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CONTENTS

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BANGLADESH RENAL JOURNAL

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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

MANUSCRIPTS SHOULD BE SUBMITTED

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Acute Renal Failure Following Bilateral Renal Intrapelvic Instillation of Povidone Iodine for Chyluria

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(Bang. Renal J. 2007; 26(1): 22-23)

Introduction

Chyluria is commonly caused by Bancroftian filariasis and is endemic in South-east Asia, China, Hong Kong, Taiwan and Japan[1]. Chyluria is milky urine due to the presence of chyle that enters the urinary tract due to fistulous communication with the renal lymphatics. Prolonged chyluria may lead to loss of weight and subcutaneous fat and protein deficiency including hypoproteinemia, lymphopenia and anaemia. Conservative management includes dietary modifications like high protein low fat diet, anti filarial drugs, bed rest and high amount of fluid intake[2]. When conservative management fails then minimally invasive techniques like renal pelvic instillation of sclerosing agents are used to cure the condition. However this procedure may be associated with serious complications like acute renal failure, life threatening hemorrhage, fulminant hepatic failure and even death[3]. In recent years Povidone Iodine has emerged as a relatively safe sclerosing agent. Here we discuss a case of acute renal failure (ARF) after bilateral renal intrapelvic instillation of povidone iodine in a patient with chyluria.

Case Report

A 90 years old hypertensive (on antihypertensive drug) nondiabetic patients was admitted on 14th January 2005 in Nephrology ward, NIKDU with complaints of oligo-anuria, haematuria and respiratory distress for 2 days. As the patient states, he was completely alright 2 years ago. Suddenly he noticed passage of frank milky urine which was intermittent for about one year. Then frequency of passing milky urine gradually increased along with dysuria and occasional hematuria. He was diagnosed as a case of chyluria possibly due to chronic filariasis and treated by different medications. During this period he was investigated and one report showed mild impairment of renal function (S. creatinine 1.7 mg/dl). But as his symptoms were not improving he went for urologic management and instillation of sclerosing agent was decided on 11.01.2005 under general anesthesia. Urethrocystoscopy and ureteric catheterization was done on both sides, and then 20 ml of diluted povidone iodine was instilled through ureteric catheter to each renal pelvis.Twenty four hours after the operative procedure the patient developed oligo-anuria, frank hematuria and features of severe renal failure. Investigation showed urine albumin (++), pus cell-plenty, RBC-plenty, S. creatinine-10.7 mg/dl, urea- 180 mg/dl. After admission other possible causes of acute renal failure were ruled out by appropriate laboratory investigation and imaging techniques. Renal biopsy could not be performed as the patient was very restless. He was managed as a case of ARF and he required ten sessions of hemodialysis and four units of blood transfusion. His renal function improved gradually (urine output 2200 ml/24 hours, urea- 58 mg/dl, S. Creatinine 2.1 mg/dl - at the time of discharge).

Discussion:

Chyluria represents chronic stage of filarial disease and is seen in 1-2% of patients of filariasis after 10-20 years of initial infection[3]. It results from obstruction of retroperitoneal lymphatics causing renal lymphatics to rupture into pelvicalyceal system leading to milky white chylous urine with haematuria and sometimes passage of chyle clots[3,4]. Although it is not life threatening but it is a debilitating condition leading to weight loss, protein loss and immunological deficiency secondary to chronic chyluria[3,4]. Our patient is a 90 years old male who is otherwise healthy, developed chyluria possibly due to chronic failariasis. His chyluria was intermittent initially for 1 year and later on he was regularly passing chylous urine along with dysuria and haematuria. He wanted to get rid of this problem by various antifilarial medications but his condition did not improve and he sought urological treatment. Renal pelvic instillation of sclerosant (RPIS) is an accepted modality of treatment for chyluria. After instillation of sclerosants the resulting inflammatory

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reaction causes edema and blockage of lymphatic channel that results in immediate relief in the form of clear urine. Permanent remission occurs when renal lymphatic inflammation heals by fibrosis[4,5]. Many sclerosing agents with different concentrations have been used over last 35 years. These sclerosing agents include hypertonic saline, hypertonic glucose, contrast (15-25% Na iodide and Na diatrizoate), silver nitrate (0.1, 01.5, 1.3 and 5%) and povidone iodine (0.2%)[4]. Of various sclerosing agents, use of silver nitrate (0.5-1%) has been common until recently and a lot of published literature showed 60-70% success rate with common complications including pain, hematuria, nausea vomiting. Serious complications are rare but include, acute renal failure, renal papillary necrosis, septicaemia, fulminant hepatic failure and death[4,5,6,7].

Recently, use of 0.2% provide iodine has been reported to be equally efficacious as well as more safe in the treatment of Chyluria[4,5,7]. In addition to advantage of being nontoxic, non irritating and antibacterial , povidone iodine is easily available and easy to reconstitute. As a selerosant it has been used in the management of renal cyst and Lymphocele following renal transplantation[7]. Although acute renal failure has often been reported after the use of silver nitrate but no such complication is reported in literature after use of povidone iodine. However there are reports of serious iodine hypersensitivities reactions (Anaphylaxis) in some patient [7]. The cause of acute renal failure in our patient with the use of a relatively safe sclerosant need some explanation. The patient is elderly, hypertensive and he might have mild renal insufficiency before surgery as previous record showed serum creatinine 1.7mg and serum creatinine was not estimated within one month before surgery. During the procedure there was bilateral renal pelvic instillation with 20 ml of diluted povidone iodine in each side in one sitting under general anesthesia. Guidelines from available literature have cautioned against such practice and it is advised never to instill sclerosing agents bilaterally at one time and never to over distend the renal pelvis[4,5,8]. Common practice is to instill 10 ml of diluted solution of povidone iodine only on one side under local anesthesia to prevent over instillation[7,8]. The reason for bilateral instillation was not clear in this case and during cystoscopy there was no record of bilateral chylous efflux from both ureters. However bilateral chylous efflux is much less common as chyluria is unilateral in 85% and bilateral in 15%[4]. Blocking the PUJ, injecting under high pressure, large volume of sclerosant and finally bilateral instillation at a time could lead to disastrous consequences like renal papillary necrosis, anaphylactic reaction, acute tubular necrosis, septicemia, renal cortical and perinephric abscess[4,5,6,8]. In order to avoid such complications utmost precautions, both preoperative and intraoperative, should be exercised during renal intrapelvic instillation of sclerosing agents. For a disease like chyluria which essentially runs a benign course, any management leading to loss of renal function or risk of death is difficult to justify.

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Vol. 26, No. 1, June 2007

Anatrophic Nephrolithotomy for Managing Large Staghorn Calculi

M NASIR UDDIN[1], AKM ZAMANUL ISLAM BHUIYAN[2], KAZI RAFIQUL ABEDIN[3], KAZI ZIKRUR RAZZAQUE[4]

Summary:

Urinary stone diseases are most common problem, that urologists, encounter in their practice. Most of the stones are associated with some complications and recurrence. Staghorn stones are frequently responsible for morbidity, even death and chances of recurrence are more. Management of large staghorn stone is a challenging issue for complete clearance. Although there are several options for their management, only anatrophic nephrolithotomy has high stone free rate in single operative procedure. Aims and objectives: To find out the outcome of anatrophic nephrolithotomy for large staghorn renal stone. Methodology: Total 27 patients underwent anatrophic nephrolithotomy in this retrospective study at National Institute of Kidney Diseases & Urology from January 2004-June 2008. Patients selected for this study were with staghorn stone in any kidney larger than 5 cm. in size sonographically. Operation was done with clamping of renal artery and using surface cooling. Patients were followed up after operation upto a period of 5-42 months. Results: 27 patients (22 male and 5 female) were included in this study. Patients were between 36-68 years with mean 52 years. In 19 patients stones were on left side and in 8 patients on right side.23 patients (85.18%) had complete clearance of stone after operation, 4 patients (14.82%) had residual stones, they were managed subsequently with ESWL. 2 patients developed urine leakage and it improved conservatively. Conclusion: Anatrophic Nephrolithotomy appears to be a standard technique for management of large staghorn stone with very high stone free rate in a single operative procedure.

Key word: Large staghorn stones, surface cooling, anatrophic nephrolithotomy, single operative procedure.

(Bang. Renal J. 2007; 26(1): 18-21)

Introduction:

Urinary stone disease is one of the common problems in urological practice. It has been estimated that in UK population the incidence is about 2%-3% [1]. The incidence of stone disease is common in Bangladesh, more in the northern part to the country affecting predominantly male over female with a ratio 3:1 [2]. Different types of stones occurred with variable sizes, biochemical compositions, clinical presentations and various morbidities. Once a patient has developed stone, the probability of a recurrence has been estimated at 50% within next 10 years [3].

Staghorn renal stone disease is a challenging problem in urology, as it can cause severe morbidity like repeated infection and even renal failure and sometimes death. There are several treatment options for managing that issue like percutaneous nephrolithotomy and anatrophic nephrolithotomy either open or laparoscopic. Minimal invasive procedure like ESWL has limited efficacy for its management even with multiple sessions.

PCNL is also a good treatment options for that but it is associated with residual stone in significant number of patients that required adjunct ESWL or another session of PCNL which increases treatment related morbidity and financial assault [4-9]. All types of stone has chance for recurrence, amongst them staghorn stone has the highest chance. Due to high incidence of recurrence of staghorn stones, particularly those associated with an infective process, the complete clearance of the stone is the ultimate goal in their management, a result that might not be attainable even after several session of PCNL or ESWL or intrarenal retrograde surgery [9].

Therefore, many investigators reserve open stone surgery as a preferred route for managing large staghorn stones, to minimize the need for secondary interventions after complete stone removal [10]. Several studies have shown better stone free rate with Anatrophic Nephrolithotomy and reduction of the morbidity and treatment cost [(4-10)].

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Patients and methods:

Although the incidence of urinary stone is high, the number of large staghorn stones is not like that. Total 27 patients with renal stones larger than 5mm underwent open anatrophic nephrolithotomy from January 2004 – June 2008 and were included in the study. Before surgery patients were evaluated with history, physical examinations and appropriate necessary investigations. Urine for RME and C/S to exclude urinary tract infection, S. creatinine to see the renal functional state, USG of KUB for stone location, size, hydronephrosis and cortical thickness of kidneys, IVU for renal anatomy, stone size, hydronephrosis and excretion of kidneys. Complete blood count, RBS and other investigations were done to assess anesthetic fitness.

Preoperatively all the patients were managed adequately. All patients underwent operation under general anesthesia with urethral catheter in situ, patients were placed in standard flank position with elevation of kidney rest. Retroperitoneal space was opened by the standard flank incision. Ureter was identified and slinged. Gerota's fascia was incised and the kidney was fully mobilized within this fascia. Renal artery and vein then dissected out. Satinsky's clamp was then applied on renal artery, ice slush were placed around kidney and surface cooling done with ice saline. Through an incision with sufficient length on the Brodel's line, the collecting system was sharply incised and the staghorn stone mobilized and removed as completely as possible. The collecting system was irrigated with normal saline and both collecting system and renal cortex was closed with 3/0 polyglactin running sutures. After nephrotomy incision was closed, Satinsky's clamp was released and renal perfusion started. The nephrotomy incision was examined carefully for bleeding. Frusemide injection was given and D-J stent kept in situ. The retro peritoneum was irrigated and aspirated. Proper haemostasis was ensured and a drain tube kept in situ. In 13 cases portable X-ray was used to seek for any significant residual stone, it included 9 patients that contain multiple stones in addition to large staghorn stone. Postoperatively all patients were managed with antibiotics and analgesics. Patients were mobilized after 48 hours of operation. At 1st POD renal functional status was reassessed. Urethral catheter and drain tube were then removed subsequently. At 7th POD plain X-ray KUB was done for any residual stones. Patient was then discharged and advised for regular follow up.

Results:

Total 27 patients underwent anatrophic nephrolithotomy. The demographics of the patients are shown in Table-I. The study was conducted from January 2004 – June 2008. Age of the patients was 36 – 68 yrs. mean 52 yrs. with male 22 and female was 5. Size of the stone was 5-8 cm, mean size 6 cm. In 19 cases stone was on the left side and rest on the right side. No patient had history of 'surgical interventions for stone diseases on that site except 2 cases who had history of open surgery 13 years before.

In all the cases stone was occupying pelvis and at least two major calyces. In 9 cases multiple stones were also present in addition to large staghorn stone. Surgical details e.g. stone size (largest diameter), ischemic time and operative duration were demonstrated in Table-II. Ischemic time was 12-28 min, means 19 min. Post operatively all patients recovered uneventfully except 2 patients who developed urine leakage and improved subsequently. 2 patients developed wound infection that was managed conservatively. X-ray KUB after operation showed 4 patients had residual stone. (3 pts had at lower calyx and 1 had at middle calyx). All of them were managed with ESWL. During follow up, patients were evaluated with history, clinical examinations and investigations including urine RME, S. creatinine, USG of KUB and IVU. Post operative investigations showed functioning kidney with significant improvement of obstruction in all of them. Follow up period was 5-42 months.

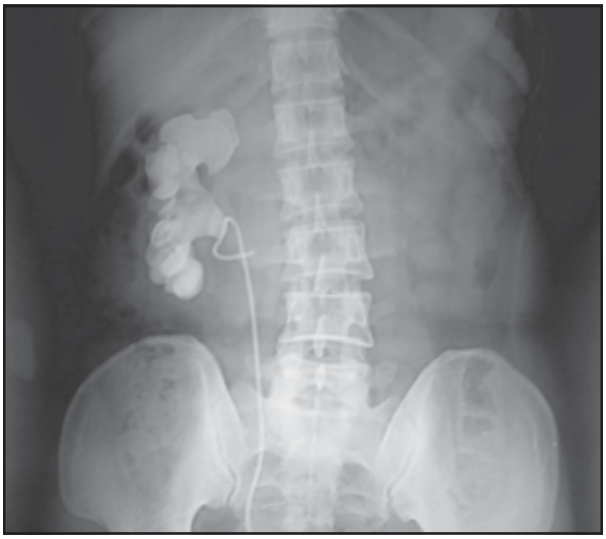

Fig-1: *X-ray KUB: Large Staghorn calculus*

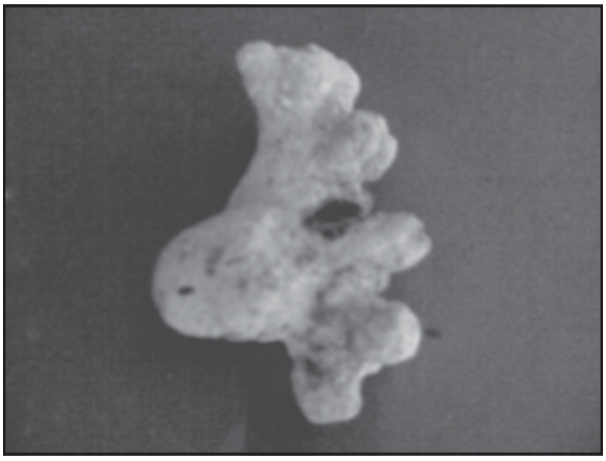

Fig-2: *After operation Large Staghorn calculus*

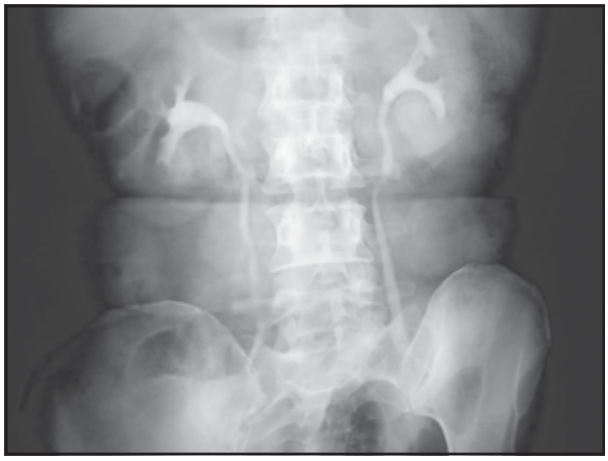

Fig-4: *Follow up IVU: Normal renal anatomy*

Table-I

Patients Demographics

Total no. of patients	27
Age	36-68 mean 52 yrs
Sex	Male- 22, Female- 5
Side of stones	19 on left, 8 on Rt
Stone size	5-8 cm,Ave. 6 cm
Study period	Jan'2004- June'2008
Follow up period	5-42 months

Table-II

Patients' operation details

Duration of operation	1.15-2.10 Hours
Ischemic time	12-28 min, ave. 19 min
Residual stone	4(14.82%)
Stone free rate	23 (85.18%)

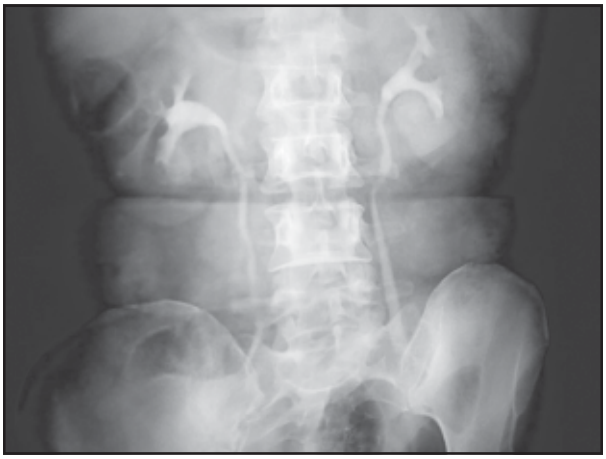

Fig-3: *IVU after operation of Large Staghorn calculus*

Discussion:

In this era, management of urinary stone diseases, almost all cases is possible by endourological procedure but for large staghorn stone, management is still challenging. Blandy and Singh (1976) [12] reported a 28% of mortality within 20 yrs of follow up in patients with staghorn calculi who were followed up nonoperatively. All survivors had persistent pain and UTI. Thus patients with staghorn calculi should not be followed up without treatment and must be removed completely to minimize the risk of continued urea splitting bacteriuria[12]. Since early 1980 with the development of less invasive procedure such as ESWL and PCNL, the role of anatrophic nephrolithotomy has diminished[13]. However anatrophic nephrolithotomy remains the gold standard for treating of large staghorn stone. Despite PCNL and ESWL minimizing the role of open surgery, several series have shown better stone free rate with anatrophic nephrolithotomy[4-10]. Matlaga and Assimos reported a stone free rate of 100% by anatrophic nephrolithotomy for large staghorn stone[4]. Essen and Kirkali et al compared the stone free rate of anatrophic nephrolithotomy with PCNL and ESWL in patients with staghorn renal stones; they reported a better stone free rate with anatrophic nephrolithotomy (80% Vs 50%)[5]. Nasser S. and Ali reza A et al showed promising results for large staghorn stone with anatrophic nephrolithotomy [10]. Similar results were reported by others who supported the preferred role of anatrophic nephrolithotomy in these patient's[6-9]. Large staghorn stone is associated with more morbidity, as it is usually associated with infection. It is also associated with high incidence of recurrence. So complete stone clearance is the ultimately goal of treatment[9]. A meta analysis by the AUA documented that for treating staghorn stones, the more invasive the

procedure the greater the stone free rate and the higher the operative morbidity expected[11-12].The need for planned or unplanned adjuvant interventions after PCNL might complicate the situation and increase the overall invasiveness, costs and morbidity[14].

At present, there is no single treatment procedure that is unique to complete stone clearance for large staghorn stone. But anatrophic nephrolithotomy is superior to other single or combined technique to achieve this target. In our study we had an excellent stone free rate after surgery (85.18%) and residual stone in 4 cases (14.81 %). It was managed subsequently with one episode and another 3 cases with two episodes of ESWL with no postoperative obstruction. Results of our study are comparable with others that were conducted by Matlaga and Assimos (100%) [4], Esens et al (80%) [5], Nasser Simforoosh et al (100%)[10]. Although our success rate is lower than Matlaga et al and Nasser et al, it can be possible to achieve almost 100% with experience, improvement of techniques and other supports. Several studies have shown that patients with such large stones endourological procedure poses a lower stone free rate, with more frequent surgery which leads to significant morbidity and increase treatment cost. Our study showed that Anatrophic nephrolithotomy is a old and gold standard surgical procedure to achieve high stone free success rate with single operative procedure.

Conclusion:

With meticulous technique, Anatrophic Nephrolithotomy can achieve successful removal of all calculi, preservation of renal function, improved urinary drainage, and eradication of infections. Stone free rates greater than 90% should be achieved. So anatrophic nephrolithotomy is a good technique for high stone free rate with a single operative procedure for large staghorn stones.

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Bangladesh Renal Journal
Vol. 26, No. 1, June 2007

Original Articles

Acute Poststreptococcal Glomerulonephritis in Children - An Ovrview

RR ROY[1], MM HOSSAIN[2]

(Bang. Renal J. 2007; 26(1): 1-5)

Acute glomerulonephritis (AGN) is constellation of clinical manifestation caused by abrupt onset of glomerular injury and inflammation that leads to a decline in glomerular filtration (GF) with retention of sodium and water[1]. It is clinically manifested by sudden onset of hematuria, edema, hypertension, renal insufficiency and mild to moderate proteinuria[2].

Acute nephritic syndrome (ANS) follows infection of variety of microorganism, when we call it 'postinfectious' glomerulonephritis[2]. Other causes of acute nephritic syndrome are listed in Table I. They are also important in day to day clinical practice. In pediatric age group, the most common cause of the acute nephritic syndrome is acute poststreptococcal glomerulonephritis (APSGN), accounting for approximately 80% of cases and is caused by group A beta hemolytic streptococci (GAS) and occasionally by group C and gropup A [1]. Some of these infections are chronic[1 3]. Other causes of acute nephritic syndrome include Henoch Schönlein purpura, systemic lupus erythematosus, membranoproliferative glomerulonephritis (MPGN), acute interstitial nephritis (AIN), idiopathic crescentic glomerulonephritis /rapidly progressive glomerulonephritis (RPGN), IgA nephropathy, Alport's syndrome, Polyarteritis nodusa, Wegener's granulomatosis [1 7].

In Bangladesh 64% of the population are below 19 years of age and more than 75% live in rural areas [3]. In resource poor communities the prevalence of scabies is about 10 % in the general population[4]. Scabies is common in children and this neglected disease can be prevented by improving hygiene.Studies show strong association of streptococcal skin infection and scabies. Scabies should be treated as it predisposes to secondary skin infection a fore bringer of ASPGN and its complication. Complications like end stage renal disease (ESRD) arising from ASPGN has huge financial cost involvent for the family[3]. Now, the discussion will concentrate on APSGN.

Acute Poststreptococcal Glomerulonephritis (APSGN)

Epidemiology and etiology

APSGN is more common in the developing countries than developed countries because of overcrowding and bad hygiene[2]. APSGN typically follows either a pharyngeal or skin infection by nephritogenic strains of GAS[1]. Most common nephritogenic GAS serotypes in postpharyngeal APSGN are M type 1, 4, 12, 25. and in post skin infection APSGN are M type 2, 49, 57, 60[1]. M is protein found on outer portion of streptococcal cell wall[1]. GAS pharyngeal infections occur primarily in winter and spring, in temperate climate in contrast to GAS skin infection which are more common in the summer and autumn in tropical climate[2,6].

The incidence of APSGN following GAS infection range from 1 to 33%, with an average of 15%[4]. Clinically apparent glomerulonephritis is less than 2% and subclinical infections are 4 to 10 times more frequent than overt clinical disease [2,6]. Within families, the clinical attack rate may be as high as 40% and asymptomatic contacts of patients of APSGN may have microscopic hematuria[2,6]. Simultaneous occurrence of acute rheumatic fever and APSGN has been reported, but is extremely rare. Common scenario of school age (5 15 years) presenting with APSGN is changing, literature search shows age range 2-15 years, and 2% patients are younger than 2 years of age and 10% above 40 years age group[7]. Boys are more affected than girls, with ratio of 2:1[1,6]. Family studies have suggested genetic predisposition for APSGN, association of the disease with HLA DRA1 and DRW4, HLA DPB1 and higher incidence of disease in siblings and relatives [6,8].

Pathogenesis

The cross reactivity of streptococcal M protein antibody with glomerular basement membrane antigen because of antigenic similarity (molecular mimicry) is well established since long [6]. Trapping of circulating immune complex, in situ immune formation and direct activation of complement have been proposed [6]. Other protein molecules that are involved in the pathogenesis are endostreptosin, cationic proteins, streptococcal pyrogenic exotoxin B (SpeB), nephritis associated plasmin receptor (NAPlr) and streptokinase[1,6].

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Streptokinase involved in the spread of bacterium through tissue, M protein contribute to virulence and progression of glomerular injury[1,6]. Immune complex mediated inflammation leads to activation of complement, infiltration of polymorphonuclear leukocytes, monocytes and proliferation of endothelial and mesangial cells, expansion of mesangial matrix. Monocyte infiltration per glomerulus (MIG) correlates with severity of disease [9]. In a small proportion of cases, epithelial cell proliferation and crescents are seen which is associated with poor prognosis because crescents compresses the glomerulus which undergoes hyalinosis and become nonfunctional[2]. Immunofluorescence examination shows granular deposits of IgG and C_3 along capillary wall and mesangium. Inflamed glomerulus have reduced filtration rate or even enhanced sodium and fluid reabsorption from distal tubules [2].

Clinical presentation

Acute nephritic syndrome follows throat or skin infection after a latency period of 1-2 weeks to 3-6 weeks, respectively [6]. In some cases, pharyngitis may be mild and have gone unnoticed[2]. Active or healed impetigo may be present when APSGN develops[2] (Table II).

Urine is typically reddish brown or smoky or cola colored[2]. Anuria is infrequent, if persistent, suggests rapidly progressive Glomerulonephritis (RPGN)[2]. Edema is usually periorbital, apparent in the morning, but as the day progresses, edema localizes in the abdomen or lower extremities[2]. In younger children, edema is usually generalized, whereas in elderly child, it is limited to face and legs[2]. Edema can be severe with pleural effusion, pulmonary edema and ascites. Edema is turgid in contrast to flaccid edema of nephrotic syndrome [2.]

Hypertension (>95th centile for age and sex) can be associated with headaches, somnolence, changes in mental status, anorexia, nausea and convulsion. Some patients present with hypertensive emergency which is defined as blood pressure greater than 30% of normal or >99th centile for age and sex, or any elevation with evidence of encephalopathy or heart failure and shock[6].

Congestive cardiac failure present with dyspnea, cough, pulmonary cracks, cardiomegaly and gallop rhythm, wrongly diagnosed as pneumonia and myocarditis[2,6].

Toxic effect and cerebral vasculitis produce central nervous system (CNS) symptoms apart from hypertension. Multiple bilateral supratentorial vasculitic infarcts are seen on magnetic resonance imaging (MRI) with severe neurological symptoms [6,10,11]. Other nonspecific symptoms include nausea, vomiting, malaise, anorexia, weakness, lumbar pain and abdominal discomfort [4,7]. APSGN can present atypically, can have subglottic edema and airway compression[2,3]. Recently some studies have shown APSGN and RPGN superimposing upon preexisting IgA[12]. There are reports of concurrent APSGN and HSP (Henoch Schonlein purpura) nephropathy [13].

Table-I

Causes of postinfectious glomerulonephritis[1 5]

Bacteria-*Staphylococcus aureus* (occult visceral abscess),*Staphylococcus epidermatidis* (shunt ephritis),*Pneumococcus* (pneumonia),*Hemophilus influenzae,Klebsiella,Salmonella typhi,*Bacterial endocarditis (*S. aureus*, *S. epidermatidis* and gram negative bacteria), *Mycoplasma pneumoniae, Mycobacterium tuberculosis, Brucella,* Syphilis, Cornebacterium, *Escherichia coli,* Campylobacter
Viruses-Hepatitis B and C,Herpes viruses, Herpes simplex, Varicella zoster, Ebstein Barr virus, Cytomegalovirus, Mumps, Measles (Rubeola), Rubella, Influenza, Echovirus,Parvovirus B 19, Human immunodeficiency virus
Parasites- Malaria,Filariasis,Leishmaniasis,Schistosomiasis,Trypanosomiasis,Toxoplasmosis, Trichinosis,
Fungi-*Candida albicans,* Aspergillus,Cryptococcus,*Pneumocytis carinii*,Histoplasmosis,Nocardia

Table-II

Clinical features of APSGN[2]

Clinical features	Percent
Hematuria	100
Proteinuria (mild to moderate)	80
Edema	90
Hypertension	60-80
Oliguria	10-50
Azotemia	25-40
Heart failure	<5
Nephrotic proteinuria	4

Diagnostic evaluation

Urinalysis reveals distorted crenated red blood cells (>5/ HPF), RBC casts and neutrophil. Presence of neutrophil does not mean infection[2]. Hyaline and granular casts are also seen at times. Proteinuria is usually mild (1+ to 2+ equivalent to 30 100 g/day). Nephrotic range proteinuria (>1 g/m^2/day) seen in 4-10% of patients and may last up to 6 months [4,7]. Early morning spot urinary protein:creatinine ratio is simpler[1]. Specific gravity of urine is more than 1020 mosmol/L[7]. Blood count may show polymorphonuclear leukocytosis with normal ESR. Anemia due to hemodilution may be noted[2].

Serum creatinine, blood urea nitrogen (BUN) and blood urea may be elevated transiently [6]. Repeated measurement of antistreptolysin titer (ASOT), antinicotinamide adenine dinucleotides show elevated titers in 80% of postpharyngitis APSGN and antihyaluronidase, antideoxyribonuclease B titers are elevated in 80 90% of postpyoderma APSGN [6]. IgG antibodies against the C region of streptococcal M protein have been claimed to be more reliable diagnostic marker for APSGN because they remain elevated for long time[14].

A group of workers felt that streptozyme test is of low sensitivity and low specificity and not recommended for routine use[2]. Anti streptolysin O titre (ASOT) is found raised in 16-18% of healthy children; it is less reliable in postpyoderma APSGN due to its lipid binding in skin[1]. ASOT begin to rise 1-3 weeks after streptococcal infection, reaches peak by 3-5 weeks and then fall to insignificant level in 8 months[2,7]. Approximately 90% patients have decreased C_3 that returns to normal in 6 8 weeks[2,7]. C_4 is usually normal. Persistent hypocomplementemia suggests (a) lupus nephritis, (b) shunt nephritis, (c) membrananonproliferative glomerulonephritis, (d) glomerulonephritis due to bacterial endocarditis, and (e) hepatitis B, C and HIV glomerulopathy[1]. In 90% cases, hemolytic complement (CH50) is also decreased[1]. Electrolytes are to be checked, usual changes are hyponatremia, hyperkalemia and metabolic acidosis[1]. Plasma proteins, calcium and phosphorous status occasionally helpful to exclude chronic glomerular disease[1].

Antineutrophil cytoplasmic autoantibodies (ANCA) were detected inn 9% of APSGN with severe glomerular disease as assessed by raised serum creatinine and crescent formation[15]. Antinuclear antibodies (ANA) and anti dsDNA antibodies are to be checked to rule out SLE and polyarteritis nodosa (PAN) if clinically suspected. Anti GBM antibody can be done if good pasture's like features are found[1].

Chest X ray and ECG in dyspneic child, ultrasonography and CT scan of abdomen to detect occult visceral abscess and CT scan/MRI of brain in patients with encephalopathy are helpful [3,6].

Renal biopsy is not indicated in typical presentation and uneventful recovery [1,6], but it is indicated in (a) anuria with progressively raised serum creatinine, that means rapidly progressive glomerulonephritis (RPGN), (b) mixed nephrotic presentation when membranoproliferative glomerulonephritis is likely underlying cause, (c) systemic features like arthralgia, rash, fever, suggesting SLE, HSP and other vasculitis, (d) delayed resolution, e.g. oliguria, azotemia >2 weeks, gross hematuria >4 weeks, microscopic hematuria >1 year, and low C_3 >3 months, (e) absence of clinical and serological evidence of APSGN[1,6].

Treatment

Uncomplicated mild cases can be treated in home[2]. Patients should be hospitalized if severe hypertension and complications like cardiac failure, renal failure, encephalopathy and severe dyselectrolytemia are present[2]. Salt and fluid should be restricted. Salt restriction means no added salt in food[1]. Fluid restriction means daily intake of 400 ml/m^2/day plus half to full of the previous 24 hour output[1].Intake output chart should be maintained[1].

Edema should be controlled with loop diuretic, e.g. frusemide at 1-2 mg/day dose, in severe cases 4-6 mg/kg IV slowly can be given[2]. Potassium sparing diuretics are generally not used because of risk of hyperkalemia[7].

Hypertension should be controlled with calcium channel blocker, loop diuretic and vasodilator[1-7].Nifedipine (0.25 mg/kg/day) and amlodipine (0.05 2 mg/kg/day), prazosin (50 100 mg/kg/day), nitroprusside are the drugs prescribed usually[2,7,] ß adrenergic blockers along with diuretics can be used in patients without heart failure[2]. Angiotensin converting enzyme inhibitors are not recommended because they can cause hyperkalemia [5.]

In hypertensive emergency, sublingual nifedipine, IV nicardipine IV (1 3 mg/kg/min IV infusion), labetalol (0.1 0.5 mg/kg slow IV) or diazoxide (0.25 0.5 mg/kg) should be used [6].

Hyperkalemia is treated with restriction of potassium containing foods, nebulized salbutamol, resin and dialysis [6]. Congestive cardiac failure is treated in conventional way, digitalis is said to be ineffective[7].

Dialysis or bloodless plebotomy can be used to treat unresponsive pulmonary edema, acute renal failure and hyperkalemia. Patient with RPGN should undergo biopsy and six pulses of IV methylprednisolone (30 mg/kg/day in 100 ml IV fluid)[6]. Early intervention gives better outcome in RPGN. Intubation and patent airway needed in encephalopathy along with other measures[3]. Penicillin or erythromycin eradicates residual GAS but does not influence the coarse or severity of the disease[1.] It is indicated in active pharyngitis, pyoderma and all contact risk group[2].

Prevention

Early treatment of sore throat and skin infection may prevent the occurrence of disease[1,6]. Prophylactic penicillin or erythromycin to contact risk group is helpful [1,6]. Some advocate oral penicillin for 10 days and few suggest single dose of intramuscular benzathine penicillin. [2,5,16].

Treatment of scabies with 5%permethrin is essential. Regular bath and washing cloth can prevent pyoderma [16].

Course and prognosis

Overall prognosis is good. About 95-97% have an uneventful recovery, less than 1% have early mortality[3 7]. Acute phase begins to resolve in 1st week and completes by 6 8 weeks[2]. Earlier research finding had not seen any evidence of regression to chronic glomerulonephritis after 12 years follow up[17].

Recent research documents overall prognosis to chronic kidney disease (CKD) at 2-10% in children and as high as 30% in adult [7]. 1-2% reaches end stage renal disease (ESRD), 20% can have persistent urine abnormalities or reduced GFR, and 8-13% have proteinuria and hypertension [6,14]. One attack of APSGN confers lifelong immunity and recurrence is low (0.7 7%)[2,6]. Anti NAPlr antibodies are protective against second attack of APSGN [6].Researchers believe that frequent APSGN is a predisposing factor for ESRD among poor Australian Aboriginals[18] .

Recommendations

APSGN patients are to be followed for 1-2 years[7]. Urinalysis at 2, 4 and 6 weeks and at 4, 6 and 12 months is indicated [7] . Cessation of follow up care when urinalysis is normal. Blood pressure, anthropometry are to be checked in each visit [7] . Serum creatinine and hemoglobin are to be monitored at 2, 6 and 12 months [7] .Research directed towards burden of PSGN and its complications in Bangladeshi children is important as prevalence of scabies, skin infection is common. Sustainable and long-term improvements in treatment of scabies, skin sores and infections like sore throat require fundamental changes that should address social and economic inequities and, in particular, living conditions and overcrowding.

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Pancreas Transplantation in Diabetes Mellitus Patients: Complications and Options for Treatment

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Abstract

Affecting millions of people worldwide, diabetes mellitus is major health problem. Amongst others, diabetic retinopathy, nephropathy, neuropathy and vasculopathy are a few mentioned complications. cell replacement therapy with pancreas or islet transplantation and intensive insulin therapy has been demonstrated to normalize HbA1C levels and thereby shown to slow down secondary complications associated with diabetes. Today pancreas transplant is considered to be the preferred treatment for selected patients with type l diabetes. Globally, more than 23,000 whole organ pancreas transplants have been performed either as simultaneous pancreaskidney or isolated pancreas. Both short term and long-term patient and graft survival have significantly improved primarily due to improvement in surgical techniques and better monitoring for rejection. Similar successes have also been reported with living donor pancreas transplants and islet cell transplantations.

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Introduction

Diabetes Mellitus (DM) is a major health problem worldwide, which affects 18.2 million individuals (6.3% of the population) in the US. Currently, the prevalence of Type 1 DM in the US is estimated to be 1,000,000 individuals, and 30,000 new cases are diagnosed each year. In addition to end stage renal disease (ESRD), DM is associated with blindness, accelerated atherosclerosis, dyslipidemia, cardio- and cerebro-vascular disease, amputation, poor quality of life, and overall life-span reduction. It accounts for more than 160,000 deaths per year in the US alone.[1,2] In 2002, the annual national direct and indirect costs of Type 1 and 2 DM exceeded $130 billion, which included hospital and physician care, laboratory tests, pharmaceutical products and patient workdays lost because of disability or premature death. From 1990 to 2001, the number of existing ESRD cases to DM increased by more than 300 per cent, while the rate per million populations increased from 167 percent to 491. The number is expected to grow ten-fold by 2030 to 1.3 million accounting for 60% of ESRD population. To date, DM is the leading indication for transplantation and is the cause of ESRD in more than 40% of transplant recipients each year.[3]

Prior to 1922, a patient diagnosed with Type 1 DM had an average life expectancy of only two years. The success of insulin, however, changed DM from a rapidly fatal condition to a chronic incurable illness, revealing the long term complications associated with Type 1 DM (e.g. neuropathy, vasculopathy, retinopathy and nephropathy) in survivors 10 to 20 years after the disease is onset. The treatments that have been demonstrated to influence the progression of secondary complications of DM (by normalizing or near normalizing HbAlC levels) are cell replacement therapy with pancreas or islet transplantation and intensive insulin therapy. Pancreas transplantation is superior to intensive insulin therapy with regard to normalization of HbA1C and has the added physiological properties of pro-insulin and C-peptide release.4,5 It has been shown to reverse the diabetic changes in the native kidneys of patients with very early diabetic nephropathy, prevent recurrent diabetic nephropathy in patients undergoing a simultaneous pancreas-kidney (SPK) transplant, reverse peripheral sensory neuropathy, stabilize advanced diabetic retinopathy, and significantly improve the quality of life. Similar glycemic control can also be achieved through islet cell transplantation, which has recently gaining popularity.

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Pancreas Transplantation

After decades of controversy surrounding the therapeutic validity of pancreas transplantation, the procedure has become accepted as the preferred treatment for select patients with Type l DM mellitus. Tradeoffs include for normal glucose homeostasis is the operative risks of the pancreas transplantation procedure and the need for chronic immunosuppression.

In 1996, Lillehei and colleagues (University of Minnesota) pioneered the first vascularized pancreas transplantation.6

The major surgical problem to be overcome was appropriate exocrine drainage of the transplanted pancreas. Fortunately, with introduction of the bladder drainage technique, further improvement in surgical techniques, and better monitoring for rejection has resulted in a significant increase in patient and graft survival. There are three circumstances where consideration for pancreas transplantation is reasonable: i) for select medically suitable patients with Type l DM who are also excellent candidates for kidney transplantation (SPK), ii) for patients with Type 1 DM who enjoy good function of a kidney transplant and are receiving immunosuppression (pancreas after kidney transplant - PAK), and iii) for select patients with Type 1 DM who have well preserved native renal function but suffer from the severity of hypoglycemic unawareness (pancreas transplant alone - PTA). The most common type of pancreas transplantation is a SPK, which is followed by isolated pancreas transplantation (PAK and PTA). Living donor pancreas transplantation has also been performed. Living donor pancreas transplantation has a decreased incidence of rejection, but the technical failure rate is similar to that of deceased donor transplantations. The International Pancreas Transplant Registry (IPTR) organized in 1980, provides historical and current data on clinical pancreas transplantation. From December 1966 to December 2004, more than 17,000 pancreas transplants performed in the United States and 6,000 abroad.[7] The number of SPK transplants has remained static since 1995, but the waiting list has doubled in size. In 2004, a total of 87, 284 patients were wait listed to receive an organ transplant - on these 1644 for isolated pancreas transplant (PTA and PAK transplant) and 2,441 SPK. From January 1988 to October 2004, of the 16,090 pancreas transplants performed in the US, the majority of the cases, 75% (n=12, 053) have been SDKs; while 25% (n=4037) have been isolated pancreas (PAK and PTA) transplants.

Patient Selection

Diabetic retinopathy is a nearly ubiquitous finding in patients with DM and is not an absolute contraindication to transplantation. Advanced coronary artery disease (CAD) is the most important co-morbidity to consider in patients with Type 1 DM - particularly those with diabetic nephropathy. Uremicdiabetic patients carry an estimated 50-fold greater risk of cardiovascular events than the general population. The prevalence of significant (> 50% stenosis) CAD in patients with DM starting treatment for ESRD is estimated to be 45-55%.8 Uremic, diabetic patients also experience an increased rate of cerebral vascular accidents and transient ischemic attacks, which tend to occur at a younger age. The extent of diabetic autonomic neuropathy manifests itself as gastropathy, bladder dysfunction, and orthostatic hypotension. Patients may have difficulty tolerating the oral immunosuppressive medications, high post void residuals, and hypotension respectively. Figure 1 illustrates an example of an algorithm for screening diabetic transplant candidates for CAD. Noninvasive screening that has high sensitivity and specificity for significant CAD can be used on low risk patients. Patients considered to be at moderate or high risk for significant CAD should undergo coronary angiography. Patients that have experienced long waiting

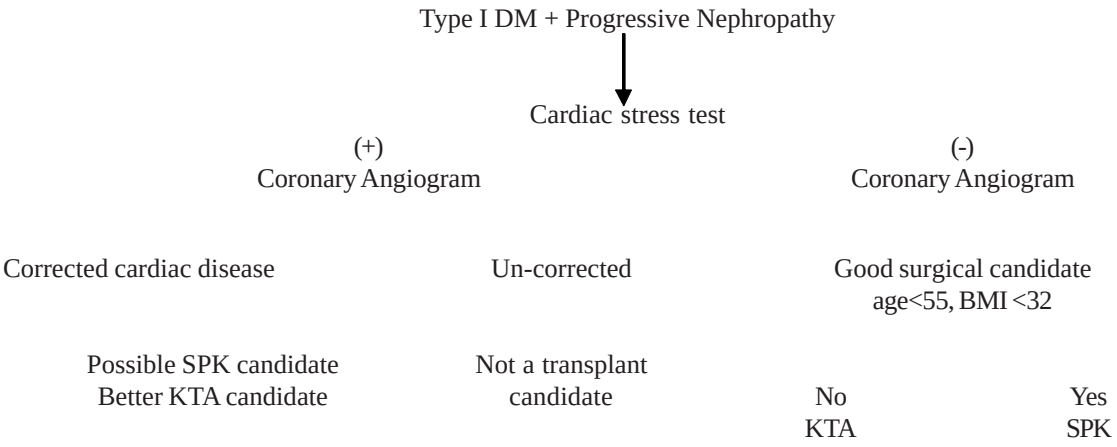

Fig.-1: *Options for potential kidney-pancreas recipients**
*modified from reference no 9

periods prior to pancreas transplantation should have their cardiac status assessed at regular intervals. The indications and contraindications for pancreas transplantation and eligibility guidelines are listed in table 1 and 2.[10]

Transplant Surgery and Surgical Complications

The pre-operative pancreas transplant care includes re-evaluation of the surgical candidacy of the recipients, careful management of pre-transplant blood sugar and a bowel preparation when time permits are important considerations. Cadaveric pancreas organ donors are typically between the ages of 10 and 55 years (table 3).[11] Obese donors with BMI >30 kg/m2 often not found to be suitable pancreas donors because of increase association of type 2 DM and higher degree of fatty infiltration. While, young and small (<30kg body weight) donors typically reflect the anticipated small size of the splenic artery precluding successful construction of the arterial Y-graft needed for allograft re-vascularization.[12,13] Hyperglycemia and hyperamylasemia are very frequently observed in cadaveric organ donors and has not been found to have any meaningful influence on post-transplant pancreas graft function. The important vascular anomaly that must be evaluated during procurement is the occurrence of a replaced or accessory right hepatic artery originating from the superior mesenteric artery (SMA). The use of marginal and non-heart beating donors for pancreas alone transplantation is selective and is made on a caseby- case basis. The hemodynamic stability and need for inotropic support are important considerations of the effect of delayed kidney graft function (DGF) in the SPK candidate. In preparation, the pancreatico-duodeno-splenic allograft is placed in chilled University Wisconsin preservation solution. The duodenum is opened, drained and irrigated into a separate container and the spleen is separated from the pancreas tail. Next, the common bile duct is cannulated and the proximal and distal duodenum are shortened appropriately. The middle colic vessels are secured and a Y-graft is constructed utilizing the donor iliac artery bifurcation graft as end-to-end anastomosis on the splenic artery and- SMA of the pancreas allograft. The portal vein is carefully mobilized to allow for appropriate length. Pancreas graft arterial revascularization is typically accomplished utilizing the recipient right common or external iliac artery. The Y-graft of the pancreas is anastomosed end-to-side and the head of the pancreas graft is positioned either cephalad or caudad. There are two choices for venous revascularization- systemic and portal. Systemic venous revascularization commonly involves the right common iliac vein, or right external iliac vein. In case of portal venous drainage, the superior mesenteric vein (SMV) and the pancreas portal vein is anastomosed end-to-side. Portal venous drainage of the pancreas is more physiologic with respect to immediate delivery of insulin to the recipient liver.[14,15]

Table I

*Indications for pancreas transplantation and eligibility guidelines**

- Presence of insulin requiring DM
  - * Documentation of insulin dose
  - * Low C-peptide levels (value)
- Ability to understand the procedure
- Willingness to follow post-transplantation guidelines and management
- Ability to withstand surgery and immunosuppression
  - * Adequate cardiopulmonary function
  - * Cardiac stress testing, with or without coronary angiography
- Presence of well-defined diabetic complications (any two)
  - * Proliferative retinopathy
  - * Symptomatic peripheral or autonomic neuropathy
  - * Microangiopathy
  - * Accelerated atherosclerosis (macroangiopathy)
  - * Glucose hyperlability, insulin resistance, or hypoglycemic unawareness
  - * Emotional and psychosocial suitability
- PAK transplant: Creatinine clearance >40 ml/min (with Calcineurin inhibitor) >50 ml/min (without Calcineurin inhibitor)
- SPK transplant: Creatinine clearance <50ml/min

* modified from reference no 10

Pancreatic exocrine drainage is handled via anastomosis of the duodenal segment to the bladder or anastomosis to the small intestine. Enteric drainage of the pancreas allograft is physiologic with respect to the delivery of pancreatic enzymes and bicarbonate into the intestines for reabsorption. The bladderdrained pancreas transplant was a very important modification and improved the safety of the enteric-drained pancreas grafts by minimizing the occurrence of intra-abdominal abscess. For portally drained pancreas transplants, bladder drainage is not an option. For recipients of a SPK transplant, enteric drainage is the technique of choice. In the cases of PAK and PTA, bladder drainage has two important advantages: i) urinary amylase monitoring for rejection and ii) placement of the graft allowing access for percutaneous biopsy for

diagnosis of rejection. When the pancreas transplant is performed simultaneously with a kidney transplant, both organs may be transplanted through a midline incision and placed intraperitoneal. Currently, approximately 75% of pancreas transplants in SPK recipients are performed with enteric drainage and the remainder with bladder drainage. Enteric drainage in the PAK and PTA recipient is performed in approximately 50% of cases. There is no conclusive evidence that portal venous drainage offers any advantage over systemic venous drainage of the pancreas allograft.

Table II

*Absolute and relative contraindications for pancreas transplantation**

A. Absolute contraindications

- Inability to provide informed consent
- Insufficient cardiovascular reserve
- Significant uncorrectable or untreatable coronary artery vdisease
- Recent myocardial infarction
- Poor ejection fraction
- Malignancy within the previous 2 to 3 year (excluding nonmelanoma skin cancer)
- Active infection
- Positive serology: Human Immunodeficiency Virus (HIV), hepatitis B surface antigen
- Active, untreated, peptic ulcer disease
- Ongoing substance abuse (drug or alcohol)
- Major ongoing psychiatric illness
- Systemic illness severely limiting life expectancy or compromised recovery
- Irreversible, hepatic or pulmonary dysfunction
- Positive cross match

B. Relative contraindications

- Age >55 years
- Extreme obesity (>150% of ideal body weight or body mass index (BMI) of > 32 kg/m2)
- Myocardial infarction, congestive heart failure, previous open heart surgery, or cardiac intervention
- Recent retinal hemorrhage
- Major amputation or peripheral bypass graft
- Cerebrovascular event or carotid endarterectomy
- Symptomatic cerebro-vascular or peripheral vascular disease
- Severe aorto-iliac vascular disease
- Hypercoagulable syndrome
- Compromised social support network
- Active smoking

*modified from reference no 10

Post-Operative Monitoring

Nasogastric tube decompression is usually maintained for 2 to 3 days, and urethral catheter drainage for 3 to 7 days (SPK recipients). Patients are serially monitored for daily fasting serum glucose, amylase, lipase renal profiles, drug levels and complete blood counts. The hormonal profiles are usually assessed by intravenous glucose tolerance tests, fasting and stimulated Cpeptide levels, lipid profiles, and HbA1C.

Complications of Pancreas Transplantation

Surgical complications are more common after pancreas transplantation compared to kidney transplantation. Non-immunologic complications of pancreas transplantation accounts for graft losses in 5-10% of cases. These occur commonly within 6 months of transplant and are important etiologies of pancreas graft loss. The different early post-transplant complications are listed in table 4, figure 2.[16]

1. Thrombosis

Approximately 3-5% of pancreas grafts will need to be removed because of portal venous thrombosis. To minimize graft thrombosis, prudent selection of donor pancreas grafts, short cold ischemia times, and meticulous surgical technique are necessary. There is no standard anti- coagulation protocol and patients are often given anti- platelet agents and/or heparin during the perioperative period.

2. Transplant Pancreatitis

A temporary and mild elevation in scrum amylase levels for 48-96 hours post-transplant is without clinical significance. Interestingly, pancreatitis is more prevalent in patients receiving a SPK transplant (compared to PAK, PTA) and is felt to be due to a greater degree of fluid retention for several days following transplant.

3. Complications of the Bladder-Drained Pancreas Transplant

Change in pH of the bladder due to drainage of bicarbonate rich fluid accounts in part for a greater increase in urinary tract infections. In some cases, a foreign body such as an exposed suture from the duodeno-cystotorny acts as a nidus for urinary tract infections or stone formation. Acute postoperative hematuria of the bladder-drained pancreas is usually due to ischemia/reperfusion injury to the duodenal mucosa or to a bleeding vessel on the suture line may be aggravated by the antiplatelet or anti-coagulation. These cases are self-limited but may require cystoscopy to evacuate the clots and/or surgical exploration of the bladder. Cystitis, urethritis and balanitis are usually managed conservatively. Urine leak from breakdown of duodenal segment is a serious complication, which usually occurs within the first 1-3 months post-transplant. Abdominal pain with elevated serum amylase, mimicking reflux pancreatitis or acute rejection, is a typical presentation. Operative repair is usually required with reexploration.

Table III

*Indications, Contraindications and risk factors to be considered during procurement of pancreas for transplantation**

Indications

- Declaration of brain death
- Informed consent
- Age of 10 to 55 year (ideal, 10 to 40 year)
- Weight of 30 to 100 kg (ideal, 30 to 80 kg)
- Homodynamic stability, with adequate perfusion and oxygenation
- Absence of infectious or transmissible diseases (i.e. tuberculosis, syphilis)
- Negative serologic findings (HIV and hepatitis B and C)
- Absence of malignancy (except skin or low grade brain cancer)
- Absence of parenchymal/intrinsic pancreatic disease

Contraindications

- History of Diabetic mellitus (type I, type 2, or gestational)
- Previous pancreatic surgery
- Moderate to severe pancreatic trauma
- Pancreatitis (active, acute or chronic)
- Significant intra-abdominal contamination
- Major (active) infection
- Chronic alcohol abuse
- Recent history of intravenous drug abuse
- Recent history of high-risk sexual behavior
- Prolonged hypotension or hypoxemia with evidence of significant end-organ (kidney or liver) damage
- Severe atherosclerosis
- Inexperienced retrieval team
- Severe fatty infiltration of pancreatic parenchyma
- Severe pancreatic edema
- Severe obesity (>150% of ideal body weight or 13M1 of >30kg/m2)
- Risk Factors
- Massive transfusions
- Prior splenectomy
- Mild to moderate obesity (125 to 150% of IDW or BMI of >27.5kg/m2)
- Aberrant hepatic artery anatomic features
- Positive venereal disease research laboratory (VDRL)/ rapid protein reagin (RPR) serologic results
- Prolonged hospital stay
- Cardiovascular or cerebrovascular cause of brain death
- Donor instability

*modified from reference no 11

Table IV

Causes of pancreas graft dysfunction

A. Rejection
B. Ductal obstruction
C. Vascular: Arterial/venous thrombosis (partial/complete) Arterial-venous fistula
D. Volume depletion
E. High calcineurin inhibitor levels
F. Graft pancreatitis (preservation, viral, bacterial, or fungal)
   - In cases of bladder drainage:
     o Reflux pancreatitis
     o Urinary tract infection
     o Anastomotic leak
     o Bladder outflow obstruction
   - In cases of enteric drainage
     o Anastomotic leak
     o Bowel obstruction

4. Complications of the Enteric-Drained Pancreas Transplant

The most serious complication of the enteric-drained pancreas transplant includes enteric leak and intra-abdominal abscess, which usually occurs 1-6 months post-transplant. Patient usually present with lever, abdominal discomfort and leukocytosis. Surgical exploration and repair of the enteric leak is frequently necessary. Incomplete eradication of the infection will result in progression to sepsis and multiple organ system failure. Peripancreatic infections can result in serious arterial rupture and transplant pancreatectomy is indicated if mycotic aneurysm is diagnosed. Gastro-intestinal bleeding occurs after the entericdrained pancreas from a combination of perioperative anticoagulation and bleeding from the suture line of the duodenoenteric anastomosis. Conservative management is usually recommended.

Immunosuppression for Pancreas Transplantation

Due to greater immunogenicity, pancreas allograft rejection is much greater than that observed with kidney transplantation. The majority of pancreas transplant programs are using induction therapy combined with microemulsion cyclosporine or tacrolimus plus mycophenolate mofetil or sirolimus and prednisone. With this combination the incidence of acute rejection has been reduced by more than half.[17] There are steroid avoidance protocols described for pancreas transplantation and reports of successful steroid withdrawal.

Pancreas Allograft Rejection

Destruction of the islet cells occurs relatively late and the diagnosis of pancreas graft rejection by hyperglycemia is

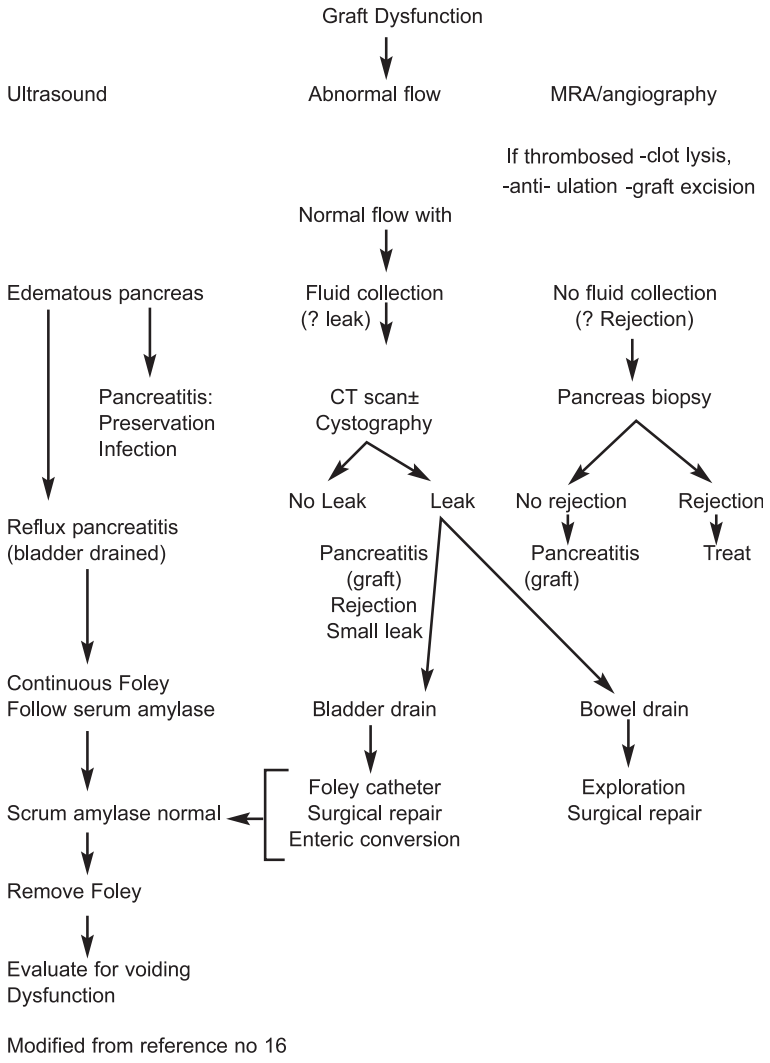

Fig-2 : *Suggested work-up for allograft pancreas dysfunction*
*modified from reference no 16

a late and often irreversible situation. The graft is usually inflamed and patients experience fever, pain and discomfort around the graft due to peritoneal irritation. This coupled with elevation in the serum amylase or lipase and if bladder-drained, reduction in urinary amylase may be the initial presentation of acute rejection.[18] Increasing serum amylase and-lipase levels suggest possible rejection but exhibit poor sensitivity and specificity for diagnosis. Levels of other serum markers, such as human anodat trypsinogen, pancreatitis associated protein, pancreas specific protein and pancreatic secretory trypsin inhibitor, become

elevated during rejection of pancreas allograft but such assays are not widely available The diagnostic sensitivity of Doppler ultrasonography, nuclear imaging with technetium-99-sestamibi, indium labeled platelets and magnetic resonance angiography for the diagnosis of rejection is poor and not well established. The diagnostics tests for pancreas allograft rejections are listed in table 5. The gold standard for confirming the diagnosis of pancreas graft rejection is pancreas graft biopsy. The biopsy may be performed by several methods including the percutaneous approach, trans-cystoscopic biopsy in a bladder-drained pancreas, or open surgical biopsy. The histologic features of acute pancreas graft rejection are listed in table 6.19 In the situation of a SPK transplant, it is the kidney allograft that is the best indicator of a rejection reaction. Although extremely uncommon in SPK transplant, isolated pancreas allograft rejection may occur in 1- 2•% of cases and the diagnosis is made by biopsies of both allografts. The success rates for reversing pancreas allograft rejection are very high in excess of 90% if diagnosed promptly. With the application of newer

immunosuppressive agents, the incidence of pancreas rejection has been reduced from approximately 80% to less than 30%.

Immunosuppression

Induction Therapy

No Federal Drug Administration (FDA)-approved immunosuppressive agents are on the market with a labeled indication of reducing rejection rates specifically for pancreas transplant recipients. Nonetheless, in 2001, 78% of solitary pancreas (PAK and PTA) transplant recipients and over 75% of SPK transplant recipients received induction therapy. By comparison recipients of other solid-organ transplants received induction therapy in 2001 in the following proportions: 59% (kidney), 15% (liver), 44% (heart), 50% (intestine), 39% (lung), and 76% (heart-lung).20 In an attempt to reduce acute pancreas allograft rejection most pancreas transplant centers employ a quadruple immunosuppressive regimen consisting of an anti-T lymphocyte agent, a calcineurin inhibitor, an anti-proliferative agent and corticosteroids. Despite favorable outcomes in SPK transplant patients treated with tacrolimus and mycophenolate mofetil (MMF) with or without induction, most centers are reluctant to eliminate induction therapy entirely because of long-term negative effect of acute rejection on graft survival.

Table V

Diagnostic tests for pancreatic allograft rejection

A. Noninvasive
• Doppler ultrasonography
• Nuclear technetium-99-sestamibi scintigraphy
• Uptake of indium labeled platelets
• Magnetic resonance angiography
B. Bio-chemical
• Hyperamylasemia, Hyperlipasemia, Hyperglycemia
• Decreased rate of glucose disappearance during intravenous glucose tolerance testing,
• Decreased insulin release after intravenous glucose or glucagon
• Decreased urinary amylase (in bladder drained patients)
• Decreased urine pH (in bladder drained patients)
• Increased serum trypsin or anodal trypsinogen
• Increased levels pancreatitis associated protein
• Increased levels pancreas associated protein
• Increases levels of pancreatic secretory trypsin inhibitor
C. Invasive
• Fine needle aspiration
• Biopsy: Percutaneous - image guided biopsy
• Cystoscopic biopsy of the pancreas or duodenal cuff (in bladder drained patients)

Table VI

*Classification of pancreas allograft rejection- grade features**

0	Normal
1	Inflammation of undetermined significance, with septal mononuclear infiltrates and the absence of venous or acinal involvement
2	Minimal rejection, with septal inflammation and venous endotheliolitis; in the absence of venous endotheliolitis, at least three of the following features also define grade II rejection: 1) septal inflammatory infiltrates with a mixed lymphocyte appearance (large activated and small lymphocytes)
3	Mild rejection, with septal inflammation consisting of a mixed population and acinar inflammation in at least three foci and with eosinophils, venous endotheliolitis, ductal inflammation, and acinar single-cell injury as a byproduct of sampling error; the latter is present as cellular apoptosis or necrosis
4	Moderate rejection, with arterial endotheliolitis and/ or necrotizing vasculitis, usually with features of grade III rejection as well
5	Severe rejection, with extensive acinar lymphoid or mixed inflammatory infiltrates, with multicellular foci or confluent acinar necrosis

*modified from reference no 19

Thymoglobulin (RATG; Genzyme, Cambridge, MA) significantly lowered the incidence of acute rejection rate in the first 6 months when compared with muromonab-CD3 (OKT3, Ortho. Cilag, NJ) and monoclonal antibody against IL-2 receptor (daclizumab, Hoffman-LaRoche, Basel, Switzerland; basiliximab, Novartis Pharmaceuticals, Basel, Switzerland) (7.7 vs 60 vs 50%).21 Similarly, others have reported their experience with induction immunosuppression using monoclonal antibody against IL-2 receptor.

From 1992-1997, virtually all cases of induction therapy involved the use of either muromonab-CD3 or Anti-thymocyte globulin. Between 1998 and 2001, basiliximab use rose from 7% to 32%, daclizumab use rose from 15% to 21%, and RATG use rose from 0.4% to 29%.[20]

Maintenance Therapy in Pancreas Transplantation

Maintenance immunosuppressive agents used for pancreas transplantation fall into the following categories: (a) corticosteroids, (b) calcineurin inhibitors (cyclosporine and tacrolimus), (c) antimetabolites (azathioprine and

MMF) and (d) other (rapamycin and cytoxan). In 2001, solitary pancreas recipients received corticosteroids in 93% of cases, tacrolimus in 91% (cyclosporine 8%), MMF in 74% (azathioprine 1%) and rapamycinin 19%. Therefore, in 2001 the most frequently used combination of maintenance therapy at discharge was tacrolimus,

MMF and corticosteroids.[20]

The dominant use of tacrolimus today represents a marked shift from earlier eras. In 1992-93 cyclosporine accounted for virtually 100% oil' the calcineurin inhibitor use in pancreas transplantation. In 2001, 92% of SPK transplant recipients received corticosteroids, 86% tacrolimus (14% cyclosporine), 82% mycophenolate mofetil, and 19% rapamycin. Based on these data, one can extrapolate that the most common maintenance immunosuppressive regimen used in SPK transplant recipients included corticosteroids, tacrolimus and MMF.

Elimination of steroid from maintenance immuno-suppressive therapy has been reported recently.

Acute Anti-rejection Treatment

In 2000, the use of corticosteroids was the most frequently employed anti-rejection agent in PAK and PTA transplant recipients (85%) and SPK transplant recipients (80%). In 2000, recipients of a PAK and PTA transplant received T-cell depleting agents in 80% of cases; the specific agents used were either muromonab-CD3 (45%) or RATG (34%). For recipients of SPK transplants, T-cell depleting agents were given in 48% of cases; the - two most frequently used T-cell depleting agents were muromonab-CD3 (27%) and RATG (17%). Compared to kidney transplant recipients, pancreas transplant recipients received more treatments with T-cell depleting agents for treatment of rejection. In 2000, kidney alone transplant recipients received a T-cell depleting agent in 38% of cases.

Antimicrobial Prophylaxis

Trimethoprim-sulfamethoxazole is given for the prevention of urinary tract infections and for pneumocystis, legionella, toxoplasma and nocardia species. It is usually given for at least 6 months following transplantation but may be administered for the lifetime of the allograft. Clotrimazole troches used orally, nystatin swish and swallow, or fluconazole are administered for the prevention of oral candidiasis, candidal urinary tract infections, and intra-abdominal fungal or yeast infection. Oral acyclovir is given to patients with history of herpes simplex infection. Valganeiclovir or Ganciclovir is given to all patients for 3-6 months following transplantation or for 3 months after treating rejection with antilymphocyte antibodies, for prevention of cytomegalovirus disease.[16]

Long-Term Outcomes and Causes of Death in Pancreas Transplants

Recurrence of Diabetes

Type 1 diabetes can recur in cadaveric pancreas allograft. This has been characterized by the recurrence of islet cell antibodies as well as antibodies directed against glutamic acid decarboxylase. Some of the reports of recurrence of type IDM commented that several of the patients were on either extremely low amounts of immunosuppression or had stopped their drugs.

Regardless of the cause, increased immunosuppression may halt the islet cell destruction. Type 2 DM can also occur in the pancreas transplant recipient. Smith et al clearly demonstrated normal to elevated C-peptide levels in pancreas transplant patients with hyperglycemia with intravenous glucose tolerance tests characteristics of a type 2 diabetic.[22] The type 2 DM may be secondary to exogenous weight gain or to the toxic effects of tacrolimus on islet cells.

PTA on Native Renal Function

One of the rationales for performing PTA has been protection of renal function in the patient with incipient diabetic nephropathy. Fioretto et al reported on 8 patients who underwent PTA and were studied with pretransplant kidney biopsies followed by biopsies at 5 and 10 years post transplant.23 All patients demonstrated reversal of diabetic nephropathy but this was not evident until at least 5 years of normoglycemia. These 8 patients started with an average creatinine clearance of 108 + 20 ml/min. Despite the normalization of the biopsies, the average creatinine clearance at 10 years was 74 ± 14 ml/min. This underscores the potential long-term toxicity of calcineurin inhibitors and the need for long-term follow-up. Furthermore, baseline renal function may be important in selecting patients for PTA.A recent paper from the Mayo Clinic demonstrated a decline in native glomerular filtration rate (GFR) from 82 ± 33 ml/min to 52 ± 26 ml/min in 23 recipients of BD PTA recipients.[24] It is unclear whether the decline was due to immunosuppressive drug therapy, volume contraction and acidosis due to BD, or a combination of both. Patients with lower GFR at the time of transplant had a greater decline of GFR.

Cardiovascular Disease after Pancreas Transplantation

According to the American Heart Association, DM is a major independent risk factor for cardiovascular disease

(CVD). The prevalence, incidence and mortality of all forms of CVD are 2 to 8 fold higher in diabetics. Nearly half of all pancreases transplant recipient deaths in national and single center reports are caused by complications of CVD.

In an interesting study, Fiorina et al showed changes in atherosclerotic risk factors in SPK recipients that may favorably influence coronary artery disease long-term.25 SPK patients demonstrated significantly lower levels of triglycerides, homocysteine and von Willebrand factor when compared to kidney-alone recipients. Jukema et al performed an observational angiographic study determining progression of coronary artery lesions in patients with and without functioning pancreas transplants.26 Mean follow-up was 3.9 years. 38% of the functioning pancreas group had regression of coronary artery atherosclerosis compared to none in the non-functioning pancreas group (p=0.035). Clinically, LaRocca et al described a lower incidence of acute myocardial infarction (AMI) in SPK compared to kidney-alone recipients (2.4% versus 17.6%, p = 0.005).27 There was a trend to fewer anginas in the SPK group (1.6% versus 8.82%, p 0.13). In a follow-up paper, the same group confirmed their previous findings in a larger cohort of patients with a significantly decreased incidence of AMI in the SPK group when compared to kidney-atone recipients (3% versus 20%, p = 0.01). No difference between the groups was found for angina.

Secchi et al noted a significant improvement in ejection fraction as measured by radionucleotide left ventriculography when comparing SPK to kidney-alone patients at four years (76.5%versus 64.3%, p = 0.003).28 This was later confirmed by the same group in 42 SPK and 26 kidney-alone recipients at four-year evaluation. Ejection fraction was significantly higher in the former group (p = 0.02). Less diastolic dysfunction was seen in the SPK group versus the kidney-alone recipients at four years ($p < 0.05$). Gaber et at confirmed these findings with 3-5 year follow-up in SPK patients.29 Kalker et al described a 19% incidence of amputation of the lower extremities at 5 years, without significant differences between SPK and kidney-alone patients.30 Morrissey et al found no difference in amputation rates between SPK and kidney-alone recipients with mean of 56 months follow-up.[31] Total peripheral vascular complications (amputation, ischemic ulcer, revascularization or failed bypass) were significantly less in the kidney-alone group (p = 0.005). Carotid disease appears to progress post-pancreas transplant.

Diabetic Retinopathy after Pancreas Transplantation

Diabetic retinopathy leading to blindness occurs 25 times more often in patients with diabetes than the general population. Available short-term studies have been uncontrolled and controlled with mixed results of the effect of pancreas transplant on eye disease. Ramsay et al did show a trend to greater stabilization of eye disease in pancreas recipients when compared to controls, but only beyond three years.[32] Longer follow-up data is available. Koznarova et al reported retinopathy outcome of 88 type 1 diabetic patients post-transplant (43 kidney-pancreas transplant versus 35 kidney transplant alone and 10 kidneypancreas transplant requiring removal of the pancreas early after the surgery).33 Follow-up of the two groups was 45 and 60 months respectively. At three years, visual acuity was significantly better in the functioning kidney-pancreas group. That same group had less macular edema, funduscopic progression, and need for laser therapy compared to the control group.

Diabetic Neuropathy after Pancreas Transplantation

Diabetic neuropathy is seen in more than 80% of type 1 diabetics with chronic kidney disease, stage 5. Lower extremity diabetic neuropathy is a strong predictor of foot ulcers and amputation. Early improvement of neuropathy post kidney-pancreas transplant may represent correction of uremic neuropathy. Navarro et al3,4 presented up to 10 years follow-up in a cohort of 115 type-1 diabetic patients post kidney-pancreas transplantation. Follow-up at intervals compared to a control group of transplant recipients with kidney only or failed pancreas transplant reveal significantly improved neurological scores and motor/sensory conduction indices at all periods. Improvement in the functioning pancreas transplant group was partial, and the patients did not achieve normal neurological testing even at 10 years. Tyden et al showed improved nerve conduction study (NCS) in recipients of kidney-pancreas transplants 8 years post surgery.35 Interestingly, no significant improvement developed between these patients and the control group of kidney only transplants until after 2 years. Autonomic dysfunction has also been assessed in long-term pancreas recipients. Autonomic indices were followed at intervals for up to 10 years after pancreas transplant in 115 patients and were significantly improved at all times. Similarly, parasympathetic autonomic dysfunction improved at 8 years post SPK in 14 patients and was significantly better than control group of kidney only recipients. Both autonomic function and NCS were significantly improved in the patients who lived 10 years as opposed to those that died.

Bone Disease after Pancreas Transplantation

Bone disease post SPK has many causes including common risks such as menopause in women, low testosterone in

men, and hyperparathyroidism. Early improvement in parathyroid hormone (PTH) levels post SPK is documented along with a decline in bone mass as measured by bone density. An increased risk of fractures can be seen early post SPK. Long-term studies (more than three years follow-up) in SPK found bone pathology and complications. Smets et al followed 31-type 1 diabetics post SPK with bladder drainage for a mean of 40±23 months.36 Osteoporosis was described in 25% and gender, age, cumulative glucocorticoid dose, PTH or GFR were not identified as risk factors. 45% of the patients developed fracture. Approximately half of the fractures were vertebral with only 16% in the feet. PTH was significantly higher in those patients with non-vertebral fractures compared to those without non-vertebral fractures. No other risk factors for fracture were detected. Osteonecrosis post kidney-pancreas transplantation has been reported.

Post-Transplant Malignancy in Pancreas Transplant Recipients

As in all immunosuppressed allograft recipients, there is an increased risk of malignancy in pancreas transplant recipient. There are however some unique characteristics of the pancreas recipient. Martinenghi et al reported on a series of 99 patients who underwent pancreas and/or kidney transplantation. Seventythree patients had SPK and 26 kidneys alone.37 There were 9 neoplasms in 7 patients after SPK and none in the 26 patients with kidney alone. The authors suggested that the greater immunosuppressive therapy given to the combined transplants might have predisposed them to a higher rate of malignancy. Roza et al reported transmission of adenocarcinoma of the pancreas with a graft from a 55 year-old donor.[38] They suggested that care should be taken when accepting a pancreas from an elderly donor. There have been 2 reported cases of bladder carcinoma arising in SPK recipients with BD. Finally, Hanaway et al examined post-transplant lymphoproliferative disorder (PTLD) in pancreas recipients from 5 large centers.39 Fifty-two recipients were identified. The authors stated that this was a higher incidence than expected, that PTLD occurred sooner after transplant compared to other organ recipients and that PTLD occurring after pancreas recipients had lower survival and shorter time to death.

Survival in Diabetics Receiving Pancreas Transplant Compared to Living Donor Transplant (LDT), Deceased Donor Transplant (DDT) or Dialysis (D)

Several studies have addressed long-term survival in patients receiving SPK versus other forms of therapy for ESRD (LDT, DDT, or D). Tyden et al compared 14 SPK patients to 15 diabetic kidney only patients over a 10-year period.40 At 8 years, the patient survival was 20% on the kidney alone group versus 80% in the SPK group. This group further refined their analysis to include non-diabetic kidney recipients and SPK patients who lost the pancreas within 2 years of transplant. The 10-year patient survival of non-diabetic kidney transplant recipients was 72% versus 60% for SPK). However, the SPK patients in whom the pancreas transplant had failed within 2 years had a 10-year survival of only 33%. Knoll et al used the United Network for Organ Sharing (UNOS) database to determine the optimal treatment strategy based on a decision analytic Markov model.[41] This approach takes into account all complications resulting from transplant as well as the outcome oil patients who lose their grafts. The outcome measures were life expectancy (LY) and quality adjusted life expectancy (QALY). LDT was associated with 18.30 LY and 10.29 QALY; Pancreas after kidney transplant was associated with 17.21 LY and 10.00 QALY; SPK was associated with 15.74 LY and 9.09 QALY; DDT was associated with 11.44 LY and 6.53 QALY; and dialysis was associated with 7.82 LY and 4.52 QALY. This approach demonstrates that SPK is better than DDT but the difference is not as dramatic as one would expect from the other analytic approach.

Outcome

Five and ten year outcomes can now be calculated for pancreas transplant recipients. In the past, the larger series as well as the registry reports have concentrated on SPK. Furthermore, enteric and bladder drainage has been compared for long term survival benefits. The UNOS/IPTR reports annually. As of December 31, 2004, more than 23,000 pancreas transplants had been reported to the IPTR; of these more than 17,000 cases were in the US and almost 6,000 were from outside the US.7 An analysis of US pancreas transplants performed between 1988 and 2003 showed a progressive improvement in pancreas graft survival rates. In this report, the 5-year graft survival worldwide for SPK performed in 1998/1999 was 69%. For PAK and for PTA the five year graft survival was 58%. These rates may be increasing. The ten-year graft survival rate for grafts performed in 1992/1993 was 46% for SPK, 17% for PAK and 17% for PTA.[7] This corresponds to the current immunosuppressive era. Long-term immuno-suppression reported during the latest time period consisted of triple therapy with cyclosporine or tacrolimus, MMF, and corticosteroids. Individual large center reports

must be examined for details regarding cause of death and comorbidities. Sutherland et al reported on experience at the University of Minnesota in 1, 194 pancreas transplant performed between December 1966 and March 2000.42 There were 498 SPK, 404 PAK, 291 PTA and 1 combined pancreas-liver transplants. The analyses were divided into five eras: era 0, 1996 to 1973 (n=14), historical; era 1, 978 to 1986 (n=148), transition to cyclosporine, duct managements and solitary transplants; era 2, 1986 to 1994 (n=461), all categories (SPK, PAK, PTA), bladder drainage, and cyclosporine based triple therapy; era 3, 1994 to 1998 (n=286), tacrolimus and MMF therapy; and era 4, 1998 to 2000 (n=275), daclizumab induction therapy. Pancreas graft survival rates 1 year have significantly improved by category and era were as follows: SPK era 2 (n=214) versus eras 3 and 4 combined (n=212), 64% versus 79%; PAK era 2 (n=610 versus era 3 (n=84) versus era 4 (n=92), 76% versus 98% versus 81; PTA era 2 (n=72) versus era 3 (n=30) versus era 4 (n=40), 67% versus 100% versus 88%. In the US, there have been 2,427 PAK and 1,008 PTA performed between October 1987 and June 2004.7 Long-term data is available on these patients. The UNOS and IPTR registry reports 10-year patient survival of 40% for PAK and 74% for PTA recipients transplanted in 1992/1993. Similarly the 10-year graft survival for the 1992/1993 eras are 17% for PAK and 17% for PTA.[7]

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Management and Prevention of Infection in CAPD

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Introduction:

Since the initiation of chronic peritoneal dialysis therapy in India in 1991 both continuous ambulatory peritoneal dialysis (CAPD) and Continuous cyclic peritoneal dialysis (CCPD) have emerged as major form of renal replacement therapy(RRT)[1]. However the drop out rate still remains high predominately due to negative patient selection. Infectious complication remains a major cause for drop out across the country. Exit site infection (ESI), tunnel infection (TI) and peritonitis are the peritoneal dialysis related infection which when appropriately treated can reduce morbidity, mortality and drop out. These infections remain most common complication resulting in hospitalization, catheter loss and failure of the peritoneal membrane.

Precautions during catheter Implantation:

The catheter insertion should be undertaken by an experienced operator, under operating room sterile conditions. This can be done either an inpatient or outpatient basis. The ideal catheter provides reliable, rapid dialysate "low rate without leaks or infections. The Tenckhoff catheter is still the most common catheter used for permanent PD. On the morning of the operation the patient should bathe or have shower with soap or detergent. Abdominal hair should be clipped. Patient's nares may be swabbed for to determine Staph. aureus nasal carrier. Nephrologist should make critical decision regarding the choice of the catheter (preferably double cuffed) and methods for placement including site of implantation (avoid locations were there may be pressure during daily activities), downwardly directed exit-site, Swan-neck design, preoperative preparation and postoperative care[2]. Prophylactic use of antibiotic therapy (inj. cephlosporin, inj.vancomycin) prior to permanent peritoneal catheter implantation has significantly reduced catheter exit-site colonization, wound infection early ESI and TI in controlled prospective studies[2,3]. Every effort should be made to avoid trauma and hematoma during catheter placement. The exit site should be round and the tissue should fit snuggly around the catheter (Fig-1). Suture at exit-site increase the risk of infection and is contraindicated. There is evidence of reduced catheter exit-site colonization, wound infection and ESI following peri-operative antibiotics(3). The factors influencing healing and early infection includes tissue perfusion, mechanical factors, sinus bacterial colonization, epithelialisation, local cleaning agent, exit direction and systemic factors.

Exit-site Care Practice:

Once catheter is placed, until the healing is completed, the dressing changes should be done by dialysis technologist/nurse by using a sterile technique. The exit site should be kept dry until well healed which precludes showers or tub bath for this period. The catheter should be immobilized and healing can take upto 2 weeks. For routine exit-site care after healing is complete antibacterial soap and water, povidone iodine or chlorhexidine are reasonable option (Table 1) (4). The catheter should always be kept immobile to prevent pulling and trauma to the exit-site which may lead to infection. Each programme should evaluate the organism causing ESI and should formulate protocols to reduce the risk as seems appropriate for the programme.

Approximately 50% of the patients are Staph. aureus nasal carriers which lead to an increase risk of Staph. aureus ESI and subsequent peritonitis[5]. A single culture may yield a false negative result since many patients are intermittent nasal carriers. Colonization with Staph. aureus, infection may come from partner, helper as well as from 1 health care worker. Therefore excellent hand hygiene is very important prior to any examination of the patients exit site by the patient, partner, helper and member of the health care team. If the water patient uses for hand washing is thought have a high bacterial count then use of an alcohol hand wash should be encouraged. The prophylactic use of mupirocin ointment at anterior hares, exit-site and short course of oral rifampicin has considerably reduced the incidence of Staph. aureus. carrier state and ESI. The emergence of gram negative ESI remains a risk factor for gram negative peritonitis but the use of gentamycin ointment at the exit-site had shown to reduce these infections[6]. Ciprofloxacin otologic solution applied daily to exit site as a part of routine care is also effective in

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reducing both Staph. aureus and P. aeruginosa infection. We are using nadifloxacin 1 cream at exit-site which is a synthetic quinolone with potent bactericidal broad spectrum activity against both gram positive, gram negative and anaerobic organisms.

ESI is defined by the presence of purulent discharge with or without erythema of the shin at the catheter-epidermal interface. A positive culture in the absences of an abnormal appearance is indicative of colonization rather than infection. A TI may present as erythema, edema or tenderness over the subcutaneous pathway but may clinically occult as shown by sonographic studies. Empiric antibiotic therapy may be initiated immediately or alternatively, the health care team may decide to differ therapy until the result of the exit-site culture can direct the choice of antibiotic. A gram stain of exit-site drainage can guide initial therapy. Oral antibiotic therapy has been shown to be as effective as intraperitoneal antibiotic therapy. Empirio antibiotic therapy should always cover Staph aureus. Severe ESI may be treated by hypertonic saline dressing twice daily as well as oral antibiotic therapy. Add I tablespoon of salt to 1 pint (500ml) of sterile water and this solution is applied to the gauze and wrapped around catheter exit-site for 15 minutes, once or, twice daily. Antibiotic therapy must be continued until exit-site appears normal. Two weeks is the minimum length of treatment time and longer may be necessary. If antibiotic fails to resolve the infection the catheter can be replaced as a single procedure under antibiotic coverage. Sonography of the tunnel has been useful in evaluating the extend of infection along the tunnel and the response to therapy. The efficacy of exit-site deroofing and cuff shaving in treating refractory infections, of the exit-site and tunnel may achieve favorable result[7]. Antibiotics must be continued during and after cuff shaving. A patient with an ESI/TI that progress to peritonitis with the same organisms will usually require catheter removal.

Connectology and Exchange Procedure:

"Flush before fill" reduces the risk of contamination and hence double bag system should be used and manual spiking system should be avoided as much as possible. Close attention must be paid to the connection-D methodology. In some programmes were they switch vendors careful attention should be paid to connection method to reduce infection rates. For automated peritoneal dialysis (APIA) if spiking is part of the system patient should be trained to use an assist device to prevent contamination (8). Patients or helpers having enhanced training to do PD have significantly fewer infections 1 every 31.8 months vs. I every 18 months). Touch contamination can be avoided by appropriate hand washing technique and drying of the hands before performing the exchange. Location for exchange must be clean, with avoidance of animal hair, dust-laden air and fan. All patients must be taught what contamination is and proper response to contamination such as presentation to the centre for a tubing change if the end of the tubing is contaminated. Prophylactic antibiotic should be prescribed if dialysis solution was infused after contamination or if the catheter administration set was open and exposed to bacteria for an extended period of time. After a known break-in technique, the nephrologist will give a 2 day course of antibiotics. A culture of the dialysis effluent if positive, is helpful in determining subsequent therapy.

Prevention of Peritonitis s and Indication for Catheter Removal:

The routes of entry of peritonitis are touch contamination, catheter related, enteric, hematogenous, and gynecological. Prior steroid use, HIV infection, and diabetes mellitus may predispose to higher peritonitis rates. Gastric acid inhibitors which are commonly use in CKD patients may increase the risk of gram negative peritonitis[9]. Upper respiratory tract infection may predispose children to peritonitis though the reason is not clear. The most common source of peritonitis is contamination at the time of exchange (touch contamination) leading to infection with predominantly gram positive skin flora. The organism involved is mainly coagulase negative staphylococcus (CONS), though diphtheroids, Corynebact eroim and Bacillus are also seen[10].

Invasive procedure such as dental work, GI scopy can produce transient bacterenmia and entry of enteric organism into the peritoneal cavity by transmural migration across the GI tract. A single oral dose of amoxicillin 2 gms two hours before extensive dental procedure is reasonable. Routine GI endoscopy is associated with Bacteremia in 2-6 % of the procedures, though esophageal dilation and variceal sclero therapy is significantly higher frequency[11]. In patient undergoing colonoscopy ampicilin 1 gm plus single dose of aminoglycoside with or without metronidozole given IV just prior to the procedure may decrease the risk of peritonitis[8]. Abdomen should be emptied of dialysis fluid prior to all procedures involving the abdomen or pelvis (Colonoscopy, renal transplantation and endometrial biopsy).

Every effort should be made in individual PD programmes directed towards prevention of peritonitis to optimize outcomes on PD. This can be done by monitoring infection rates on an yearly basis. This should include ESI, TI, peritonitis, cultured organisms, and frequency of relapsing peritonitis episode. If necessary patient technique should be reviewed and retraining should be performed. Causative organism and presumed etiology should be reviewed in a regular fashion by the PD team, including clinical coordinator, microbiologist and the nephrologist. This will facilitate interventions if infection rates are raising or unacceptably high. The individual centre peritonitis rate should be no more than I episode every IS patients months[8].

Over burdening of the dialysis technologist/ nurse with excessive numbers of patients will result in shorten training times and difficulty in retraining as needed. Home visit by clinical coordinators or nurses can be carried out periodically in detecting problem with exchanges. All PD patients should be instructed during training on the

Early Catheter Immobilization and Healthy Exit-site

Table-I

Antimicrobial spectrum and characteristics of hand-hygiene antiseptic agents

Group	Gram-Positive bacteria	Gram-negative bacteria	Myco-bacteria	Fungi	Viruses	Speed of action	Comments
Alcohois						Fast	Optimum Concentration 60-90%; Non-persistent activity. Inactivated in presence of organic matter.
Chlorhexidine						Intermediate	Persistent activity; rare allergic reactions Not inactivated in presence of organic matter
Iodine compounds						Immediate	Causes skin burns usually too irritating for hand hygiene. Inactivated in presence of organic matter.
Quaternary ammonium Compounds						Slow	Used only in combination with alcohols or chlorhexidine Ecological concerns.
Activity : Excellent Good Flair No activity							

Current recommendation *Say that alcohol chlorhexidine combination is the best solution.
*CDC guidelines on prevention of surgical site infection.

importance regular bowel movement and avoidance of constipation. Some patients will require laxatives or lactulose for treating constipation. Hypokalemia which can worsen bowel immobility should be treated. There is association between severe constipation, enteritis and peritonitis due to enteric organisms. The majority of fungal peritonitis are preceded by course of antibiotics. Prophylactic use of oral nystatin or fluconozole given during antibiotic therapy may prevent fungal peritonitis.

Indications for peritoneal dialysis catheter removal are refractory peritonitis, relapsing peritonitis, refractory exit-site and tunnel infection, fungal peritonitis. In mycobacterial peritonitis and multiple enteric organims peritonitis catheter should be removed if not responding to therapy[8].

Microbiological Aspects of Peritoneal infections:

Antimicrobial drug resistant has been recognized as a problem since the advert of antimicrobial therapy more than 60 years ago. Staphylococci because of their natural habitant of the skin has always been leading cause of peritonitis in patients receiving peritoneal dialysis (PD). These organisms have demonstrated a remarkable ability to develop resistance to antibiotics, first with penicillin, methicillin and more recently strains expressing resistance to vancomycin have emerged[12]. Enterococci are normal inhabitant of gastrointestinal tract have shown emergence of resistance to vancomycin in many areas.

In the past decade, community acquired methicillin resistant staphylococcus aureus (CA-MRSA) have become a growing problem in the USA and in other part of the world including India. These CA-MRSA strains differ from the classic nosocomial MRSA in that CA-MRSA strains usually possess the type IV chromosomal cassette (SCCmec), which includes methicillin resistance genes. Prompt and accurate detection of microbial isolates is important so that appropriate therapy and infection control measures can be instituted. Staphylococcus aureus strains with reduced susceptibility to vancomycin may be difficult for microbiology labs to detect. These organisms often appear vancomycin susceptible when tested by disc diffusion and some automated susceptibility testing systems[12]. Broth microdilution, agar dilution, and agar gradient diffusion are recommended for detecting these strains.

Other important aspects of therapy for these organisms are removal of catheters and other indwelling devices and good local wound care. Strict contact isolation is recommended to prevent spread of these strains to other patients. In addition, persons who are colonized or infected with these strains should undergo decolonization with intranasal mupirocin ointment and other measures.

Frequency of infectious complication remains high in infants on peritoneal dialysis than in older children and adults, although automated cyclers, disconnect system has reduced overall pediatric peritonitis rates[13,14]. Possible explanation for the infant experience include proximity of the PD catheter exit-site to the diaper area feeding gastrostomy tube, as well as the greater use of single cuff catheter with upward facing exit-site.

Mycobacterium tuberculosis peritonitis (MTB) is under diagnosed in developing countries. Patients who while being initiated on chronic peritoneal dialysis should be evaluated for the presence occult tuberculosis (thorax abdomen) and full course antituberculus treatment with isoniazid, rifampicin, pyrazinamide, quinolone should be initiated along with B6. Ethambutol is not usually recommended because of the high risk of optic neuritis in end stage renal disease. Streptomycin even in reduced doses may cause ototoxicity after prolonged use. Tuberculus peritonitis evades diagnosis and can present at any point in time in the course of chronic peritoneal dialysis

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Abstract from NUTS of SAARC 2005

Estimation of GFR from Serum Creatinine in detection of CKD

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At present there are more than 250,000 patients on hemodialysis in Japan. Every year in Japan, approximately 25,000 patients who are receiving haemodialysis die, but approximately 35,000 new patients require haemodialysis, so the number of these patients increases every year by approximately 10,000. One of the main causes of this rise in the number of patients with ESRD is the large increase in the number of patients with diabetes over the last two decades. Last year, the diabetic patient accounts for 41.5% of the new dialysis patients. The incidence of hypertension is also increasing and this is also contributing to the rise in the numbers of CKD patients. There were previously no national data on CKD in Japan, and with such large and increasing numbers of people affected by renal diseases, the Japan (Chronic Kidney Diseases Initiatives) KDI was set up with the aim of assessing renal function in the general population of Japan and copes with the issue from increasing CKD population.

Kidney function should be assessed by measuring glomerular filtration rate (GFR), although this is quite difficult to measure in clinical practice. There are at least two commonly used methods for measuring GFR: the Cockcroft-Gault formula and the modification of diet in renal disease (MDRD) equation, which requires an ethnic coefficient for use in certain groups such as African Americans. The MDRD equation was used to analyze GFR data obtained from Japanese laboratories. This showed that the MDRD formula underestimates GFR in Japanese people and that a Japanese coefficient is required so that the MDRD can be used in Japan.

The Japan CKDI then obtained data from 248 volunteers to calculate a Japanese coefficient for the MDRD. The Japanese coefficient was determined as 0.881. Therefore, the modified MDRD equation for Japanese is as follows:

GFR (mL/min/1.73m^2) = 186.3-Age$^{-0.203}$ Cr$^{-1.154}$ l 0.881 l (if female x0.742)

With this coefficient, we calculated the data gathered from approximately 360,000 people from 7 areas of Japan at their annual health check program to estimate GFR in the general population. This revealed that overall, GFR is lower in Japanese people, and the proportion of patients with CKD stage 3 (Table 1) appears to be several times higher in Japan than in the USA.

These results do not necessarily mean that all these people have CKD stage 3 as it is possible that Japanese people may have a naturally lower GFR. One possibility is that the definitions of the different stages of CKD (Table I) need to be redefined, at least for Japanese people. The reason for this proposal is that the comorbidity of CKD in general population was not different from that in hypertensive and diabetic population when the cut-off GFR was 60ml/min defined for stage 3 CKD. In contrast, the cormobidity of CKD was increased in hypertensive and diabetic population, when the cut-off GFR was 45ml/min. Next, the effect of age can not be overlooked in Japan since the proportion of patients with low GFR increased with advancing age. So the increase in the average age of Japan's population may also be contributing to the low overall GFR seen in Japan.

I stressed that there continues to be concern about the apparently low GFR of the Japanese population, and that the best method for accurately estimating GFR in Japanese population needs to be established in future by JCKDI. Lastly, I welcome the Asian nephrologists who are interesting in the cooperation to make a formula to estimate the GFR for Asian population. JCKDI will take a prompt action to determine the original formula for Asian population.

Table-I

Distribution of estimated GFR in general population in USA and Japan

GFR	USA	(%)	Japan	(%)
	(million)		(million)	
90<	114.0	(64.3)	5.8	(5.6)
60-89	55.3	(31.2)	76.0	(73.7)
30-59	7.6	(4.3)	21.2	(20.5)
15-29	0.4	(0.2)	0.16	(0.15)
<15	0.3	(-)	0.06	(0.06)

Is Albuminuria An Isolated Risk Factor for Progression of Cardiac Disease in Hypertensive Patients with Renal Disease

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Introduction: Cardiovascular disease is the predominant cause of end-stage renal disease accounting for >50% deaths.' As in diabetic patients, microalbuminuria in hypertensive patients is also associated with several markers of cardiovascular disease[1-2].

For this reason to accept microalbuminuria as an independent risk factor for atherosclerotic disease adjustment for traditional and novel risk factors is mandatory [2-3].

Antihypertensive therapy however can lower the albumin-creatinine ratio thus modifying the level of risk indicator and confounding the relationship between microalbuminuria and cardiovascular disease[4].

Several studies 5-8 have reported that the prevalence of cardiovascular disease is significantly higher among hypertensive patients with microalbuminuria than patient without microalbuminuria, in such patients with microalbuminuria and cardiovascular disease, the amount of albumin in the urine was also significantly higher than in those who did not present with cardiovascular disease

Objective: Purpose of doing this study was to determine the importance of early detection of albuminuria in patients with hypertensive renal disease and the measures to control its progression that may be beneficial in preventing progression of cardiovascular morbidity and mortality.

Methods: This is a prospective study conducted on 216 patients followed in our institute of Nephrology and transplantation, LNH over a span of 2 years (Jan 2003-Dec. 2004). We selected 60 patients with essential hypertension with glomerular filtration rate between 15-90 ml/min and excluded those with preexisting cardiovascular disease, secondary hypertension, urinary tract infection, pregnancy and renal disease secondary to any pathology other than hypertension.

In all patients complete blood picture, biochemical renal profile, lipid profile, urine analysis, renal sonograms and electrocardiograms were done as baseline investigations. Test for microalbumiuria was done only in those patients in whom urinalysis was normal. Echocardiogram were done only on those patient who have positive EKG findings of cardiovascular disease because of financial constrains.

Serial measurements of blood pressure and albuminuria were done on monthly and quarterly basis.

Results: Out of 216 patients screened, the study group comprised of 60 patients. 20% patients developed CVD. 60% of the total patients were between the age group of 30-60 years and out of them 33.3% developed CVD. There was no gender discrimination in association of CVD as 25% of males and 25% of females were affected.

It was found that the patient who fell in CKD V did not develop CVD but 25% each of those falling in CKD III and IV stages developed CVD.

Out of 40 patients developing CVD, 8 had microalbuminuria, 36 had proteinuria <1 gm and 16 had proteinuria >1gm and 16 had proteinuria >1gm

There was significant relationship between overt proteinuria > 1 gm with the development of CVD as 66.6% of this group developed the complication (p. value 0.000842).

Conclusion:

In a follow up of 2 years on 60 patients with albuminuria and renal disease, 20% of patients developed cardiovascular complication Higher prevalence of CVD (33.3%) was found in age group between 30-60 years. There was no gender predisposition as female and males both developed CVD in equal proportion (25% each). Patients with stage II and III CKD developed CVD in equal proportion (25%) but there was no CVD occurrence in CKD V and in patients with microalbuminuria over 2 years. Hence in our study overt proteinuria more than 1gm/day is a definite marker of CVD.

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Comparative Study of Two Different Dosages of Erythropoetin in Respect of Response to Anemia in Patients with ESRD On MHD

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Background: Anemia is a widespread finding in chronic kidney disease (CKD), affecting up to 90% of patients. The introduction of rhuEPO is the most important therapeutic advances in the treatment of anemia in dialysis patients. The efficacy and safety of epoetin for treating renal anemia is well established. A reduced dose is both clinically and economically desirable and is particularly important when long-term anemia management is necessary. This study was carried out to see effectiveness of once weekly s/c epoetin-B at lower doses in correction of anemia in ESRD patients while maintaining iron parameters at an optimum level.

Methods: Thirty seven (37) end-stage renal disease (ESRD) patients, 21 (56.8%) male and 16 (43.2%) female, stable on MHD, twice weekly (8 hours duration) session with a minimum 3 months duration of dialysis (mean±SE = 6.69±1.38 months) and age ranged from 20 to 76 years (mean±SE = 46.6±3.73 yrs) were included in this study. They were divided into two groups, group-A, higher dose group (EPO: 80±10 IU/kg/week; n = 17, 45.95%) and group-B, lower dose group (EPO: 50±10 IU/kg/week; n = 20, 54.05%). All subjects included in the study have had optimized level of iron parameters (Ferritin $\geq$ 250 µg/l or TSAT $\geq$ 20%) before enrollment into the study and it was maintained throughout the study period by i.v. iron therapy (Iron sucrose/dextran). The duration of study was 6 months and during this period, Hb/Hct level was measured at 2 weeks interval.

Results: At 3rd month of epoetin therapy Hb/Hct rises significantly in both groups: 10.08±1.36 gm/dl (Mean±SD) in group A and 8.98±0.82 gm/dl in group B ($p<0.001$) compared to baseline Hb/Hct of 7.19gm/dl & 6.99gm/dl respectively. At 6th month of epoetin therapy Hb/Hct further rises significantly in both groups: 11.30±1.25 gm/dl (Mean±SD) in group A and 10.23±0.91 gm/dl in group B ($p<0.001$). The rise of hemoglobin per month was 0.68 gm/dl and 0.55 gm/dl in group A & B respectively. Target Hb of 10 gm/dl had been achieved in 82% of patients in group A and in 65% of patients in group B.

Conclusion: From this study it was concluded that Erythropoietin beta administration in two different doses causes (group A: 80±10 IU/kg/wk and group B: 50±10 IU/kg/wk) significant rise of Hb/Hct level in both groups provided there should be optimum level of iron parameters. Rise in Hb/Hct is significantly more in higher dose group compared to lower dose group and lower dose of erythropoietin (50±10 IU/kg/wk) can achieve and sustained a target Hb level of 10 gm/dl up to 65% of the patients.

Detection of Chronic Kidney Disease (CKD) in Adult Disadvantageous Population

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Background: Chronic Kidney Disease is increasingly being recognized as a significant cause of morbidity and mortality all over the world. With the increase of diabetes, hypertension the prevalence of Chronic Kidney Disease (CKD) is also alarmingly going up, particularly in disadvantageous population. Although exact data of CKD in our country are not available, it seems to put considerable burden on our scarce health resources. Faced

with this background, we conducted this study among urban disadvantageous population to findout the prevalence of CKD and their relationship with demographic and other putative risk factors.

Materials and Methods: A multistage sampling, following a simple random sampling procedure, was done to choose the study area (Mirpur Slums) and a total of 1000 adult population ranging from 15 - 65 years as study sample. Data were collected from the participants using a structured questionnaire addressing all the variables of interest. The test statistics used to analyse the data were descriptive statistics, Chi-square (X^2) and Fisher's Exact Probability Test.

Results: Out of 1000 participants 160(16%) were found to have CKDs based on corrected CCr for male and female and/or proteinuria. Nearly 11% had Stage-III, 3.4% had Stage-II, 1.3% had Stage-I, 0.3% Stage-IV and only 0.1% stage-V diseases. However, based on classic CKD criterion of serum creatinine >1.5 mg/dl in male and >1.3 mg/dl in female only of study population was considered as having CKD (1.3 male and 2.7% female). The analysis showed that 55% of the participants were young and early middle aged (from 15-40 years of age), while the rest 45% were middle aged and elderly (from 41-65 years of age;). The mean age was observed to be 34.39 ± 0.40 years. A female preponderance was observed among the participants (66.6%). Majority of the participants was married (84.7%) and illiterate (78.8%). In terms of occupation, the house-wives comprised the main bulk (39.9%), followed by garment-workers 17.4%, small-business 9.4%, service 9%, day-labour 5.4%, riksaw-puller 4.3%, other jobs 10.6%. The rest 4% were unemployed. BMI study categorised 575(57.5%) participants as normal, 218(21.8%) as underweight, 174(17.4%) as 30(3%) as obese and 3(0.3%) as morbidly obese. A total of 41(4.1%) participants were diabetics. Of them 20 were self-reported diabetics and 21 were diagnosed during the survey, Of the self-reported diabetics 1%(45%) reported having regular antidiabetic agents, although only 5(55%) of them reported to achieve a control over the disease. Likewise a total of 116(11.6%) participants were hypertensives. Of them 50(43.1%) were established hypertensives and the rest 66(56.9%) were discovered so from the collected data. Of the self-reported hypertensives 25(50%) reported taking regular antihypertensives, although only 5(20%) of them had a history control. Approximately 22% participants had smoking habit and nearly one quarter (23.7%) informed about the habit of chewing tobacco. Urine albumin analysis using multi-sticks demonstrated that 77(7.7%) participants had albuminuria - 57(5.7%) had '+'. 16(1.6%) had '++' and 4(0.4% '+++' albuminuria. About 2% participants had diabetes with proteinuria, 3.7% had HTN with proteinuria, 0.7% had DM and HTN along with proteinuria, While 2.8% had isolated proteinuria. Association of demographic factors with CKD showed that age >40 years were significantly prone to develop CKD than those having age < 40 years ($p<0.001$). However, the disease was not found to be associated with, respect to sex ($P>0.05$). More than one-quarter (25.6%) of the CKD population were overweight and obese compared to 19.6% of those without CKD, although the difference between the two groups did not reach the level of significance ($p = 0.086$). Smoking habit was found almost equally distributed in both CKD (22.5%) and normal population (21.7%), although habit of chewing tobacco found to be almost double in CKD (39.4%°) than that in normal population (20.7%) ($P<0.001$). Those having CKD 10.6% of them had diabetes and 31.9% had HTN compared to 2.9% and 7.7% of the normal population, showing statistically significant associations of CKD with diabetes and HTN ($p<0.001$). Combined prevalence of DM and HTN in CKD group was also demonstrated to be significantly higher (3.8%) than that to normal population (0.6%) ($P<0.005$). Though all the diagnosed CKD cases were advised to have their serum checked for creatinine and urine for albumin 3 months after the first check up, only 25(15.63%) of 160 cases attended complying to the advice. Out of them 23(92%) were confirmed as having CKD - 20% were in Stage 1, 12% Stage II, 52% in Stage III and 8% in Stage IV disease.

Conclusion: CKD is a silent killer disease. Patients of CKD presented to the nephrologists are usually in advanced stages and represent only tip of the iceberg, the large portion of which remain undiagnosed in the community. Early identification and intervention can help prevent or slow progression to ESRD.

Is Left Ventricular Hypertrophy A Predictor of Cardiac Event in Cases of End Stage Renal Disease Patients on Hemodialysis?

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Introduction : Cardiovascular disease is highly prevalent in the population with chronic kidney diseases[1-3]. Left ventricular hypertrophy (LVH) is the most frequent cardiac

abnormality in end-stage renal disease (ESRD), with 74% of patients demonstrating LVH by the time of starting dialysis[4-6]. This compares to a prevalence of 20% in the general population7. Progressive cardiac enlargement is common and evident particularly in the first year of dialysis[8]. Such effects are profoundly deleterious for long term survival of patients with ESRD. Upon starting dialysis, 40% of patients already have a previous episode of heart failure, doubling the risk of death[9]. The prevalence of coronary artery disease approaches 40% among patients starting dialysis[10]. We aimed for a study on ESRD patients who developed cardiovascular disease alter initiation of haemodialysis, to identify their modifiable risk factors that play role during the course of renal replacement therapy.

Objective : To identity the risk factors for progression of cardiovascular disease (CVD) after initiation of haemodialysis, in patients with end stage renal disease (ESRD), hypertension and LVH and compare it with the group of patients who did not have pre existing left ventricular hypertrophy (LVH) but have developed CVD after 6 months of Hemodialysis

Our analysis of identified modifiable risk factors would help us to control of progression of CVD in patients with LVH and those without LVH which play role after initiation of hacmodialysis (HD).

Methods and Material : This was prospective case control study conducted over the span of 2 years (from Jan 2003 to Dec. 2004) at the Dialysis Centre of Institute of Nephrology &Transplantation, Liaquat National Postgraduate Medical Center, Karachi. All ESRD patients who were hypertensive, with or without LVH were included.

We screened 139 patients from our unit and selected those who were on maintenance hemodialysis for at least 6 months. These patients were divided in 2 groups of diabetes and non diabetes with pre-existing LVH and were compared with their controls.

We excluded 55 patients who had history of ischemic heart disease, valvular heart disease, Cor-pulmonale, infective endocarditis, cardiomyopathy or had any evidence of heart disease on EKG and/or echocardiograms prior to initiation of Hemodialysis had their base line investigations, serum parathyroid hormone, ECG and echocardiogram done serially at monthly and quarterly basis or as per need.

Results : Our study group comprised of 85 patients. In diabetic group (1) 28.6% of patients with LVH developed CVD. While 80% of those who did not have LVH developed CVD. (p. value 0.0015). In this group other risk factors identified for development of CVD were uncontrolled HTN in 91%, hyperparathyroidism in 58.3%, dyslipidemia in 50%, high BMI (>25) in 41% hypoalbuminemia in 75% patients 33.3%. patient had anemia and uncontrolled Hyperglycemia each. None of them were smokers, Kt/v was done for all patients and dry weight was obtained. Proteinuria was present in all patients. In the non diabetic group (11) there was association of CVD with LVH as 62.5% patients with LVH developed CVD as compared to 50% in those without LVH. The association was not significant (p-value 0.0324870) in this group all patients had uncontrolled HTN, BMI was high in 40%, hypoalbuminemia in 60% patients. 20% of these patients were smokers.

Conclusion: We screened 139 patients who had ESRD with HTN on haemodialysis for > 6 months and studied 84 patients who were meeting our criteria. They were divided in two groups of diabetic (I) and diabetics with LVH and were compared with their controls. In group I, 63% patients developed CVD, LVH was not identified as a risk factor for CVD as only 28% patients with LVH developed CVD. Risk factors identified in this group were uncontrolled HTN, hyperparathyroidism, dyslipidemia, high BMI and hypoalbuminemia. In group II, 55% developed CVD, LVH was found to be insignificant risk factor (p-value 0.324870) for CVD. Other modifiable risk factors in this group were high BMI, hypoalbuminemia and smoking.

Thus in our study LVH is a marker of CVD only in non diabetic patients who had HTN. LV dysfunction was the most common cardiovascular complication developed in both groups. So it is important to correct the other easily identifiable risk factors other than LVH in our dialysis population, specially in diabetics.

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Study of Acute Renal Failure in Rhabdomyolysis

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A total of twenty four cases of acute renal failure due to rhabdomyolysis were studied in Dhaka Medical College in last 3 years in terms of clinical presentation, biochemical parameters including prognosis after treatment. Mean age (mean±SD) were 32±10 years ranged from 22 to 72 years, male 22 and female 2 cases. Common presentation were anorexia, nausea & vomiting 22 (91.66%), decreased urine output 20 (83.33%), generalized body ache 12 (50%), painful swelling of limbs 6 (25%), fever 3 (15%), convulsion & fracture of lower limb 2 (8.33%) each, abdominal pain in one case. Main causes were physical assault 12 (50%), near-drowning 3 (12.5%), vigorous exercise 3 (12.5%), road traffic accident (RTA) 2 (8.3%), convulsion, self induced trauma, septicemia, post partum eclampsia with convulsion I in each case. Mean haemoglobin was 11.66 gm/dl, total count of WBC 13400/cumm of blood with neutrophil 77.38%, urinary albumin 1+ in 14 cases, 2+ in 10 cases and mean urinary RBC 4/HPF and pus cell (WBC) 6/HPF. Mean blood urea and serum creatinine were 161 mg/dl and 10 mg/dl respectively. Mean serum potassium (K+) 5.9 mmol/L (K+ > 6.0 mmol/L in 12 cases). Mean serum CPK was 2341 IU/L, LDH 1300 IU/L, aldolase 1636 IU/L SGOT 199 IU/L, blood sugar 5.8 mmol/L. Among 24, 6 patients (25%) were treated conservatively and 18 (75%) received dialysis treatment. 14 (58.3%) patients was given peritoneal dialysis (IPD) and 4 (16.66%) received haemodialysis (HD). Twenty (83.33%) patients were cured completely and 2 patients (8.3%) were discharged with risk bond (DORB) and 2 patients (8.3%) expired. It is concluded that rhabdomyolysis may lead to acute renal failure and prognosis is good if adequate treatment is administered early including dialysis therapy.

Screening for Diabetes Mellitus, Hypertension, Proteinuria and Chronic Kidney Disease in an Adult Community in Rural Area

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A total of 1263 people of ages 15-65 yrs. were studied in a rural union, Bongao of Savar for 17 month to detect proteinuria, hypertension, diabetes and chronic kidney disease. Detailed history, clinical examination including height, weight, BP measurement was done in all cases. Blood and urine tested for random sugar, creatinine and multistick evaluation in every cases. CKD was defined as per DOQI guideline and Ccr (Creatinine clearance rate) was determined with Cockroft-Gault formula. Hypertension was defined as JNC VII and Diabetes Mellitus (DM) when random blood sugar was ≥ 11.1 mmol/L as per WHO criteria. Proteinuria detected by multistick test.

The result showed among 1263 people 468 (37%) male and 795 (63%) female. 237 (I8.76%) were hypertensive out of which 155 (66.4%) were newly diagnosed. Diabetes mellitus

were detected 44 (3.88%) amongst them 27 (55.1%) were newly diagnosed, proteinuria was detected 78 (6.18%). Corrected Ccr with body surface area 30-59 ml/min was detected 172 (13.62%) and Ccr 29-15 ml/min was 3 (0.24%) and <15 ml/min was 2 (0.16%). Total 228 (17.97%) detected to have CKD. 50% of known hypertensive and diabetic was not on any treatment.

It is observed that 66% of Hypertensive & 55% Diabetic are not aware of their disease and were not in any form of treatment. About 18% of people is detected to have chronic kidney disease and 6% have isolated proteinuria.

EFFECT OF CALCIUM CARBONATE AND ORAL CALCITRIOL ON PTH IN MHD PATIENTS

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Background : Secondary hyperparathyroidism is common in MHD patients. Accumulated evidence suggests that PTH is a major uremic toxin. Sometimes it is difficult to suppress PTH in MHD patient. Oral calcitriol and calcium carbonate therapy can effectively reduce elevated PTH level.

Methods : 45 MHD patients were prospectively studied to see the effect of oral calcitriol and calcium carbonate on PTH.

Total duration of study was 36 months. Initial 4 weeks were washout period, remaining 32 weeks were study period. During this study period all the subjects received calcium carbonate 500 mg thrice daily with meal and oral calcitriol 0.25 µg once daily. Serum PTH (midregion), Calcium, Alkaline phosphatase, Inorganic phosphate, Albumin, were measured at the end of wash out period and at 9th months of study period.

Results : Elevated Serum PTH (mid region), alkaline phosphates, hyperphosphataemia, hypocalcaemia, was observed at beginning and decreased PTH, inorganic phosphate, alkaline phosphatase and increased calcium level was observed at the end of study.

Median Serum PTH (mid region) Beginning of study vs end of study was, 490.56 pmol/L vs 176.82 ($p<0.05$) Mean±SD Serum alkaline phosphatase: Beginning of study vs end of study was 307.33±133.4µ/L vs 219 12±86.44µ/L ($p<0$ 01).

Mean±SD inorganic phosphate: Beginning of study vs end of study: 2.60±0.59 mmol/L vs 1.79t0.31mmoVL ($p<0.01$)

Mean ± SD S calcium: Beginning of study vs end of study was 1.92±0.92 mmol/L vs 2.39 ±0.12 mmol/L ($P<0.001$).

Conclusion: It is concluded that oral calcitriol and calcium carbonate can effectively reduce Serum PTH, alkaline phosphatase, inorganic phosphate and increase calcium in MHD patients.

Diagnosis and management of Renal bone disease

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Renal bone disease (RBD) is an important complication of chronic renal failure. The monitoring, diagnosis and management of RBD adds considerable cost to the care of patients with End stage renal disease on renal replacement therapy. Abnormalities in hormonal and mineral metabolism begin early in the course of Chronic Kidney disease when the GFR falls below 60 mls/min/1.73m2. There are many forms of RBD including Osteitis fibrosa, mixed lesions, Osteomalacia, Adynamic bone disease and Amyloid bone disease. In addition cardiovascular diseases and vessel and soft tissue calcification have been associated with abnormalities or a consequence of their treatment.

While bone biopsy will provide definitive diagnosis of RBD, in most instances in clinical practice the diagnosis is made on various other parameters. Parathyroid hormone (PTH) assay which indirectly reflects bone turnover has now largely replaced “skeletal surveys” as a regular test to detect bone disease due to hyperparathyroidism. Desferrioxamine test is still done in some centres to diagnose the presence of Aluminium bone disease but its use is declining with patients having less exposure to aluminium. The pathogenesis of secondary hyperparathyroidism which may eventually lead to tertiary hyperparathyroidism and osteitis fibrosa is rather well understood and provides the basis for treatment to prevent RBD. Progressive kidney damage disease leads to declining glomerular filtration rate (GFR) leading to phosphate retention; in addition there is diminished production of calcitriol. This leads to hypocalcemia as well as an increase in parathyroid hormone (PTH) whose synthesis is repressed by calcitriol.

Management strategies in preventing secondary hyperpara-thyroidism include controlling serum phosphate level and suppressing the PTH level. The control of serum phosphate level requires dietary phosphate restriction and the use of various forms of phosphate binders. The former approach is often not successful and almost all patients on dialysis treatment will be on phosphate binders. Aluminium based phosphate binders which were widely used more 10-15 years ago hardly find a place in present day practice because of complications of encephalopathy, bone disease and anaemia. If at all its use is restricted to short duration in patients with difficult to control hyperphosphatemia. The mainstay phosphate binders used in most Asian countries are calcium based binders: calcium carbonate or calcium acetate. In recent years there have been concerns about calcification of vessels and soft tissues and the associated cardiovascular morbidity and mortality and thus there a move to use less of the calcium binders particularly if there is concomitant use of Vitamin D3 analogues. Two new non-calcium based phosphate binders were introduced to clinical practice recently. Sevelemer, containing cross-linked poly-allymine hydrochloride has been shown to be an effective phosphate binder. It also lowers serum cholesterol and low-density lipoproteins. The second non calcium based phosphate binder is Lanthanum carbonate which like Aluminium is a trivalent cation. It is as efficacious as Aluminium based binder and studies up to 36 months do not show

significant accumulation in bones. The cost of these two new binders is quite prohibitive and their use is limited in Asian countries.

Suppressing elevated PTH level is another major aspect of the management of secondary hyperparathyroidism. Vitamin D3 (1, 25 dihydroxy cholecalciferol) is used to suppress PTH levels and is given either orally or intravenously. The later route is often used if hypercalcemia, which is a complication of Vitamin D3 therapy, occurs. New forms of Vitamin D3 analogues eg paracalcitol and doxercalciferol are available which cause less hypercalcemia but suppresses PTH to a greater extent. The use Vitamin D3 should be monitored with regular measurement of PTH which should not be allowed to be overly suppressed to prevent the development of adynamic bone disease. A new novel class of drugs to prevent secondary hyperparathyroidism is the calcimimetics. These agents are calcium receptor-sensing agonist that act on the parathyroid gland calcium sensing receptors increasing their sensitivity to calcium. They suppress PTH without increasing serum calcium or requiring Vitamin D3. The use of the newer Vitamin D3 analogues and calcimimetics provide greater flexibility in managing secondary hyparathyroidism but these agents are costly and their use is presently limited.

When all efforts at medical treatment fail to control secondary hyperparathyroidism, the patient most probably has to undergo parathyroidectomy. Either subtotal or total parathyroidectomy with reimplantation can be performed. Patients require careful pre operative preparation and close monitoring after the surgery for complications such as “hungry bone” syndrome.

Renal bone disease continues to pose challenges to the nephrologists. Early diagnosis and management with regular monitoring of markers of secondary hyperparathyroidism may help prevent serious complications. Newer drugs including a new class of agents provide greater flexibility to manage RBD patients and with less iatrogenic complications.

Acute Coronary Syndrome in Patients with Kidney Disease

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Introduction: Ischemic heart disease is the common cause of death in patients with chronic kidney disease. The increased prevalence of CVD in patients with renal dysfunction has been attributed to lack of effective prevention and less utilization of effective therapy[1]. The optimal treatment of ischemic heart disease in patients with kidney disease is still controversial. CKD is associated with adverse outcomes after coronary interventions (PCI) but it is unclear which of these revascularization strategies is associated with lower risk for morbidity and mortality in CKD population[2]. Keeping this is view we designed a study in which we analyzed 60 patients who had CKD stage II to III and compared their prognosis in terms of survival and resolution Vs recurrence of the coronary symptoms between those who underwent PCI/CABG and those who were given medical treatment without invasive therapeutic intervention.

Objective: To compare the prognosis and outcome of CKD patients with ACS between those who underwent therapeutic invasive intervention Vs those who were treated medically without any invasive intervention.

Patients and Methods : This is prospective case control study done over a span of 3 years conducted at our institute. We identified 30 patients who had CKD 2-3 and had clinical symptoms of ACS who underwent coronary angiography with angioplasty + stenting or CABG and compared with another group which was equally matched in terms of number, risk factors and clinical symptoms but did not undertake any invasive intervention and were treated medically.

Participants were followed for a mean of 3 years after their intervention. We evaluated whether randomization to CABG or PCI Vs medical treatment was associated with different outcome among participants with CKD. An interesting data regarding whether CABG/PCI or medical treatment offers better clinical outcome with CKD patients has come to light and will be presented in the symposium.

Results: We had a total study group of 123 patients with chronic kidney disease 2-4, who had angina, EKG changes or ECHO findings were counseled to undertake coronary Angiography, these patients were then divided into 3 groups: Group I - 34 patients who refused for Coronary Angiography, Group II - 50 patients who underwent Invasive Therapeutic intervention including both PTCA ± stenting or CABG and Group III- 39 patients who although underwent diagnostic coronary Angiography and with proven CAD but were treated medically either advised by the physician or opted by the patient themselves.

In group I of 34 patients, 42% of the patients became worse and the worsening parameters were left ventricular dysfunction (73.5%) Congestive heart failure (64.7%) and Mitral regurgitation (38.2%). In the medical treatment group, patients with SVD survived without deterioration, but those with 2VD and 3VD had a worsening rate of 40% and 75% respectively.

Invasive Therapy group had a better outcome (52%) as compared to medically treated patients in group Ill (17.9%). Better prognosis was seen in patients with 3VD undertaking CABG (52%) when compared to 3VD patients on medical treatment (18%), p. value: 0.0021 17. CABG is still a viable mode of treatment in pts with 3 vessel disease because in the study 40.9 % of chronic kidney disease patients became better. (p.value: 0.024831)

In pts with 2 vessel disease CABG was not identified as a treatment modality of choice as 50% worsened with CABG while only 12.5% deteriorated with PTCA. PTCA in 2VD showed a clinical outcome (75%), while with CABG it was 50%. We also found that renal functions did not determine the cardiac outcome in any of these groups.

Conclusion: In the study, we concluded that in chronic kidney disease lI -IV invasive therapy for CAD had a better outcome Significantly better prognosis was seen in patients with 3VD undertaking CABG In pis with 2 vessel disease CABG was not identified as a treatment modality of choice. We also found that renal functions did not determine the cardiac outcome in any of these groups.

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HCV Infection in Renal Replacement Therapy

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Liver disease is an important cause of morbidity and mortality in patients with chronic renal failure treated by dialysis and transplantation. Biochemical abnormalities in liver function are seen in 7-24% of transplant recipients. Further, liver failure is the cause of death in 8-28% of long-term survivors after renal transplantation. In the past, approximately half of these cases of liver disease were attributed to viral infections such as hepatitis B virus (HBV), Epstein-Barr virus or cytomegalovirus, drugs such as alcohol, azathioprine or cyclosporin, and hemosiderosis. The remaining cases were attributed to non-A, non-B hepatitis (NANBH). In 1989, the hepatitis C virus (HCV) was cloned, and identified as the major cause of parentally transmitted NANBH. The transmission of HCV by transfusion of blood products and by sharing of needles among intravenous drug abusers has been unequivocally demonstrated. After tests becoming available to detect antibodies to multiple HCV antigens (anti-HCV), and the presence and titre of HCV RNA, new avenues to study the prevalence, transmission and natural course of HCV infection in transplant recipient had opened up.

In India, seroprevalence of HCV infection in community is approximately 1%. The prevalence of HCV infection in patients of CKD before start of dialysis is not very well studied. In a study conducted by our own center, it was found that of the 279 consecutive patients of CKD attending for the first time renal outpatients at our hospital and screened for HCV infection, only 3 (1.07%) patients were positive for anti-HCV tested by fourth generation ELISA test (Unpublished data). Thus, it seems that CKD patients themselves are not a high-risk group for HCV infection. In contrast to pre-dialysis patients, patients on maintenance haemodialysis (MHD) is a high-risk group for HCV infection. There are two major risk factors for increasing the risk of HCV infection in patients on MHD; number of blood transfusion and duration of MHD. With the development of screening of blood for HCV infection, blood as a source of HCV has almost being eliminated. However, duration of MHD still remains a major risk factor and causes increase in HCV infection through nosocomial transmission. In a study conducted at our hospital and funded by Indian Council of Medical Research (ICMR), it was found that HCV prevalence at the start of MHD was 3.4% but it increased to 42% during MHD just before the renal transplantation (RT). All these patients were given HCV negative blood if they required blood during MHD. This clearly showed that nosocomial transmission is a major route of HCV transmission during MHD. Further, while conducting another study again funded by ICMR, we have showed that isolation of these HCV positive patients in separate room has decreased the transmission of HCV infection in same dialysis unit setting and two years study outcome was that prevalence only increased to nearly 10% rather than 42% at the end of MHD. However, here it is necessary to state that there is no substitute of following "Universal Precautions" in a dialysis unit. Isolation is not alternative to universal precautions. Every body in dialysis unit MUST follow universal precautions and in addition, these patients need to be isolated.

These patients are usually asymptomatic and diagnosis is made by high ALT value or a positive anti-HCV test. We do monthly ALT and anti-HCV test for screening the HCV infection in our dialysis unit. Patients who have raised ALT but negative anti-HCV test and have no other obvious cause of raised ALT, we usually go for HCV-RNA testing for diagnosis of HCV infection as nearly 15-20% patients who are anti-HCV negative in fact are found to be HCV-RNA positive and thus needs to be isolated. We do liver biopsy in all these patients and had shown that there is no significant correlation between ALT values and histological finding of liver biopsy. Many a times histology shows active hepatitis and ALT values are nearly normal. So, decision of liver biopsy in MHD setting is NOT based on ALT values. If the liver biopsy shows cirrhosis, only then we decide against RT, otherwise even patients with active hepatitis are subjected to RT. Ideally all these patients should be treated before RT with anti viral therapy for HCV. However, because of cost of therapy, majority of patients seen in our hospital are not treated. Recently, we have started trial of Peg-interferon (Peg-INF) alone in these patients. The results and tolerability of the drug will be known in near future.

Once these patients are transplanted, we have shown that these patients have higher risk of infections in post transplant period and there is high mortality due to infections. However, some of these patients also have mortality directly related to liver disease. Mostly, chronic liver disease develops after many years following transplantation. However, in some of the patients, serious liver disease does develop within few years following RT. The factors causing rapid deterioration of liver disease are not known. It may be related to genotype of the HCV virus and degree of immunosuppression given to these patients. There is recommendation that these patients need less immunosuppression but which drug and how much doses are far from clear. At our center we use mostly triple immunosuppression (CsA+ Steroid+Azathioprin) in majority of patients. After some times (Usually 6-12 months), we try to decrease and then stop Azathioprin and keep only two-drug regimen. Post RT we are using Amantadine and Ribavarin as antiviral drugs in these patients as INF cannot be used due to risk of acute rejection. However, results of this non-interferon therapy are not encouraging.

We do not take HCV positive donors for RT.

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Announcements

FUTURE CONGRESSES OF THE ERA–EDTA

Year	Venue	Date
2007	Barcelona (Spain)	June 21–24
2008	Stockholm (Sweden)	May 10–13

For more information please contact: ERA–EDTA Congress Office, Via Spolverini 2, 43100 Parma, Italy. Tel: +39 0521 989078; Fax: +39 0521 959242; Email: congress@era-edta.org

EUROPEAN RENAL ASSOCIATION
European Dialysis and Transplant Association

The New ERA-EDTA website

http://www.era-edta.org

visit the new ERA-EDTA website:
you will find all the information
regarding our Association and our Congresses

Practical-lecture course "Podocytes in-vitro" 7–9 June in Dublin City University, Dublin, Ireland

The course, partially funded by the ERA-EDTA, will consist of lectures by the leading scientists and developers of podocyte cultures (for details, please visit www.cbas.ie).

Deadline for applications is 20 May 2007

For inquiries, please contact Joan.Kelly@dcu.ie

Renal Disaster Relief Task Force (RDRTF): call for volunteers

The RDRTF takes care of interventions during mass disasters such as earthquakes whereby large numbers of acute renal failure (ARF) occur, and support is offered to the local medical and nephrological communities. The RDRTF intervened at the Marmara earthquake in Turkey in 1999, the Bam earthquake in Iran in 2003 and most recently in Kashmir in Pakistan. The RDRTF – European Branch is looking for young doctors, nurses and dialysis technicians who volunteer to take part in our actions. Missions last approximately 10 days. People who are interested, with experience in acute renal failure and/or intensive care nephrology, organising skills, respect for foreign cultures and diplomatic talent are asked to contact Raymond Vanholder, the current chairman of the RDRTF at the following e-mail address: Raymond.vanholder @ugent.be

WE ARE HAPPY TO ANNOUNCE THE 6th ANNUAL CONFERENCE ON

PREVENTION IN RENAL DISEASE

TORONTO,

September 28-29, 2007

For details and registration form, those interested should visit: <http://www.nephroprevention.com>

ERA-EDTA CME COURSES

The ERA-EDTA CME course programme after the first two years is already well established.

The programme that was developed in 2006 was widely appreciated and I must thank all the organizers for the efforts made, starting from their inputs in the programme refining to looking for collateral economical supports, and finally to entertaining in such a kind way both the speakers and the attendants.

19 events were organized, each at a very good level and extremely successful.

The programme for 2007 has been finalized and is available at our web-page.

Considerations

- The success of the CME courses is greater than planned and it is constantly increasing: the Society is receiving high recognition for this activity.
- The organizers are key-persons in Nephrology in Europe, and they must be thanked.
- The programmes are covered by the most famous experts in the various fields, who report the experience of a lifetime activity and must be greatly thanked for this.

The 2007 CME courses will include:

5 COURSES BEFORE THE XLIV CONGRESS IN BARCELONA (JUNE 21, 2007)

AREAS:

- Basic Science and Translational Applications
  "Beginner's guide to Molecular Biology for the Clinical Nephrologist": J. Floege & R. Coppo
- Immunopathology

"Renal Histo-Immunopathology at square two": V. Nickeliet, F. Ferrario, MP Rastaldi

- Clinical Nephrology

"Renal ultrasound and renal doppler for the Clinical Nephrologist": J. Radermacher

- Chronic renal disease

"Organizing CKD care: integrating knowledge and practice": A. Levin, AM Castelao

- Epidemiology

"The Epidemiology of CKD in Europe: National surveys and initiatives": P. De Jong, C. Zoccali

Highlights

"ASN Highlights" in Europe and "ERA-EDTA Highlights" in USA

- "ASN Highlights" at the ERA-EDTA Congress, Barcelona, June 22, 2007
- "ERA-EDTA Highlights" at the ASN, San Francisco, November, 2007

"ERA-EDTA Highlights" in Europe:

- At the Italian Society of Nephrology, Bari, October 10, 2007
- At BANTAO, Belgrade, Serbia, September 16–17, 2007
- Nephrology meeting, Parma, Italy, November 16–17, 2007
- At the Turkish Society of Nephrology, Antalya, 14–17 November, 2007

CME COURSES FULLY SPONSORED BY ERA-EDTA:

AREAS:

- *Basic Science and Translational Applications: 1.*

NEW! Laboratory hands-on skills working with cultured podocytes + clinical lectures "Podocytes in vivo and in vitro – from molecular biology to translational applications": H. Holthofer, Dublin, Ireland, July 4–7, 2007.

- *Immunopathology: 2.*
- NEW! "European Nephropathology course": S. Florquin & J. Weening, Amsterdam, the Netherlands, June 27–29, 2007.
- "Frontiers in Renal Science: inflammation, genetics and repair": T. Cook, P. Maxwell, C. Pusey, Oxford, UK, July, 11–13, 2007.
- *Continuous practical development: 1.*

"Ultrasound training course" and "Kidney biopsy and histopathology training course": J. Beige, Leipzig, Germany, May 31, 2007.

- *Clinical Nephrology & Basic Science: 1.*

"Reina Sofia Inst. &K/DIGO": J. Cannata-Andia, Madrid, Spain, November, 2007.

- *Transplantation: 2.*
- "Cancer and Renal Transplantation Updates": J. Campistol, Barcelona, Spain, February 23–24, Satellite to Catalan Congress.
- "Proteinuria in Renal Transplantation: pathophysiology, diagnosis, treatment": M. Salvadori, Florence, Italy, March, 21–22, 2007.
- *Epidemiology &/Statistics: 2.*
- ERA-EDTA Registry, QUEST C. Zoccali, Thessaloniki, Greece, February 10–12, 2007.
- ERA-EDTA Registry, C. Zoccali, Leiden, the Netherlands, September 22–24, 2007.
- *Multiple topics full Courses: 2.*
- "Renal Failure Academy": A. Covic, Constanta, Romania, June 7–10, 2007.
- "CKD, Epidemiology and Registry": Tirana, Albania, May 4–5, 2007, G. Spasovski.

CME COURSES IN COLLABORATION WITH ISN (2–3 LECTURERS SPONSORED BY ERA-EDTA).

- Prague, Czech Republic, January 27–30, 2007, V. Teplan & A. Wiecek.
- Budapest, Hungary, August 25–30, 2007, L. Rosivall.
- Pristina, Kosovo, UNMIK, May 24–26, 2007, M. Zeier & N. Lameire.
- Kiev, Ukraine, September 14–15, 2007, D. Ivanov.
- In collaboration with ISN and ESPN
- Moskow, Russia, September 22–24, 2007. N. Tomilina, A. Tsygin,

2007 CME COURSES SUMMARY

- 5 in Barcelona, June 21, 2007, ERA-EDTA Congress.
- 6 Highlights (5 ERA-EDTA, 1 ASN).
- 12 ERA-EDTA full CME courses.
- 5 in collaboration with ISN.

ERA-EDTA CME Activities

Chair: Rosanna Coppo

CME Courses Coordinators

Basic Science & Clinical Nephrology: R. Coppo and P. Ronco.

Chronic Renal Failure, Hypertension, Clinical Epidemiology: C. Zoccali and G. London.

Dialysis: R. Vanholder, S. Davies, C. Wanner.

Transplantation: C. Ponticelli, A. Torres and K. Olgaard.

Collaboration with ISN for courses in Eastern Europe: N. Lameire, A. Covic.

(www.era-edta.org. Section Education, CME Courses)

14TH BUDAPEST NEPHROLOGY SCHOOL

(Nephrology, Hypertension, Dialysis, Transplantation)
Under the Auspices of ISN, ERA 25 August – 30 August, 2007
To be held at the Semmelweis University with the participation of distinguished international faculty.
For further information and application please write to:
László Rosivall, MD, PhD, DSc,
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Semmelweis University, Institute of Pathophysiology
Nephrology Research and Training Center
Nagyvarad ter 4, 1089 Budapest, Hungary
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XXXIV. CONFERENCE OF THE EUROPEAN SOCIETY FOR ARTIFICIAL ORGANS

Campus Krems, Krems, Austria, September 5-8, 2007
Sponsoring Organization: Fresenius Medical Care

(Main Sponsor)

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