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Bangladesh Renal Journal is the official organ of the Bangladesh Renal Association. The Journal publishes two issue in a year i.e. June and December. The Journal is devoted to continuing education in kidney diseases.

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Editorial

Cardiovascular Risk Factors in Chronic Kidney Disease

Prof Brig Gen Mamun Mostafi

(Bang. Renal J. 2012; 31(1): 1)

Cardiovascular disease is the primary cause of morbidity and premature mortality in chronic kidney disease. While it is well established that patients with chronic kidney disease stage 5 are at high risk of cardiovascular disease morbidity and mortality [1], patients with earlier stages of chronic kidney disease also experience a high rate of fatal and nonfatal cardiovascular events [2]. Recent guidelines and position statements have therefore defined chronic kidney disease as a cardiovascular risk equivalent, and patients in all stages ofchronic kidney disease is considered in the "highest risk group" for development of cardiovascular disease [3].

Elevated urea in patients with CKD dissociates to form cyanate, which causes carbamylation of proteins. Carbamylated LDL causes progression of atherosclerosis through endothelial cell injury, increased expression of cell adhesion molecules, and proliferation of vascular smooth muscle cells. It also causes endonuclease G activation that results in cellular injury and generation of oxidants. Elevated carbamylated LDL independently predicted an increased risk of CAD, future AMI, stroke, and death[4].

Statins were proved to have substantial CV benefits in primary and secondary prevention, including in patients with CKD stages 1–4; however, randomized controlled trials have not shown similar benefits in dialysis patients. In the AURORA study, rosuvastatin lowered LDL cholesterol in HD patients, but had no significant effect on the composite primary endpoint of death from CV causes, nonfatal AMI, or nonfatal stroke [5].Studies in this subject led to the identification of multiple nontraditional risk factors like proteinuria, anaemia, abnormal calcium and phosphate metabolism, CRP and hyperhomo-cysteinaemia that might play a direct causal role, and of markers for pre-existing CVD or other factors that increase the risk of CVD [6]. Studies have shown that traditional risk factors are not adequate to account for the excess CVD in patients with CKD and a concert of both traditional and nontraditional factors makes the situation critical [7].

In this issue of BRJ RD Gupta et al studied the cardiovascular risk factors in CKD patients. Like most of the studies the traditional risk factors were found tobe significant in respect to cardiovascular events but according to them the other nontraditional factors like homocystienaemia, CRP, anaemia etc. were not significant. We require more studies with larger population to come to a national conclusion.

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Original Articles

Cardiovascular Risk Factors in Chronic Kidney Disease (CKD)- Traditional or Non-traditional ?

Ratan Das Gupta[1], M. Muhibur Rahman[2], Mesbah Uddin (Noman)[3], Nazrul Islam[4], Dilip Kumar Debnath[5], Syed Mahbub Morshed[6], HM Nazmul Ahsan[7]

Abstract:

Cardiovascular disease is the leading cause of death and morbidity in chronic kidney disease and hemodialysis patients. Both traditional and nontraditional cardiovascular risk factors may contributable but the excess burden of cardiovascular disease in chronic kidney disease cannot be explained by traditional risk factors alone. Here we evaluated impact of traditional and nontraditional risk factors on cardiovascular disease of chronic kidney disease. Study conducted in Nephrology department of Dhaka medical college with 70 patients of CKD and MHD. In this cross sectional study, we examined the relationship between several traditional and non-traditional cardiovascular risk factors and the presence or history of cardiovascular events. Chi-squre test and unuvariate and multivariate logistic regression analysis used to determine association. 54.5% patients had cardiovascular disease. Most of traditional risk factors smoking, hypertension, diabetes ,age and dyslipidaemia associated with cardiovascular disease but no non-traditional cardiovascular risk factors (hyperhomocyteinemia, hyperfibrigenaemia, increased CRP, factor VII activity and anaemia) independently associated with cardiovascular disease.

Key words: Nontraditional risk factor, CKD. Cardio-vascular risk.

(Bang. Renal J. 2012; 31(1): 3-11)

Introduction:

Cardiovascular events are the most common cause of death and morbidity in end stage renal disease. Mortality rates are 10-20 times higher among patients with end-stage renal disease, compared with the general population, with 50% of this excess burden being attributable to cardiovascular disease[1]. Though the prevalence of traditional risk factors for cardiovascular disease, including diabetes and hypertension, are common among patients with CKD and may partially account for the excess risk for cardiovascular disease among these patients[2], however, several prospective cohort studies indicate that, this excess risk is not entirely explained by elevated traditional risk factors[3]. Non-traditional risk factor such as elevated level of homocysteine, fibrinogen, Factor VII, C-reactive protein has been associated with an increased risk for cardiovascular disease[4]. Traditional risk factors are limited predictors of cardiovascular morbidity and mortality in ESRD[5]. Non-traditional risk factors e.g. hyperhomocysteinemia has been found more commonly than traditional risk factors in ESRD patients on hemodialysis and is contributing independently to excess incidence of fatal and non-fatal cardiovascular outcomes[6]. Therefore, much recent interest has focused on non –traditional risk factors, as promoters of atherosclerosis. Several non-traditional factors, such as hyperhomocystenemia, anaemia, thrombogenic factors elevated fibrinogen and factor VII and elevated inflammatory markers especially elevated fibrinogen, factor VII, and CRP are associated with cardiovascular events in CKD patients.

The objectives of this study are to 1) Identification of cardiovascular disease in CKD and hemodialysis dependent patients.; 2) Determine the association of traditional and non-traditional risk factors to cardiovascular disease.

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Methods and material:

This cross sectional study was designed for identification of cardiovascular disease and traditional , non-traditional risk factors in CKD and haemodialysis dependent patients and also to determine the association of cardiovascular risk factors to cardiovascular events. The study was conducted at the department of Nephrology and dialysis department of Dhaka medical college hospital, Dhaka, Bangladesh during the period 2007 and 2008.

Subject:

Total 70 patients were selected from Nephrology and Hemodialysis department of DMCH. 48 cases of CKD never receive hemodialysis or peritoneal dialysis treatment and 22 cases of MHD patients received regula hemodialysis 4-5 hour in one session, and two to three session in a week for at least six months. Patients were selected according to specific selection criteria. All of the selected patients were evaluated clinically. Laboratory investigations were done to identify cardiovascular disease by ECG, Echocardiography, stress test or angiography and to identify cardiovascular risk factors (both traditional and non-traditional risk factors). All patients gave informed consent. The study protocol was reviewed and approved by the Dhaka medical college Ethics committee.

Laboratory tests:

Blood sample were drawn in the fasting state and had rested for at least 10 minutes before blood sampling. Venous blood collected from the right ante-cubital vein of CKD patients and healthy controls with minimal stasis and without frothing using standard equipment. In hemodialysis patients the arterio-venous fistula punctured with an arteriovenous needle immediately before the start of hemodialysis. 1 ml EDTA blood used for complete blood count. 1.8ml (9 volumes) blood mixed with 0.2 ml sodium citrate (1 volume), centrifuged at 2000 g for 20 min. Plasma was separated, aliquoted and stored at -70ºCuntil used for assay of factor VII activity and plasma fibrinogen level. 2 ml of serum separated, aliquoted and stored at -7^0 C until used for assay of total serum homocysteine , C-reactive protein , serum lipid profile, and kidney function tests including creatinine and urea. All investigations were done in single specialized diagnostic center in Dhaka.

Statistical analysis:

Data analyzed by computer using the statistical package SPSS for Windows 11.5 version. All values are expressed as mean ±SD or median and range or frequency and proportion. The patients were divided into cardiovascular disease positive and cardiovascular disease negative and group were compared by the student t test. Nonparametric tests chi-square was used for qualitative data. Univariate and multivariate regression analysis used to assess association of risk factors with cardiovascular disease and to determine best predictor of cardiovascular disease. For all test p-values less than 0.05 were considered statistically significant.

Results:

We studied 70 chronic kidney disease patient of stage III-V and haemodilysis dependent. 64.6% were male and mean age 49 years.

Baseline characteristics study population:

Clinical and biochemical parameters CKD patients.(n=70)

Table-1

Clinical and biochemical parameters of CKD patients.

	Mean±SD / %
Age	49.00±13.579
Male	64.6%
Smoking	29.2%
Hypertension	87.5%
Diabetes	37.5%
Cardiovascular disease	52.1%
Hemoglobin level gm/dl	8.08±1.94
CRP mg/dl	52.59±12.16
Fibrinogen mg/dl	264.10±67.81
Factor VII %	103.97±14.41
Homocysteine µmol/L.	22.99±8.70
Blood sugar mg/dl	7.01±2.48
Serum creatinine mg/dl	7.57±3.38
Creatinine clearance ml/min	12.15±8.59
Total cholesterol mg/dl	173.50±51.10
LDL mg/dl	93.43±41.99
HDL mg/dl	35.91±6.25
TG mg/dl	216.43±94.44

Cardiovascular disease:

55.7 % (39) patients were found suffering from cardio-vascular disease among both non-dialysis CKD and hemodialysis dependent CKD patients. 26(54.2%) non-

dialysis groups and 13(59.1%) hemodialysis group had cardiovascular disease . Mean age of patient having cardiovascular disease 52.92±11.14 years. CKD patient both non-dialysis and hemo-dialysis group having cardiovascular disease mean 66.7% (16) male, 46.2% (18) currently or previously smoker, 33.33% were taking anti lipid drugs, 100% are hypertensive, mean systolic blood pressure 155.13±26.864 mm of Hg, diastolic blood pressure 90.51±12.183 mm of Hg, mean hemoglobin level 8.89±1.83 gm/dl, CRP 46.23±88.50mg/L, Fibrinogen 276.58±66.57mg/dl, Factor VII 105.79±14.92%, Homocysteine 28.79±33.86µmol/L. Table 16 shows comparison between cardiovascular disease negative and cardiovascular disease positive patient of both non-dialysis and hemodialysis dependent patients.

Comparison between cardiovascular disease–Ve and cardiovascular disease +ve patients:

Table-II

*Comparison between cardiovascular disease–ve and cardiovascular disease +ve patients: * chi-square test used.*

Variable	Cardiovascular disease -ve mean±SD /% n=31	Cardiovascular disease +ve mean±SD/% n=39	P-value
Age of patient	42.10±13.245	52.92±11.148	.001
Male	31	39	.205*
Smoking	6	18	.001*
Diabetes	5	20	.006*
Hemoglobin level	8.04±2.16	8.89±1.83	.92
CRP	35.56±38.11	46.23±88.50	.130
Fibrinogen	245.19±60.26	276.58±66.57	.087
Factor VII	103.25±13.86	105.79±14.92	.076
Homocysteine	22.92±10.47	28.79±16.86	.127
Total cholesterol	144.58±33.29	197.69±75.73	.001
LDL	74.60±31.10	113.05±70.48	.006
TG	163.54±38.11	148.97±98.91	.001
HDL	35.35±6.74	36.38±5.88	.449

Only 2 (5.12%) patients with cardiovascular disease have normal hemoglobin (>12gm/dl), 14(35.89%) and 23 (58.97%) patients have hemoglobin 8-12 gm/dl and less than 8 gm / dl in patient who have cardiovascular disease in non-dialysis CKD and hemodialysis dependent patients.

Associations between risk factors and cardiovascular disease:

All traditional and non- traditional cardiovascular risk factors tested in variable models. Age, hypertension, diabetes, smoking and dyslipidaemia were significantly associated with cardiovascular disease. Non-traditional risk factors homocysteine , fibrinogen, CRP, factor VII and hemoglobin were not significantly associated with cardiovascular disease although these factors and cardiovascular disease were more common in CKD and hemodialysis patients. Univariate logistic analysis shown that age, smoking, hypertension, diabetes and dyslipidaemia were strongly associated with cardio-vascular events. Fibrinogen , homocysteine, CRP, factor VII and anaemia were not significantly associated withcardio vascular events in CKD and hemodialysis dependent patients.

Univariate logistic models for the associations between variables and cardiovascular disease

Table-II

Univariate logistic models for the associations between variables and cardiovascular disease

Variable	Odds ratio	95% CI	P value
Age	1.34	1.33-10.35	.012
Male sex	.629	.71-4.94	.205 (NS)
Smoking	2.79	2.08-30.76	.001
Hypertension	21.465	11.224-34.325	<.001
Dyslipidaemia	1.73	1.679- 12.755	.003
Diabetes	1.75	1.742-17.195	.004
Homocysteine µmol/L	.937	.967 -9.686	.169 (NS)
Fibrinogen mg/dl	.362	.691 -2.987	.337 (NS)
CRP mg/L	-.798	.162-1.253	.126 (NS)
Factor VII %	.531	.623- 4.642	.300 (NS)
Hemoglobin gm/dl	-.385	.294 – 1.574	.368 (NS)

Cardiovascular risk factors were common in both non-dialysis and hemo-dialysis patients. There was a high prevalence of both traditional and non-traditional cardiovascular risk factors. To analyze the influence of these risk factor, we performed a step wise multiple linear regression analysis in a model constructed with six traditional (increased age >55 years), smoking, high blood pressure, hyperglycemia, dyslipidaemia) and five non-traditional (decreased hemoglobin level, increased CRP, Fibrinogen, Homocysteine, and factor VII) risk factors. Traditional risk factors hypertension, diabetes, dyslipidaemia, smoking and increased age were found

independently associated with cardiovascular events as univariate and multivariate analysis shows significant association of these risk factors to cardiovascular disease. But None of non-traditional cardiovascular risk factors hyper-homocystenemia, increased fibrinogen, factor VII, and CRP and decreased hemoglobin level were independently associated with cardiovascular events although these factors were increased in CKD patient (both non-dialysis and hemodialysis groups) in comparison to control normal population.

Multivariate analysis of traditional risk factors and association of cardiovascular disease

Table-III

Multivariable logistic models for the association between cardiovascular disease and traditional risk factors:

Risk factors	Odds ratio	95% CI	P value
Hypertension	14.476	5.047 - 27.143	<.001
Diabetes	1.431	1.019-17.164	.047
Dyslipidaemia	1.190	.994 - 10.876	.051
Smoking	2.154	1.463-50.802	.017
Age	1.006	.803 – 9.313	.017
Sex	- .587	.089 - 1.902	.256

Multivariate analysis of traditional cardiovascular risk factor in association to cardiovascular disease hypertension (p-<.001), diabetes (p-.047), smoking (p-.017), age (.017) and dyslipidaemia (p-.051) significantly associated with cardiovascular disease but sex not significantly associated with cacrdivascular disease.

Multivariate analysis of traditional risk factors + non traditional risk factors and association with cardiovascular disease:

Table-IV

Multivariable logistic models for the association between cardiovascular disease and traditional and non-traditional risk factors:

Model	Odds ratio	Cardiovascular disease (95% CI)	P value
1. Traditional+ Homocysteine	-.765	.426- 10.857	.354
2. Traditional + CRP	- .568	.156-2.056	.388
3. Traditional + Fibrinogen	.299	.519-3.499	.539
4. Traditional + Factor-VII	-.183	.231-3.001	.779
5. Traditional+ Haemoglobin	-.414	.216-2.022	.468

Multivariate analysis of traditional risk factors and each individual non-traditional risk shows that Non-traditional risk factors were not significantly associated with cardiovascular disease. Multivariate logistic regression analysis of all traditional and non-traditional cardiovascular risk factors shows hypertension (p-<.001), diabetes (p- .044), and smoking (p- .046) significantly associated with cardiovascular disease. Non non-traditional risk factors (hyper-homocysteinemia, hyper-fibrinogenemia, increase CRP, factor VII activity and decreased hemoglobin) not significantly associated with cardiovascular disease.

Multivariate logistic regression analysis of all traditional and non-traditional cardiovascular risk factors and association of cardiovascular disease:

Table-V

Multivariate logistic regression analysis of all traditional and non-traditional cardiovascular risk factors and association of cardiovascular disease:

Variable	Odds ratio	95% CI	P value
Age	1.133	.824 - 11.690	.047
Sex .060	.099 - 3.300	.491	
Hypertension	21.400	16.400 - 31.357	<.001
Diabetes	1.561	1.004 – 21.724	.044
Dyslipidaemia	-.964	.743 – 9.259	.134
Smoking	1.987	1.033 – 51.443	.046
Hemoglobin	-.075	.275 – 3.130	.905
Homocysteine	-.745	.396 – 11.197	.382
Fibrinogen	.409	.503 – 4.502	.465
CRP	-.785	.110 – 1.889	.374
Factor VII	-.085	.232 – 3.632	.903

Multivariate logistic analysis shown that age (.047), hypetension (p-<.001), diabetes (p-.044), smoking (.046) independently associated with cardiovascular events but no non-traditional risk factors independently associated with cardiovascular events in chronic kidney disease and hemodialysis dependent patients.

Independent risk factor for cardiovascular disease in CKD and Hemodialysis dependent patients:

Table-VI

Independent risk factor for cardiovascular disease in CKD and Hemo-dialysis dependent patients:

Variable	Odds ratio	95% CI	P value
Age	1.133	.824 - 11.690	.047
Smoking	1.987	1.033 – 51.443	.046
Hypertension	21.400	16.400 - 31.357	<.001
Diabetes	1.561	1.004 – 21.724	.044

Discussion:

The principle finding of this study that patients with chronic kidney disease and hemodialysis dependent patients are increased risk of cardiovascular events. 55.7% of both non-dialysis and hemo-dialysis dependent patients have cardiovascular disease. Cardiovascular diseases are more common in hemo-dialysis dependent patients 59.1%. Both traditional and non-traditional risk factors are common in non-dialysis and hemo-dialysis dependent group in comparison to normal control group which maybe associated with increased cardiovascular events in CKD and hemo-dialysis dependent patients. Though increased prevalence of both traditional and nontraditional cardiovascular risk factors age >50 years, hypertension, diabetes, and smoking are independently associated with cardiovascular events in chronic kidney disease.

Chronic kidney disease (CKD) patients are highly prone to develop cardiovascular disease. End stage renal disease (ESRD) patients are higher risk of cardiovascular disease than the general population. Cardiovascular disease is by far the leading cause of morbidity and mortality in chronic kidney disease, accounting for almost 40% of hospitalization and almost 50% of death[7]. Prevalence of coronary artery disease is approximately 40% and prevalence of left ventricular hypertrophy is approximately 75% in chronic kidney disease and hemodialysis patients[8]. Prevalence of IHD in hemodialysis dependent patients of Bangladesh (study done in BSMMU) 48.6%[9] Most patients on the renal replacement therapy are treated with maintenance hemodialysis (76%), and have the highest mortality, particularly due to cardiovascular disease (70%). The HEMO study also identified cardiovascular disease, particularly ischemic heart disease, to be a major cause of cardiac hospitalizations and cardiac death. According to the EDTA Registry, death rate from ischaemic cardiac disease was 16-19 folds more common in RRT patients than age and sex matched population without renal disease[10]. In this study, 55.7% of both non-dialysis and hemodialysis dependent patient having cardiovascular disease. In hemodialysis dependent patients and non-dialysis CKD patients' cardiovascular disease were 59.1% and 55.4% respectively.

Our study documented a significant increase in several risk factors for cardiovascular disease among patients with chronic kidney disease and hemo-dialysis dependent patients. Both traditional and non-traditional risk factors are common in CKD and hemodialysis dependent patients.

Traditional risk factors increase age, hypertension, diabetes, dyslipidaemia, smoking, male sexes, positive family history of cardiac disease are established risk factors for cardiovascular disease. In a community –based cohort, showed that the prevalence of all the major traditional cardiovascular risk factors was significantly higher in patients with even mild renal failure (serum creatinine >1.5mg/dl) than in those with normal renal function. Hypertension is a frequent finding at all stages of CKD. The prevalence of hypertension increases nearly linearly as renal function falls, and so vast majority of patients with significant renal failure present high blood pressure[11]. Hypertension appeared as major factors of cardiovascular atherosclerotic accidents, especially high systolic blood pressure. An adverse role for systolic blood pressure was also reported in other studies both in renal replacement therapy patients and in the general population[12]. Conversely, a low incidence of cardiovascular death has been noted in dialysis patients with optimal blood pressure control. In this study documented that 87.5% of non-dialysis CKD patient and 90.09% hemodialysis patients were hypertensive and mean systolic blood pressure 151.87±24.01mm of Hg, 150.23± 26.20 mm of Hg in non-dialysis CKD, hemodialysis respectively. Mean diastolic blood pressure 88.96±11.66mm of Hg, 89.32± 11.47mm of Hg in non-dialysis CKD, hemodialysis and control normal group respectively. Hypertension is significantly associated with adverse cardiovascular events.

Several studies have noted that higher coronary heart disease (CHD), cardiovascular disease among the person with diabetes mellitus. With compared to non-diabetic individuals, diabetic patients have more severe LV hypertrophy and also develop more frequently ischaemic heart disease[13]. Diabetes is one of the established risk factor for cardiovascular disease in both patient with or without kidney disease. Diabetes also most important cause of chronic kidney disease. Diabetic patients with end-stage renal failure have particularly high cardiovascular morbidity and mortality. With compared

to non-diabetic individuals, diabetic patients have more severe LV hypertrophy and also develop more frequently ischaemic heart disease[14] . In this study 18 (37.5%) were found diabetic in non-dialysis groups and 7 (31.8%) were diabetic among hemodialysis group. Patient having cardiovascular disease 51.3% (20) were found diabetic. As expected, diabetes was found to be strongly associated with cardiovascular disease (p-002).

In chronic kidney disease dyslipidaemia , namely low HDL-cholesterol level, is a major independent risk factor, all the more deleterious that lipid disturbances develops early in course of CKD[15]. Plasma total cholesterol and LDL cholesterol, triglyceride levels all are significantly higher and HDL cholesterol lower in CVD+ than in CVD- patients. Lipid parameters are significantly altered in CKD patients as a whole, compared to healthy controls, but significantly greater extent in the CVD+ than in the CVD- group[16] . Several other studies also documented those lipid abnormalities are present in non-dialysis CKD patients and hemidialysis patients. The lipid abnormalities, as observed in this study are in agreement with finding of other authors in non-dialysis and dialysis dependent patients. Dyslipidaemia also significantly associated with cardiovascular disease in CKD and hemodialysis patients (p-001).

Cigarette smoking revealed a very important, independent cardiovascular risk factor. Cigarette smoking may be especially atherogenic in CKD patients because it enhances free radical generation and subsequent lipid per-oxidation which is already increased in CKD patients[16]. In our study smoking found to significantly associated with cardiovascular events (p-.001).

Age also important traditional cardiovascular risk factor. Age is the most powerful independent risk factor for atherosclerosis. Pre-menopausal women have much lower rates of disease than age- and risk-matched males; however, the gender difference disappears rapidly after the menopause. In our study age is correlated with cardiovascular disease. In non-dialysis dependent CKD and hemodialysis dependent CKD patients' age > 50 years were found significantly associated with cardiovascular events. Sex is not significantly associated with cardiovascular disease in our study result.

Several prospective epidemiologic studies have identified a positive association between plasma fibrinogen level and risk for cardiovascular disease[18]. A meta-analysis of prospective studies in the general population suggested that an increase in plasma fibrinogen levels of approximately 1 gm/L corresponds to a 1.8 fold increase in the risk for coronary heart disease[18]. A few clinical studies have suggested that fibrinogen levels are higher in patients with CKD and treated with hemodialysis or peritoneal dialysis[19]. Irish examined plasma fibrinogen levels among 126 patients with chronic kidney failure and 31 healthy controls. Mean levels of plasma fibrinogen were significantly increased in patients with chronic kidney failure compared with those in the control groups (12.38 μmol/L vs. 7. 88 μmol/L; p<0.001). Elevated levels of plasma fibrinogen in a large representative sample of patient with chronic kidney disease[20]. Fibribinogen is a classical acute phase reactant protein and is an independent predictor of cardiovascular events[21]. The risk of myocardial infarction (MI) almost doubles if fibrinogen level exceeds 300 mg/dl[22]. In our study, we documented elevated level of plasma fibrinogen in chronic kidney disease and hemodilysis dependents patients. Mean fibrinogen level 264.10±67.81mg/dl, 259.59±60.92mg/dl in non-dialysis CKD and hemodialysis group. Increase fibrinogen level may be associated adverse cardiovascular event but in current study fibrinogen is not independently associated with cardiovasculear disease in CKD and hemodialysis dependent patients.

Individuals in the lowest quartiles for serum folate, vitamin-B2 or vitamin B6 have significantly higher concentrations of homocysteine[23]. Hyper-homocystenaemia revealed a strong independent atherogenic risk factor in CKD patients, as already observed in the general population. Important finding of our study was increase level of plasma homocyeine level in CKD and hemodialysis dependent patient in comparison to normal control groups. Plasma homocysteine level increased in those patients with cardiovascular disease than those not have cardiovascular disease in both non-dialysis CKD and hemodialysis groups, but did note prove as independent cardiovascular risk factor in CKD and hemodialysis dependent patients. One study shows hyperhomocystinemia is not independent risk factor for cardiovascular disease in CKD in pre-dialysis group[17]. Hyper-homocystenemia has been found in adult patients with ESRD and predialysis CKD. Elevated Homocysteine concentrations have been associated with an increased risk of atherothrombotic events in adults[24]. Several clinical studies have supported that blood homocysteine concentration is an important risk factor for atherosclerosis. Mild hyperhomocysteinemia has been found in about 30% of patients with premature

cerebral, peripheral, or coronary vascular disease[25]. Risk factor analysis showed a significant association of hyperhomocysteinemia with premature vascular disease, even after adjustment for other atherogenic factors, including serum cholesterol, hypertension, or cigarette smoking, supporting the view that hyperhomocysteinemia is an independent risk factor for atherosclerosis. A positive association between plasma homocysteine level and carotid artery intimal- medial wall thickening in asymptomatic adults[26]. Thus recent literature suggests that blood homocysteine level may be of considerable importance as a risk factor for vascular atherothrombosis. Experimental studies have confirmed the atherogenic and thrombogenic effects of homocysteine . The parenteral administration of homocysteine derivatives caused arterial plaques and endothelial damage in rabbits and primates.

In chronic kidney disease, atherosclerosis is a major problem that to a great extent determines the prognosis of chronic uraemic patients, either dialyzed or not. Several hypotheses have been put forward to explain the development of atherosclerosis in chronic renal insufficiency. Among those, dyslipidemia, insulin resistance, and secondary hyper-parathyrodism have been favored.

C- reactive protein is an acute phase protein and a predictor of cardiovascular mortality in non-renal patients population[27]. Meta-analysis of several prospective studies of CRP and cardiovascular disease reported that CRP to be predictive of cardiovascular disease[28]. Although a variety of mechanisms by which CRP might promote thrombosis and atherosclerosis have been proposed, there is no proven relevance for these or any other putative mechanism. ESRD patients have also demonstrated an association between elevated CRP levels and all –cause and cardiovascular mortality[29]. Several studies also demonstrate that CRP is elevated in a significant proportion of ESRD patients without any apparent reason. In prospective cohort analysis of hemodialysis patients, Zimmermann et al showed that all cause and cardiovascular mortality was higher in patients with elevated CRP[30]. Two cross sectional studies demonstrates that elevated CRP levels were associated with surrogate markers for atherosclerotic vascular disease in both hemodialysis dependent patients and non-dialysis CKD patients[15]. In current study CRP level were elevated in patients with CKD and hemodialysis patients. Mean CRP level 17.31 ± 18.42 mg/dl and 52.59±82.16 mg/L in CKD non-dialysis and hemodialysis dependent patients respectively. Patient with cardiovascular disease and without cardiovascular disease CRP level 46.23±66.57 mg/L and 35.56±38.11 mg/L respectively. CRP is not independently associated with cardiovascular disease.

Erythropoietin is produced in the kidney, and anemia resulting from a deficiency of erythropoietin is present in the majority of patients with ESRD. Smaller reductions in hemoglobin occur in mild to moderate renal impairment. Anemia which is thought to make a substantial contribution to the development of cardiac abnormalities in CKD patients is a very frequent complication. There is increasing evidence that early and complete anemia correction may slow down the progression of CKD thus preventing cardiovascular and overall morbidity and improve survival in dialysis population. A number of observational studies have shown that it inversely correlates with residual renal function, yet its prevalence is already high during the earlier stage of CKD[31]. LVH as well as cardiovascular disease is very common in CKD patients. The Canadian multi-center study of renal anemia in patient with various stages of CKD found that the prevalence of LVH progressively increased with declining renal function from 30% prevalence at early CKD stage. Evidence suggests that low hemoglobin is a risk factor for cardiovascular disease. a recent analysis of the ARIC data found a 40% increased risk of CVD in subjects with anaemia compared with patients with normal hemoglobin[32]. Low hemoglobin also increases the risk of death in patients with heart failure independent of renal failure. It is widely known that patients with a GFR <60 ml/min per 1.73m^2 are much more likely to have anaemia and the prevalence and severity of anemia increase with declining renal function. The association between increased risk of cardiovascular disease and high creatinine in patients with anaemia might be explained by impairment in the physiologic mechanism. When hemoglobin concentration is <10gm/dl, non-hemodynalmic factors become inadequate, and increased cardiac output and blood flow begin to compensate for tissue hypoxia. In this study hemoglobin level was low and mean hemoglobin level 9.46± 1.87 mg/dl and 8.08±1.94 gm/dl in non-dialysis CKD and hemodialysis dependent patients respectively. Prevalence of low hemoglobin also more common in patients with cardiovascular disease. In this study low hemoglobin is not independently associated with cardiovascular disease.

In general population, activation of blood coagulation is associated with hyperlipidaemia via an increase in mass and activity of factor VII[33]. Northwick Park Heart Study

suggested that elevated activity of factor VII, measured as factor VII coagulant activity (VIIc), was predictive of future CVD events in men. Patients on hemodialysis and non-dialysis CKD have increased factor VII antigen and VIIc when compared with healthy controls.. Patients with cardiovascular disease are compared with those without cardiovascular disease, no significant difference in factor VIIc[15]. Clinical and epidemiological data suggest that factor VII may be involve in pathogenesis of cardiovascular disease. An elevated Factor VII activity level has been shown to be related to increase risk of MI[34]. In this study documented that factor VII activity increased in CKD non-dialysis patients and hemodialysis patient in compared to normal control group. Factor VII activity in patient with cardiovascular disease and patients without cardiovascular disease 105.79 ± 14.92% and 103.25 ± 13.86% respectively not independently associatedwith cardiovascular disease which correlates with other studies.

Conclusion:

Cardiovascular disease is strikingly higher in Non-dialysis chronic kidney disease (CKD) patients and Hemodialysis dependent CKD patients leads to increase morbidity and mortality of these groups. Both traditional and non-traditional risk factors are increased in CKD and hemodialysis dependent patients who may be responsible for increased cardiovascular morbidity and mortality in CKD and hemodialysis patients. Age, smoking, hypertension, diabetes, were found independently associated with cardiovascular event but non-traditional risk factors such as anaemia, hyperhomocysteinemia, hyperfibrinogenomia, increase C-reactive protein and increase factor VII activity were not independently associated with cardiovascular events although these factors were found strikingly higher in Non-dialysis CKD and hemodialysis dependent patients. Traditional risk factors are more important than non-traditional risk factors causing cardiovascular disease. So traditional cardiovascular risk factors should get first priority to prevent cardiovascular disease. We can-not comment on the effect of the duration of renal dysfunction and hemodialysis on the risk of adverse cardiovascular outcomes. We evaluated a limited number of non-traditional risk factors in limited number of study population, not exactly represent total populations. Further large scale study is required to establish association of non-traditional cardiovascular risk factor and cardiovascular events in chronic kidney disease and hemodialysis dependent patients.

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Dyslipidaemia and Progression of Chronic Kidney Disease

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Abstract

Background : CKD is a worldwide problem and patients with CKD are more likely to die of cardiovascular disease (CVD) than general population.

Objective: To see the pattern of dyslipidaemia in chronic kidney disease. *Methods:* ***A prospective study was carried out at Department of Nephrology, Dhaka Medical College Hospital. All admitted and OPD patients of CKD during the study period according to inclusion and exclusion criteria. Patients of CKD with diabetes mellitus, CKD stage 5 or ESRD, CKD with thyroid and liver diseases, patients on lipid lowering drugs or immunosuppressive drugs were excluded. eGFR was measured using MDRD equation. Progression of CKD was defined as reduction of eGFR from baseline or changes of stages of CKD downward during follow up after 6 months.***

Results: Out of 74 cases regarding relation between CKD stages with lipid abnormalities elevated TC were significantly higher in stage 1 75% (p<0.05) and TG is higher is stage 4 which was 44.4% (p<0.05). No significant difference in elevated LDL-C with stage 1 to stage 4 (p>0.05), and HDL-C was significantly reduced in stage 4 (66.7%) and p value <0.05. Among the lipid abnormalities of study population, mean total cholesterol, LDL-c and TG were significantly associated with the decline of GFR in all patients (P<0.001). HDL-c was not significantly associated with the rapid decline of GFR (P=.446).

Conclusion: Almost all of the patients of CKD have some form of lipid abnormalities. Lipid abnormalities influence the progression of chronic kidney disease. Specifically, elevated levels of total cholesterol, LDL-c and TG promote further progression of renal insufficiency.

Key words: Chronic Kidney Disease, Dyslipidaemia,Progression.

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Introduction

The prevalence of Chronic Kidney Disease (CKD) is increasing worldwide as a consequence of a rise in the prevalence of disorders that damage the kidneys, such as hypertension and diabetes mellitus.[1] CKD is a worldwide problem and patients with CKD are more likely to die of cardiovascular disease (CVD) than general population. Indeed, the Kidney Disease Outcome Quality Initiative (K/DOQI) and National Cholesterol Education Program (NCEP) guidelines recognize CKD as a CVD risk equivalent.[2] The majority of patients (58%) of CKD die from cardiovascular cause, making CVD the leading cause of death in patients with CKD.[3] Patients with CKD are at an increased risk for CVD and have a higher prevalence of hyperlipidaemia than the general population. Therefore, it is important to screen all patients with CKD for dyslipidaemia and treat them as they are considered a very high risk group for cardiovascular disease.[4] Dyslipidaemia is an almost universal consequence of renal disease, the exact pattern being influenced by the degree of renal failure, type of renal replacement therapy or transplant status of the patients.[5] Dyslipidaemia associated with chronic kidney disease is characterized by a low plasma concentration of high density cholesterol (HDL-c), a high concentration of triglycerides (TG) and the presence of small dense low density lipoprotein (LDL) particles.[6] Small dense LDL particles contain less cholesterol but they are more easily oxidized than larger LDL particles.

Methodology:

A prospective study was carried out at Department of Nephrology, Dhaka Medical College Hospital during the Period of 2007-2008. All admitted and OPD patients of CKD during the study period according to inclusion and

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exclusion criteria were enroll. Patients of CKD with diabetes mellitus, CKD stage 5 or ESRD, CKD with thyroid and liver diseases, patients taking lipid lowering drugs or immunosuppressive drugs were excluded. eGFR was measured using MDRD equation. Progression of CKD was defined as reduction of eGFR from baseline or changes of stages of CKD downward during follow up after 6 months. Risk factors influencing progression of CKD were addressed in every patient and appropriate measures were taken accordingly. Dyslipidaemia was defined as raised level of total cholesterol (≥200mg/dl), raised LDL-c(≥130mg/dl), Low HDL-c(<40mg/dl) and raised TG level (≥150mg/dl) (NCEP ATP 111, 2001). Different lipid abnormalities were categorized as : Normal = (TC <200mg/dl; HDL-c≥ 40mg/dl; LDL-c<130mg/dl and TG <150mg/dl). High = (TC 200-239mg/dl; LDL-c-130-159mg/dl and TG 150-499 mg/dl). Very high = (TC≥240mg/dl; LDL-c160mg/dl and TG ≥500 mg/dl). HDL-c level was categorized as normal (≥40mg/dl) & low (<40mg/dl). Data were collected from all respondents by direct interview and using structured questionnaires containing the variables of interest. Informed consent was obtained from all participants. All patients were evaluated by clinical history, physical examinations and relevant investigations. CKD patients was diagnosed and staged as per K/DOQI guideline 2002. Blood sample for serum lipid profile was taken after an overnight (≥12 hrs) fast. Levels of TC, HDL, TG were measured by autoanalyzer in the fresh state & LDL-c was calculated by Friedewald formula. Data were processed and analyzed using computer software SPSS (Statistical Package for Social Science) version 12. Results were expressed as frequency, percentage, and mean±SD. For statistical analysis one way ANOVA (Analysis of variance) test were used for numerical data. The association between baseline values and the rate of progression of disease (declining GFR) was analyzed by Spearman's correlation test. The level of significance was 0.05. P value < 0.05 was considered significant.

Results

The mean age of the study patients was 41.28±11.10 years. Mean BMI was 19.7±3.2. Mean SBP was 158.12±12.14 mm of Hg and mean DBP was 92.84±10.28 mm Hg (table 1). Out of all patients , CKD was due to glomerulonephritis in 65 patients (87.83%), followed by hypertensive nephrosclerosis in 4 patients (5.40%),lupus nephritis in 3 patients (4.05%) and Autosomal Dominant Polycystic Kidney Disease in 2 patients (2.70%) (Table 2). Out of 74 study populations, 4 patients were in stage I CKD (5.40%), 17 patients were in stage 2 CKD (22.97%), 35 patients (47.29%) were in stage 3 CKD and 18 patients (24.32%) were in stage 4 CKD. Mean level of Total cholesterol was 286.18±72.26mg/dl in stage 1, 215.62±66.27mg/dl in stage 2 CKD, 222.62±66.72mg/dl in stage 3 CKD and 226.21±68.11mg/dl in stage 4 CKD. Mean level of HDL-c was 44.13±6.28mg/dl in stage I, 36.71±5.78mg/dl in stage 2 CKD, 33.18±6.70mg/dl in stage 3 and 32.63±6.80mg/dl in stage 4 CKD. Mean level of LDL-c was 212.52±72.15mg/dl in stage 1 and 147.56±37.10mg/dl in stage 2, 142.72±41.02 mg/dl in stage 3 and 138.16±32.66 mg/dl in stage 4 CKD.(Table-IV).

Table-I

Base line patient's characteristics: Anthropometric and physical variables

Demographic variables	Mean ±SD	Range (Min-max)
Age (years)	41.28±11.10	Range 28-56 years
Body weight (kg)	52.86±6.73	Range 42-76 kg
BMI	19.71±3.23	Range 17-26
Systolic blood pressure (mm of Hg)	158.12±12.14	Range 125- 170
Diastolic blood pressure (mm of Hg)	92.84±8.26	Range 70-110

Table-II

Distribution of patients by gender

Sex	Number	Percentage
Male	46	62.16
Female	28	37.83

Table-III

Distribution of patients by aetiology of CKD.

Causes	Number	Percentage
Glomerulonephritis	65	87.83
Hypertension	04	5.40
Systemic inflammatory disease (lupus nephritis)	03	4.05
Inherited Kidney disease (ADPKD)	02	2.70

Regarding relation between CKD stages with lipid abnormalities elevated TC were significantly higher in stage 1 which was 75% (p<0.05), elevated TG is higher is stage 4 which was 44.4% (p<0.05). No significant difference in elevated LDL-C with stage 1 to stage 4 (p>0.05), and HDL-C was significantly reduced in stage 4 which was 66.7% and p value <0.05 (Table-V).

Table-IV

Fasting lipid profile among different stages of CKD

CKD stages	Mean±SD			
	Total cholesterol	HDL-cholesterol	LDL-cholesterol	Triglyceride
Stage 1 (4)	286.18±72.26	44.13±6.28	212.52±72.15	228.02 ±58.62
Stage 2 (17)	215.62±66.27	36.71±5.78	147.56±37.10	271.71± 89.22
Stage 3 (35)	222.62±66.72	33.18±6.70	142.72±41.02	265.01± 86.58
Stage 4 (18)	226.21±68.11	32.63±6.80	138.16±32.66	256.31 ±63.18

Table-V

Prevalence of Lipid abnormalities across the CKD stages

	Stage 1 n=4(%)	Stage 2 n=17(%)	Stage 3 n=35(%)	Stage 4 n=18(%)	P value
Elevated TC (n=22)	03(75)	05(29.4)	06(17.1)	08(44.4)	0.03
Elevated TG (n=14)	00	02(11.8)	04(11.4)	08(44.4)	0.01
Elevated LDL-C (n=11)	01(25)	02(11.8)	03(8.6)	05(27.9)	0.27
Reduced HDL-C (n=23)	01(25)	03(17.6)	07(20.0)	12(66.7)	0.002
Dyslipidaemia (44)	3(75)	10(58.8)	16(45.7)	15(83.3)	0.06

Among the lipid abnormalities of study population, mean total cholesterol (252.42±35.28 mg/dl) was significantly associated with the decline of GFR in all patients (P<0.001). HDL-c (mean 32.43±6.12 mg/dl) was not significantly associated with the decline of GFR (P=.446). Mean LDL-c (138.12±28.22 mg/dl) and mean TG level (261.24±56.46 mg/dl) was also significantly associated with the decline of GFR (P= <0.001 and <0.01 respectively) (Table-VI).

Table-IV

Association of fasting lipid profile with the declining GFR in all patients

Fasting lipid profile	Mean ±SD	r	p
Total cholesterol (mg/dl)	252.42±35.28	.428	<0.001
HDL-cholesterol (mg/dl)	32.43±6.12	.082	0.428
LDL-cholesterol (mg/dl)	138.12±28.22	.342	<0.001
Triglyceride (mg/dl)	261.24±56.46	.365	<0.01

Discussion

This study was conducted in Nephrology department of Dhaka Medical College Hospital to find out the pattern of lipid abnormalities in different stages of CKD and their role in the progression of CKD. In present study among the 74 patients the mean age was 41.28±11.10 years, 46 patients (62.16%) were male and 28 patients (37.83%) were female. Similar results was found in study of Rao et al.[7] they showed the mean age was 49.41 ± 13.66 years. In another Adejumo OA et al[8] study also reported the mean age of the CKD subjects were 47.57±15.97 years, male:female ratio of 1.7:1 this results support our study.

In current study revealed that common cause of CKD was due to glomerulonephritis in 65 patients (87.83%), followed by hypertensive nephrosclerosis in 4 patients (5.40%), lupus nephritis in 3 patients (4.05%) and Autosomal Dominant Polycystic Kidney Disease in 2 patients (2.70%). In study of Adejumo OA et al.[8] found cause of CKD were hypertensive nephropathy 34 (32.4) Diabetic nephropathy 31 (29.5), Chronic glomerulo-nephritis 35 (33.3%). Rao et al.[7] study revealed common causes of CKD were diabetes mellitus 30%, hypertension 34%, lupus nephritis 04%. that findings is approximately similar to our study.

In present study regarding relation between CKD stages with lipid abnormalities elevated TC were significantly higher in stage 1 which was 75% (p<0.05), elevated TG is higher is stage 4 which was 44.4% (p<0.05), no significant difference in elevated LDL-C with stage 1 to stage 4 (p>0.05), and HDL-C was significantly reduced in stage 4 which was 66.7% and p value <0.05. In Adejumo OA et al[8] study showed significant increase in the prevalence of

reduced HDL-C and elevated TG with worsening GFR, hence early evaluation and management of dyslipidaemia should be advocated in these patients in order to retard progression of CKD to ESRD and prevent development of cardiovascular disease. There was association between dyslipidaemia and severity of CKD unlike previous reports.[9,10]

In our present study, there was also no significant difference of lipid abnormalities between different stages of CKD except that in stage 1 CKD patients, HDL-c level was normal. In every other stages of CKD there was raised TC-c, raised LDL-c, raised TG level and low HDL-c level but there was no significant fall of lipoprotien in advancing CKD. Adejumo OA et al study also found similar results.[8] Kachhawa et al.[11] study reported Serum lipid profile (total cholesterol, triglyceride [TG], LDL, and very low density lipoprotein [VLDL]) except high density lipoprotein cholesterol (HDL C) was showed significantly increased compared to control subjects. Some other studies also shown similar results.[12,13]

Harper and Jacobson [14] study showed CKD causes profound dysregulation of lipoprotein metabolism, resulting in multiple lipoprotein abnormalities. Dyslipidemia develops during the early stages of CKD, and significant changes in apolipoproteins usually precede changes in plasma lipid levels. Decreased high density lipoprotein (HDL) levels and increased trigiyceride rich lipoproteins are the major lipid abnormalities. Dyslipidaemia is a common cardiovascular risk factor in CKD especially in females and older CKD patients. Some lipid abnormalities such as reduced HDL-C, elevated TG tend to increase with worsening renal function. They recommend early evaluation of CKD patients for dyslipidaemia and cardiovascular risk using ratio of lipid components at all stages with the aim of management with both lifestyle modification and therapeutic intervention.

Conclusion

Almost all of the patients of CKD have some form of lipid abnormalities. Most common lipid abnormalities were low HDL-c and high TG level. The results of this prospective study also support the concept that lipid abnormalities influence the progression of chronic kidney disease. Specifically, elevated levels of total cholesterol, LDL-c and TG promote further progression of renal insufficiency.

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Quality of Life of Chronic Kidney Disease Patient on Hemodialysis

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Abstract

Background: Chronic Kidney Disease (CKD) is one of the common chronic illnesses among elderly people due to increasing incidence of hypertension, diabetes mellitus and vascular disease. Among the renal replacement therapy hemodialysis is the cornerstone to improve quality of life (QOL) of the CKD patients. Objectives: To evaluate the quality of life of CKD patient on hemodialysis therapy & also to compare this QOL with that of healthy control. Patients and method: This is a descriptive cross sectional study carried out in dialysis unit of Rangpur Medical College Hospital. WHOQOL-BREF questionnaire was used to assess the quality of life. Higher QOL score corresponds to better quality of life. Results: A total of 60 patients on hemodialysis and 30 healthy subjects (attendant of the patient) has been included in this study. The quality of life of CKD patient on hemodialysis was significantly lower (p <0.05) than healthy people especially in physical, psychological & social domain. There was no significant difference between two groups in environmental domain. Female hemodialysis patient showed significantly lower QOL scores (p <0.05) than male patient especially in psychological & social domain. Higher educational qualification showed better quality of life than lower educational qualification. Conclusion: The quality of life of CKD patient on hemodialysis was found to be significantly lower in comparison to healthy general people in this study.

Key words: quality, domain, hemodialysis.

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Introduction

Quality of life, an important parameter of health and well-being, getting popular now-a-days. Quality of life (QOL) is an important outcome representing a person's concerns. This also is an important indicator of other outcomes, such as mortality and hospitalization due to any disease.[1,2] In 1991, the World Health Organization(WHO) introduced a pilot project to develop a QOL questionnaire (WHOQOL) for generic use and defined QOL as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns.[3,4,5] Modern civilization includes better health facilities, thus increasing proportions of elderly people, with a resulting increase in the incidence and duration of chronic illnesses. This chonic diseases are being treated by different newer & better therapeutic procedure, bringing to the center the need for a dignified QoL of patients.[6] An increasing interest in QoL is observed in patients who suffer from chronic diseases, including those with chronic kidney disease (CKD).[7] Data from different studies in Bangladesh reveal an alarmingly high burden of chronic kidney disease. These groups of patient are increasing day by day on the part of diagnostic advances. Patients with CKD on Hemodialysis therapy, is an important subgroup of them who needs long term monitoring & prognostic evaluation. Although HD therapy prolongs life, there often several factors which may affect QOL of CKD patient.[8] Chronic renal patients who depend on renal replacement therapy (continuous peritoneal dialysis and hemodialysis) have a limited daily life and go through many bio-psychosocial changes and losses which interfere in their quality of life.[9]

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When dialysis came up, the main concern was to prolong the survival of chronic renal patients, but now it is more important to evaluate their quality of life with this therapy. Being under hemodialysis three times a week or under peritoneal dialysis on a daily basis has consequences for the patients regarding physical, emotional and social aspects of their lives. Depression is the most common mood disorder among these patients, and usually represents an answer to a real or imagined loss, thus configuring persistent depressive mood, bad self-image and pessimistic feelings, besides physiological complaints such as generalized weakness, sleep disorders, changes in appetite and weight, diminished sexual interest, among others.[10]

Bangladesh is a developing country, nephrology services are in the earlier stage of development. In this era, there is improvement in the awareness about kidney diseases in Bangladesh. There are only about 40 formally trained nephrologists for a population of 180 million (compared to the United States with more than 5000 nephrologists for a population of about 300 million).[11] There are only 12 Government institute in Bangladesh where dialysis facility is present. Beside these there are some private institute developing in recent years but bothers high cost load. According to the Hospital Data, there are about 20,000 patients who are receiving dialysis in Bangladesh. Rangpur Medical college hospital is a tertiary level hospital in the northern part of Bangladesh where dialysis unit has been established in 2011. Now in this hospital total 16 dialyzer machine is working out of which 03 machines are dedicated for hepatitis B & C positive patient. A total of 114 CKD patients are enrolled in this hospital for dialysis from starting up to 30th June of 2013 out of which only 80 patients are currently on regular schedule. Among them 10 patients are irregular in respect to their need i.e. under dialyzed. Even most of the patients who receive dialysis are "under dialyzed" (about 75% get dialysis twice per week, 12.5% also get irregular dialysis). Under dialysis affects not only survival of the patients (1- to 2-year survival is 40.5%), but even quality of life (QOL) is also poor in these patients. Health-related QOL (HRQOL) represents the "physical, psychological, and social domains of health that are influenced by a person's experience, beliefs, expectations, and perceptions. We know that there are many factors that affect QOL of these patients.[13] Causes of CKD also affect QOL of the patient. Adequacy of dialysis, daily dialysis, financial capacity and transport facility all may affect QOL.[14]

Long term HD therapy often results in loss of freedom, dependence on family members, and disruption of marital, social & family life, reduced financial income. In our setting it is estimated that about 75,000 Tk (BD) is needed only dialysis purpose. Private institute requires double cost than that of govt. institute. As hemodialysis therapy is expensive, patients often willingly do not follow the standard dialysis frequency, use of less costly dialyzers& most of them do not receive erythropoietin therapy at all. In overall, end-stage renal disease patients have to cope with many adversities, like physical symptoms, special diet schedules, changes in their body image while the outcome of treatment is not satisfactory. The concept of quality of life in chronic disease is a new thinking in Bangladesh. There are very few studies dealing with this topics & most of them are from developed countries. So, my interest on this topics to judge the feedback of HD patient not to be satisfied by ourselves that the patient is getting appropriate treatment but also to see the patients view.

For many years scientists are working to measure the quality of life of human being .Their attempt shows tremendous need for this QoL in modern civilized world .QoL reflects every aspect of life especially psychological aspect which is solely related with many chronic diseases like CKD, coronary heart disease & diseases causing disability. In part of this development WHO has developed a WHOQOL group who has adopted a new instrument for measuring QoL by working in different centers in various countries, named WHOQOL-100 score. It contains about 276 questions with 06 domains .Very limited studies were done by this.[16,17,18] But the WHOQOL-100 score has very soon lost its expected popularity due to following reason: very clumsy, time consuming& definitely expensive.

After a while the WHOQOL group ,for their convenience and in the interests of parsimony has developed the 26 item WHOQOL-Bref. It is short & easily interpretable.Now a days it is widely used to interpret QoL in health sector as well as many sociological perspect. The international WHOQOL-Bref has been shown to have good psychometric properties and to provide a valid and reliable alternative to the WHOQOL-100. The WHOQOL-BREF is available in approximately 20 languages, including those of both developed and developing countries, and in Christian, Islamic, and Hindu culture settings, with several studies in developing countries having demonstrated its cross-cultural and content validity.[19,20,21] In Bangladesh,

Izutsu et al. developed the Bangla version of the WHOQOL-BREF, showing it to be a valid and reliable assessment tool of QOL in an adolescent population.[15] Finally, it is very important to know the quality of life of chronic kidney disease patient on hemodialysis. Thus we can ensure a positive attitude towards HD treatment so that we can improve the overall quality of life in this group of people.

Materials and methods

This was an observational cross-sectional study, carried out in dialysis unit of Rangpur Medical college Hospital, Rangpur, Bangladesh. Chronic kidney disease patients on hemodialysis for at least 2 months duration, twice in a week, admitted between 1st January 2013 to 30th June 2013 in Rangpur Medical College Hospital, Rangpur were enrolled. Convenient purposive sampling procedure was used, the study objectives were explained to the patient/ guardian of the patient and informed written consent was taken. Patients having malignancies, multiple organ system failure, major hearing impairment (inability to hear loud speech even with a hearing aid), any major surgical interventions in the previous three months and who did not give consent to take part in the study were excluded from the study. A total of 60 cases enrolled for the study. Thirty (30) apparently healthy individuals were taken as control from the caregivers of the patients.

Procedure of data collection and analysis

Each patient or attendant was directly interviewed & the data was collected via WHOQOL-BREF questionnaires (Bangla Version). After collection of data it was coded and checked manually. Data analysis was done according to the objectives of the study by using SPSS-17.0 (Statistical Program for Social Science) software program. Descriptive statistics were expressed as mean ± standard deviation for continuous variables and percentage for categorical variables. Statistical significance was set at a two-sided P-value of <0.05. The result of the clinical study and statistical analysis is presented in the form of text, table, bar and chart.

Operational definitions:

Chronic kidney disease (CKD) refers to an irreversible deterioration in renal function or evidence of renal damage for at least 03 months. According to the serum creatinine data in the study cohort, the estimated GFR (eGFR) was calculated using the Modification of Diet in Renal Disease four-variable equation.[22] CKD was identified & stages of CKD were originally defined by the US National Kidney Foundation Kidney Disease Quality Outcomes Initiative 2002. Hemodialysis patient means CKD patients who were on regular at least twice a week hemodialysis therapy. Hemodialysis means purification of blood by ultrafiltration in a dialyzer machine. Anxiety means emotion of anxiety, worrisome thoughts, avoidance behavior and the somatic symptoms of autonomic arousal. Depression means episodes of low mood & disinterest. Demographic and medical data including age, sex, marriage, education, religion, occupation, annual income, and co-morbidities were obtained from medical records and interviews with the patients. Regarding educational status primary means upto class V level, secondary means S.S.C & H.S.C level and graduate means university education. The designated level of income; low was <TK(BD)30,000 per year, middle was between TK 30001-180,000,which was approximately the average annual income of the general population in Bangladesh, whereas upper class was designated as annual income >Tk (BD)180,000. Cardiovascular disease was defined as a history of congestive heart failure, angina pectoris or myocardial infarction. Diabetes mellitus (DM) was defined as those with the history or on anti-diabetic medications. Definition of hypertension was those patients with blood pressure >140/90 mmHg or on anti-hypertensive medications.

Tools of Investigation:

The WHOQOL-BREF consisted of 2 global items, G1 for overall QOL and G2 for general health, and 26 items in the physical, psychological, social relations, and environment domains. Specifically, there were 7, 6, 4, and 9 items in the physical, psychological, social relations, and environment domains, respectively. Application method, reference time point, and item scoring were performed as described for the original WHOQOL-BREF. Four domains are defined for the WHOQOL-BREF, based on its 24 items: domain 1, physical health, is on activities of daily living, dependence on medicinal substances and medical aids, energy and fatigue, mobility, pain and discomfort, sleep and rest, and work capacity. Domain 2, psychological health, includes bodily image and appearance, negative feelings, positive feelings, self-esteem, spirituality, religion, personal beliefs, thinking, earning, memory, and concentration. Domain 3, social relationships, covers personal relationships, social support, and sexual activity. Domain 4, environment, assesses financial resources, freedom, physical safety and security, health and social care (accessibility and quality), home environment, opportunities for acquiring new information and skills, participation in and opportunities

for recreation and leisure activities, physical environment (pollution, noise, traffic, and climate), and transport. The raw score of each domain was then transferred to standardized score of 4 to 20, in order to maintain uniformity in the scores. The method of inferring the score is available elsewhere.[21] Higher scores mean the better quality of life of patients. The QOL index of each domain and their associations with demographic factors were assessed.

Ethical implications:

Written, informed and voluntary consent was taken and confidentiality assurance was provided to those who agreed to participate in the study.

Results

During the study period, 60 patients who fulfill the criteria & 30 healthy attendants had been studied. The mean age of the patients in our study was 40.63 (SD ±14.25) years with a range of 16 to 70 years & of control group was 32.03 ± 11.58 (mean ± SD) years with a range of 17 to 60 years. (Table I)

Table-1

Demographic characteristics of the studied subjects & Healthy control group

Variables	Hemodialysis group (n=60)	Healthy control group (n=30)
Age(Years)		
<30	18 (30%)	18 (60%)
31-60	38 (63.3%)	12 (40%)
>60	04 (4.70%)	00
Sex		
Male	38 (63.3%)	14 (46.7%)
Female	22 (36.7%)	16 (53.3%)
Marital status		
Married	52 (86.7%)	5 (16.7%)
Unmarried	8 (13.3%)	25 (83.3%)
Educational status		
Primary	23 (38.3%)	16 (53.3%)
Secondary	13 (21.7%)	07 (23.3%)
Graduate	20 (33.3%)	07 (23.3%)
Illeterate	04 (6.7%)	00
Occupation		
Farmer	07 (11.7%)	06 (20%)
Service holder	11(18.3%)	02 (6.7%)
Businessman	11 (18.3%)	07 (23.3%)
Housewife	19 (31.7%)	13 (43.3%)
Retired person	04 (6.7%)	00
Student	08 (13.3%)	02 (6.7%)

Comparison of WHOQOL-BREF QOL scores:

The scores in a WHOQOL-BREF scale range from 0 to 100. In hemodialysis group highest QOL score was observed in the environmental domain (40.23 ±11.86) and lowest in social relationship domain (30.22±14.34). (Table II) Where as in the healthy subjects the QOL score was highest in social domain 82.66± 9.94 and lowest in psychological domain 78.19± 8.59. The over all QOL score in haemodialysis patient was 38.06±16.13 and in healthy subjects was 77.50±7.63 (p value 0.0001).

Table II

WHOQOL-BREF scores of hemodialysis patients & healthy control group

Domains group	Mean ±SD (QOL scores)	*p* value
Physical Domain:		
HD(n=60)	35.89±11.68	0.0001
HCG(n=30)	81.15±6.39	
Psychological Domain:		
HD(n=60	37.42±12.67	0.0001
HCG(n=30)	8.19± 8.59	
Social Domain:		
HD(n=60)	30.22±14.35	0.0001
HCG(n=30)	82.66± 9.94	
Environmental Domain:		
HD(n=60)	40.23±11.86	0.0001
HCG(n=30)	81.67±6.02	
Overall QOL :		
HD(n=60)	38.06±16.13	0.0001
HCG(n=30)	77.50±7.63	

**P* value <0.05 is considered as statistically significant

SD: standard deviation, HD: Hemodialysis patient, HCG: Healthy control group

Effect of various demographic characteristics upon QOL:

Among the 60 CKD patient on hemodialysis, the female patient showed lower QOL score in psychological domain(35.23±10.10) & social domain (29.35±16.08) in comparison to male CKD patient(38.79±13.84 &31.16±13.52 respectively) (p <0.05) (Table III). Among patient of different educational status of the CKD patient illiterate having over all QOL score 36.39 and in graduate patient QOL score 39.90.

Table-III

Association between Demographic variables & WHOQOL-BREF scores of Hemodialysis Patients

Variables	QOL Scores in WHOQOL Domains			
	PD	PSD	SD	ED
Sex:				
Male(n=38)	36.09±10.89	38.79±13.84	31,16 ± 13.51	39.75±10.82
Female(n=22)	36.20±12.6	35.23±10.10	29.35±16.08	41.62± 13,39
P- Value	<0.05	<0.05	< 0.05	<0.05
Educational status:				
Primary(n=23)	32.61±10.67	35.84±11.01	27.36±14.38	35.24±10.62
Secondary(n=13)	35.99±12.83	39.10±10.28	26.92±14.50	39.66±10.70
Graduate(n=20)	39.66±12.92	39.03±17.08	35.13±11.62	45.79±11.99
Illeterate(n=4)	35.72±2.91	34.37±5.24	31.25±23.93	44.25±14.39
P-Value	<0.08	<0.05	<0.05	<0.05

(Illeterate Vs.Graduate), QOL: quality of Life; PD: Physical Domain; PSD: Psychological Domain; SD:Social Domain; ED: Environmental Domain

Discussion

This is the first report of quality of Life of patients on HD therapy in Bangladesh. Quality of life of patients on hemodialysis is poor as compared to attendance of them in all domains except for the environment domain. It means patients on hemodialysis have poor a QOL in physical health, psychological health, and social relationship domains than their attendance. Since attendance of the patients live with them in same socioeconomic conditions, availing same transport, sharing same home and physical environment, it is reasonable that they have the same level of QOL in the environment domain. Similar observation have been reported in other studies comparing quality of life of CKD patient on hemodialysis with that of general healthy people.[23,24] One important thing is that majority of CKD patient in this study were economically poor. They had not enough economical security, even though they didn't show significantly lower QOL score in environmental domain than healthy control group. The hemodialysis patient were satisfied with the health care facilities in the hospital, also showed no significant difference with that of healthy group.

Educational qualifications have positive effect on QOL scores. Study population with higher educational status showed significantly higher QOL in all dimension of health. This observation is consistent with previous studies.[25] The role of economical security also showed better QOL in all domains. Another cause of this difference is that higher educated people have more income source, become financially capable of bearing the cost of dialysis. It also affects their psychological wellbeing & mental soundness. People with low economy show more depressive & other mental problem than others.

This study showed significantly lower scores in psychological & social domain in female patients than their male counterpart. The cause may be female patients were not the decision maker of their family& majority of them were not income generating person, being dependent upon family income. Another factor may be the cultural factors & biases regarding care & supervision of female patient. Other studies in different parts of world also showed same result in case of gender analysis of QOL. 26 Many of the CKD patients were dissatisfied with them & suffering from anxiety, depression, pessimistic feeling. Many of them thought themselves as burden of the family. This may be an important cause of lowered QOL in psychological domain of CKD patients than healthy people. The majority of study subject especially male were not satisfied in sexual life after initiation of hemodialysis.

Limitations of the present study:

1. The sample was relatively small.
2. Duration of dialysis couldn't be evaluated which may affect QOL of CKD patient.
3. Etiology of CKD couldn't be included in the present study.
4. Co-morbidity of patient was not included.

Conclusion:

Quality of life score of CKD patients on hemodialysis is significantly lower in comparison to healthy individual. Hemodialysis therapy affects negatively the quality of life of CKD patients.

Recommendations:

Proper counseling of the CKD patients should be done before dialysis.

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Case Reports

21 Years of Haemodialysis with Healthy Life: A Case Report

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Abstract

Mortality among the end stage renal disease (ESRD) patient remains unacceptably high despite progress in the management of Renal Replacement Therapy (RRT) even in the most developed countries. Those patient on Renal Replacement Therapy, the life can be prolonged up to 30 years is possible. Nevertheless, due to the advance and modern technique in RRT, the surveillance of these patients could be long with reasonable quality of life (QoL). The number of patients requiring dialysis is increasing worldwide and so do Bangladesh. It is believed that there is a 6% growth of dialysis patients per year. These patients remain on dialysis for a long period, the reason being transplantation beyond their reach for cost andlong waiting time for transplantation, also scarcity of donor. Life span of hemodialysis patients not very long, its average less than 10 years. Among hemodialysis patients, long and very long term survivals were associated with younger age, nondiabetic status, black race and male gender. Patient survival for periods of up to 30 years is possible on hemodialysis.

Here we present a case history of a women who spent 21 years on hemodialysis and is still going on with good health. While her set off was not so impressive but is going to exceptional journey of hemodialysis.

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Background

Hemodialysis is a method that is used to extracorporeal removal of waste products such as creatinine and urea and free water from the blood when the kidneys are in a state of failure. Haemodialysis is the one of three modes of renal replacement therapy (RRT) other two being renal transplant and peritoneal dialysis. In 1960s, haemodialysis was introduced to the world when Belding Scribner initiated a chronic haemodialysis program in Seattle, Washington[2]. Long-term haemodialysis first became a reasonable possibility in 1966 when the arteriovenous fistula was described, and there is now a group of survivors' worldwide[3]. In Bangladesh, hemodialysis started only in the late 1970s. First hemodialysis in Bangladesh was done in 1978. Two centers provided dialysis at that time, BSMMU (Bangabandhu Sheikh Mujib Medical University) then known as IPGMR, being one.

There are about 18 million people with renal disease in Bangladesh and about forty thousand die per annum due to it. There are about 40 dialysis centers with 300 functioning dialysis machine across Bangladesh[4]. Long term haemodialysis is very rare and beyond the imagine in developing countries like Bangladesh where the patient has to bare all the expenses.

The haemodialysis unit in BSMMU is providing dialysis services since 1978 and till date around thousands of people have been benefited. BSMMU, is also one of the pioneer institute for providing renal transplantation in Bangladesh.

Case History

A 34-yr-old unmarried lady, born 11th June 1981, was only 14 years old when she received her first session of haemodialysis. Twenty-two years back, she initially presented with fever and leg swellings diagnosed as glomerulonephritis and renal biopsy performed. She was a case of membranous nephropathy and received steroid and cyclophosphamide but failed to achieve remission.

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Her renal function deteriorated continuously and became End Stage Renal Disease (ESRD).

She introduced to hemodialysis in 1995. She was in her young, tender age when dialysis started. The disease and the dialysis process hampered her both physically and mentally. Initially for some days she discontinued her study but later on she continued her study became graduate.

She is the eldest daughter of the 3 siblings. Her mother was willing to donate her kidneys but she refused and continuing hemodialysis.

When she started haemodialysis, it was in primitive stage in Bangladesh. She has been receiving 3 session dialysis each week, each session is 4 hours duration. Her journey was not even full, during this period faced vascular access problems, one AV fistula failed, she also suffered from pneumonia, tuberculosis and became hepatitis C seropositive. Now she is HCV negative, normotensive with medication, not anaemic with erythopoetin, serum albumin 3.2 gm/dl, serum calcium 9mg/dl, serum phosphate 3.6 mg/dl but she has hyper urecaemia and mild arthritis and peripheral neuropathy.

Discussion

Mortality of hemodialysis patient remain very high but some cases of long time survival not impossible. Factors associated with long survival are younger age, normotensive and no diabetic. Survival more than 20 years in developing country are rare, our patient survive 21 years in BSMMU which is low resource dialysis center long time survivor of haemodialysis patient also suffer from multiple comorbidities including cardiovascular disease, osteodystrophy, 2 Microglobulin associated with amyloidosis leading bone pain, arthritis. Long term dialysis on several studies have shown that the patient who were non diabetic, had less severe hypertension, availability of long-lived dialysis access, blood transfusion leading to hepatitis B and C, and disability due to bone disease; hence indicating that these were the important points to be considered. It would thus appear that many of these problems can be identified early and prevented or treated without any delay.

Dialysis treatment sometimes can significantly prolong life with normal life and can offer appreciable quality of life. There is no registry of extremely long-lived haemodialysis patients, information on this group is scattered. Piccoli described a group of 56 patients who had been on uninterrupted dialysis for at least 20 years. None of the patients were diabetic; 82.1% had severe vascular disease; 46.4% had severe cardiac disease; 89.3% had severe bone disease; and 48.2% of the patients had had a parathyroidectomy. Hypertension were less common in the long-lived patients on haemodialysis. Dialysis treatment sometimes can significantly prolong life, sometimes more than expected[7].Appropriate dialysis and treatment of complication should address in long time survivor of hemodialysis patient.

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Atypical Complications of Dengue Fever: A Case Report

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Abstract

Dengue is common but may present with atypical manifestations. Here, we report case history of a 55-year-old man, diagnosed case of diabetes mellitus, hypertension and chronic kidney disease, who presented with history of fever, headache, retro-orbital pain, myalgia, nausea and vomiting, followed by severe epigastric pain and anuria. Diagnostic work-up revealed dengue fever complicated with acute pancreatitis and acute kidney injury. Patient was managed conservatively and by intermittent hemodialysis. Physicians should be aware of the atypical presentation/complication of dengue fever.

Key words: Dengue fever, Acute pancreatitis, Acute kidney injury, Hemodialysis.

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Introduction

Dengue is the most rapidly spreading mosquito borne disease with increasing geographic expansion to newer regions and even from urban to rural settings.[1] Patients infected with dengue virus may remain asymptomatic and symptomatic patients present with fever, myalgia, retro-orbital pain, cough, skin rash, leucopenia and thrombocytopenia. A case of severe dengue is defined as a suspected dengue patient with one or more of the following: severe plasma leakage that leads to shock, severe bleeding and severe organ impairment. Dengue infection may present with atypical manifestations, which are often under reported and may lead to misdiagnosis. Atypical abdominal presentations include hepatitis, acalculous cholecystitis, splenic rupture, febrile diarrhoea and acute pancreatitis.[2]Atypical renal presentations include acute kidney injury (AKI) and haemolytic uraemic syndrome.[2] A case of severe dengue with atypical manifestations is presented here.

Case Report

A 55-year-old male presented with history of high grade fever, headache, retro-orbital pain, myalgia, nausea and vomiting for five days followed by severe piercing pain in epigastrium that radiated to back, associated with gradual reduction of urine output followed by cessation of urine output for one day. He is known diabetic for last 16 years, hypertensive for 3 years and chronic kidney disease (CKD) patient for last 2 years. He had no history of gall stone disease, alcohol abuse or any drug intake.

On examination, he was mildly dehydrated. His pulse was 112 b/m, blood pressure was 150/90 mm of Hg, respiratory rate 16 breaths/min, temperature 102^0 F, maculopapular rash was present mostly in limbs and on trunk. There was bruise at venipuncture site and he had oedema. Abdominal examination revealed mildly distended abdomen with diffuse epigastric tenderness and ascites. He had non-proliferative diabetic retinopathy with maculopathy on both eye and diminished touch and pin prick sensation in both distal lower limbs. Other systemic examination findings were unremarkable.

Laboratory investigations showed leukocytosis (total white cell count 15,900/mm^3, polymorph 76% lymphocyte 7%, monocyte 14%), normal haematocrit (34.8%) and low platelet count (43,600/mm^3). Urine routine test showed haematuria (red cells 8-10/high power field) and proteinuria (++). He had raised aspartate aminotransferase (AST 76 U/L), alanine aminotransferase (ALT 54 U/L), blood urea (197 mg/dl), serum creatinine (8.9 mg/dl), phosphate (7.3 mg/dl), low serum sodium (121 mmol/L) and bicarbonate (19 mmol/L). He had uncontrolled blood glucose (fasting blood glucose 8.3 mmol/L, glycated haemoglobin 7.8%), and normal lipid profile (TG 179 mg/dl, HDL 18 mg/dl, LDL

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74 mg/dl). Serum amylase level was 2568 mg/dl and lipase level was 8492 mg/dl. His dengue serology (IgM by ELISA) was found to be positive. D-dimer was positive. Blood culture revealed no growth. Ultrasonogram(USG) revealed mildly swollen and hypo-echoic pancreas and ascites. Computed tomography (CT) scan revealed swollen pancreas (Figure 1) and left sided minimal pleural effusion and pelvic collection.

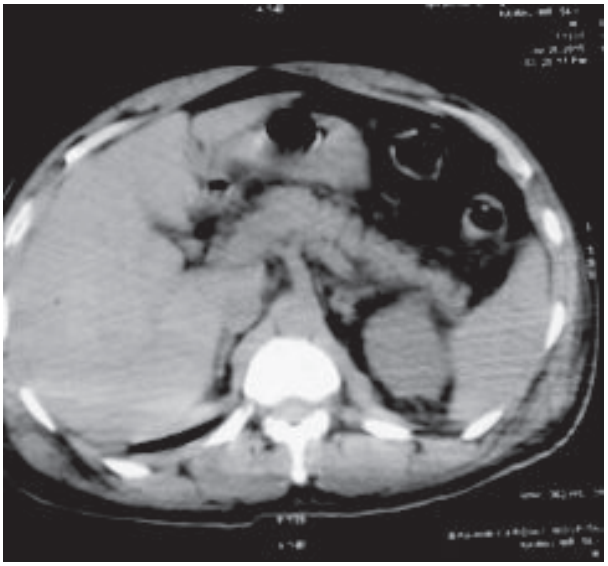

Fig.-1: *CT scan of abdomen showing swollen pancreas*

He was diagnosed as severe dengue fever with acute pancreatitis with AKI on CKD. He was managed conservatively by intravenous fluid,intravenous antibiotics, pancreatic enzymes and insulin. He required 6 sessions of hemodialysis. He was discharged with a serum creatinine of 5.5 mg/dl without requiring further dialysis.

Discussion

Acute pancreatitis is a rare complication of dengue fever.[3,4]Setiawas et al. conducted a study that included 148 children with dengue haemorrhagic fever and abdominal pain to assess the pancreatic involvement by abdominal USG. Enlarged pancreas and increase serum amylase and lipase levels were found in 29% of patients.[5]

Involvement of the pancreas may be due to direct viral invasion or hypotension in dengue haemorrhagic fever. There are no reports of pancreatic histological findings in dengue infection to document direct viral invasion. This may be due to difficulty in obtaining samples. More definitive studies are required to determine the pathogenesis with subset of dengue patients developed pancreatitis.[2]

AKI is a complication of dengue fever which has not been studied much. There are multiple proposed mechanisms for etiopathogenesis of renal involvement in dengue virus infection. Dengue causes capillary leakage and loss of fluid from the intravascular compartment leading to shock[6,7] which may lead to decreased kidney perfusion and acute tubular necrosis. Possible etiological factors for AKI in dengue include hypotension with either hemolysis or rhabdomyolysis and shock as reported in various case reports.[8-11]The presence of viral antigen in tubular epithelial cells has been demonstrated.[12]

Conclusion

Dengue infection can have varied and multi-system manifestations, which might be unrecognized and unreported because of lack of awareness. Early diagnosis and prompt management of dengue related complications is necessary to avoid serious morbidity and mortality.

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ABBREVIATIONS

Angstrom	A
body surface area	BSA
body weight	body wt.
centimeter	cm
celius	C
complement components	C1,C2,C3
Correlation coefficient	r
creatinine clearance	Ccr.
curie (s)	Ci
Equivalents	Eq
Fahrenheit	F

Glomerular fitration rate	GFR
gram (s)	g
Grams per cent	g/100mi
half-time	tf1/2
hour (s)	hr
inch	inch
International Unit (s)	IU
Intramuscular	im.
intraperioneal	i.p.
intravenous	i.v.
inulin clearance	Cln
Kilogram (s)	Kg
liter (s)	L
meter (s) or milli	m
microns (s) or micro	µ
milligram (s) per cent	mg/100ml
minute (s)	min
molar	M
mole (s)	mole (s)
Molecular weight	molwt
nanogram (s) (millimicrogram)	ng
nanoliter (s) (millimicroliter)	nl
normal (concentration)	N
not significant	NS
optical density	OD
osmole (s)	Osm
probability	P
second (s)	sec
standard deviation	SD
standard error	SE
standard error of the mean	SEM
ultraviolet	UV
unit (s)	U
volt	V

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