staging and TSH status (n=100)

	High TSH		Normal TSH		
	No	%	No	%	Chi square 1.08 DF 2 P value 0.5815
CKD III	5	55.6	4	44.4	
CKD IV	9	36.0	16	64.0	
CKD V	26	39.4	40	60.6	
TOTAL	40	40.0	60	60.0	

From the above table it had been found that proportion of high TSHstatus is highest in CKD-III stage (55.6%). 36.0% of all CKD-IV patients and 39.4% of all CKD-V patients showed high TSH status. Overall 40.0% of all patients reported to have high TSH. The difference was not found to be of statistical significance (p = 0.581)

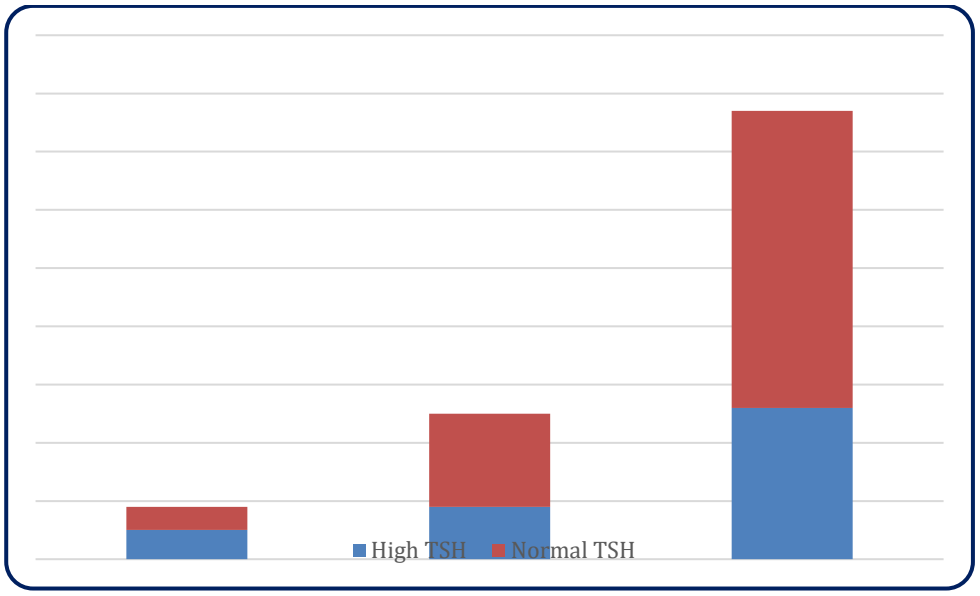

Fig …….:Compound Bar diagram showing stages of CKD and level of TSH among study participants (n = 100)

Table 21 :Mean and SD of the Thyroid value of study subjects

	Mean	SD
T_3 (ng/ml)	0.67	0.46
T_4(µg/dl)	5.77	2.04
TSH (µIU/ml)	6.98	6.24

It has been showed from above table that calculated mean for T_3, T_4, TSH are 0.67 (ng/ml),5.77(µg/dl),6.98(µIU/ml) respectively.Standard deviation for T_3, T_4, TSH are0.46,2.04,6.24 respectively.

Table 22 : Level of T_3 according to sex (n=100)

	No	%	Level of LDL		
			Mean (ng%)	SD (ng%)	t = 0.14 DF = 98 p = 0.889
Male	71		0.66	0.43	
Female	29		0.68	0.54	
Total	100	100.0			

From the above table it has been shown Mean and SD of T_3 in male patients are 0.66±0.43 and 0.68±0.54 in female. p=0.889 is not significant.

Table 23 : Level of T_4 according to sex (n=100)

	No	%	Level of T_4		
			Mean (µg%)	SD (µg%)	t = -.06 DF = 98 p = 0.949
Male	71		5.77	2.19	
Female	29		5.75	1.66	
Total	100	100.0			

From the above table it has been shown Mean and SD of T_4 in male patients are 0.5.77±2.19 and 5.75±1.66 in female. p=0.949 is not significant.

Table 24 : Level of TSH according to sex (n=100)

	No	%	Level of TSH		
			Mean (µIU/ml)	SD (µIU/ml)	t = -.0.82 DF = 98 p = 0.416
Male	71		6.65	5.51	
Female	29		7.78	1.66	
Total	100	100.0			

From the above table it has been shown Mean and SD of TSH in male patients are 6.65±5.51 and 7.78±1.66 in female. p=0.416 is not significant.

Table 1: Distribution of patients according to Age and Sex (n=100)

Age (years)	Male		Female		Total	
	No	%	No	%	No	%
≤ 30	12	75.0	4	25.0	16	100.0
31 – 60	41	66.1	21	33.9	62	100.0
> 60	18	82.8	4	18.2	22	100.0
Total	71	71.0	29	29.0	100	100.0
Mean age 50.56, SD 13.72						

It is observed from the above table that the maximum number of study subjects were male(71%) and 29% were female. Highest proportion of participants found in age group of 31-60 years of age, of which 66.1% were male (41 patients) and rest were female (34%, 21 patients).Total 62 patients in this age group.
Among the patients less than or equal to 30 years of age male patients were 12 in number (75%) and female patients were 4 in number (25%).
Above 60 years of age 82% (18 in number) were male and 18% (4 in number) were female. Mean age is 50.56 and SD 13.72

DISCUSSION

The present topic "a study of lipid profile and thyroid hormone status in chronic kidney disease patients attending the deptartment of general medicine, BankuraSammilani Medical College and Hospital, Bankura"
A descriptive, cross-sectional, hospital based study conducted over a period of one year from 1st july 2016 to 30thjune2017 among the patients suffering from chronic kidney disease attending in-patient and out-patient department of Medicine, BankuraSammilani Medical College and Hospital (BSMC&H), Bankura. A total of 100 patients presenting with features of chronic kidney disease were studied. The objective of the proposed study is to find out the occurrence of lipid & thyroid disorders in patients of chronic kidney disease. Various studies were conducted about dyslipidaemia and thyroid dysfunction in CKD patients and had been shown different results.
The study started after obtaining ethical clearance of institutional ethics committee of BSMC&H and approval of the West Bengal University of Health Sciences Kolkata. Before beginning the sample collection, written informed consent obtained from each patient who will agree to take part in the study.
The results and observation of the study are discussed below.
Table 1 reveals that the mean age of the population of the study is 50.6 years and SD is 13.7. It is observed from the above table that the maximum numbers of study subjects were male 71% and 29% were female. Highest proportion of participants found in age group of 31-60 years of age, of which 66.1% were male (41 patients) and rest were female (34%, 21 patients).Total 62 patients in this age group. Among the patients less than or equal to 30 years of age male patients were 12 in number (75%) and female patients were 4 in number (25%) . Above 60 years of age 82% (18 in number) were male and 18% (4 in numbers) were female. This is in agreement with the findings of Saharet al[35] who reported a mean age of 52.50±14.96 and in study of Ganta et al[36] mean age was 55.14±12.27. In some study done by Szu-Chia Chen et al[37] found to have a older age group participants (mean age was 63.56). Two other Indian study done by Rajapurkar M.M.et al[38] (50.1±14.6) &Modi G.K.et al[39] (47 years) has closer value to our study. In our study majority are male participants (71%) like the study of Gantaet al[36]where 63.57% are male patients.
In table no 2 & 3 highest percentage of patients are in CKD stage V (66%) and mean eGFR is 12.6±8.7. This trend is also found in the study of Gantaet al[36] and Swaminathan et al[40] where maximum no. of patients are in CKD-V. Szu Chia et al[40] and Saroj et al[41] found a slightly in high range of eGFR i.e. 24.76, 28.2 respectively. Different studies show variation in range of urea and creatinine. The range of mean urea of our study (107.34) is similar to Saroj et al[41] (106.3) but Rashmi et al[42] (mean urea 137.75) and Sahar et al[35] (mean urea 188.25) have found high mean urea than our study andRaju et al[44] had a lower range of finding (90.46).
In Table no. 4 ultra sonographic findings revealed that majority of bparticipants had bilateral contracted kidney (84%) than loss of cortico-medullary differentiation (16%) and there was a significant difference in level of urea (p=0.0007). As CMDL occurs earlier than BLCK in sonographic findings so it may reflect in level of urea which is higher in BLCK stage when the damage in kidney is more than CMDL stage. This trends was exist in value of creatinine also but no significant difference (p=0.115).

Several studies on lipid profile in CKD patients observed hypertriglyceridemia, hypercholesterolemia, increased LDL and decreased HDL [10-15].In general, the prevalence of hyperlipidemia increases as renal function declines, with the degree of hypertriglyceridemia and elevation of LDL cholesterol being proportional to the severity of renal impairment.[4] CKD affects lipoprotein metabolism, leading to hypercholesterolemia, hypertriglyceridemia and excess LDL cholesterol.[26] Many studies have reported rise in level of lipid parameters and dyslipidemia prevalence in patients with CKD, which may further assist in renal disease progression.[10] In our study we found mainly hypercholesterolemia, low HDL, high VLDL. High triglyceride and LDL value also exist but not as profound as other lipid fractions.

According to table 6 over all hypercholesterolemia was observed in our study is 49%, male had much higher percentage (71%) and there was a increasing trend of hypercholesterolemia from CKD III to CKD V (CKDIII has 44.44% hypercholesterolemia, CKD IV 48%, CKD V 50%) though not significant (p=0.946). Mean cholesterol of our study was 193.97±78.1 similar to sarojet al[41] (191.9±31.7). Different study showed hypercholesterolemia like Saroj et al[41] (34.4%), Ghanta et al[36] (22.86%), Poudel B et al[45] (33.75%). Few studies like Rashmiet al[43] and Gerald Appel[44] found even low level of cholesterol in CKD.

In table 8 in our study 25% of cases had hypertriglyceridemia. Mean is 120.58±45.07. Study done by Rashmiet al[43] had mean triglyceride of 163.87 and Raju et al[46] had much higher value 209.80. Michel et al[17] study found similar triglyceride value to our study (124). Ghantaet al[36] and Khalidah et al[44] had much lower mean value of trigleceride 116 &113.8 respectively.

Table 10 showed 84% of study subjects had low level of HDL of mean value 33.91±6.72 and similar mean value of HDL was found in the study of Rashmi et al[42] (31.75) , Raju et al[43] (35.28), Khalidah et al[44] (33.68). Some of studies done by VeerenGantaet al[36] and Saroj et al[41] had found much higher mean value of HDL 43.15±16, 42.1±5.9. In our study 84% of participants had high HDL and highest number of patients (56 patients) having high HDL value are in CKD stage V though p=0.3096 is not but there was a tendency of increasing HDL as CKD is worsening. High HDL cholesterol was found in 22.86% of patients in study done by VeerenGanta et al[36],Saroj K et al[41] study also showed 34.1% had high HDL value. In a comperative study done by Rashmiet al[42] between CKD patients and control group, there was decreased HDL seen in CKD group.The significant decrease of HDL-C in CKD can be attributed to

(i) Decreased levels of apolipoproteins AI and AII; the main protein constituents of HDL [34].

(ii) Diminished activity of LCAT; the enzyme responsible for the esterification of free cholesterol in HDL particles [35].

(iii) Increased activity of Cholesteryl Ester Transfer Protein (CETP) that facilitates the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins [36].

All these factors combinedly act to reduce the serum concentration of HDL-C.

From table 12, high LDL value has been found in 29% of cases and mean value is 83.20±27.52. Mean value of our study is much closer to study done by VeerenGanta et al[36] (83.81±34.76), Khalidah et al[45] (87.44±24.30). Few studies like Raju et al[46] (105.22±26.15) ,Saroj et al[41] (103.6±28.1),Sahar et al[35] (139.60±6.26) found higher value than our study. Rashmi et al[42] study did not reveal any difference between CKD and control group , even they found lower mean value of LDL in CKD group (63.23±46.47). Percentage wise high LDL value was found in study by VeernerGanta et al[36] (12%) which is lower than our study and Poudel et al[46] found higher percentage 38.03%.

Elevated plasma LDL cholesterol is common in nephrotic syndrome but it is not a typical feature of patients with advanced CKD, especially those who are on hemodialysis.In CKD patients, the hepatic LDL receptor gene expression is not altered until there is significant glomerulosclerosis or heavy proteinuria [9].

Table 14 showed that there was a trend of high VLDL from CKD III to CKD V. In our study 54% of patients have high VLDL level among all cases. Mean value of VLDL in our study is 31.67±12.27. Similar findings have been found in study done by Rashmiet al[42] (32.57±13.55) and Raju et al[47] (41.96±6.48).The factors which explain the increase in serum VLDL are

(i) the increased activity of CETP which increases transfer of cholesterol ester to VLDL and promotes more VLDL formation [36].

(ii) Increased apo C-III, which is an LPL inhibitor inhibitng the degradation of VLDL [23]. These factors increase the level of serum VLDL-C in CKD patients.

The present study identifies thyroid dysfunction and dyslipidemia as a common disorder in CKD patients. From table 17 to table 24, it had been shown that thyroid dysfunction was found in (41) % CKD patients, the most common being subclinical hypothyroidism (15%), followed by low T_3 syndrome (13%), overt hypothyroidism (9%), low T_3 and low T_4 syndrome together (5%), only low T_4 syndrome (4 %). Study by Lo et al[23] found that the prevalence of hypothyroidism increased with lower levels of GFR (in units of mL/min/1.73 m^2), occurring in 5.4 % of subjects with GFR greater than or equal to 90, 10.9 % with GFR 60–89, 20.4 % with GFR 45–59, 23.0 % with GFR 30–44, and 23.1 % with GFR < 30 ($p < 0.001$ for trend). They reported that 56 % of hypothyroidism cases were subclinical. Studies of Sarojet al[41] and Song et al[48] also found an increasing trend of low T_3 as GFR decreases.

In general population, prevalence of subclinical hypothyroidism is 4-10%. Our study is similar to study done by Saroj et al[41] who found thyroid dysfunction 38.6%, subclinical hypothyroidism 27.2%,overt hypothyroidism 8.1%.

In our study, over all low T_3 value among all CKD patients was found in 37% of patients; 5 cases are in CKD III, 6 patients in CKD IV, and 26 cases in CKD V. Over all low T_4 value was found 22% of patients; 2 cases in CKD III, 5 patients in CKD IV, and 15 cases in CKD V. High TSH value was found in out of 100 participants was 5 cases in CKD III, 9 cases in CKD IV, 26 cases in CKD V; total 40% cases have high TSH value. So there was a trend of increasing TSH and low T_4 ,T_3 value from CKD stage III to CKD stage V.

Studies done by Jingxianet al[49] and Swaminathan et al[39] found a lower percentage of subclinical hypothyroidism (4.7%) & (8%) respectively; but Jingxian found a higher percentage of total low T_3 value (47%) and a lower percentage of low T_4 (5.4%) than present study. Swaminathan study had a much higher percentage of low thyroid hormone status among all CKD patients (low T_3 66%, low T_4 24%).

Mean value of different Thyroid hormones of our study was T_3 (0.67±0.46), T_4 (5.77±2.04), TSH (6.98±6.24). So here a trend of high TSH and low normal range of T_3,T_4 was found in our study though value is not significant.

Various studies have been studied by comparing CKD patients on conservative Management and patients on HD by Ramirez[50] and Kayimaet al[51]. In uremia the mean values of T_3& T_4 were significantly low as depicted in various international studies by Ramirez G et al[50] , Lim VS et al[52], and Pagliacci MC et al[53].

However, few studies showed different results, like a studies by Swaminathan et al[39] ,Rajagopalan B[54], Spector et al[55], Ramirez et al[56]Dudani et al[57], Karunanidhi et al[58]in CKD patients found that both T_3 and T_4 were significantly reduced whereas TSH remains to be unchanged in patient group compared to controls.These studies depicted abnormality in hypophyseal mechanism of TSH release in uraemicpatients as the TSH response to the TRH was blunted.

Another study which was conducted by Joseph et al andHardy et al[36,58] revealed low T3 T4 level with high TSH level suggesting maintenance of pituitary thyroidaxis. Low T3 had been reported in Ramirez etal[56], Hegedus et al[60], Beckett et al[61], PonAjil Singh et al[62]P Igleasias and JJ Diez[63]and many others. Ramirez and Spector et al[55,] study showed linear correlation between mean serum T3 and T4 and severity of renalfailure.

CONCLUSION

- In patients with CKD Thyroid dysfunction occurs in 48 % of the patients.
- Incidence of hypothyroidism is increased in patients with chronic kidney disease.
- Number of patients with low T3 and T4 syndrome progressively increase with the severity of chronic kidney disease.
- Excluding patients with hypothyroidism T3 level is low in 38 % of the patients, T4 level is low in 17.5 % of the patients.
- Serum level of T3 and T4 and TSH has no correlation with the severity of chronic kidney disease.

CONFLIT OF INTEREST: Nil

LIMITATIONS OF THIS STUDY

- Thyroid dysfunction was studied in patients with CKD irrespective of the etiology. Hence correlation of the etiology of CKD with thyroid dysfunction could not be studied.
- As lipid levels in a normal person and a CKD patients can be varied by different etiological factors, so correlation among lipid profile, CKD and its etiology could not be studied.
- Study sample is small.
- The study had conducted in General Medicine ward in a tertiary care peripheral hospital. So the referral patients loads are higher. So the results of the study cannot be generalized with the medical patients of the district or rural hospitals.
- As it is a hospital-based study the results of this study cannot be generalized with the true picture of the community.

SUMMARY

The present topic “a study of lipid profile and thyroid hormone status in chronic kidney disease patients attending the deptartment of general medicine, BankuraSammilani Medical College and Hospital, Bankura”

A descriptive, cross-sectional, hospital based study conducted over a period of one year from 1st july 2016 to 30thjune2017 among the patients suffering from chronic kidney disease attending in-patient and out-patient department of Medicine, BankuraSammilani Medical College and Hospital (BSMC&H), Bankura. A total of 100 patients presenting with features of chronic kidney disease were studied. The objective of the proposed study is to find out the occurrence of lipid & thyroid disorders in patients of chronic kidney disease. Various studies were conducted about dyslipidaemia and thyroid dysfunction in CKD patients and had been shown different results.

The study started after obtaining ethical clearance of institutional ethics committee of BSMC&H and approval of the West Bengal University of Health Sciences Kolkata. Before beginning the sample collection, written informed consent obtained from each patient who will agree to take part in the study.

The results and observation of the study are discussed below.

- Number of Male patients are 71, Female patients 29
- Below 30 years Male=12, Female=4 ; between 30-60 years Male=41, Female21 ; above 60 years Male=18, Female=4
- Mean age-50.56 ± 13.72
- Age varied between 19-78 years.
- Duration of symptoms 4 months -64 months. Mean duration of symptoms with SD
- Urea Creatinine
- Mean urea = 107.34 ± 28.69, Mean creatinine = 6.68 ± 4.03
- Creatinine clearance- Mean creatinine clearance =
- Mean eGFR= 12.6±8.7
- The study range T_3
- Number of patients in CKD III is 9, CKD IV- 25, CKD-V 66.

- Total hypercholesterolemia is 49%. Range of cholesterol - In CKD III - 44.44%, CKD IV- 48.00% and in CKD V- 50% patients have hypercholesterolemia.
- Total hypertriglyceridemia was 25%. Range of triglyceride In CKD-III 22.2%, CKD IV-24%, CKD-V 25.8%.
- Low HDL in 84% of patients, Range 6 patients in CKD-III, 22 patients in CKD- IV, 56 patients in CKD- V.
- High LDL value in 29% of cases. Range 4 cases in CKD-III, 7 cases in CKD-IV, 18 cases in CKD-V.
- High VLDL in 54% of cases. Range 4 cases in CKD-III, 14 cases in CKD-IV, 36 cases in CKD-V.
- Mean value of cholesterol (193.97±78.), Triglyceride (120.58±45.07), HDL (33.91±6.72) , LDL (83.20±27.52) , VLDL (31.67±12.27).
- Total number of patients in Low T_3 syndrome is (13%) , Low T_4 (4%), Low T_3 & Low T_4 syndrome is (5%), Subclinical hypothyroidism (15%), Overt hypothyroidism(9%), Euthyroid (59%)
- Total Low T_3 was 37 cases. In CKD III 5 cases, CKD IV 6 cases and in CKD V 26 cases.
- Total Low T_4 was 22 cases. In CKD III 2 cases, CKD IV 5 cases and in CKD V 15 cases.
- Total high TSH was 40 cases. In CKD III 5 cases, CKD IV 9 cases and in CKD V 26 cases.
- Mean T_3, T_4, TSH are 0.67,5.77,6.98

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