BANGLADESH RENAL JOURNAL

ISSN 1015-0889
Abstracted by
EXCERPTA MEDICA

OFFICIAL ORGAN OF RENAL ASSOCIATION, BANGLADESH

VOLUME 30 NUMBER 1 DHAKA, JUNE, 2011

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BANGLADESH RENAL JOURNAL

(A Journal of continuing education in kidney diseases)

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Any statistical method used should be detailed in the method section of the paper.

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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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Published by Bangladesh Renal Association, and Printed at Asian Colour Printing, 130 DIT Extension Road, Fakirerpool, Dhaka. Phone : 9357726, 8362258, E-mail: asianclr@gmail.com

Original Articles

Raised Erythrocyte Sodium-Lithium Counter Transport Activity in Bangladeshi Type 2 Diabetic Subjects With Family History of Hypertension

Md Anisur Rahman[1], Harun Ur Rashid[2], Habibur Rahman[2], Liaqat Ali[3], Habib Sadat Chaudhury[1], AHM Nurun Nabi[1], Karabi Biswas Farhana[1], Md Jakir Hossain[1] and Md Abul Mansur[1]

Abstract

Background and aim : Raised sodium- lithium counter transport activity (SLCT) in erythrocyte is claimed to be an early marker of nephropathy in type 1 diabetes. However the role of the transport system in type 2 diabetes is still controversial. This study in Bangladeshi type 2 diabetic patients was to evaluate whether SLCT in RBC is influenced by familial predisposition to hypertension in presence or absence of nephropathy. Method: Sixty three newly diagnosed Bangladeshi type 2 diabetic patients (age in years 45±4; BMI 24.0±3.4 kg/m2) and twenty age- and BMI-matched control subjects (age 47 ±9, BMI 22.4 ±3.8) without any family history of diabetes and hypertension were investigated. The diabetic subjects were divided into two groups as diabetes with family history of hypertension (n=37) and diabetes without family history of hypertension (n=26). Diabetic subjects were further divided into normo (n=16) and microalbuminuric (n=16) subgroups. Serum glucose was measured by glucose-oxidase; C-peptide by ELISA; lipid profile, blood urea, creatinine (serum and urinary) by enzymatic-colorimetric methods and albumin by immunoturbidimetry method. Lithium was measured by atomic absorption spectrophotometry. Results: The red cell sodium-lithium counter transport activity(SLC) was significantly elevated in diabetic subjects with familial predisposition to hypertension when compared to control [median (range), 0.067 (0.022-0.153) vs 0.046 (0.004-0.115) µmol Li/g RBC protein/h, p<0.006] and to diabetic subjects without familial predisposition to hypertension [0.072±0.032 vs 0.039±0.017 µmol Li/gRBC protein/h, p<0.001]. When SLC activity was compared between normo- and microalbuminuric diabetic subjects with familial predisposition to hypertension, no significant difference was observed among themselves. Conclusion: Raised SLC activity in erythrocyte can be a marker of genetic predisposition to hypertension in diabetic population irrespective of presence of nephropathy.

Key words: sodium- lithium counter transport activity, diabetes mellitus, familial predisposition to hypertension, nephropathy.

(Bang. Renal J. 2011; 30(1): 1-5)

Introduction:

Diabetic nephropathy is the leading cause of End-stage Renal Disease (ESRD) requiring dialysis in developed countries[1] and it is the second common cause of ESRD in Bangladesh[2]. Diabetic nephropathy occurs only in a subset of diabetic patients who are genetically predisposed, approximately 30 to 4o percent in type 1 diabetes and 30 percent in type 2 diabetes of more than 10 years of duration[3,4].

The red cell sodium- lithium counter transport activity (SLC), which is largely genetically determined and associated with risk of essential hypertension[5], have been shown to be greater in proteinuric type 1 diabetic patients than matched long-term normoalbuminuric controls[6,7]. It raises the possibility that the genetics of essential hypertension and diabetic nephropathy may partially overlap.Thus any candidate gene proposed for essential hypertension can also be considered as a susceptibility gene for diabetic nephropathy[8]. In a study Fujita et al. 1994 showed that SLC activity is more influenced by family history of hypertension than hypertension itself [9].

The association of elevated SLC activity in red cells of essential hypertension [5] and diabetic nephropathy in type 1 diabetes[7] raised the possibility of elevated SLC activity identify a subgroup of type 1 diabetic patients who are genetically predisposed to hypertension are at increased risk of nephropathy, although there are conflicting reports[10].

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The aim of this study is to evaluate the red cell SLC activity in Bangladeshi healthy population and type 2 diabetic patients with familial predisposition to hypertension.

Subjects and methods

This cross sectional case- control study was carried out in the Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka in collaboration with Biomedical Research Group, BIRDEM and Analytical Division, BCSIR,Dhaka during the period of 1998-2000. Eighty-three subjects were included in this study of which 20 were healthy controls (16 men and 4 women) and 63 were newly detected untreated type 2 diabetic subjects(42 men and 21 women). Controls were selected from hospital staff, patient,s friends and voluntary participants. They were free from any disease, not taking any drugs and had no family history of diabetes or hypertension upto second-degree relatives. Diabetic subjects were selected from Outpatient Department of BIRDEM General Hospital. They were considered diabetic according to WHO consultation Report (Alberti and Zimmet 1998).

The diabetic subjects were studied by dividing them into several groups in the following way:

A. Based on family history of hypertension: a) Diabetes with family history of hypertension, FH (+)ve group, (n=37). b) Diabetes without family history of hypertension, FH (-)ve group,(n=26).

B. Based on presence or absence of hypertension: a) Diabetes with hypertension, hypertensive group,(n=17). b) Diabetes without hypertension, normotensive group,(n=46).

C. Based on presence or absence of microalbuminuria: a) Diabetes with microalbuminuria, microalbuminuric group,(n=18). b) Diabetes without microalbuminuria, normomicroalbuminuric group, (n=45).

Medical history of the patient was taken carefully. Clinical parameters (age, sex, body mass index (BMI), blood pressure and family history of hypertension) were recorded in a predesigned data sheet for the study. A positive family history of hypertension was recorded if one or both parents had been diagnosed hypertensive or were undergoing treatment for hypertension.

Specific laboratory investigations (blood glucose fasting and 2 hours post glucose load, fasting serum C-peptide, post glucose load serum C-peptide, lipid profile, serum urea, serum creatinine, albumin creatinine ratio (ACR),sodium-lithium counter transport activity (SLC) in RBC were done in each patient. Biochemical parameters were recorded in a predesigned data for the study.

Serum glucose was measured by glucose-oxidase method. Serum C-peptide was measured by ELISA. Lipid profile, serum urea and creatinine (serum and urinary) were measured by enzymatic-colorimetric methods. Urinary albumin (microalbuminuria) was measured by immunoturbidimetry method.

Sodium- lithium counter transport activity (SLC) in RBC was measured according to the method described by Canessa et al.(5)with slight modifications. Briefly, 8ml of venous blood was collected after an overnight fast into heparin(10 µl/ml of blood) treated tube and centrifuged(at 3000 rpm at 4^0C). Plasma and buffy coat was discarded. The RBC packed cells were washed with ice cold washing solution (75 mM $MgCl_2$, 85 mM sucrose, 10 mM glucose, 10 mM Tris, 10 mM MOPS)and centrifuged for 2 minutes. The washing was repeated for three times. Then 1.5 ml washed RBC was incubated in a lithium-loading solution(150 mM lithium chloride, 10 mM glucose, 10 mM Tris, 10 mM MOPS) in a shaking water bath at 37^0C for 3 hours. After incubation the lithium loaded RBC was transferred into test tubes and centrifuged at 4^0C for 5 minutes. Then RBC packed cells were washed with ice cold washing solution and centrifuged for 2 minutes. The washing was repeated for four times. After the final washing, 1 ml of lithium-loaded erythrocytes was incubated in either 8.0 ml of sodium free solution(75 mM $MgCl_2$, 0.1 ml ouabain, 85 mM sucrose, 10 mM Tris, 10 mM MOPS)or sodium-enriched solution(150 mM NaCl, 0.1 mM ouabain, 10 mM glucose, 10 mM Tris, 10 mM MOPS) in shaking water bath at 37^0C. Portions of the samples were taken at 15 and 30 minutes of incubation and immediately centrifuged and preserved in a freezer at -70^0C for future determination of lithium. 500 µl of RBC packed cells was taken into a microcentrifuge tubes and added to it 200 µl of 1% triton-X 100. The cell suspension was vortexed properly to ensure lysis of all cells.The whole cell suspension was preserved in a freezer at -70^0C for future determination of total RBC protein content. Lithium concentration of the preserved sample was determined by atomic absorption spectrophotometry (AA-680). SLC was determined by calculating the difference between lithium efflux from erythrocytes in the sodium-free and sodium-enriched solutions by means of linear regression curves and expressed as µmol Li/g RBC protein/h.

Statistical Analysis:

All variables are expressed as mean±SD unless otherwise stated. Albumin creatinine ratio (ACR), sodium-lithium counter transport activity (SLCT), Serum triglyceride, C-peptide levels are expressed as median (range). The comparison between the groups was made either by unpaired Student's t-test or Mann-Whitney U test by using SPSS windows package 12.0 version and *p* value below 0.05 was considered significant.

Results:

Sixty three diabetic subjects was matched for age, BMI,blood pressure, C-peptide level, lipid profile and renal function tests with twenty healthy controls. These two groups were studied for microalbuminuria and sodium-lithium counter transport activity (SLC). Table 1 shows the comparison between healthy controls and diabetic subjects.The incidence of microalbuminuria is significantly higher in diabetic subjects but SLC activity was not significant in diabetic subjects than controls [median (range) 0.049 (0.008-0.153) vs 0.046 (0.004-0.115) µmol Li/g RBC protein/h, $p<0.09$].

Table-I

Comparison in DM and Control subjects

Features	Control (n=20)	DM (n=63)	*P* value
ACR (mg/mmol)	1.03(0.00-3.09)	1.80(.28-9.43)	0.001
SLC(µmol Li/g RBC protein / hour)	0.046 (0.004-0.115)	0.049 (0.008-0.153)	0.09

Twenty six diabetic subjects without family history of hypertension FH (-)ve group was matched for age, BMI,blood pressure, C-peptide level, lipid profile and renal function tests with twenty healthy controls. These two groups were studied for microalbuminuria and sodium- lithium counter transport activity (SLC).Table 2 shows the comparison between them. The incidence of microalbuminuria is significantly higher in diabetic subjects but SLC activity was not significant in diabetic subjects without family history of hypertension FH (-)ve group than healthy controls [median (range) 0.046(0.004-0.115) vs 0.039±0.017 µmol Li/g RBC protein/h, $p<0.08$].

Table –II

Comparison in healthy controls and diabetic subjects without family history of hypertension FH (-)ve group

Features	Control (n=20)	FH (-)ve (n=26)	*P* value
ACR (mg/mmol)	1.03 (0.00-3.09)	1.52 (.29-3.91)	0.02
SLCT(µmol Li/g RBC protein/ hour)	0.046 (0.004-0.115)	0.039±0.017	0.08

Thirty seven diabetic subjects with family history of hypertension FH (+)ve group was matched for age, BMI,blood pressure, C-peptide level, lipid profile and renal function tests with twenty healthy controls. These two groups were studied for microalbuminuria and sodium-lithium counter transport activity (SLC). Table 3 shows the comparison between them. The incidence of microalbuminuria is significantly higher in diabetic subjects with family history of hypertension FH (+)ve group. SLC activity was also significantly higher in FH (+)ve group than healthy controls [median (range) 0.046(0.004-0.115) vs 0.072±0.032 µmol Li/g RBC protein/ hour, $p<0.006$].

Table-III

Comparison in healthy controls and diabetic subjects with family history of hypertension FH (+)ve group

	Control (n=20)	FH (+)ve (n=37)	*P* value
ACR (mg/mmol)	1.03(0.00-3.09)	2.23(0.28-9.43)	0.001
SLCT (µmolLi/g RBC protein/ hour)	0.046 (0.004-0.115)	0.072±0.032	0.006

Thirty seven diabetic subjects with family history of hypertension FH (+)ve group was matched for age, BMI, glycaemic status, c-peptide levels, lipid profile and renal function tests with twenty six diabetic subjects without family history of hypertension FH (-)ve group and were studied for sodium- lithium counter transport activity (SLC). Table 4 shows the comparison of SLC activity between them. SLC activity was significantly higher in FH (+)ve group than FH (-)ve group[0.072±0.032 vs 0.039±0.017 µmol Li/g RBC protein/h, $p<0.001$].

Table IV

Comparison of diabetic subjects with family history of hypertension FH (+)ve and without FH (-) ve

Features	FH (+)ve (n=37)	FH (-)ve (n=26)	*p value*
Systolic BP (mmHg)	127±16	110±14	0.001
Diastolic BP (mmHg)	81±9	72±11	0.001
ACR (mg/mmol)	2.23 (0.28-9.43)	1.52 (.29-3.91)	0.03
SLCT (µmol Li/g RBC protein/hour)	0.072±0.032	0.039±0.017	0.001

Grouping of diabetic subjects by using presence or absence of microalbuminuria with albumin creatinine ratio (ACR) > 2.77 mg/mmol as a cut-of value. Fourty five diabetic normoalbuminuric(ACR <2.77 mg/mmol) subjects were match for age,BMI,blood pressure, glycaemic status, C-peptide levels, lipid profile and renal function tests with eighteen diabetic microalbuminuric(ACR > 2.77 mg/mmol)subjects. This two groups were studied for sodium-lithium counter transport activity (SLC) . Comparison of SLC activity was found no significant difference between diabetic normoalbuminuric and diabetic microalbuminuric subjects [median (range) 0.042(0.008-0.153)vs 0.065(0.018-0.153) µmol Li/g RBC protein/h, *p* = NS]

Fourty six diabetic normotensive subjects were match for age, BMI, glycaemic status, c-peptide levels, lipid profile, renal function tests and microalbuminuria with seventeen diabetic hypertensive subjects and were studied for sodium- lithium counter transport activity (SLCT). Comparison of SLCT activity was found no significant difference in diabetic normotensive and diabetic hypertensive subjects [median (range) 0.046(0.004-0.153) vs 0.064(0.022-0.126) µmol Li/g RBC protein/h, *p*=NS].

Discussion:

In this cross sectional study, the SLC activity in diabetic subjects, as a group, is comparable with healthy controls. This result is similar to a study on young diabetic subjects of Bangladeshi population by Hada 1998.[11] Contrary to this, Jensen et al. 1990 in type 1 diabetes and Gall et al. 1991 in type 2 diabetes found SLC was raised for diabetes per se irrespective of diabetic nephropathy and hypertension when compared to healthy controls[10,12]. The reason for the discrepancy, however, still to be clearly understood. Herman et al. 1993 commented that this could be due to confounding variables or it might be due to racial heterogeneity existing between Danish and different study populations.[13] Racial variation of SLC has also been reported by others.[14,15] The finding in this study favors the idea that diabetes per se is not responsible for raised SLCT activity in red cells of type 2 diabetic subjects.

To see the relation of SLCT activity with microalbuminuria, the diabetic subjects were studied after dividing them into microalbuminuric and normoalbuminuric groups. These two groups were matched for age, BMI, blood pressure, blood glucose, lipid profile and renal function tests. Diabetic patients with normoalbuminuria showed similar level of SLC activity with diabetic microalbuminuric subjects. Hada (1998) and Iqbal (2000) also found similar results in type 2 diabetic study subjects[11,16]. Contrary to this, increased SLCT has been reported in type 1 diabetic patients with microalbuminuria[17] and overt proteinuria[6,7]. This was also reported in type 2 diabetic subjects with nephropathy [13]. But in most of those studies, the elevated SLC and nephropathy were found to be related to hypertension and / or family history of hypertension. In a study by Mangili et al. 1998 showed that the absence of elevated SLC in non-diabetic renal disease has excluded the probable effect of altered internal environment due to nephropathy on SLC. Fujita et al. (1994) in their study in type 2 diabetic nephropathy found that normotensive subjects without family history of hypertension had similar SLC activity to that in hypertensive subjects without family history of hypertension. They also found similar SLCT activity both in Control and microalbuminuric diabetics in the absence of family history of hypertension[9]. The above findings indicate that it is still unsettled whether microalbuminuria is a confounding variable of SLC activity in type 2 diabetic subjects.

To see the relation of SLC activity with hypertension, the diabetic subjects were studied after dividing them into hypertensive and normotensive groups. Who were matched for age, BMI, blood pressure, blood glucose, lipid profile and renal function tests. Diabetic normotensive subjects showed similar SLC activity with hypertensive group. This result was similar with the other study in the same population [16]. In the absence of family history of hypertension, SLC activity has been similar in diabetic subjects with or without hypertension [9].

In the present study, the type 2 diabetic subjects with family history of hypertension were studied to observe the possible genetic influence on the red cell SLC activity. The diabetic subjects with family history of hypertension showed significantly high SLC activity in comparison with

diabetic subjects without family history of hypertension and healthy controls. This result is supported by majority of the literatures that SLC activity is raised when there is a family history of hypertension and / or nephropathy. Cannesa et al. 1980 and Clegg et al. 1984 showed raised SLC activity in essential hypertension only with family history[5,18]. Monciotti et al. 1997 showed increased SLC activity in nephropathy subjects only when they have parents with hypertension and raised SLC activity[19]. Fujita et al. 1994 in their study in type 2 diabetic subjects with nephropathy found that normotensive subjects without family history had similar SLC activity to Controls and microalbuminuric diabetics in the absence of family history of hypertension[9]. Contrary to this Jensen et al. 1990 did not find raised SLC activity in parents of diabetic subjects with nephropathy[10]. In the present study, it is found that high SLC activity in type 2 diabetic subjects with family history of hypertension have high prevalence of microalbuminuria in comparison with diabetic patients without family history of hypertension. This result supports the earlier claims that the nephropathic patients have elevated SLC activity in diabetic subjects with family history of hypertension.

Therefore, raised red cell SLC activity can be a marker of familial predisposition to hypertension in diabetic population irrespective of presence or absence of hypertension or nephropathy.

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Risk Factors for Development of Renal Failure in Eclampsia Patients - A Prospective Study

Fahmida Khan[1], M Muhibur Rahman [2], Shila Rani Das[3], Kazi Shahnoor Alam[2], Ferdous Kamal Bhuiyan[4]

Abstract:

This prospective study on the risk factors for renal failure in eclamptic patients was carried out in the Eclampsia ward of Dhaka Medical College Hospital from July 2009 to December 2009. Study group comprised of 50 diagnosed cases of eclampsia and 50 patients with uncomplicated pregnancy was taken as control. About 30% of eclamptic patients were found to have impairment of renal function and incidence was significantly increased among the patients coming from the lower socioeconomic status, patients above 25 years of age and in multi-gravida eclamptic patients. Patients with ante-partum eclampsia and the onset of convulsion at gestational age < 36 weeks were significant risk factors for the development of impaired renal function in eclampsia. Blood pressure was significantly increased and platelet count was significantly low in the impaired renal function group of eclamptic patients compared to the normal renal function group. There was an association between increased level of proteinuria and impairment of renal function. So, the risk factors which may predispose the eclamptic patients to impaired renal function are age above 25 years, multi-gravida, ante-partum eclampsia, onset of convulsion at or before 36 weeks of gestation, increased level of proteinuria and thrombocytopenia. The need for proper antenatal care for all pregnant women to prevent renal impairment in eclampsia cannot be over emphasized.

Key words: Eclampsia, renal failure, proteinuria, antenatal care

(Bang. Renal J. 2011; 30(1):6-10)

Introduction:

Eclampsia is an important cause of maternal and peri-natal morbidity and mortality.In different studies conducted in Dhaka Medical College Hospital the incidence of eclampsia has been found to be 4-9% among the patients admitted in the obstetric wards[1,2,3] In Bangladesh, the obstetric causes contributed 70% of the total maternal mortality among which 11% were due to eclampsia[4]. The most common causes of maternal mortality in eclampsia are cerebrovascular accident, pulmonary oedema, post-partum shock, renal failure and sepsis. The main causes of foetal death in eclampsia are pre-maturity, foetal asphyxia and acidosis[5,6]. There is association of eclampsia with some risk factors. Young primigravidas below the age of 20 and both primigravidas and multi-gravidas over the age of 35 years have increased incidence of hypertensive disorder of pregnancy[7,8]. The possible explanations given in the young are social negligence, poor dietary habits, ignorance and poor maternal care. The reasons in the older age group have been suggested as increasing incidence of essential or latent essential hypertension[9,10]. The fact that preeclampsia and eclampsia are essentially diseases of the primigravidas has long been known. Renal biopsies performed on women considered toxaemic during gestation demonstrated glomerularendotheliosis in only 80% of primiparas and a minority of multiparas[11]. Majority (82%) of proteinuric women were primigravidus, confirming the concept that eclampsia is primarily a disease of the first pregnancy[12]. The relative risk for preeclampsia in a first pregnancy is 7-10. The prevalence of preeclampsia and eclampsia in daughters was significantly higher than the daughters-in-law. The relative risk of preeclampsia for daughters of women with preeclampsia is 4, for sisters of women with preeclampsia are 7[11,13]. Eclampsia and preeclampsia are found to occur in women with lower socioeconomic status and may be related with poor dietary habit, ignorance or illiteracy and poor antenatal care. In tropics the incidence of eclampsia is higher in cool humid condition and lower in dry condition. It has been postulated that the tendency for convulsions is reduced by the dehydration in dry seasons. This increased incidence in the winter is likely to be caused by the rise of blood pressure resulting from the bodily response to cold by vasoconstriction and increased secretion of adrenaline and thyroid hormones necessitating extra heat production[14]. The incidence of both pregnancy induced hypertension and chronic hypertension is seen to be increased in obese women[15]. Eclampsia is associated with

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hydatidiform mole, multiple pregnancy, polyhydramnios, nonimmune foetal hydrops and some Medical conditions like chronic hypertension, chronic nephritis, and Diabetes mellitus. This study was done to identify any associated risk factor or factors affecting renal function in eclampsia patients and to determine the effect of impaired renal function on pregnancy outcome.

Materials and Methods:

This prospective study was done in the Dhaka Medical College Hospital from July 2009 to December 2009. A total of 3894 non-eclamptic patients and 403 eclamptic patients were admitted in the Department of Obstetrics and Gynaecology in Dhaka Medical College Hospital during the study period. From the eclamptic group a total of 50 diagnosed eclampsia patients admitted in the Eclampsia Ward were selected at random. From the 3897 non-eclamptic patients admitted during the study period, 50 patients matched by parity and age was selected at random as the control group. Those who delivered by normal vaginal deliveries were not kept in the hospital due to acute shortage of hospital beds and huge load of patients. So they could not be included in the study. Therefore, control group was from the post-caesarean patients who stayed nearly the same duration as the study group in the hospital. Patients who were known cases of Essential hypertension, Diabetes mellitus, Chronic renal disease, Liver disease, Epilepsy, Psychiatric problems and who were incompletely investigated were excluded. For data collection a pre-designed protocol was used to record the information. It has covered the predisposing factors (age, parity, socioeconomic background etc.), antenatal visits, gestational age, time of first convulsion, number of convulsions, interval between convulsion and hospital admission etc. Information was collected from clinical history given by the attendants in case of the study group and directly from the patients themselves in the control group. A thorough clinical examination was done. Further information was obtained by doing laboratory investigations. After collection blood sample was sent for estimation of haemoglobin, platelet count, random blood sugar, blood urea, serum creatinine, serum uric acid and serum electrolytes. 24 hours urine sample was collected in pre-marked clean plastic container sprayed with toluene as preservative, for estimation of 24 hours urinary total protein. Heat coagulation test for protein was done at the bedside. A sample of urine was also sent to the laboratory for routine and microscopic examination. The data collected were compiled with the help of a personal computer and appropriate statistical analysis was carried out using SPSS program. Student's t test and Chi-square test were done to compare the results between the different groups. The difference was considered significant when the p value was <0.05. The results are shown in the form of tables in the following section.

Results:

A total of 3894 non-eclamptic patients and 403 eclamptic patients were admitted in the Department of Obstetrics and Gynaecology in Dhaka Medical College Hospital. From the eclamptic patients, a total of 50 patients were selected at random as study group and from the 3894 non-eclamptic patients, 50 patients matched by parity and age was selected at random as the control group. The incidence of eclampsia was found to be 9.38% during the study period. Types of eclampsia were antepartum (72%), intrapartum (12%) and postpartum (16%).

Most of the patients in the study (52%) and control (48%) group belonged to the age group of d"20 years. Mean age of the patients in the study group was 23.6±6.2 and that of the control group was 23.9±5.7. There was no significant difference in the age distribution between these two groups ($p=0.9$). In the impaired renal function group of eclamptic patients 46.6% was above 25 years of age in contrast to 11.5% of the patients in the normal renal function group ($p<0.05$).

There was statistically significant difference ($p=0.004$ & 0.005) both in the systolic and diastolic blood pressure between the study and the control group. Mean systolic blood pressure was 153±23 and 116±12 mmHg and mean diastolic blood pressure was 105±14 and 71±8 mmHg in the study and control group respectively. All the patients in the study group had detectable proteinuria and 54% of the patients had more than 2+ proteinuria. In contrast 86% of the patients in the control group had no proteinuria, 12% had 1+ proteinuria and only 1 patient had 2+ proteinuria. The blood urea nitrogen, serum creatinine, serum uric acid and 24 hours urinary total protein were significantly higher in the study group. There was no significant difference in 24 hours urinary volume between the study and the control group ($p=0.41$).

This study shows that out of 50 cases of study group, 70% of the patients had normal renal function and 30% had impaired renal function (serum creatinine level >0.9 mg/dl and blood urea nitrogen >13 mg/dl). It has been evident from this study that 93.3% of the patients with impaired renal function and 57.1% of the patients with

normal renal function of the study group was from the lower socioeconomic status (p<0.05).

Table-I

Comparison of renal function between the study and control group (on admission)

Parameters	Study group (n=50) Mean ± SD	Control group (n=50) Mean ± SD	P value
BUN(mg/dl)	11.26±5.64	8.73±2.75	0.004
Creatinine (mg/dl)	0.87±0.33	0.71±0.12	0.009
Uric acid (mg/dl)	6.88±1.89	3.97±0.8	0.005
UTP (g/24hr)	2.51±2.18	0.27±0.11	0.001
UTV (ml/24hr)	1515.2±854.0	1484±359.6	0.41

This study shows that 66% in study group and 68% in control group were primigravida. About 66.6% of the patients with impaired renal function of the study group were multigravida in contrast to 20% of the patients with normal renal function. There was a statistically significant difference between these two groups (p<0.05). (Table-II).

Table-II

Parity distribution between study and control group.

Parity	Study group (n=50)		Control group (n=50)
	Impaired renal function (n=15) (%)	Normal renal function (n=35) (%)	Control patient (%)
Nil	5 (33.4)	28 (80.0)	34 (68)
1	2 (13.3)	4 (11.4)	9 (18)
2	3 (20.0)	3 (8.6)	4 (8)
3	2 (13.3)	-	1 (2)
4	1 (6.7)	-	2 (4)
>5	2 (13.3)	-	-

About 58% of the patients in the study group had no booking in contrast to the control group where 82% of the patients had antenatal booking (p<0.03). In the control group 56% of the patients and in the study group only 16% of the patients had 3 or more antenatal visits. There was no significant difference in the antenatal care between the patients with impaired renal function and normal renal function of the study group. Both systolic and diastolic blood pressure was significantly higher among the impaired renal function group (SBP = 161±28 mmHg, DBP = 107±18 mmHg) than the normal renal function group (SBP = 146±14 mmHg, DBP = 98±8 mmHg) (P = <0.05).

It was found that 68% of the patients in the study group had foetal complications, in contrast 26% of the patients in the control group had foetal complications and that foetal complication was significantly higher among the patients with impaired renal function group. 40% of the patients with impaired renal function had still birth compared to only 8.6% of the patients with normal renal function (Table-III).

Table- III

Comparison between the impaired and normal renal function groups

Parameters	Impaired renal function group (n=15) Mean± SD	Normal renal function group (n=35) Mean± SD	P value
Blood urea nitrogen (mg/dl)	15.64±6.38	8.15±3.28	0.004
Serum creatinine (mg/dl)	1.24±0.33	0.72±0.09	0.003
Serum uric acid (mg/dl)	8.5±1.83	6.09±1.35	0.01
Total urinary protein (g/24hr)	2.71±0.92	1.67±1.03	0.02
Urinary volume (ml/24hr)	487±223	1541±849	0.001

Table- IV

Comparison of foetal outcome between the impaired and normal renal function groups

Foetal outcome	Impaired renal function group (n=15) No of patients (%)	Normal renal function group (n=35) No of patients (%)	P value
Mature live birth	2 (13.3)	14 (40)	0.005
Fetal Complications	13 (86.7)	21 (60)	0.005
IUGR	3 (20.0)	9 (25.7)	
Premature	4 (26.7)	7 (20)	
Stillbirth	6 (40.0)	3 (8.6)	
Neonatal death	0 (0)	2 (5.7)	

Most of the patients (86.6%) with impaired renal function had antepartum eclampsia. From this study it has been

found that 73.3% of the patients with impaired renal function group had onset of convulsion at or <36 weeks' gestation whereas 71.4% of the patients with normal renal function had onset of convulsion at e"37 weeks' gestation (Table-IV). Eleven (11) eclamptic patients developed maternal complications and one patient developed severe renal failure and one patient died in the impaired renal function group.

Table-V

Gestational age of the impaired and normal renal function group

Gestational age (weeks)	Impaired renal function group (n=15)		Normal renal function group (n=35)	
	Total No	%	Total No	%
<28	2	13.3	0	
29-32	6	40.0	5	14.3
33-36	3	20.0	5	14.3
>37	4	26.7	25	71.4

Discussion

Kidney involvement in preeclampsia and eclampsia has been observed by many observers[16,17]. A number of pathological changes, which tend to parallel in severity of the clinical condition, occur in the kidney. Severe renal involvement may produce extensive arterial thrombosis and infarction resulting in bilateral renal cortical necrosis which is often fatal [18].

The incidence of eclampsia was found to be 9.38% in this study. In another study incidence of eclampsia has been reported to be 11% in Bangladesh[4]. Small hospital based studies show variation in the incidence of eclampsia in Bangladesh. Some previous studies showed incidence of eclampsia in Dhaka Medical College Hospital as 8.6%, 4.14%, 7-10% of obstetric cases[1,2,3]. A study from Sir Salimullah Medical College and Mitford Hospital in 1989-90 showed the incidence of eclampsia as 7.7% of obstetric cases[15]. In our neighbouring countries India and Nepal the incidence is 1.4% and 1.3% respectively [4]. This observation shows that the incidence of eclampsia is still very high in this subcontinent especially in Bangladesh. Like other studies most of the eclamptic patients (66%) in this study were primigravida. The number of patients in the study group (58%) who had no booking was significantly higher than the number of patients without booking (18%) in the control group. Other researchers have also observed that the incidence of eclampsia is higher among the unbooked patients[2,17].

Significant difference in renal function was observed between the study and control group in this study. Mean serum uric acid level was significantly higher in the study group compared to the control group. Higher serum uric acid level in the eclamptic patients has also been observed by other investigators[19,20,21].

In this study had impaired renal function MacKay et al found impaired renal function in 15% of the eclamptic patients[20] but Sibai et al reported that 48% of the patients with eclampsia had impaired renal function[22]. About half of the patients in the impaired renal function group was above 25 years of age whereas only 11.5% of the patients in the normal renal function group was above 25 years of age. Of 6 eclamptic patients above 30 years of age, 5 patients (83.3%) had impaired renal function. Mattar et al studied 399 patients with eclampsia in E. H. Crump Women's Hospital and Perinatal Center in Memphis USA and found that acute renal failure was more common with maternal age < =35 years. This may be due to decrease in renal reserve with increasing age.

It is seen that the socio-economic status has inverse relationship with the incidence of eclampsia. 93.3% of the patients in the impaired renal function group of the eclampsia patients belonged to the lower socioeconomic status whereas 57.13% of the eclamptic patients with normal renal function came from lower socioeconomic status. So lower socioeconomic status appears to be a risk factor for impaired renal function in the eclamptic patients. It may be due to pre-existing sub clinical renal disease in this class of patients which has not been detected before.

In this study 66% of the eclampsia patients were primigravida. Eclampsia was also observed in a number of multigravidas in this study. Similar observation was also made by other investigators[17,20]. Of 15 eclamptic patients with impaired renal function 33.3% were primigravida whereas 80% of the patients with normal renal function were primigravida. 67.3% of patients in the impaired renal function group were multigravida compared to only 20% of patients in the normal renal function group. So it appears from these results that multigravida eclamptic patients are at risk of developing impairment of renal function.

Mean 24 hour urinary total protein of the impaired renal function group was 2.71±0.92 gm and that of the normal

renal function group was 1.67±1.03 gm (p=0.02). Similar observation was also made by Sibai et al[22]. They showed that the eclamptic patients with renal impairment had significantly more proteinuria than the eclamptic patients with normal renal function. So degree of proteinuria may act as a predictor for impaired renal function in the patients with eclampsia.

Impairment of renal function is common among the patients with eclampsia. So special attention should be paid to the assessment of renal function in these patients. The risk factors which may predispose the eclamptic patients to impaired renal function are age above 25 years, multigravida, antepartum eclampsia, onset of convulsion at or before 36 weeks of gestation, increased level of proteinuria and thrombocytopenia. The need for proper antenatal care for all pregnant women to prevent eclampsia cannot be over emphasized.

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Relationship between Birth Weight of New Born Baby and Kidney Volume

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Abstract:

Low birth weight predisposes to renal disease later in life. This could be due to reduced nephron numbers, which might be reflected in lower kidney volume, at least early in life. In this study the association of birth weight with renal volume was evaluated. Four hundred and one new born baby were included in the study .Kidney dimensions were measured by ultrasound by a single observer, and kidney volume was calculated from the formula KV(ml)=Length×Width×Depth×0.52.Mean birth weight was 2.8±.52kg and 28% had been low birth weight(<2.5kg).Male babies tended to have larger kidney than female babies(mean total volume 22.14±5.35ml versus 21.17±4.61 ml, p= 0.053).The combined kidney volume was significantly lower in low birth weight group than normal birth weight group baby(17.9±3.98 ml versus 23.14±4.6 ml, p=0.001).There were significant correlations between the weight at birth and the volume of kidney(r=0.424, p=0.001). Low birth weight baby had significantly lower kidney volume than normal birth weight baby. This finding is compatiable with the proposition that intrauterine growth retardation is associated with reduced nephron endowment.

Key words: Low birth weight, Kidney volume, reduced nephron, intrauterine

(Bang. Renal J. 2011; 30(1): 11-14)

Introduction:

A growing body evidence suggest that fetal exposure to an abnormal intrauterine environment has lasting effect on arthropomorphic and metabolic development that lead to increased risk of disease later in life (Nelson, 2003). Abnormal intrauterine exposure to growth retardation, diabetes,& Vit-A Deficiency contribute disproportionately to the rising incidence of kidney disease by reducing nephron mass in developing country because they encounter these exposure more frequently than people from developed country[1].

Low birth weight (LBW) baby is an important public health problem in developing country like Bangladesh as a consequence of malnutrition and poverty. In Bangladesh LBW prevalence varies between 23-60%[2]. Brenner and Chertow (1994) proposed that nephrogenesis is impaired in people of LBW because of a critical shortage of fuels necessary for fetal development[3].The low nephron mass. in turn. hightens the risk of kidney disease later in life

Low protein diets are experimentally associated with LBW,a decrease number nephron and increase risk of hypertension. Mackenzie, Lowler nad Brenner(1996) postulated that low nephron number, genetically determined or acquired, is a likely explanation for increase risk of hypertension in children with LBW. Demographic studies have shown that population with a very high incidence of essential hypertension have a relatively small kidney size, suggesting decrease number of nephron[4].

The total number of nephron is a biological variable that is defined prior to birth.Nephron development begins during the fifth week of gestation and approximately 60% of the nephron population occurs during the third trimester of pregnancy upto 36 weeks. No new nephrons are formed after birth. The number of nephron is a critical variable in the progression of chronic kidney disease(CKD) because reduction in nephron number result in glomerular hypertension in the remaining nephron population which in turn. trigger a vicious cycle of progressive loss of functional unit. Reduced number of nephron at birth may be associated with a diminished resistance to any mechanism of renal damage in adult life[5].

In fetuses & newborn infants, nephron number is reflected in renal volume & both are powerfully linked to body weight[6]. However there is no study of birth weight & nephron number or renal volume in Bangladesh. The present work was done to explore the relationship between weight at birth & the volume of kidney in newborns..

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Materials & Method

Four hundred and one new born baby were included in this study. The study was approved by the regional institutional ethics committee & consent was obtained from each newborn baby's parents at the time of assessment.

Both kidneys were examined by ultrasound on a single occasion by one designated radiologist who was blinded to the children's birth weight. The maximum length, width & depth (at the mid point)were measured & recorded. The renal volume was calculated using the formula (kidney volume‹ml›=Length.Witdh.Depth.0.523)^2. Left and Right kidney volume were added for the combined kidney volume.

All the babies were categorized into two groups, low birth weight (<2.5 kg) and normal birth weight(e"2.5kg)& kidney dimensions were compared using student t-test.

All data were presented as the mean±SD. Statistical analysis were performed using computer based programme, statistical package for social science(SPSS) windows version 11.5.

Results:

The average birth weight was 2.85±.52 kg. Female babies had lower birth weight than male babies 2.79±.48kg versus 2.9±.55kg) & were more often low birth weight.

Kidney dimension of study participants are shown in Table-I.

Table-I

Kidney dimensions of study participants:

Parameters	Value
Average Length (mm)	40.76±2.81
Average Width (mm)	21.47±2.74
Average depth (mm)	23.26±2.27
Right kidney volume (ml)	10.98±2.84
Left kidney volume (ml)	11.08±9.37
Combined kidney volume (ml)	21.67±5.02

As expected, the left kidney was longer than right. Male babies tended to have bigger kidneys than female babies (mean total volume of 22.14±5.35 ml versus 21.17±4.61 ml, p=.053).Babies of normal birth weight had larger kidney than those of low birth weight(mean length 41.47±2.64 ml versus 39.98±2.40 ml, (P=<0.01).

The relationship of kidney volume to birth weight was also evident when data were examined by birth weight category.

Table-II Compares kidney dimensions by birth weight category.

Table-II

Kidney dimensions by birth weight category

Parameters	*LBW (n=133)*	*NBW (n=288)*	*P-value*
Average length (mm)	39.98±2.40	41.47±2.64	0.001
Average depth (mm)	21.53±2.07	23.94±1.97	0.001
Average width (mm)	20.35±2.96	21.97±2.52	0.001
Right kidney volume (ml)	9.12±2.52	11.72±2.69	0.001
Left kidney volume (ml)	8.79±1.94	11.99±10.87	0.001
Combined kidney volume (ml)	17.91±3.98	23.14±4.6	0.001

Note: LBW-low birth weight ;NBW-normal birth weight

All dimensions of kidney was significantly lower in low birth weight baby. Both male & female babies show this trend, with combined kidney volume of 17.91±3.98 ml versus 22.66±4.17 ml(p=0<.001) in low birth weight & normal birth weight female babies and 17.84±4.22 ml versus 23.55±4.92 ml (p=<0.001) in low birth weight & normal birth weight male babies.

There was a significant positive correlation between weight at birth & combined kidney volume.(Fig:1).

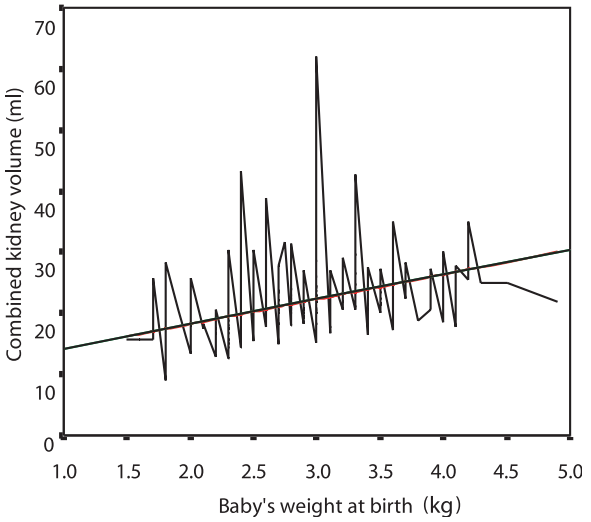

Fig.-1 *Graph showing positive correlation (r = 0.424, p < 0.01) of baby's weight at birth with combined kidney volume.*

The relationship of kidney volume to birth weight was also evident when data were examined by birth weight category. Table 3 compares characteristics of low birth weight & normal birth weight children. There was almost 1-kg difference in average birth weights. The low birth weight group had more girls.

Table-III

Characteristics of participants by birth weight category.

	Low birth weight (n=113)	Normal birth weight (n=288)	P value
Birth weight (Kg)	2.24±0.21	3.07±0.42	0.001
Female	62/113	133/288	0.05
Mother's BMI (Kg/m^2)	22.23±3.29	23.05±3.22	0.05

NOTE: Values are the mean (SD).

Discussion:

Low birth Weight(LBW) are common in children in developing community. Most of the underweight babies like those in other aboriginal communities and in the developing world, had Intrauterine growth retardation (IUGR). The prevalence of LBW baby in Bangladesh is 23-60%[2], which is similar to 28% found in this study. Many factors contribute to this intrauterine growth retardation including generalized maternal malnutrition, lack of fresh food (specially fruit and vegetables), vit-A and other deficiencies, maternal infection, placental dysfunction, toxemia of pregnancy and hypertension, multiparity, maternal disease like heart disease, tuberculosis, renal disease, bronchial asthma genetic/ chromosomal disorder, teenage pregnancy, smoking etc[7]. LBW may be due to IUGR, prematurity or both; epidemiologic studies do not always separate clearly the two conditions. However other lines of evidence support a link between IUGR,oligonephropathy and hypertension in later life [8]. It is possible that the decrease in renal size that is seen in the fetuses with IUGR is due to alteration in renal artery blood flow.

Sato et al (1985) looked at the kidneys, by ultrasound scan, of fetuses with IUGR and normally grown fetuses and found that the kidney area in fetuses with IUGR was significantly smaller than the kidney area of fetuses who were appropriately grown[9]. Spencer et al. (2001) have shown that low birth weight people have smaller kidneys in postnatal life, when inspected in the context of current body size[10]. Lori E, Silver et al, 2003. looked at the kidney by ultrasound scan, of fetuses with IUGR and Non IUGR fetuses found that kidney volume was significantly smaller in the fetuses with IUGR than the fetus without IUGR[8].

The present study is consistent with all these studies. Low birth weight baby had significantly lower kidney volume than normal birth weight baby. Lower kidney volumes are association with reduced nephron mass. One important determinant of nephron mass is nephron number. Birth weight is an important determinant of nephron number.Our study is inconsistent with naturally occurring LBW in rats is not associated with a reduction in the glomerular number or with a change in glomerular volume.

In full term pregnancies with LBW there is decreased to 20% in the number of nephron[11]. Manalich et al (2000) have documented a 20% reduction in nephron number in children with low birth weight baby.In the present study was seen a 23% reduction in renal volume in baby with low birth weight[12].

In a study of 174 children Spencer J et al (2001) have shown that girls had lower renal volumes than boys[10]. The higher rates of renal disease in aboriginal females than males are probably related, in part to this inherent difference which is accompanied by lower birth weight among females. A study was done by Schmidt IM et al (2004) on 717 healthy children age 0-18 months. They showed boys had significantly larger kidney volumes than girls[13].

Manalich et al. (2000) have found a positive relationship between weight at birth and the number of glomeruli, indirectly reflected in renal volume[12]. On the other hand Jones et al (2001) showed that there was no linear relationship between birth weight & glomerular number[14]. In present study there was a significant positive relationship between weight at birth and the renal volume.

It is concluded that low birth weight is directly related to reduced renal volume.A further prospective study with a large number of babies should be carried out and a long term follow up should be carried out to explore the association of congenital reduced renal volume and hypertension, diabetes mellitus and chronic kidney disease in later life.

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Protocol Biopsy at 0, 14 and 90 Days to Identify Renal Allograft Dysfunction - Single Center Study

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Abstract:

To identify histological changes of renal allograft by protocol biopsy for detection of early graft dysfunction. Thirty five kidney transplant recipients were included in this study over a period of two years in the Department of Nephrology, BSMMU, Dhaka. All received cyclosporine based immunosuppressive treatment. Serum creatinine was done daily for first 14 days and then weekly for three months. Cyclosporine blood (C_2) level was done 7th and 14th POD and monthly for three months. Protocol transplant kidney biopsy was done at day 0, day 14 and day 90. For histopathology haemotoxilyne and eosin (H&E) and periodic acid Schiff (PAS) stain was done. Among 35 recipients 23(66%) show normal graft function and 12(34%) showed early graft dysfunction. Among 35 biopsies, per operative 26 showed normal histology (no sclerotic glomeruli), 6 showed 10% sclerotic glomeruli and 3 showed 16% sclerotic glomeruli. Protocol biopsy at 14th post operative day showed 57.1% (n=20) normal histology 14.3% (n=5) had clinical rejection (elevated serum creatinine along with histological features of rejections). 14.3% (n=5) had sub clinical rejection (normal serum creatinine with histological features of rejections), cyclosporine toxicity 5.7% (n=2), ATN 5.7% (n=2) and 2.9% (n=1) had recurrent GN. Rejection episodes are further categorized by Banff-97 classification. Banff grade I (20%) (n=1) grade II (60%) (n=3) and grade III (20%) (n=1) were found in clinical rejection group and Banff grade I (80%) (n=4) and grade II (20%) (n=1) in sub clinical rejection group. Adequate histological evaluation is helpful for detection of clinical and subclinical rejection. So routine allograft biopsy should be practiced in different transplant center of Bangladesh.

Key words: protocol biopsy, transplant rejection, banff classification

(Bang. Renal J. 2011; 30(1): 15-18)

Introduction:

Renal allograft biopsies have traditionally been performed in the setting of acute graft dysfunction. However, several groups have performed graft biopsies at times of stable graft function, referred as subclinical rejection and its maximal prevalence is reached during the first 3 month.[1] Early subclinical rejection as a risk factor for late chronic humoral rejection.[2] Presence of subclinical rejection in early protocol biopsies is associated with a shortened graft survival.[3,4,5,6,7] The treatment of sub clinical rejection has been shown to reduce IF/TA[8] and improve graft function in two randomized studies in recipients of deceased or living donor kidney.[9] Protocol renal biopsy is practiced in different transplant center at different interval. Some center practiced it at day 7, day 14, and day 30 and some center practiced it 1, 2 and 3 post transplant month.[10] Isehcamic acute renal failure known as ATN is the important cause of DGF. Post transplant ATN increases the risk of both acute rejection and graft loss. Its occurrence has been shown to reduce one year graft survival.[11] Less than 50% rise of Serum creatinine from baseline associated with high cyclosporine blood level which is histologically characterized by tubular vaculation, intimal thickening and focal infiltration is defined as Cyclosporine toxicity. Post transplant glomerulonephritis may be due to novo GN or recurrence of original kidney disease. But little data are available concerning impact of post transplantation glomerulonephritis on graft out come.[12]

Materials and Methods:

In this study, thirty five renal allograft recipients were selected in the department of nephrology, BSMMU. All received same immunosuppressive drugs (cyclosporine 8mg/kg/body weight, mycophenolate mofetil 500mg 12 hourly and prednisolone 0.5mg/kg/day). It is an observational study. All of them were followed up for 1st three months. Serum creatinine was done daily for first 14 days and then weekly for three months. Cyclosporine blood

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(C_2) level was done on 7th and 14th POD and monthly for three months. Per operative protocol biopsy was done just after completion of vascular anastomosis. Tissue was obtained from upper pole of transplanted kidney by a scalpel. Tissue was preserved in a test-tube with 10% formalin. Tissue was immediately sent for histopathological examination. For histopathology haemotoxilyne and eosin (H&E) and periodic acid Schiff (PAS) stain was done. A protocol biopsy of transplanted kidney was done at 14th POD and at the end of three months (day 90) by 7.6cm, 18G trucut kidney biopsy needle. Upper pole of the transplanted kidney was selected for biopsy. Tissue was preserved in formalin (10%) and was sent for histopathology. Histopathological slides were examined by same histopathologist (light microscopic examination). Histopathological slides were stained with haemotoxilyne and eosin (H&E) and periodic acid Schiff (PAS) stain and categorized according to Banff 97 classification. According to Banff classification of renal transplant pathology, rejections are classify as hyperacute, borderline change and acute rejection grade I, II and III. Banff grade I is classified as sub clinical rejection characterized by tubulointerstitial mononuclear infiltration identified from biopsy specimen.[13]

Results:

A total of 35 subjects were selected for the purpose of the study. Among them 12 patients who had s. creatinine level > 140 µmol/L 7 days following transplantation were defined as graft dysfunction and 23 patients who had s. creatinine level < 140µmol/L were defined as normal graft function.

Distribution of recipients by graft status:

Of the 35 recipients who underwent kidney transplantation, 12(34%) exhibited early graft dysfunction (Fig. 1).

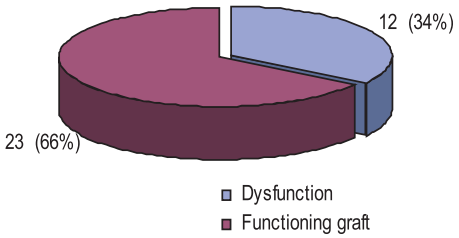

Fig. -1: *Distribution of recipients by graft status*

Serum creatinine level on 7th POD, 14th POD and on 3 months are shown at Table-I

Table-I

Postoperative S. creatinine level at different interval between groups

Serum creatinine (µmol/L)	Group		p-value
	Dysfunction (n=12)	Functioning (n = 23)	
S. creatinine on 7th POD	248.9 ± 37.4	135.1 ±2.5	0.041
S. creatinine on 14lh POD	200.8 ± 52.9	134.0 ±4.49	0.050
S. creatinine in 3 month	215.2 ± 13.5	137.4 ±2.1	0.017

Blood cyclosporine level (C_2) at different intervals are shown in Table-II

Table–II

Postoperative blood cyclosporine level (C_2) at different interval between groups.

Cyclosporine level (C_2) (ng/ml)	Group		p value
	Dysfunction (n=12)	Functioning (n=23)	
Cyclosporine on 7th POD	1593.2± 320.4	1439.1 ± 199.5	0.140
Cyclosporine on 14th POD	1384.7± 295.3	1348.1 ±257.8	0.706
Cyclosporine at 3 month	1364.8 ±263.7	1114.2 ± 145.1	0.032

Result of preoperative protocol biopsy is shown in Fig. -2

Among 35 biopsies, per operative 26 showed normal histology (no sclerotic glomeruli), 6 showed 10% sclerotic glomeruli and 3 showed 16% sclerotic glomeruli.

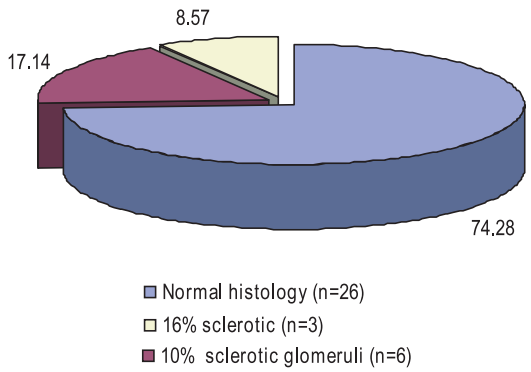

Fig. 2: *Per Operative protocol biopsy*

Result of protocol biopsy at 14th POD in shown in Fig.-3

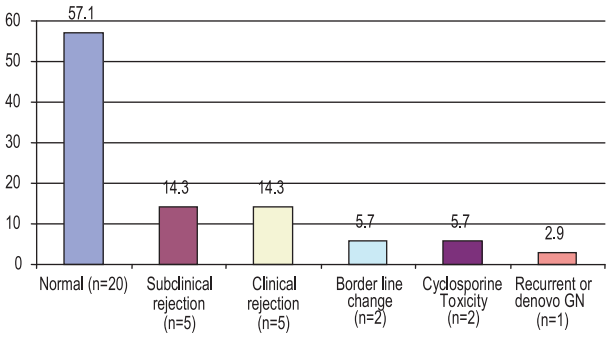

Fig. 3: *Protocol biopsy at 14th POD*

Protocol biopsy at 14th post operative day showed 57.1% (n=20) of patients were normal 14.3% (n=5) had clinical rejection (elevated serum creatinine along with histological features of rejections). 14.3% (n=5) had sub clinical rejection (normal serum creatinine with histological features of rejections) cyclosporine toxicity 5.7% (n=2), ATN 5.7% (n=2) and 2.9% (n=1) had recurrence of GN.

Banff numerical scoring for the biopsies according to the pathological grade of rejection showed, Banff grade I (20%) (n=1) grade II (60%) (n=3) and grade III (20%) (n=1) in clinical rejection group and Banff grade I (80%) (n=4) and grade II (20%) (n=1) in sub clinical rejection group.

Histological correlation with serum creatinine level at 14th and 90th POD in shown Table-III.

Table-III

Histological correlation with serum creatinine level at 14th and 90th POD.

Histological group	Serum creatinine level (µmol/L)		p value
	14th POD	90th POD	
Normal histology	128±4 (n=20)	130±3 (n=18)	0.09
Clinical rejection	280± 35 (n=5)	230±32 (n=4)	0.06
Sub-clinical rejection	134±2 (n=5)	130±4 (n=7)	0.16
Cyclosporine toxicity	198±6 (n=2)	180±18 (n=2)	0.33
Acute tubular necrosis/border line changes	231±55 (n=2)	130±44 (n=2)	0.18
Recurrenvr or denovo GN	191±42 (n=1)	170.4±31 (n=1)	0.19

Histological correlation with cyclosporine blood level at 14th and 90th POD in shown in Table – IV.

Table-IV

Histological correlation with cyclosporine level at 14th and 90th POD.

Histological Group	Cyclosporine blood level (C_2) ng/ml		pP value
	14th POD	90th POD	
Normal histology	1248±250 (n=20)	1110±198 (n=19)	0.07
Clinical rejection	1262±230 (n=5)	1125±135 (n=4)	0.32
Sub-clinical rejection	1389±140 (n=5)	1166±110 (n=7)	0.08
Cyclosporine toxicity	1880±260 (n=2)	1580±185 (n=2)	0.31
Acute tubular necrosis/ border line changes	1430±253 (n=2)	1180±247 (n=2)	0.42
Recurrenceor denovo GN	1490±220 (n=1)	1070±186 (n=1)	0.39

Protocol biopsy performed in all 35 patients after 3 months of transplantation and 54.28% (n=19) showed normal histology 11.42% (n=4) had clinical rejection, 20% (n=7) sub clinical rejection, 5-7% (n=2) borderline changes, 5.7% (n=2) cyclosporine toxicity and 2.8% (n=1) recurrence or denovo GN. According to Banff, numerical scoring of clinical rejection Banff grade I (25%) (n=1), grade II (50%) (n=2), grade III (25%) (n=3). In subclinical rejection, Banff grade I (70%) (n=5) and grade II (30%) (n=2).

Result of protocol biopsy at 90th POD is shown in Fig. – 4.

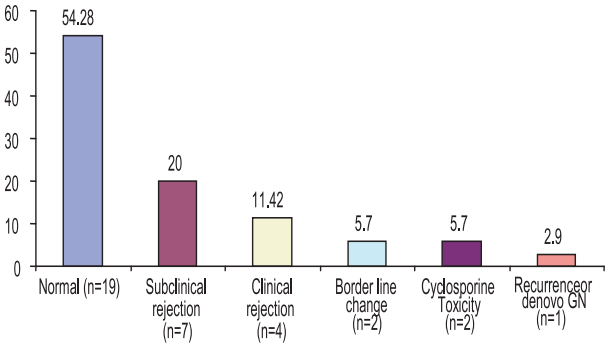

Fig.-4: *Protocol biopsy at day 90 (n=35)*

Discussion:

The present study describe the histological changes of renal allograft by protocol renal biopsy at different interval for identification of early graft dysfunction. In this study we have observed that the biochemical values correlate with histological features of graft dysfunction that has some similarity with other studies[14]. Histological classification of clinical and sub clinical rejection was made and they were categorized by Banff 97 criteria. The Presence of subclinical rejection in another study was found 30%[15]. In this study subclinical rejection was detected in 14.3% at 14th postoperative day and 20% at the end of three months. The majority of subclinical rejection in Banff criteria is Banff grade I. A center published data on seventy renal allograft biopsies done routinely at 1, 2, and 3 months post transplant[16]. The histological diagnosis was made according to the Banff schema. Of these biopsies, 30% showed sub clinical rejection. Data in different study suggests that donor glomerulosclerosis greater than 20% increases the risk of delayed graft function and poor outcome.[13] In the study per operative protocol biopsy 3 kidney showed 16% sclerotic glomeruli which are more common in dysfunction group. Recurrence of GN was reported to be important cause of impaired renal function and consequence graft losts. Recurrence of GN is the 3rd most common cause of graft loss[12]. In the study recurrence or denovo GN was found in 2.9% of the patient at protocol biopsy. It is very difficult to interprete whether patient is suffering from recurrence of GN because native kidney biopsy was not done. Hence we have clarified it as denovo or recurrent.

Acute cyclosporine toxicity in the important cause of early graft dysfunction and usually it is reversible.[17] As it has narrow therapeutic index so its blood level and toxicity in individualized. Cyclosporine toxicity and acute rejection often co-exist and its toxicity sometimes is sub clinical. In this study we have found 5.7% patients of cyclosporine toxicity at protocol biopsy which had clinical correlation with histology.

The major cause of delayed graft function is ATN.[18] Post transplant ATN increases the risk of acute rejection and graft loss. In this study we have shown 5.7% cases of graft dysfunction due to acute tubular necrosis. Tubular cell flattening and degeneration is the characteristic feature of ATN. But mild acute rejection or borderline changes can be confused with ATN. It may be conclude that adequate histological evaluation is helpful for detection of clinical and subclinical rejection. So routine allograft biopsy should be practiced in different transplant center of Bangladesh.

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Abstract from Current Literature

(Bang. Renal J. 2011; 30(1): 19-22)

Spectrum of acute kidney injury in a tertiary care hospital in Cairo.

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Introduction: Data concerning the spectrum of acute kidney injury (AKI) in Egypt are scarce. The study aims to describe the spectrum of AKI in a tertiary hospital in Cairo.

Methods: We retrospectively collected the data of all cases of AKI who were treated at Dar El Shefa Hospital, Cairo, Egypt, from January 2006 to January 2007.

Results: There were 51 cases of AKI during the study period (29 males and 22 females). Their age ranged from 19 to 81 years with a mean of 48 years. Pre-renal azotemia and acute tubular necrosis (ATN) accounted for 53% of all cases. These were due to cardiovascular disease in ten patients, sepsis in six patients, obstetrical complications in five patients, post surgical in four patients, trauma in one patient and gastroenteritis in one patient. Contrast induced nephrotoxicity was responsible for AKI in eight cases (15.7%), glomerulonephritis/vasculitis in eight (15.7%), obstructive uropathy in five (9.8%) acute interstitial nephritis in two (3.9%), and acute urate nephropathy in one (2%). Thirty cases were treated conservatively, nineteen received hemodialysis, and two received peritoneal dialysis. Average duration of hospital stay was 11.7 days. Out of the fifty one cases, thirty-three recovered normal renal function (64.7%), eleven expired, five progressed to chronic kidney disease and two were lost follow up. Overall mortality was 21.5%.

Conclusion: The common causes of acute kidney injury in our setting were pre-renal azotemia and ATN due to acute cardiovascular disease (19.6%), contrast induced nephrotoxicity (15.6%), glomerulonephritis (15.6%) and sepsis induced ATN (11.7%). Most cases were managed conservatively and two thirds recovered their normal kidney function.

Arab J Nephrol Transplant. 2011 May;4(2):83-6.

Membranous glomerulopathy in a patient with selective IgA deficiency: is there a link?

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We report a 42-year-old woman, who presented with proteinuria (3.85 g/day) and malleolar oedema. She had a medical history of Graves' disease, recurrent upper respiratory tract infections, episodes of Raynaud phenomenon and dysphagia. Biochemistry showed a selective IgA deficiency (SIgAD). Percutaneous renal needle biopsy showed diffuse global thickening of the glomerular basement membranes on light microscopy and granular deposits of IgG and C3 along the glomerular basement membranes on immunofluorescence. The pathological diagnosis was membranous glomerulopathy stage II. A treatment with dietary salt restriction and an angiotensin-converting enzyme inhibitor was initiated, resulting in a reduction of proteinuria. Despite the fact that selective IgA deficiency is associated with various autoimmune disorders, the association with glomerular disease is rather rare and the pathogenesis is not fully understood

Acta Clin Belg. 2011 May-Jun;66(3):228-30.

Short-term effects of soy protein diet in patients with proteinuric glomerulopathies.

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Introduction: It has been suggested that soy protein can slow renal disease progression by decreasing plasma cholesterol and proteinuria in patients with nephropathies. This study was designed to evaluate the effect of soy protein on proteinuria and dyslipidemia, in patients with proteinuric glomerulopathies.

Patients and methods: Patients were divided into three groups: Control Group (n = 9) received diet with 0.8 g/kg/day of animal protein; Study Group 1 (n = 9), 0.8 g/kg/day of soy protein; and Group 2 (n = 9), 0.8 g/kg/day of soy protein plus fibers. The study period corresponded to eight weeks. During the baseline period and by the end of the study, patients were submitted to laboratorial and anthropometric evaluation.

Results: There was no statistically significant difference between baseline and post-diet periods among the three groups in anthropometric parameters or body composition, neither in proteinuria levels (Control: 0.7 ± 0.6 versus 0.8 ±

0.6; Group 1: 2.0 ± 1.7 versus 1.9 ± 1.8; Group 2: 2.0 ± 1.4 versus 2.1 ± 2.0). However, a slight decrease in triglycerides (244.8 ± 275.9 versus 200.5 ± 34.0), total (234.0 ± 59.4 versus 181.2 ± 110.3) and LDL (136.0 ± 59.1 versus 104.1 ± 39.4) cholesterol in Group 1 was observed, although not significant.

Conclusion: We have not observed beneficial effects when using soy protein instead of animal protein with the aim of attenuating proteinuria and hyperlipidemia, but we have shown that soy protein has not caused deleterious changes in body composition, ensuring an adequate nutritional state.

J Bras Nefrol. 2011 Apr-Jun;33(2):150-9.

Tunneled central venous catheters: Experience from a single center.

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In the past vascular surgeons were called in to place tunneled central venous catheter (TVC) for hemodialysis patients. Advent of percutaneous technique has resulted in an increasing number of interventional nephrologists inserting it. A single centre three year audit of 100 TVCs with a cumulative follow up of 492 patient months is presented here. From 2007 to 2010, 100 TVCs were placed by nephrologists in a percutaneous fashion in the operative room or the interventional nephrology suite. Those who completed minimum of three months on the catheter were included in analysis. There were 69 males and 31 females with a mean age of 52.3±13.6 years.(range: 25-76). Chronic glomerulonephritis was the commonest cause of CKD (45%) followed by diabetes (39%).Right internal jugular vein was the preferred site (94%). TVC was utilized as the primary access to initiate dialysis in 25% of patients in whom a live donor was available for renal transplant. The blood flow was 250-270 ml/min. The Kaplan-Meier analysis showed that 3 months and 6 months catheter survival rates were 80% and 55%, respectively. The main complications were exit site blood ooze, catheter block and kink. Catheter related bacteremia rate was low at 0.4/1000 patient days. Primary cause of drop out was patient death unrelated to the TVCs. Those under the age of 40 years showed better survival, but there was no bearing of gender, catheter site, and etiology of CKD on survival. Tunneled central venous catheters could find a niche as the primary access of choice for pretransplant live donor renal transplants in view of its immediate usage, high blood flows, low infection rates and adequate patency rates for 3-6 months.

Indian J Nephrol. 2011 Apr;21(2):107-11. doi: 10.4103/0971-4065.82133.

Collapsing glomerulopathy in a renal transplant recipient: potential molecular mechanisms.

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Background: In this case report, we describe a predisposed renal transplant patient who developed FSGS with cellular and collapsing features after sirolimus exposure and discuss the potential molecular mechanisms.

Case Report: A 35-year old African American female with end stage renal disease due to lupus nephritis received a living related renal transplant from a brother. She had immediate function achieved serum creatinine level of 1.7 mg/dl post day 4. Following a slow rise in the creatinine, first renal allograft biopsy performed on post op day 14 that showed thrombotic microangiopathy (TMA) involving arterioles and glomerular capillaries without any sign of rejection. The serological work up was negative for donor specific and antiphospholipid antibodies. The TMA was attributed to tacrolimus which was subsequently discontinued. It was replaced with sirolimus with loading dose of 10mg once and then 5 mg daily maintenance dose at day 21. At day 35, the patient was noted to have nephrotic range proteinuria, 12 gm/24 hrs. A second renal biopsy performed that revealed de novo focal segmental glomerulosclerosis with cellular and collapsing features, mild mesangial proliferative glomerulonephritis with immunoflourescence consistent with early recurrence of lupus nephritis ISN/RPS class 2. The etiology of cellular and collapsing FSGS was thought to be related to sirolimus based on timing of exposure and negative work up for secondary causes of collapsing FSGS. Sirolimus was switched to cyclosporine. At day 105, proteinuria decreased to 1.6 grams/day and serum creatinine leveled off 1.6 mg/dL.

Conclusions: We report a case of possible sirolimus-induced collapsing FSGS in a renal transplant recipient who may have been predisposed to develop a podocytopathy possibly due to TMA and altered WT1 expression resulting from m-TOR exposure

Ann Transplant. 2011 Apr-Jun;16(2):113-6.

Endothelin but Not Angiotensin II May Mediate Hypertension-Induced Coronary Vascular Calcification in Chronic Kidney Disease.

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To understand the relationship between putative neurohormonal factors operative in hypertension and coronary artery calcification (CAC), the relevant cellular actions of angiotensin (Ang II) and endothelin-1 (ET-1) are reviewed. There is compelling evidence to implicate ET-1 in CAC. ET-1 increases phosphate transport with a 42 to 73% increase in V(max). Increased cellular phosphate may induce CAC through increased Ca x phosphate product, transformation of vascular smooth muscle cells into a bone-producing phenotype or cell apoptosis that releases procalcific substances. ET-1 is increased in several models of vascular calcification. ET-1 inhibits inhibitors of calcification, matrix Gla and osteoprotegerin, while enhancing pro-calcific factors such as BMP-2 and osteopontin. In contrast, Ang II inhibits phosphate transport decreasing V(max) by 38% and increases matrix Gla. Ang II also stimulates bone resorption. Vascular calcification is reduced by ET-1 A receptor antagonists and to a greater extent than angiotensin receptor blockade although both agents reduce blood pressure

Int J Nephrol. 2011;2011:516237. doi: 10.4061/2011/516237. Epub 2011 May 31.

A comparative study of renal dysfunction in patients with inflammatory arthropathies: strong association with cardiovascular diseases and not with anti-rheumatic therapies, inflammatory markers or duration of arthritis.

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Aims: The aim of this study was to investigate the prevalence of chronic kidney disease (CKD) among comparable patients with rheumatoid arthritis (RA) and seronegative inflammatory arthritis, and to explore any predictive factors for renal impairment.

Methods: Consecutive patients with peripheral joint disease (oligo and polyarthritis) were recruited from our inflammatory arthritis clinics. We divided patients in two groups: RA group and seronegative inflammatory arthritis group. The cohort consisted of 183 patients (RA = 107, seronegative arthritis = 76 [psoriatic arthritis = 69, undifferentiated oligoarthritis = 7]). Estimated glomerular filtration rate (eGFR) was calculated using the established Modification of Diet in Renal Disease equation. Demographic details, disease-specific characteristics, anti-rheumatic drugs and the presence of cardiovascular diseases were recorded.

Results: In total, 17.48% (n = 32) of the cohort had CKD. There was no statistically significant variation between the two groups as regards baseline demographics, disease characteristics, use of anti-rheumatic drugs and the presence of individual cardiovascular diseases. We found that eGFR and the presence of CKD were similar among these groups. Among patients with CKD, 72% had undiagnosed CKD. No association of statistical significance was noted between CKD and the use of corticosteroids, disease-modifying antirheumatic drugs and anti-tumor necrosis factor agents. The association of cardiovascular diseases with CKD remained significant after adjusting for confounders (age, gender, duration of arthritis, high C-reactive protein, use of anti-rheumatic drugs).

Conclusions: Patients with inflammatory arthritis are more prone to have CKD. This could have serious implications, as the majority of rheumatology patients use non-steroidal anti-inflammatory drugs and different immuno-suppressives, such as methotrexate. No association of kidney dysfunction was noted with inflammatory disease-specific characteristics; rather it appears to have a positive independent association with cardiovascular diseases

Int J Rheum Dis. 2011 Aug;14(3):255-60. doi: 10.1111/j.1756-185X.2011.01594.x. Epub 2011 Apr 4.

Thyroid status and kidney transplantation outcomes.

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Introduction: It is known that end-stage renal disease patients can display abnormal thyroid gland function, which may cause autoimmune hypothyroidism or subclinical alterations. The impact of thyroid function on graft outcomes is not completely clear among renal transplant patients. The aim of this study was to evaluate thyroid function among a cohort of 136 consecutive renal recipients in correlation with clinical parameters of graft function.

Materials and methods: We performed a cross-sectional study on 136 subjects including 84 males and 52 females of overall mean age of 49.71 ± 10.98 years who underwent renal transplantations between 2005 and 2009 and had a mean follow-up of 28.3 ± 15.7 months. All patients were treated with a calcineurin inhibitor, steroids, and mycophenolate mofetil. The exclusion criteria were age below 18 years, multiorgan transplantation, graft failure in the first 6 months, or presence of a thyroid neoplasm. We

evaluated levels of serum FT3, FT4, and thyroid-stimulating hormone (TSH) in relation to the following parameters: body mass index (BMI), serum creatinine, estimated glomerular filtration rate estimated glomerular filtration rate (eGFR) by Modification of Diet in Renal Disease (MDRD) formula, proteinuria/24 hours, serum sodium, potassium, calcium, phosphorus, cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, and hemoglobin (Hb).

Results: Only 6.4% of our transplant recipients were treated with levothyroxine sodium. The patients showed an average FT3 of 3.24 ± 0.5 mg/dL; average FT4 of 0.84 ± 0.1 mg/dL, and mean TSH of 1.29 ± 0.8 mg/dL. The study showed no relationship between thyroid hormones and age of the transplant, while there was a significant difference in FT3 levels between men and women. We also observed a significant correlation between FT3 and serum creatinine, eGFR, serum sodium, BMI, and Hb; whereas there was no correlation with other variables. The correlations between FT4 and TSH and all examined variables were not significant.

Conclusions: The interactions between the thyroid and the kidney have been incompletely studied among patients with renal transplants. Our data showed that the presence of low serum FT3 levels correlated with worse graft function, anemia, BMI, and serum sodium. Thus low FT3 levels could be predictive of graft function, especially in the 5 years posttransplantation.

Transplant Proc. 2011 May;43(4):1042-4. doi: 10.1016/j.transproceed.2011.01.126.

Salmonella typhi infection complicated by rhabdomyolysis, pancreatitis and polyneuropathy.

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Introduction: Typhoid is a common infection that can have serious complications. Here we present a severe case of Salmonella typhi infection complicated by rhabdomyolysis and acute kidney injury.

Case report: A 42-year-old male presented with shortness of breath, generalized body aches and upper abdominal pain two weeks after returning from India. Investigations revealed severe metabolic acidosis (arterial blood pH 6.9), high serum creatinine (12.7 mg/dl), hyperuricemia (16.4 mg/dl), hypocalcemia (4.1 mg/dl), hyperphosphatemia (16.1 mg/dl), high serum amylase (1458 u/L), thrombocytopenia (59,000/mm3) and disturbed coagulation profile. The diagnosis of rhabdomyolysis was confirmed by an elevated creatine phosphokinase level of 17,000 U/L. The patient was started on hemodialysis, and two days later he developed broncho-pneumonia and required mechanical ventilation. Blood cultures grew Salmonella typhi; parenteral imipenem-cilastin and ciprofloxacin were initiated. After one week, the patient continued to have fever despite improvement of biochemical parameters and negative blood and stool cultures. Antibiotic drug-fever was suspected and antibiotics were stopped. Subsequently, fever and rash disappeared and the patient was switched to ceftazidime two days later. The patient eventually regained normal kidney function but continued to have weakness in both lower limbs. Electromyography (EMG) and nerve conduction studies revealed diffuse axonal sensorimotor polyneuropathy that progressively improved over time.

Conclusion: Common infective agents, including salmonella typhi, can present in unusual ways. The possibility of a severe systemic infection being the underlying cause of rhabdomyolysis should not be overlooked

Arab J Nephrol Transplant. 2011 May;4(2):91-3.

Outcomes of renal transplantation in recipients with Wegener's granulomatosis.

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Wegener's granulomatosis (WG) is the leading cause of rapidly progressive glomerulonephritis-induced end-stage renal disease (ESRD). In this study, we compared transplant outcomes between recipients with ESRD caused by WG to recipients with ESRD secondary to other causes. Using OPTN/UNOS data from 1996 to 2007, 919 recipients with WG were identified. Post-transplant outcomes included rates of delayed graft function, acute rejection within one-yr post-transplant, overall and death-censored graft survival, and patient survival and were compared between recipients with ESRD secondary to WG versus ESRD from other causes. Recipients with ESRD because of WG had superior unadjusted and adjusted rates of graft loss, patient death, and functional graft loss (adjusted hazard ratio [HR] 0.711, 0.631, and 0.625 respectively, $p < 0.001$). When we compared the WG cohort to a non-WG, non-diabetic population, the HR for graft loss was still significant, but patient death and death-censored graft loss were not. Subgroup analysis of recipients aged over 60 conf000000000000irmed that WG recipients had better unadjusted outcomes. This study supports the notion that renal transplantation is an effective treatment option for patients with ESRD secondary to WG. They fare similarly, if not better, than other patients.

Clin Transplant. 2011 May-Jun;25(3):380-7. doi: 10.1111/j.1399-0012.2010.01248.x. Epub 2010 Apr 11.

Announcements

(Bang. Renal J. 2011; 30(1): 23-24)

Important Announcement of the ERA/EDTA

On 19th May the European Parliament adopted legislation setting out common quality and safety standards of organs for transplantation. EKHA representatives, of which ERA-EDTA is a founding member, was present at all stages of the legislation preparation, providing expert input at the European Commission's stakeholder group during the drafting of the proposal as well as advising the European Parliament and the Council on various amendments such as those pertaining to living donation. The consolidated text of the final Directive can be found at the following link: http://www.europarl.europa.eu/sides/getDoc.do?

The accompanying Action Plan instead can be found here: http://ec.europa.eu/health/ph_threats/human_substance/oc_organs/docs/organs_action_en.pd

Apply for an ISN Educational Ambassador to Visit Your Center

ISN COMGAN and its Education Committee believe the most effective teaching takes place in face-to-face, hands on settings. ISN is now extending its traditional CME lecture program to offer renal centers in emerging countries the opportunity to invite an established expert (ISN Educational Ambassador) from outside to come to your institution and remain for a period of 1–4 weeks to provide hands on teaching and help to establish new programs that would benefit patient care. Experts may be selected directly by the center, or ISN will match the needs of the center with qualified experts who have volunteered to become educational ambassadors. Costs of travel will be covered by ISN, centers are asked to provide local accommodations.

Tired of reading journals, reviews and textbooks written by distant experts that cannot answer your questions or give advice? Invite the expert to come to you! This new program offers support for a unique opportunity to start new programs and expose your students, residents, fellows and practioners to in depth contact with an established ISN teacher whose experience and expertise matches your needs.

More information and application forms are available at http://www.nature.com/isn/society/outreach/isn_20090. html

Become an Educational Ambassador for ISN

The ISN seeks qualified nephrologists willing to visit a renal center in a developing country for as little as 1–2 weeks to help establish or upgrade a new clinical program (e.g. peritoneal dialysis, management of AKI, pediatric nephrology, renal pathology, many others). Expertise will be matched with needs outlined in applications for assistance from developing country centers. Timing is flexible and negotiable. Both all nephrologists with a hospital or university teaching position and an existing or potential interest in international renal health care are welcomed. Travel costs are paid by ISN, and local accommodations will be provided by host centers.

You can volunteer to visit a developing renal center that needs your help in a part of the world you would not ordinarily see, experience a unique professional opportunity for service and interaction with local providers, make a contribution to improving renal care in the emerging world and promote international understanding and collaboration. If you are someone who sees yourself as a concerned citizen of the global health community, this program is a way to demonstrate that commitment by sharing your expertise where it is most needed.

If you are an emerging center that would like to benefit from the visit of an Educational Ambassador ISN is now also welcoming application requests for training! Applications must be received by May 1st.

More information and application forms are available at http://www.nature.com/isn/society/outreach/isn_20090. html

RENAL PHYSIOLOGY FOR THE CLINICIAN

Fluids, electrolytes and acid-base 4-6 May 2011 Sir William Wells Atrium, Royal Free Hospital, London NW3

This course aims to integrate physiological principles with day-to-day clinical practice. It will feature formal, introductory lectures each day, and clinical case-based and interactive discussions with our faculty designed to illustrate and build upon the day's presentations. It is intended for Specialist Registrars in Nephrology, and will also be of interest to more senior General (Internal) Medicine SPRs and SPRs in Intensive Care Medicine. Consultant Nephrologists and General Physicians with an interest in fluid and electrolyte disorders are welcome to attend as a "refresher" course.

Dialysis 2011

A comprehensive three-day course on dialysis and the management of patients with end stage renal failure

15-17 June 2011 Sir William Wells Atrium, Royal Free Hospital, London NW3

The management of end stage renal failure by dialysis forms a central component of all renal units. However, it is often the least intensively taught aspect of nephrology training. This in-depth course is a thorough introduction to dialysis, from basics to new developments. Expert faculty will provide comprehensive coverage of all aspects of dialysis and ESRF through a mixture of informal lectures and workshops. Although the course is aimed at Specialist Registrars in nephrology, it will also be of interest to other health care professionals involved in the management of patients with chronic renal failure.

REGISTRATION OPENS 1 DECEMBER 2010 CLOSING DATE FOR REGISTRATION 13 May 2011

For registration information, please contact the Course Administrator: Pamela Fong Whitehead Tel: +44 (0)20 7830 2930 Fax: +44 (0)20 7317 8591 UCL Centre for Nephrology Royal Free, Rowland Hill Street, London, NW3 2PF UK **EMAIL:** pf.whitehead@medsch.ucl.ac.uk COURSE DIRECTORS Dr Chris Laing Dr Andrew Davenport Professor Ken Farrington Dr David Wheeler Dr Suresh Mathavakkannan

ERA-EDTA Research Programme

1,000,000.00 EUR has been budgeted for the second call of this initiative aimed to support research in Nephrology. The application deadline will be the 31st of March 2011. All the necessary information, as well as the instructions on how to apply, is available in the ERA-EDTA website www.era-edta.org, under the "Research Programme" section.

Oxford–Ghent Dialysis and Transplantation Summer School 17-21 September 2011

Location: Corpus Christi College, Oxford

Organised by: Paul Harden, Oxford, Wim Van Biesen, Ghent, Raymond Vanholder, Ghent.

An INTERACTIVE course for young nephrologists (fluency in English is mandatory). Education is provided in interactive tutorials in small groups of 10–12 participants.All tutorials start from a clinical problem.The major aim of the course is to disperse available knowledge among young nephrologists (last year of training or just finished training). Topics covered include: Predialysis strategies, Non-renal problems in dialysis patients, Haemodialysis strategies, Peritoneal dialysis strategies, Transplantation, Ethical and economical issues of dialysis. A large faculty of opinion leaders with clinical experience in their field moderates the debate.The course is hosted in the stimulating setting of Corpus Christi College in medieval Oxford. The atmosphere of this college and the city of Oxford provide an ideal climate for discussion and learning. For organisational reasons, this year, the course will be restricted to applications from the following countries: The Netherlands, Belgium, Ireland, United Kingdom, Austria, Germany, Finland, Greece, Turkey, Denmark, France, Croatia, Slovenia and Spain.**For application:** Mail to ivandorpe@gmail.com to obtain the official application form or contact your local Genzyme representative for more information.