DISSERTATION ON

A STUDY OF VOLUNTARY KIDNEY DONORS – POST TRANSPLANT

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

M.D. GENERAL MEDICINE

(BRANCH – I)

THANJAVUR MEDICAL COLLEGE,

THANJAVUR - 613 004

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

APRIL - 2013

CERTIFICATE

This is to certify that this dissertation entitled **"A STUDY OF VOLUNTARY KIDNEY DONORS – POST TRANSPLANT"** is the bonafide original work of **Dr. LALITH NARAYAN B.** in partial fulfillment of the requirements for **M. D. Branch - I (General Medicine)** Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in APRIL - 2013.

The period of study was from February - 2012 to October - 2012.

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DECLARATION

I, **Dr. LALITH NARAYAN B.**, solemnly declare that dissertation titled **"A STUDY OF VOLUNTARY KIDNEY DONORS – POST TRANSPLANT"** is a bonafide work done by me at Thanjavur Medical College, Thanjavur during **February - 2012 to October - 2012** under the guidance and supervision of **Prof.Dr.S.MANOHARAN, M.D.,** Unit Chief M-IV, Thanjavur Medical College, Thanjavur.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University towards partial fulfillment of requirement for the award of **M.D. Degree (Branch - I) in General Medicine**.

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Period of Study : **February - 2012 to October - 2012**

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Dissertation Topic : **A STUDY OF VOLUNTARY KIDNEY DONORS – POST TRANSPLANT**

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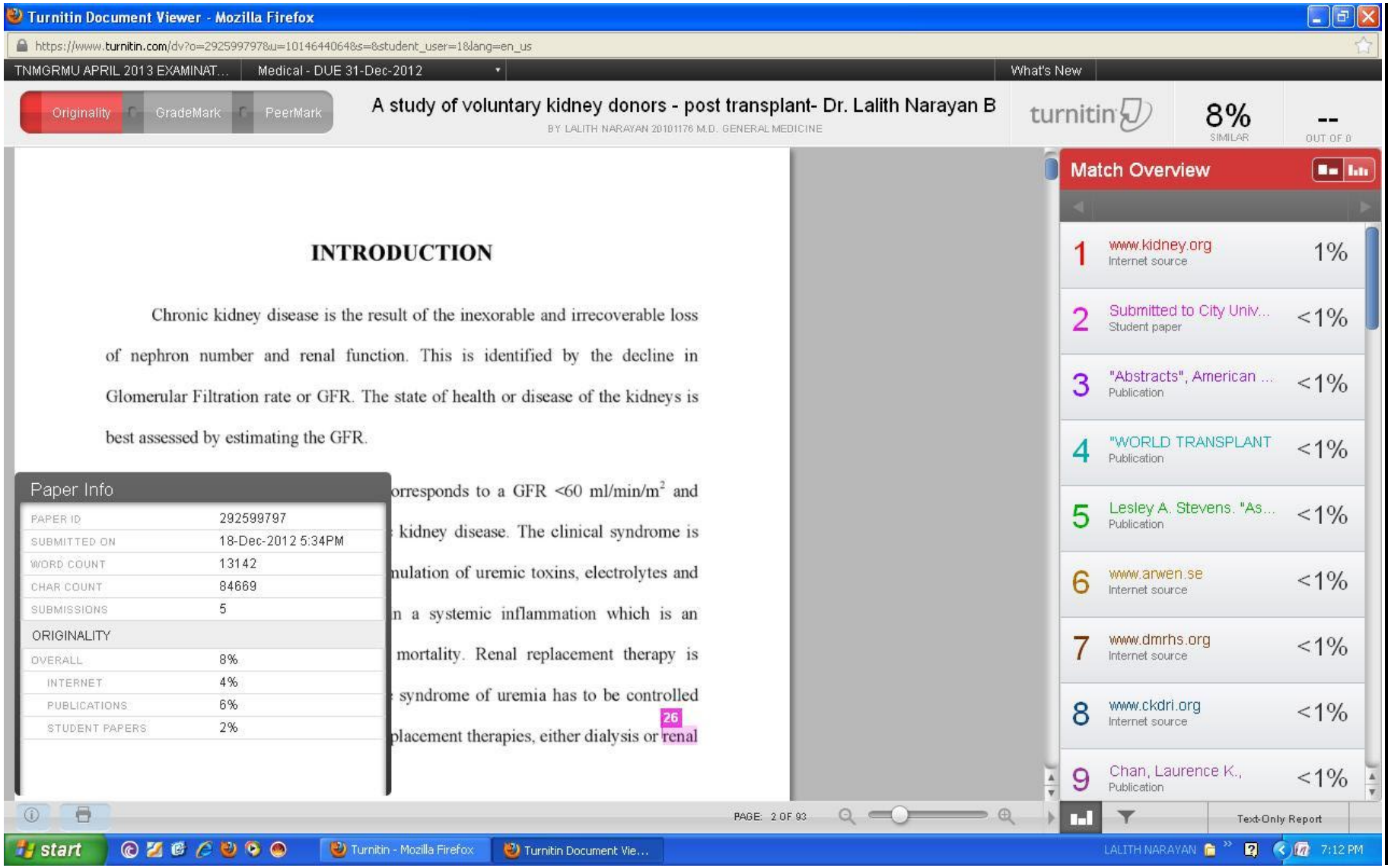
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26
Paper Info
PAPER ID 292599797
SUBMITTED ON 18-Dec-2012 5:34PM
WORD COUNT 13142
CHAR COUNT 84669
SUBMISSIONS 5
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ACKNOWLEDGEMENT

I gratefully acknowledge and thank **Prof. Dr.C.Gunasekaran M.D.,D.C.H.**, Dean(i/c), Thanjavur Medical College, Thanjavur, for allowing me to do this dissertation and utilize the institutional facilitites.

I am extremely grateful to **Prof. Dr. S. Muthukumaran M.D.**, Head of the Department of Internal Medicine, Thanjavur Medical College, Thanjavur, for his full fledged support throughout my study and valuable suggestions and guidance during my study and post graduate period.

I am greatly indebted to **Prof. Dr.S.Manoharan, M.D.,** my Professor and Unit Chief, who is my guide in this study, for his timely suggestions, constant encouragement and scholarly guidance in my study and post graduate period.

I fondly remember my former unit chief **Prof. Dr. P. Krishnamurthy M.D.**, who has been a continuous support and whose teachings I will always remember.

I profoundly thank my respected professors

Prof.Dr.P.G.SankaranarayananM.D., Prof.Dr.K.NagarajanM.D., Prof.Dr.C.GanesanM.D., Prof.Dr.D.NehruM.D.,D.M.R.D., Prof.Dr.V.RajendranM.D., Prof.Dr.K.Parimala DeviM.D. and **Prof. Dr.M.SivasankaranM.D.** who have all taught me the art of medicine during my post graduate period.

This study would not have been possible without the motivation, support and guidance of the nephrologist at Thanjavur Medical College, **Dr.T.Rajendran M.D.,D.M.(Nephro)** to whom I am greatly indebted.

My sincere thanks to my Assistant Professors **Dr.C.SundararajanM.D., Dr.V.P.KannanM.D., Dr.S.VetrivelM.D., Dr.R.T.Shriram GaneshM.D.,** for their motivation and encouragement.

A special thanks to all the donors who took their time and effort to come from far away places to participate in this study, for their kind cooperation.

I would like to thank my family and friends who have been a constant source of encouragement and support during the study period.

I invoke the blessings of the Almighty for making all this possible.

Dissertation on

'A study of voluntary kidney donors – post transplant'.

ABSTRACT

BACKGROUND AND OBJECTIVE:

The incidence and prevalence of chronic kidney disease is increasing in India. CKD stage V is reached earlier in life. Renal transplantation is the best choice of treatment for CKD stage V. Living donor kidney transplantation represents about 95% of renal transplantations in India. Uninephrectomy for kidney donation puts the donor at risk for renal failure and the development of glomerular hyper-filtration syndrome. Studies from the West have have documented the safety of living kidney donation. There are limited numbers of studies from India regarding kidney donors.

MATERIALS AND METHODS:

The voluntary kidney donors of 50 transplant recipients attending the Department of Nephrology-Transplant OPD were chosen and enrolled in the study after informed consent. The donors had a post nephrectomy period ranging from <1 year to 27 years. They were screened for hypertension, proteinuria and renal failure. Their attitude toward kidney donation was studied.

RESULTS:

39 female donors and 11 male donors were enrolled. Wives were the single major group of donors. The mean age of the donors studied was 49 years, with a mean post donation period of 6.58 years. Female donors had a mean age at donation less than the males. The mean systolic blood pressure was 122.32±13.65 mmHG and mean diastolic blood pressure was 79.16±9.85 mmHg. The prevalence of hypertension among the donors was similar to the population based studies. None of the donors had proteinuria. Only one donor had elevation of urea and creatinine. The mean time taken by the donors to return to normal life was 4.08 weeks. All the donors had a positive attitude towards donation.

CONCLUSION:

The donors seem to have no additional prevalence of hypertension as compared to the general population. No proteinuria or major deterioration in renal function was noted. All the donors had a positive attitude towards kidney donation. Living kidney donation appears to be safe in the Indian scenario also. Larger prospective studies are needed to confirm this.

KEYWORDS:

Kidney donors, living kidney donation, glomerular hyperfiltration, renal transplantation.

CONTENTS

INTRODUCTION

INTRODUCTION

Chronic kidney disease is the result of the inexorable and irrecoverable loss of nephron number and renal function. This is identified by the decline in Glomerular Filtration rate or GFR. The state of health or disease of the kidneys is best assessed by estimating the GFR.

The term chronic renal failure corresponds to a GFR <60 ml/min/m^2 and occurs during stage III to V of chronic kidney disease. The clinical syndrome is called uremia and is produced by accumulation of uremic toxins, electrolytes and dysregulation of hormones resulting in a systemic inflammation which is an independent risk factor for increased mortality. Renal replacement therapy is initiated at a GFR <15 ml/min/m^2. The syndrome of uremia has to be controlled and reversed by the initiation of renal replacement therapies, either dialysis or renal transplantation.

The best form of renal replacement therapy is renal transplanation. However there is an increasing mismatch between the demand and supply of kidneys for transplantation. This led to the increase in living donor transplantations over deceased donor transplants. Further expanded criteria for selecting donors and kidneys of brain dead patients were accepted to increase the pool of available

kidneys for transplantation. Recent improvements in post transplant graft support have made outcomes similar in related and unrelated kidney transplants.

The most common type of renal transplantation in India is living donor transplantation. It has the advantage of immediate availability of kidneys. However it involves an operation and removal of a vital organ from a healthy individual. Therefore it is obvious that strict selection criteria for donors and recipients are followed. The safety of renal donation has been studied and confirmed by many studies in the western world. Data from India about renal donors and the safety of renal donation are scarce. This study aims to assess the effects of renal donation by assessing the renal function in the donors and the impact of renal donation on their psychosocial functioning.

AIMS AND OBJECTIVES

AIMS OF THE STUDY

Uninephrectomy for renal donation results in an obvious loss of nephron mass. Surgical ablation of kidneys in animals has proven to result in the syndrome of glomerular hyper-filtration in the remaining kidney.

This study aims to evaluate kidney donors for the following

1. Development of systemic hypertension.
2. Development of proteinuria.
3. Development of renal failure by estimation of urea and creatinine values.

The quality of life after kidney donation was analysed by the following

1. Time taken to return to normal activities following surgery
2. Their attitude about kidney donation

REVIEW OF LITERATURE

Chronic Kidney disease

The NKF-KDOQI[1] (The National Kidney Foundation Kidney Disease Outcome Quality Initiative Work Group - 2002) defined Chronic Kidney Disease (CKD), identified the stages of the disease and developed practice guidelines.

It also established criteria for laboratory assessment of chronic kidney disease. It correlated the level of kidney function with the complications of CKD and stratified the risk for progressive loss of renal function and the risk of cardiovascular disease.

Definition[1]

The operational definition adopted by the Work Group was as follows:

Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, that can lead to decreased GFR, manifest by either:
• Pathologic abnormalities; or • Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
GFR < 60 mL/min/1.73 m^2 for ≥ 3 months, with or without kidney damage

The Work Group preferred to use the word ‘kidney’ instead of ‘renal’ to simplify communication between the doctors and patients.

Chronic kidney disease included any condition that affected the kidney with the potential to cause progressive loss of renal function, or the complications arising out of the decreased renal function. Thus irrespective of the diagnosis, kidney damage or decreased renal function for 3 or more months was sufficient for a diagnosis of CKD. The National Institute of health and clinical excellence (NICE) modification-2008 of the K-DOQI 2002 guidelines is as follows:

CKD Stages	Definition
1	Normal or increased GFR; some evidence of kidney damage reflected by microalbuminuria, proteinuria, hematuria, as well as radiologic or histologic changes
2	Mild decrease in GFR (89-60 mL/min/1.73 m^2) with some evidence of kidney damage reflected by microalbuminuria, proteinuria, hematuria, as well as radiologic or histologic changes
3	GFR 59-30 mL/min/1.73 m^2
3a	GFR 59-45 mL/min/1.73 m^2
3b	GFR 44-30 mL/min/1.73 m^2
4	GFR 29-15 mL/min/1.73 m^2
5/ESRD	GFR <15 mL/min/1.73 m^2; when renal replacement therapy in the form of dialysis or transplantation has to be considered to sustain life

CKD = chronic kidney disease; K/DOQI = Kidney Disease Outcomes Quality Initiative; NICE = National Institute of Health and Clinical Excellence; GFR = glomerular filtration rate; ESRD = end-stage renal disease. The suffix "p" should be added to the stage in patients with proteinuria (proteinuria >0.5 g/24h).

Stages of Chronic Kidney Disease		
Stage	**GFR**	**Action Plan ***
1	≥90	Diagnosis and treatment. Treatment of co-morbid conditions, slowing progression, CVD risk reduction
2	60-89	Estimating progression
3	30-59	Evaluating and treating complications
4	15-29	Preparation for kidney replacement therapy
5	<15 (or dialysis)	Replacement (if uremia present)
***Includes actions from preceding stages**		

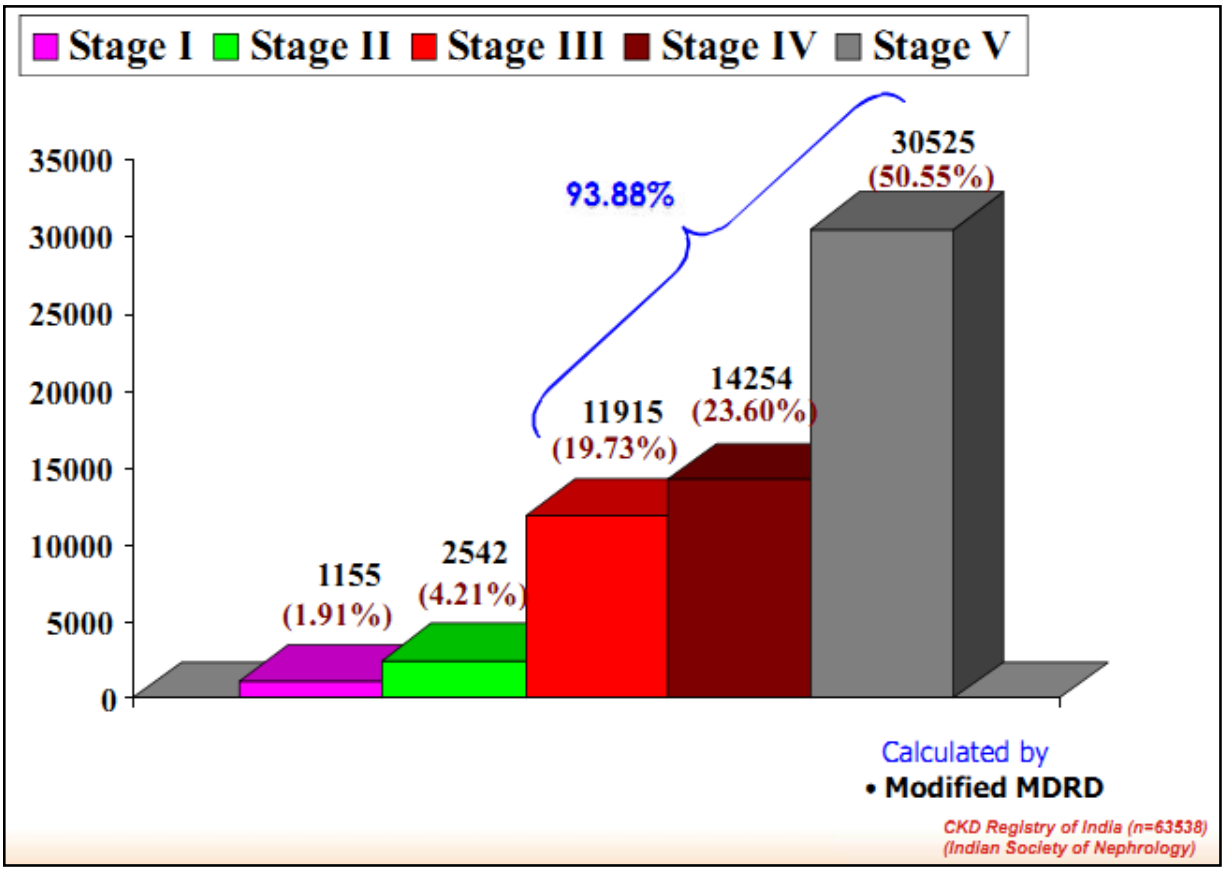
Indian scenario of CKD

CKD in India has sporadically been studied previously[2-5]. There were no regional or national reports on incidence or prevalence of CKD. The crude and age-adjusted incidence rates of ESRD were found out to be 151 and 232 per million populations respectively, in a study by Modi GK et al. [6,7]. Varma PP et al. showed the prevalence of reduced glomerular filtration rate and microalbuminuria was 13% and 10% respectively in healthy adults[8]. Agarwal et al found low GFR 0.8% of 4972 persons surveyed in Delhi[10]. These data are in contrast to those in the West where CKD occurs in about 12-20% as estimated by NHANES [11-13].

The CKD Registry of India created in 2005 with the help of the Indian society of Nephrology aims to document and study the various aspects of CKD in India.

The 2011 report of the CKD registry of India[14] noted a total of 63538 reports of CKD. Males constituted 70.6% and females 29.4% of the reported cases. The mean age for males was 50.7+14.6 years and 48.1 + 14.3 years for females. The overall mean age was 50.0 + 14.6 years with an age range of 19 to 98 years. A stable trend was observed in the past 6 years with regard to the age and gender distribution. In south zone of India, the highest reports of CKD were in the age group of 51 to 60 years. This was consistent with the reports from the other three zones.

Stage I CKD was observed in 1.91% cases, stage II in 4.21%, stage III in 19.73%, stage IV in 23.60% and stage V in 50.55% of cases. This pattern was similar in the reports from all four zones of the country. Patients with CKD stages III to V constituted 93.88% of the total reported. Thus it is easily seen that CKD stage V constitutes the majority of cases and these are the patients who need expert care and renal replacement therapy.



Irrespective of their educational status, 74.2% patients report to nephrologists after stage IV CKD. 74.0% patients irrespective of their income report to Nephrologists after stage IV CKD. As family income increases the patients come earlier to the nephrologists.

The most common etiology associated with CKD was diabetic nephropathy, seen in 30.9% cases. CGN was the second most common etiology identified with 13.3% cases. The etiologies of CKD showed a similar trend in all four zones of the country.

ZONEWISE CURRENT MANAGEMENT

	East	North	South	West	Total
Conservative + Palliative	5415 (71.62%)	14005 (82.88%)	19504 (81.86%)	10990 (72.05%)	49914 (78.56%)
Dialysis – MHD	1814 (23.99%)	2126 (12.58%)	3678 (15.44%)	3423 (22.44%)	11041 (17.38%)
Dialysis – CAPD	159 (2.10%)	579 (3.43%)	276 (1.16%)	376 (2.47%)	1390 (2.19%)
Renal Transplantation	173 (2.29%)	188 (1.11%)	368 (1.54%)	464 (3.04%)	1193 (1.88%)
TOTAL	7561	16898	23826	15253	63538

Renal Transplantation

CKD patients in India enter into stage V much earlier (42 years) as compared to the developed countries (61 years)[22]. Therefore, CKD occurs in the prime period of life. This is the age when patients have to earn and secure their families. The earlier occurrence of CKD stage V maybe due to delay in starting treatment or measures to slow progression of CKD.

Thus patients in their productive years need a therapy that is cost effective in the long run and also provides a better quality of life. In these regards, renal

transplantation has emerged as the therapy of choice for CKD stage V. The costs of the transplant procedure and the follow up immunosuppressive therapy remain prohibitive for many patients. But they are still somewhat comparable to the costs of maintenance hemodialysis. CAPD is a conducive alternative, as it reduces the need to travel to hemodialysis centres, but has its own limitations with regard to availability and infection control issues for the patient. CKD often affects the poor in our country who cannot afford the costs for these procedures. Despite this, transplantation should still be considered wherever possible.

The first successful renal transplantation was performed between identical twins by Joseph Murray and his team, at the Peter Bent Brigham Hospital in Boston, Massachusetts, in 1954. Study of the immune responses to allogenic grafts led to the identification and understanding of the the Human Leucocyte Antigens (HLA). Recipient T cells identify allograft HLA antigens and mount a vigorous immune response to knock out the graft tissue. The development of azathioprine as an immunosuppressant made it possible to perform transplants between non-identical persons. Azathioprine was used in conjunction with corticosteroids. The development of more potent molecules like mycophenolic acid, cyclosporine, tacrolimus and monoclonal antibodies has improved acute rejection outcomes. The problem of chronic rejection still remains a major issue.

Kidney transplants are of 2 major types:

1. Living donor transplantation.

2. Deceased donor transplantation.

The living donors may be classified further as identical twin, biologically related and biologically unrelated donors. The biologically unrelated donor pool has fast grown over the last decade. This is mainly due to the improvement in graft survival in unrelated donation which now approximates that of the HLA matched transplant. The biologically unrelated donors may further be classified as emotionally related e.g. spouse, friend, etc. or altruistic donor. Spousal donation is on the increase in India. There are social issued regarding live kidney donation like organ trafficking. Spousal donation reduces the incidence of such malpractices, strengthens the marital bond and makes preemptive transplantation possible by reducing the waiting period for the kidney. However given the male dominant society in India, donation of kidney by women by compulsion must be carefully excluded in every case. Living donor transplantation is now more commonly practiced in India.

Living Donor Transplantation

In the United States, about 40% of all transplants performed from living related donors. It is lesser in Europe and Australia[15]. It is now the commonest form of kidney transplantation in India. In addition, many programs will now accept living, non-blood-related or distantly related donors (spouses, cousins, uncles, aunts, altruistic donors etc.) Living related kidney donor transplantation is no longer controversial. There has been concern for many years about the long-term outcome of a healthy donor. In particular, the concerns regarding the possibility of long-term renal dysfunction resulting from hyper-filtration in the solitary kidney have prompted transplant centers to re-evaluate their living-related donor program. Several long-term follow-up studies have not revealed any adverse problems in living related donor with a single kidney[16]. The donor mortality risk has shown to be less than 0.1%. Life expectancy in the donor remains unaffected. Further studies and follow-up of kidney donors are necessary. In view of the shortage of cadaver kidneys, transplantation of a graft from a compatible living related donor should be considered if there is a suitable donor. Outstanding results with living unrelated donors have been obtained.[17]

Expansion of the living donor pool

As patient and graft survival rates for kidney transplant recipients with living unrelated donors have been shown to be equivalent to living related donor transplant recipients, a greater willingness by society and the transplant community to consider the unrelated donor has emerged. An extension of living nonrelated donation is the non-directed kidney donor, an individual who contacts transplant centers wishing to donate a kidney for purely altruistic reasons, to no specific recipient in particular. Unlike the non-directed kidney donor, two other circumstances have been specifically proposed to increase the number of potential living donors. The first, a paired exchange program, attempts to identify two potential donors who wish to donate to a family or friend but are unable to due to blood group incompatibility or a positive cross-match. Two such donors and their prospective recipients are then paired, with donor A donating to recipient B and donor B donating to recipient A. An extension of this concept is the mixed donor exchange in which an incompatible donor donates to the cadaveric waiting list in exchange for their paired recipient moving to the top of the deceased donor list in their given blood type. These efforts are currently being tested for their equity and effect on transplantation rates in small pilot studies. The second circumstance is the matched donor in which a prospective recipient pays a monthly fee to a coordinating site, which presumably has access to a list of potential parties

interested in donating their kidney. This strategy circumvents the UNOS waiting list and currently is under significant criticism from the American Society of Transplantation and UNOS.

Living donor evaluation

Live donors are usually first-degree relatives who are one or two haplotype matched. However, there is good evidence that zero haplotype-matched relatives can donate kidneys that provide excellent chance of short- and long-term graft survival. Similarly, good results have been reported with emotionally related living donors. Most living nonrelated donors are spouses or companions with long-standing emotional ties. This practice will likely become an important source of organs for transplantation. By 1995, about 10% of transplants were from living unrelated donors. Initial screening should concentrate on related donors and tissue typing should be used to help choose the best potential donor among ABO-compatible candidates.

The attitude toward the use of unrelated live donors varies considerably among centers. In general, live-donor transplantation is fraught with potential psychological problems and it is important to establish that the prospective donor has not been subject to family pressure. A very careful psychological evaluation will be needed to determine that the motivation to donate the kidney is, indeed,

genuine. HLA genotyping should be used to decide on the most suitable donor if there are several family members who are all keen to give a kidney. The initial series of tests which include ABO blood group and HLA tissue typing can be completed at a brief outpatient visit. Possible live-donor transplantation can then be considered with the individuals best matched to the recipient. The living donor not only needs a thorough medical evaluation, with particular attention to renal function and the urinary tract, but also a renal angiography or magnetic resonance angiography to identify vascular or anatomical variation of the kidneys or the collecting systems. It is important to ascertain that both kidneys are of normal size and configuration and that a donor kidney with a single renal artery can be obtained.

Exclusion criteria for live kidney donors

- Age <18 or >65 to 70years
- Significant medical illness (e.g. cardiovascular or pulmonary diseases, recent malignancy)

  History of recurrent kidney stones
- History of thrombosis or thromboembolism
- Psychiatric contraindications

- Obesity (30% above ideal weight)
- Hypertension (>140/90 mmHg or necessity for medication)
- Proteinuria (>250 mg/24 hr)
- Microscopic hematuria
- Abnormal glomerular filtration rate (<80 mL/min)
- Diabetes (abnormal glucose tolerance test or hemoglobulin A_{1c})
- Urologic/vascular abnormalities in donor kidneys

Suggested evaluation process for potential live donors

- Donor screening
- Educate patient regarding cadaveric and live donation
- Take family and social history and screen for potential donors
- Review ABO compatibilities of potential donors
- Tissue type and cross-match ABO-compatible potential donors
- Choose primary potential donor with patient and family

- Educate donor regarding process of evaluation and donation
- Donor evaluation
- Complete history and physical examination
- Comprehensive laboratory screening to include
    1. Complete blood count,
    2. Chemistry panel,
    3. human immunodeficiency virus,
    4. very low-density lipoprotein,
    5. hepatitis B and C serology,
    6. cytomegalovirus,
    7. glucose tolerance test (for diabetic families)
- Urinalysis, urine culture, pregnancy test (where appropriate)
- Protein, 24-hr urine collection
- Creatinine, 24-hr urine collection
- Chest radiogram, exercise treadmill for patients older than 50 years of age

- Helical computed tomography urogram
- Psychosocial evaluation
- Repeat cross-match before transplantation

Cadaver donor transplantation

Better quality kidneys are available with the increase in certification of brain death. [18] Better preservation techniques have been developed. Organ sharing programs help to find appropriate recipients[19]. Although there is a slight influence of donor age on renal function in transplant recipients, acceptable donors are between age 3 to 65 years old and, in some centers, even younger and older donors are being considered. There should be no evidence of primary renal disease and no generalized viral or bacterial infection. A major consideration is the risk of transmitting infection with the allograft to an immunosuppressed recipient. Because of the possibilities of HIV transmission, HIV screening should be performed. All donors who are confirmed positive for HIV antibody should be excluded from donation. Those donors at high risk for HIV infection generally should not be accepted for donation because there is a period of seronegativity in early HIV infection before antibodies appear. HIV antigen testing should be performed in such donors.

Extended criteria donor

In an effort to improve utilization of cadaveric organs, UNOS has defined and established guidelines for the use of organs that have traditionally resulted in excellent short-term function but diminished long-term function (extended criteria donors, ECD). These kidneys meet ECD criteria if they arise from

1. donors over the age of 60 or
2. donor is between the ages of 50 to 59 with atleast two among the following criteria:
    a. Cerebrovacular accident as a cause of death
    b. Prior diagnosis of hypertension or diabetes
    c. Serum creatinine greater than 1.5 mg/dL.

These donor kidneys provide improved outcomes when compared to dialysis for a significant portion of the dialysis population, particularly elderly patients and patients with diabetes who generally have poorer outcomes on dialysis. Additional attempts to increase the organ donor pool have addressed the use of donors who have died by cardiopulmonary arrest rather than brain death, termed deceased by cardiac death donors (DCD).

Cadaver donor - Criteria

- Diagnosis of brain death
- Preconditions
    - Positive diagnosis of cause of coma (irremediable structural brain damage)
    - Comatose patient, on ventilator
- Exclusions
    - Severe metabolic or endocrine disturbances
    - Drugs
    - Primary hypothermia (<33°C)
- Tests
    - Apnea (strictly define)
    - Absent brainstem reflexes
- No preexisting renal disease

- No active infection, Tests:
    - HBsAg; 5 antibodies to cytomegalovirus and hepatitis C virus
    - HIV antibodies
    - HIV antigen in high-risk patients

Transplants So Far in Tamil Nadu[24]:

It is not surprising that kidneys are the most frequently transplanted organs. This is due to the fact that kidney transplantation is now a well established technique and many centers have come up with the facility. There is also more number of patients on the kidney waitlist every year. The cadaver kidneys function satisfactorily post transplantation in many cases. Although inferior to living kidney donation, for patients with no available donor, cadaveric transplantation is a new hope for a better life. It has been studied that the rate of commercial kidney donation has been curtailed by the success of the cadaver transplantation programme in Tamil Nadu by Georgi Abraham et al.[26] It is a proud fact that Tamil Nadu had a 1.3 per million population in 2011[24]. For a programme that is developing and functioning well, this donation rate maybe expected to increase.

So far 53 hospitals were approved for kidney transplantation in Tamil Nadu as on 13th February 2012.

Performance Report : From Oct 2008 to Nov 30, 2012

Donors From TN	**301**
Heart	49
Lung	11
Liver	275
Kidney	**555**
Total Major organs	**890**
Heart Valve	350
Cornea	476
Skin	1
Total Organs	**1717**

Barriers to deceased donor transplantation in Tamil Nadu

1. Lack of awareness of brain-death concept
2. Lack of organ donation awareness
3. Misunderstood concept that renal transplantation is very expensive in the long run
4. False perception of reduced survival after transplantation
5. Limited availability of state run kidney transplantation centers which function at low cost.

Pre-transplant preservation of the kidney graft

Effective preservation of the kidney is an integral part of a kidney transplantation program and has evolved on the basis of known principles of preservation because of a need for longer storage of kidneys[20]. The ability to preserve kidneys provides time for tissue typing and cross-matching and the selection of the most appropriate recipients for a particular donor on the basis of matching, as well as the preparation of the patients selected, who often may need dialysis before transplantation, and, finally, the transport of the kidneys to a center where an appropriately matched recipient may be awaiting a transplant. The target is to achieve a core temperature of 0ºC.

Commonly used methods:

1. Continuous perfusion with oxygenated colloid solution.
2. Storage in ice after complete flushing with cold solution.

In general, preservation methods do not affect cadaver renal allograft outcome[21]. Storage in ice after flushing is now widely used. It is simple and preserves the kidney for 24 hours, and even up to 48 hours with newer approaches to preservation.

Before nephrectomy, the blood in the kidney is flushed out with hypothermic solution. This is done through the aorta and renal artery. Many different flushing solutions have been used (Collins, citrate, University of Wisconsin solution). The aim of these maneuvers is to prevent post-transplant acute tubular necrosis. The University of Wisconsin solution has revolutionized the preservation of livers and pancreas, but whether it represents an improved method of preservation for kidneys has not yet been clearly established.

When there has been no warm ischemia, kidneys preserved up to 24 hours function immediately. However, kidneys stored for more than 24 hours begin to function slowly. The delay may even be up to several weeks. As the storage time increases there is a greater risk that some function will be permanently lost.

It has been suggested that for short-term outcome, local use of kidneys with poor HLA matching is as good as shared use with good matches. Since 18 to 36 hours is an adequate time for most units and also allows time for transport of kidneys within a region or country, there has been widespread adoption of the simple cold-storage technique for preservation.

The second approach of machine preservation is costly and complex. But it is not very beneficial. In this albumin or plasma protein fraction is used. The circuit oxygenates the colloid during the perfusion process. Either a pulsatile or a continuous flow pattern can be utilized. Both the temperature and the pressure of the perfusate are monitored and the flow is generally kept at 1 to 3 mL per gram of kidney per minute. However, normal perfusion characteristics are no guarantee of organ viability and function.

Cadaveric organ transplantation - The Tamil Nadu model

Certification of brain death has been made compulsory in the 3 medical college hospitals in Chennai. This is to promote organ donation after brain death. The next process depends on where the harvesting takes place. If it is done in a place where only kidney transplantation is done, the other kidney, heart, lung and liver are available for other hospitals where the appropriate transplantation facility is available.

There has been a recent interest among non government organizations (NGOs) in this area. Now, an organ sharing network has been established and is functioning well. All the enlisted hospitals are instructed to update the details of the waitlist of patients and the transplantation procedures periodically. There has also been a government order[25] to conduct periodic training programmes and workshops to increase the general awareness regarding organ donation. The lack awareness about the organ donation programme is by itself a major impediment, which has to be overcome. With the passage of time, if this system in TamilNadu works successfully, more people may become willing to donate organs once brain death is pronounced and thereby more patients on the waitlist for organs will benefit. This is particularly true for older patients in whom cadaveric transplantation is a reasonable option ahead of live kidney transplantation in view of the overall short life expectance post transplantation. Most of the transplant facilities are presently available only with the private hospitals. With further government interest in this issue, more number of medical colleges may be upgraded into transplant centres whereby, even the poor people in India may benefit. It has already been shown that renal transplantation in the long run is not costlier than maintenance hemodialysis or CAPD, but provides a better life. Thus the initial cost of the transplant surgery may also become affordable with the

addition of more state run transplant centers. Listed below are some of the organizations taking active interest in organ transplantation across India.

1. The Narmada Kidney Foundation
2. The Foundation for Organ Transplantation and Education- FORTE in Bangalore
3. Organ Retrieval Banking Organization - ORBO in New Delhi
4. Multi-Organ Harvesting Aid Network–MOHAN in Chennai and Hyderabad
5. Zonal Transplant Co-coordinating Committee - ZTCC in Mumbai
6. Delhi Organ Procurement Network and Transplant Education – DONATE in Delhi

Outcomes in kidney transplantation

In the 1960s and early 1970s, many patients were transplanted when there were no supportive facilities if the graft failed. In those days, the high mortality was related to uncontrolled infection when excessive immunosuppression was used for rejection processes. With improvement in clinical care and use of more specific immunosuppression, patient survival has been shown to improve both in the

cadaveric and in the living related renal transplant recipients. Mortality at the end of the first year is currently less than 5% for living donor and under 10% for cadaver donor. Indeed, recent data indicate that patients currently receiving cadaver donor transplants generally survive longer than patients treated by dialysis. Infectious complications of immunosuppressive therapy and cardiovascular diseases are the most important cause of death. Based on UNOS registry data, during the first post-transplant year, cardiovascular diseases (26%) and infection (24%) were the reasons for dying in cadaver kidney transplant recipients.

Graft Survival

Acute rejection is the most frequent cause of graft failure within the first year. Although there has been a progressive improvement in patient survival, rates of graft survival after cadaver transplant have remained virtually unchanged in the 1970s and early 1980s. The failure to improve these results is due to the lack of more specific forms of immunosuppressive therapy. In the years immediately following 1983, there were dramatic gains in cadaver graft survival probably related to the introduction of cyclosporine. The overall cadaver graft survival has increased from about 65% to about 80% to 85% at 1 year. The race of recipients also influenced outcomes. Asian recipients had a better outcome than Caucasians who fared better than African Americans.

Monozygotic Twins

Provided that there are no technical mishaps as a result of the operation itself, one should expect twin kidney transplants to survive indefinitely without the need for immunosuppression . However, there has been a significant incidence of recurrent glomerulonephritis when this was the original disease in the recipients. In a series of 30 identical-twin transplants followed for up to 27 years, 9 developed recurrent nephritis, 1 as late as 16 years after transplantation. Of 41 renal transplants between monozygotic twins having recorded by the European Dialysis and Transplant Association, 36 were alive with functioning grafts from 1 to 14 years after transplantation. Two grafts failed from recurrent nephritis, two due to de novo glomerulonephritis and one died in a traffic accident. This has been considered an indication for continuous low-grade immunosuppression in those patients where there is a risk of recurrent disease, but perhaps of greater importance is the withholding of transplantation until the original disease is completely quiescent.

HLA Identical Siblings

The HLA identical sibling transplant is ideal and there have been recent reports of 3-year graft survival rates of 90% to 95% in such patients. Immunosuppression is still necessary since rejection does occur in a substantial

number of patients and may even occasionally result in loss of a graft from rejection[27]. These rejection episodes no doubt reflect recognition of, or sensitization to, minor histocompatibility antigens in the donor or to genetic recombination at the HLA-DR locus. As excellent results are obtained with azathioprine and prednisone, this would seem to still be the immunosuppressive therapy of choice at this time, in view of the nephrotoxicity associated with cyclosporine. However, some centers cover the recipient with cyclosporine for several months in case of unexpected rejection and then taper and discontinue the drug after 4 to 6 months. Steroids can usually be discontinued after 1 or 2 years if renal function is stable, although withdrawal of steroids should be done very cautiously over a period of at least 6 months.

HLA Non-identical Parent to Child or Siblings

A transplant may be performed between a patient and a child who will differ for one HLA haplotype or between the two siblings who differ either for one or both HLA haplotypes. The results of transplantation were related to the degree of HLA disparity, that is, two haplotype-disparate pairs were less successful than one haplotype-disparate pair and both were significantly worse than the results of transplantation between HLA identical siblings. However, Cyclosporine treatment and donor-specific blood transfusion have substantially improved the results of transplantation between HLA non-identical family members.

Actuarial graft survival is now very close to that achieved for transplantation between HLA identical siblings[28].

Living Unrelated Transplantation

A case can be made for the use of emotionally related donors, such as a spouse or more distantly related members of the family, such as cousins, and perhaps even between very close friends, now that the expectation of a successful transplant is quite high[17]. Despite greater histoincompatibility, the survival rates of these kidneys are greater than those of cadaveric kidneys. Living donor kidneys have performed better probably because the injury by shock in about 10% cadaver kidneys which occurred before removal. Living unrelated donors have thus become a major source of organ for kidney transplantation[29].

Cadaver Transplantation

The majority of kidneys used for transplantation have been from cadavers. Even though there may be variations from center to center, there has been a steady improvement in the results of cadaver transplantation in terms of both patient and graft survival over the last 10 years[30]. Patient survival is now around 96% at 1 year and graft survival is approaching 80%; in selected groups of patients, such as those who have been transfused and who are receiving a first graft, graft survival is over 85%. This improvement in patient survival is due to use of less

immunosuppression and, in particular, the use of low-dose steroid protocols. Cardiovascular disease has replaced infectious complication as a major cause of morbidity and mortality. The results of cadaveric transplantation are now approaching a level at which, if there were an adequate supply of cadaver kidneys, there probably would be little justification for continuing living related transplantation, except when high sensitization of the recipient makes cadaver transplant unlikely or impossible.

Is HLA typing relevant today?

The improved graft survival, which obviously is due in part to improved patient survival, can be attributed to the recognition of the transfusion effect, HLA matching, and, more recently, to better immunosuppression. However, controversy still exists as to whether matching is of any relevance because of the better results achieved with better immunosuppression. Although this question has not been resolved, data are gradually accumulating suggesting that matching, and, in particular, matching for HLA-DR, does exert the same influence on graft survival in patients treated with cyclosporine as with those on conventional immunosuppressive therapy. The 6-year half-life of kidney transplants from cadaveric donors has been unchanged since the early 1970s.

This is in comparison with the 20- to 25-year half-life for the same period in HLA-identical sibling transplants, emphasizing the effect of histo-compatibility differences on graft survival[30].

Futuristic aspects of transplantation in India

The central government has understood the importance of a national and regional level body for the implementation, regulation and monitoring of the organ transplant programmes. It has come out with a new directive in this purpose.

1. National Organ Transplant Programme (NOTP).
2. State Organ Procurement and Distribution Organization (SOPDO)
3. National Organ Procurement and Distribution Organization (NOPDO)

Adaptation of kidney to injury

Aristotle (384 – 322 B.C.) noted that a single kidney was sufficient to sustain life in animals, and that such kidneys were enlarged. The first successful nephrectomy was performed by the German surgeon Gustav Simon on August 2, 1869 in Heidelberg. Prior to this he studied the effects of uninephrectomy in dogs.

He found that the size of the remaining kidney increased to 1.5 fold at 20 days post nephrectomy[32].

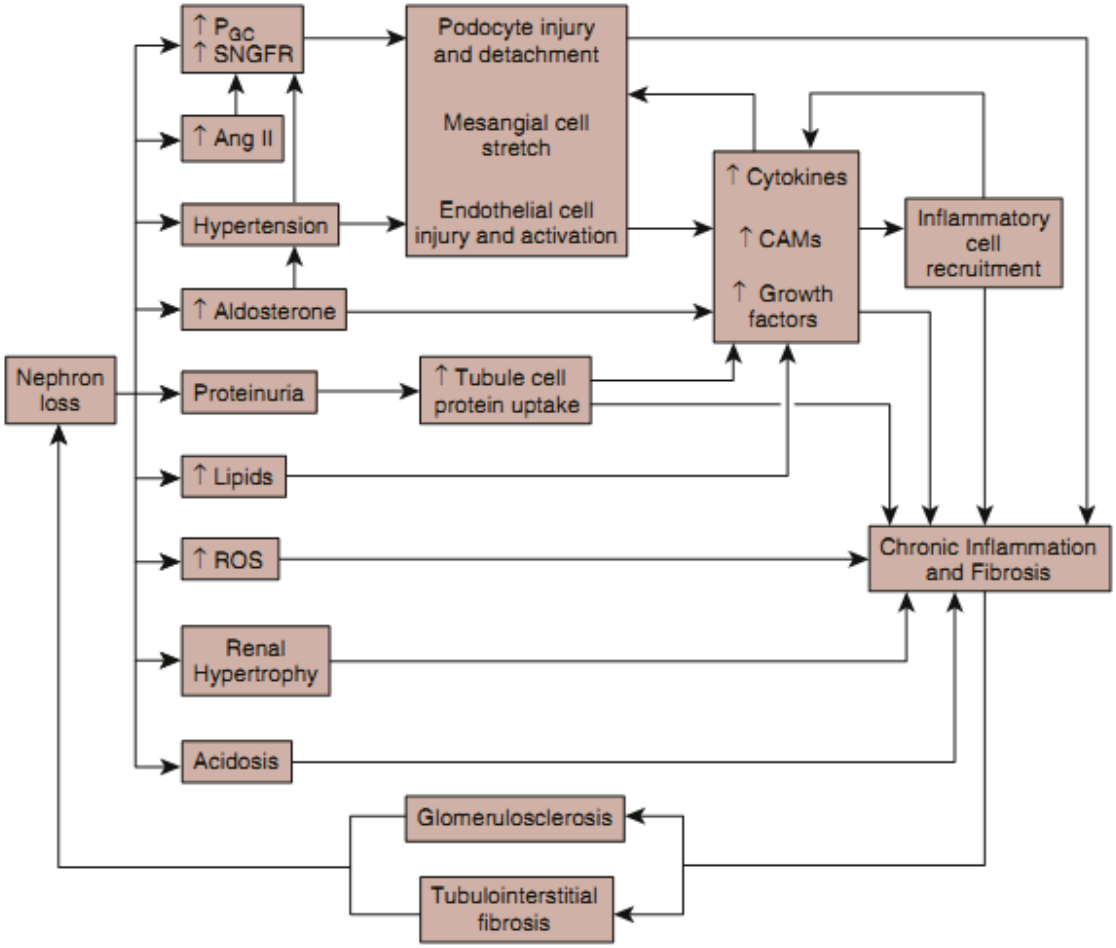
It is clear that the cause of renal failure is loss of functioning nephrons. The loss of nephrons is initiated by various insults. When the insult is removed prior to a certain threshold, the further loss of nephrons is avoided and there are sufficient numbers of healthy nephrons left to carry on the normal function of the kidneys. However once the threshold is crossed, the progression of renal failure is a self sustained process.

This is particularly relevant in chronic kidney disease. The loss of nephrons is not localized. The healthy nephrons adjacent to the scarred and defunct nephrons adapt structurally and functionally to maintain normal renal function. Thus the normal nephrons must overwork to maintain renal function.

This is more easily observed in persons with normal kidneys and renal function, who undergo uninephrectomy for either kidney donation or traumatic injuries.

This adaptive response of the kidney is identified by an increase in the size of the nephrons[33] and a compensatory increase in the glomerular filtration rate of the surviving nephrons. This is called ‘glomerular hyperfiltration’.

However like in many physiological compensations, over a period of time, glomerulosclerosis and tubular atrophy supervene which further reduces the functioning nephron mass and can lead to reduced renal function.



Intact nephron hypothesis of Bricker[34]

In 1960, Bricker postulated the following;

1. Diseased kidneys reduced nephron mass.

2. Some of the problems in CKD occur due to changes in body fluids and reduced nephron mass. It is not entirely due to change in nephron structure.

3. The ability to adapt decreases with loss of nephrons.

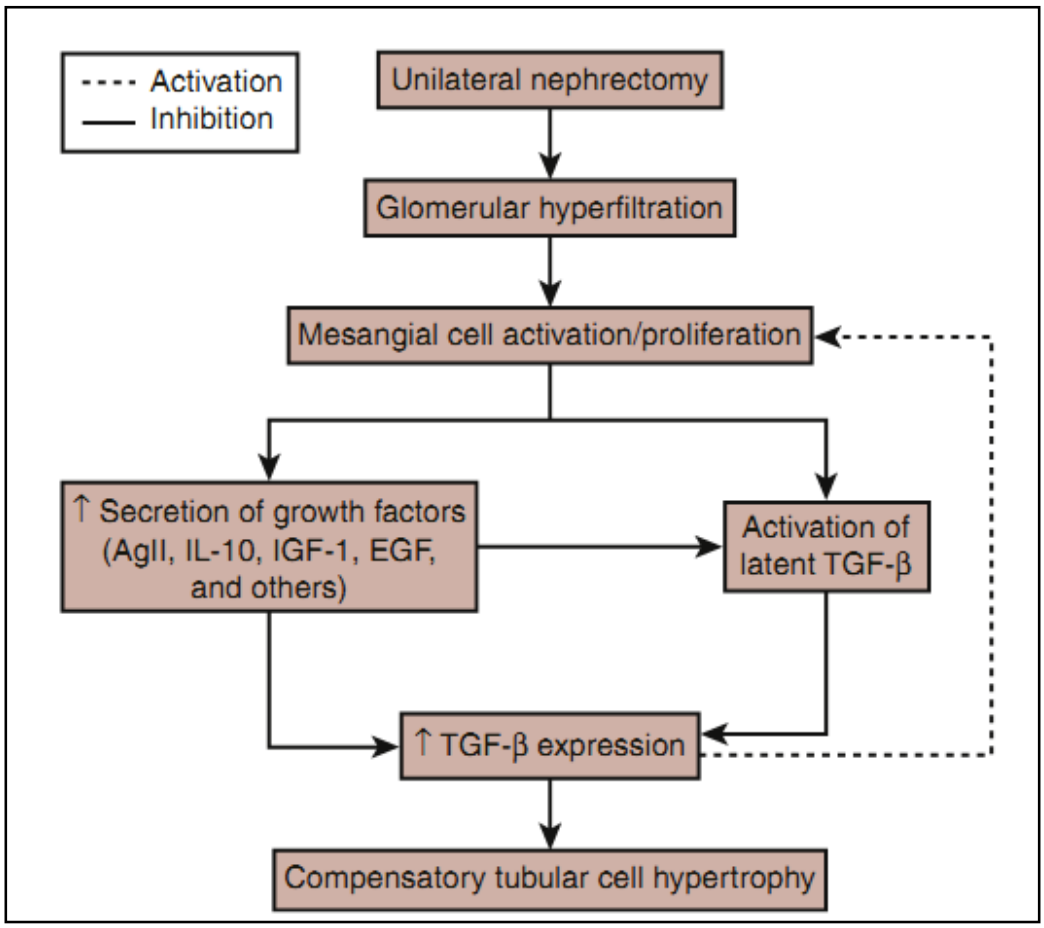
4. Excretion for all substances follows an orderly and predictable pattern.

Whole kidney hypertrophic responses

The earliest changes in the remaining kidney after uninephrectomy are the biochemical changes that precede normal cell growth. This is an increase in the incorporation of choline, activation of ornithine decarboxylase, increased RNA synthesis and suppression of factors inhibiting growth and apoptosis[35]. DNA synthesis is increased at 24 hours. It has a maximum of 5 to 10 fold increase that is reached within 2 to 3 days. The weight of the kidney was to found increase as early as 2 to 3 days. The renal mass continued to increase for 1 to 2 months, by when a 40 to 50% increase would be expected[35]. Most of the increase in weight would be due to hypertrophy of the existing nephrons and only minimally by hyperplasia. This is due to the fact that the number of nephrons is determined shortly before birth, a phenomenon called '**Nephron Endowment**'.

The assessment of renal hypertrophy after nephrectomy in humans has been analysed with the help of radiological studies. The volume of the remaining kidney increased 27.6 ± 9.7% on an average, at 6 months post donor nephrectomy[36].

In another ultrasound based study, the increase was 19 to 100% [37]. Computed tomography based studies showed an increase in renal cross sectional area of 30 to 53%.[38]. However a meta-analysis of these studies could not provide statistically significant prognostic data. The hypertrophy is still an observation that is to be evaluated for a clinical correlation.



Changes in GFR post transplantation

Glomerular Filtration Rate

The GFR is the amount of plasma filtered through glomeruli per unit of time. Although the term can refer to the function of a single nephron, GFR most often refers to the sum filtration rate of all functioning nephrons. The normal GFR is approximately 120–130 mL/min/1.73 m^2, and it reduces with age.

The level of GFR is accepted as the most useful index of kidney function in health and disease. The GFR begins to fall before clinically evident CKD occurs . CKD is defined as GFR, 60 mL/min per 1.73 m2 in addition to markers of kidney damage.

The severity of CKD is also determined by the level of GFR. Kidney failure is defined as GFR, 15 mL/min per 1.73 m^2. Kidney failure is associated with uremic symptoms and laboratory findings, such as anemia, malnutrition, bone and mineral disorders, neuropathy, and decreased quality of life. There is a graded relationship between the severity of these signs and symptoms at intermediate reductions in GFR in patients with kidney disease.

The level of GFR is also associated with progression to kidney failure and cardiovascular disease. In addition, drug dosages will need to be adjusted for the level of GFR.

Measuring GFR

The gold-standard method to measure GFR is urinary clearance of an ideal filtration marker. An ideal filtration marker is one that is (1) freely filtered at the glomerulus; (2) present at a stable plasma concentration; and (3) not reabsorbed, secreted, or metabolized by the kidney. The ideal filtration marker is inulin. However, this is rarely used and alterative markers such as iohexol and iothalamate are more commonly used.

Clearance concept

For a substance that is cleared by urinary excretion, the clearance formula may be written as:

$$\mathbf{C_A = U_A \times V/P_A}$$

where U_A is the urinary concentration of A and V is the urine flow rate. The term $U_A \times V$ represents the urinary excretion rate of A. If substance A is freely filtered at the glomerulus, then urinary excretion represents the net effects of glomerular filtration, tubular reabsorption, and secretion.

Estimation of GFR in the clinic

GFR is usually estimated from endogenous filtration markers. The level of all known endogenous filtration markers is determined by factors other than GFR, including generation from muscle mass and diet, tubular secretion, and extra-renal elimination. GFR estimating equations use the filtration marker

in combination with demographic variables to overcome some of the limitations from non-GFR determinants. The most commonly used filtration marker is serum creatinine. The most commonly used equation is the MDRD Study equation, but a more accurate equation, the CKD-EPI equation, has recently been published.

Estimating equations combine the endogenous filtration marker(s) with other variables, such as age, sex, race, and body size, as surrogates for non-GFR determinants of the filtration markers and, therefore, can overcome some of the limitations of the filtration marker alone. An estimating equation is derived using regression techniques to model the observed relationship between the serum level of the marker and measured GFR in a study population.

The Cockcroft-Gault formula

The creatinine clearance or GFR is calculated as:

[(140-Age) × Body Weight (in kg)] \ [72 × Serum creatinine (in mg/dL)]

If the patient is female, multiply the above by 0.85

It was developed in 1973. It is not adjusted for body surface area.

Modifications of the Cockcroft and Gault equation using ideal body weight instead of actual body weight are sometimes used but have not been validated.

The MDRD equation

It was developed in 1999. It estimates GFR adjusted for body surface area and is more accurate than measured creatinine clearance from 24-hour urine collections or estimated by the Cockcroft-Gault formula.

$$\mathbf{GFR = 175 \times Serum\ Creatinine^{-1.154} \times age^{-0.203}}$$

[× 1.212 (if patient is black), × 0.742 (if female)]

CKD-EPI Formula

The CKD-EPI equation is a new equation to estimate GFR from serum creatinine, age, sex, and race. The CKD-EPI equation was as accurate as the MDRD Study equation in the subgroup with estimated GFR less than 60 mL/min/1.73 m2 and substantially more accurate in the subgroup with estimated GFR greater than 60 mL/min/1.73 m2.

The CKD-EPI equation:

$GFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018[\text{if female}] \times 1.159[\text{if black}]$

$\kappa = 0.7$ if female
$\kappa = 0.9$ if male

$\alpha = -0.329$ if female
$\alpha = -0.411$ if male

min = The minimum of Scr/κ or 1
max = The maximum of Scr/κ or 1

Various online e-GFR calculators are available; however, cockroft-gault formula continues to be the most frequently used equation due to its ease of application. There was a debate as to which formula estimates GFR better in persons with single kidney and persons with normal renal function. There was a general agreement that the MDRD formula was the closest. However, its application in renal donors has been argued, stating that it tends to underestimate GFR in normal individuals and post uni-nephrectomy and may falsely classify donors under a CKD stage leading to unnecessary hassles.

Single nephron GFR

The single-nephron GFR refers to the work per formed by a single functioning nephron. It can be affected by hemodynamic alterations or structural damage.

As part of the adaptation of the kidney to injury, uninjured nephrons undergo hypertrophy and hyper-filtration to compensate for the loss of functioning nephrons (compensator y hyperfiltration). Thus, total GFR remains relatively normal despite a decrease in functioning nephrons. As such, the GFR is dependent on the number of nephrons (N) and the single-nephron glomerular filtration rate (SNGFR):

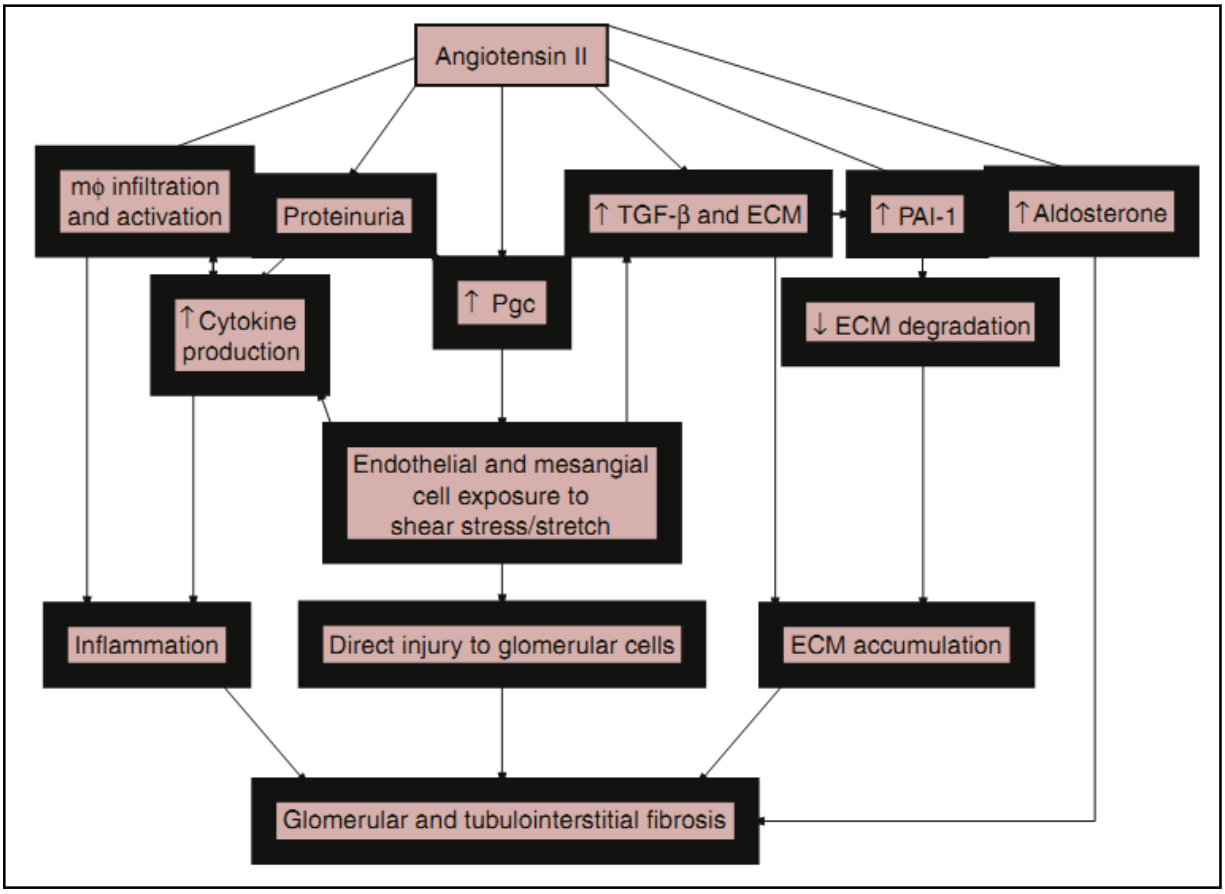
$$GFR = N \times SNGFR$$

Mechanisms inducing change in GFR

Alterations in glomerular hemodynamics after renal mass ablation are due the interplay of various vasoactive factors. Vasodilator prostaglandins and natriuretic peptides dilate the afferent arterioles. Bradykinin dilates both afferent and efferent arterioles. Angiotensin II, vasoconstrictor prostaglandins and endothelins constrict efferent arterioles more than afferent arterioles. The nett effect of the interplay of various factors is an increase in the 'Single Nephron GFR' (SNGFR).

Renin angiotensin system

The effects of the renin angiotensin system in humans are obtained from studies showing the effects of pharmacological inhibition of the renin angiotensin aldosterone system (RAAS) in preventing the progression of glomerular injury. Studies by inducing infarction to produce 5/6 nephrectomy have showed increases in the intrarenal renin levels. The study showed that the increases were more adjacent to the infarct site[39].



The renoprotective effects of ACE inhibitors and Angiotensin Receptor Blockers have been proved in subsequent studies to be due to decreases in intrarenal angiotensin levels.

Endothelins

Endothelins act via 2 types of receptors ET-A and ET-B. ET-A is found in vascular smooth muscle and mediates vasoconstriction and cellular proliferation. ET-B is found in the vascular endothelial and renal epithelial cells and functions as clearance receptors. Intrarenal endothelin studies by micropuncture techniques are yet to be published but current studies show evidence that endothelins are increased by chronic infusions of aldosterone and the effects are atleast partially mediated by prostaglandins[40].

Natriuretic peptides

Both Atrial and Brain derived natriuretic peptides are found to be increased in post nephrectomy state. They mediate increases in GFR in the remaining nephrons. They are also vasoactive and dilate the afferent arteriole and constrict the efferent arteriole[41].

Eicosanoids

Prostaglandin production is increased in the setting of reduced nephron mass. Both vasodilatory and vasoconstrictive are produced in the glomerulus. That net effect is mediated by the interaction of both the dilator and constrictor types. The balance is in favor of vasodilation[42].

Nitric oxide

Intrarenal effects of nitric oxide are studied from studies of infusions of nitric oxide inhibitors. The extremely short half life of Nitric Oxide precludes direct intrarenal measurements. As a vasodilator, it was thought to increase GFR. Studies have shown that post nephrectomy, intrarenal nitric oxide synthase and nitric oxide levels are both reduced, whereas systemic production is increased[43]. Indeed the role of nitric oxide in adaptation to nephron loss is not fully understood.

Bradykinin

This vasodilatory peptide is increased in the remnant kidney. Acute and chronic infusions of bradykinin increased renal plasma flow but not the GFR. The effects of bradykinin on the afferent and efferent are mediated by prostaglandins and cytochrome P450 metabolites[44]. Further studies are needed to understand the role of bradykinin after nephron loss.

Urotensin

Urotensin II is the most potent vasoconstrictor identified till date. Urotensin II is produced in the kidney and the levels are increased after nephrectomy[45]. However the role of urotensin II in adaptation to nephron loss remains to be fully elucidated.

Alterations in renal auto-regulation

Marked readjustment of renal autoregulatory mechanisms are noted after renal mass ablation. The role of myogenic mechanisms is believed to be to protect the glomerulus from increased systemic blood pressure. The tubuloglomerular feedback is also reset to adjust for the increases in the SNGFR[46]. These changes are noted as early as 20 minutes after uninephrectomy.

Hypertension

The current classification of hypertension proposed by the report of the 7th Joint National Committee is based on the average of two or more properly measured, seated BP recordings on each of two or more office visits. This includes a new category called ‘prehypertension’ which includes systolic blood pressure from 120 to 139 mmHg and diastolic blood pressure from 80 to 89 mmHg.

The stages 2 and 3 of hypertension in the JNC 6 report were combined. The new classification proposed in 2003 which is still in vogue is shown in Table 1.

JNC 7 Classification of Hypertension		
BP CLASSIFICATION	**SBP**	**DBP**
NORMAL	<120	<80
PRE-HYPERTENSION	120-139	80-89
STAGE 1	140-159	90-99
STAGE 2	≥160	≥100

About 50 million people in the United States of America suffer from hypertension. The incidence and prevalence of hypertension is expected to increase in the future. A 90% life-time chance of developing hypertension was noted even among people with normal BP at 55 years of age[47]. When the systolic BP increased by 20 mmHg and diastolic BP increased by 10mmHg, the risk of cardiovascular disease double across the BP range 115/75 to 185/115 mmHg[48].

It was initially thought that diastolic blood pressure was the most important predictor of cardiovascular events. Later studies have shown that systolic blood pressure is a more important predictor. Therefore the importance of diagnosing Isolated Systolic Hypertension (ISH) as a separate category was emphasized. This group of patients included those with a systolic blood pressure ≥140 mmHG and a normal diastolic blood pressure ≤ 80mmHg.

Accurate measurement of blood pressure in office

A calibrated standardized instrument should be used. The auscultatory method of BP recording should be followed. At least two measurements should be made. The BP recording is done with the person sitting in a chair with arm supported at heart level and feet resting comfortably for atleast 5 minutes. A cuff bladder encircling at least 80 percent of the arm is an appropriate size. SBP and DBP are measured at Korotkoff phases 1 and 5 respectively.

Hypertension due to renal disease

Hypertension is common in renal disease. This is especially when the disease process affects the vasculature, either inside the kidney or outside. There have been a few models to suggest that even essential hypertension could be an intrinsic renal disease related to poor sodium excretion. Cross transplantation studies have proved that the kidney definitely mediates persistent systemic hypertension. When the kidney of the normo-tensive person from a family without history of hypertension, was transplanted, hypertensive recipients became normo-tensive without the need for anti-hypertensive drugs. The glomerulus is sensitive to pressure. The intra-glomerular pressure reflects to the systemic BP. Thus glomerular diseases tend to present with more severe hypertension.

Proteinuria

Proteinuria usually implies that there is a defect in glomerular permeability. In general, proteinuria can be classified into persistent or transient. Among the causes of persistent proteinuria, there are three types:

(1) Glomerular proteinuria

(2) Tubular proteinuria

(3) Overflow proteinuria

- Glomerular proteinuria includes diabetic nephropathy and other common glomerular disorders. It is usually caused by increased filtration of albumin across the glomerular capillary wall.

  Other causes of glomerular proteinuria have a rather benign course, such as orthostatic and exercise-induced proteinuria. These latter causes are characterized by significantly lesser degrees of proteinuria, ranging < 2 g/day.

- Tubular proteinuria is usually seen in those with underlying tubulointerstitial diseases. They usually have defective reabsorptive capacities in the proximal tubules, such that, instead of the proteins being normally reabsorbed, they are excreted in the urine. In contrast to

glomerular proteinuria, whereby macromolecules such as albumin are leaked out, in tubular proteinuria it is mostly low molecular weight proteins, such as immunoglobulin light chains, etc. Proximal tubular injury leads to increased low molecular weight proteinuria e.g. intestinal alkaline phosphatase, n-acetylglucosaminidase, retinol binding protein, tissue specific alkaline phosphatase, α glutathione S transferase, β2 microglobulin and α1 macroglobulin. β2 microglobulin is freely filtered at the glomerulus and is almost completely absorbed in the proximal tubule. Thus it is used as a marker of proximal tubular proteinuria. In contrast, Tamm-Horsfall protein and α glutathione S transferase are markers of distal tubular proteinuria. Tubular proteinuria rarely exceeds 2 grams per day.

- Overflow proteinuria (also called overproduction proteinuria) is exemplified by multiple myeloma, in which there is an overabundance of immunoglobulin light chains secondary to overproduction. Simply put, proteinuria occurs as a result of the amount of protein produced basically exceeding the maximum threshold for reabsorption in the tubules. Dipstick testing may be negative in this case and testing for serum electrophoresis and urinary Bence Jones Protein is necessary. Other examples include amyloidosis and some reticuloendothelial disorders.

Whereas both glomerular and tubular proteinuria are secondary to abnormalities involving the glomerular capillary and tubular walls, respectively, in overflow proteinuria, the problem lies in overproduction of certain proteins.

Quantification of the degree of proteinuria is accomplished by performing a 24-hour urine collection, which can be cumbersome, especially in elderly individuals or in those with concomitant fecal or urinary incontinence.

The urine protein-to-creatinine (using a random urine specimen) ratio has been shown to have a good correlation with the 24-hour urine protein determination.

In transient proteinuria conditions, there is a transient change in glomerular hemodynamics causing increased excretion of urinary protein. These are usually benign and self-limited. Examples include congestive heart failure, fevers, strenuous exercise, seizure disorders, and even extremes of stress. Orthostatic proteinuria falls under this category.

Glomerular proteinuria

The principal mechanisms of glomerular proteinuria are two.

1. Increased permeability of glomerular filtration barrier to proteins.

2. Incomplete absorption of the filtered protein in the proximal tubule, either due to proximal tubular defect or due to the large amount of protein filtered.

The glomerular filtration barrier is both charge and size selective. Therefore a defect in either feature will likely result in proteinuria.

Structure of the glomerular filtration surface

The three layer concept of the filtration surface includes

1. Glomerular capillary endothelium
2. Glomerular basement membrane
3. Epithelium - podocyte

Glomerular endothelial cells are the most fenestrated in the circulation, with a pore area in the peripheral zone that occupies from 20% to 50% of the cell surface[49]. The glomerular endothelial cells retain cell, but not protein. Large proteins are filtered out by the basement membrane. Only water and solutes pass through the slit diaphragms of the podocytes. Most of the protein is retained[50]. The glycosaminoglycans, glycoproteins and membrane associated proteoglycans or glycocalyx form the negative charge on the basolateral surface of the filtration

barrier which prevents negatively charged smaller sized proteins from being filtered freely.

Diagnosis of proteinuria

Healthy individuals excrete <150mg of protein or <30mg of albumin in urine per day. Microalbuminuria is urinary excretion of 30 to 300mg / 24 hours and macroalbuminuria is >300mg / 24 hours. Nephrotic range of proteinuria is defined as proteinuria >3.5gm/day. Tubular proteinuria rarely exceeds 2gm/day.

Dipsticks are currently available for rapid screening or urine samples for albumin. However they miss out on detecting other significant proteins in the urine, like the Bence Jones Protein of multiple myeloma. The copper based Biuret method and the dye-binding method using Coomassie brilliant blue as the indicator are more sensitive than the commonly used turbidimetric methods like sulphosalicylic acid and trichloroacetic acid methods.

Selectivity of proteinuria

Patients with glomerular disease typically have a non selective proteinuria[51]. However, minimal change disease caused by fusion of foot processes is characterized by selective proteinuria in which albumin is preferentially lost.

The selectivity of proteinuria is measured in the laboratory by comparing the clearance of IgG to albumin or tranferrin. Both plasma and spot urine samples are required.

IgG (urine) / IgG(plasma) × transferrin (plasma) / transferrin(urine)

Selective proteinuria – ratio <0.10

Non selective proteinuria – ratio >0.20

Microalbuminuria

Microalbuminuria is urinary excretion of 30 to 300mg / 24 hours.

Radioimmunoassay is the most sensitive method for diagnosis of microalbuminuria. It can detect albuminuria >30mg in a normal protein range of 150mg in a 24 hour urine sample. Microalbuminuria is an independent risk factor for not only progression of renal failure but also for increased cardiovascular morbidity and mortality.

Normal urinary protein should not exceed 150 mg/day. Among these urinary proteins are albumin and Tamm-Horsfall mucoproteins (also called uromodulin). Urinary dipsticks only detect the presence of albumin; however, they are notorious for being poor indicators of the presence of urinary globulins and Bence Jones proteins (commonly seen in multiple myeloma). It is important to recognize that the dipstick measurement of urine protein is

dependent on the concentration of the urine specimen so that a patient with a small volume of concentrated urine may test 21 for protein, but when a 24-hour urine collection is obtained the actual daily concentration is much smaller. However, a patient with a large volume of dilute urine may test trace positive for protein but may have a large amount of total 24-hour urine protein excretion. Thus, it is important to quantitate the amount of proteinuria found on dipstick testing. A more reliable test for the presence of non-albumin proteins is called the sulfosalicylic acid test, which is more reliable in detecting the presence of albumin, globulin, and Bence Jones proteins in the urine, even in low amounts.

URINARY DIPSTICKS	
Dipstick	**Proteinuria(mg/dl)**
Trace	**10-30**
1+	**30**
2+	**100**
3+	**300**
4+	**≥1000**

SULFOSALICYLIC ACID TEST		
Dipstick	**Appearance**	**Proteinuria(mg/dl)**
Trace	**Slight turbidity**	**10-30**
1+	**Print visible through specimen**	**30**
2+	**Print invisible**	**100**
3+	**Flocculation**	**300**
4+	**Dense precipitates**	**≥1000**

The collection of a 24 hour urine sample for estimation of protein is the best method to calculate proteinuria. It nullifies the effect of diurnal variation in urine output and proteinuria. However, the method of collection is difficult and changes occur with the reagents used for the analysis. So, although it is a gold standard method, a repeat testing maybe necessary at times. The procedure is also difficult to understand and follow for old people and has its limitations in the out patient setting.

The protein-creatinine ratio uses urinary creatinine excretion as a parallel marker of proteinuria. It is easy to perform as only a spot urine sample is required. The diurnal variations are eliminated. Water intake and urine output do not influence the result. Thus it has become a very useful clinical screening test

Spot PCR matches well with the 24 hour sample results. When the spot PCR is normal, it effectively rules out the possibility of proteinuria. But the results of spot PCR are less reliable in the setting of gross proteinuria and a 24 hour sample must be analysed. Therefore urine spot PCR finds its value as a screening test for proteinuria in the outpatient setting.

MATERIALS

AND METHODS

Materials and Methods

Setting	**:**	Donors of transplant recipients, Department of Nephrology – Out patient department Thanjavur Medical College Hospital, Thanjavur.
Ethical committee approval	**:**	Obtained.
Design of study	**:**	Single center, observational study.
Period of study	**:**	February - 2012 to October – 2012
Sample size	**:**	50 subjects.

Selection of study subjects

Inclusion Criteria

- ✓ Voluntary kidney donors.
- ✓ Related and unrelated donors were included.
- ✓ Both male and female donors were included.
- ✓ No age limits were set.
- ✓ No limits for the time period since donation.
- ✓ Pre-existing diseases or current co-morbid illnesses were accepted.

Exclusion Criteria

- × No major exclusion criteria were fixed.

Methodology

The study was carried out in the Nephrology Outpatient Department of Thanjavur Medical College Hospital. Voluntary kidney donors of the transplant recipients who were attending the Department of Nephrology OPD were traced and included in the study. A total of 50 kidney donors were included. All the donors who participated in the study were informed about the purpose of the study.

The clinical examination and laboratory investigations were done with due consent from them. The proforma designed for the study was used for all the subjects and the details entered. The name, age and sex, relationship to the recipient, date of transplant, blood pressure, blood urea, serum creatinine, urine protein, urine spot protein creatinine ratio were documented. The quality of life of the donors was assessed by the time taken to return to normal day to day activities after surgery and their attitude towards kidney donation.

The blood pressure measurement was done according to the current guidelines for office BP recording, i.e. after min 5 minutes rest, at least 30 min after drinking a beverage or smoking. Seated blood pressure recordings were taken from both arms. The average of 3 recordings made from each arm taken with at least 5 minute interval between two successive recordings from the same arm. Auscultatory method of blood pressure measurement and a standard mercurial manometer apparatus with appropriate sized bladder cuff was used.

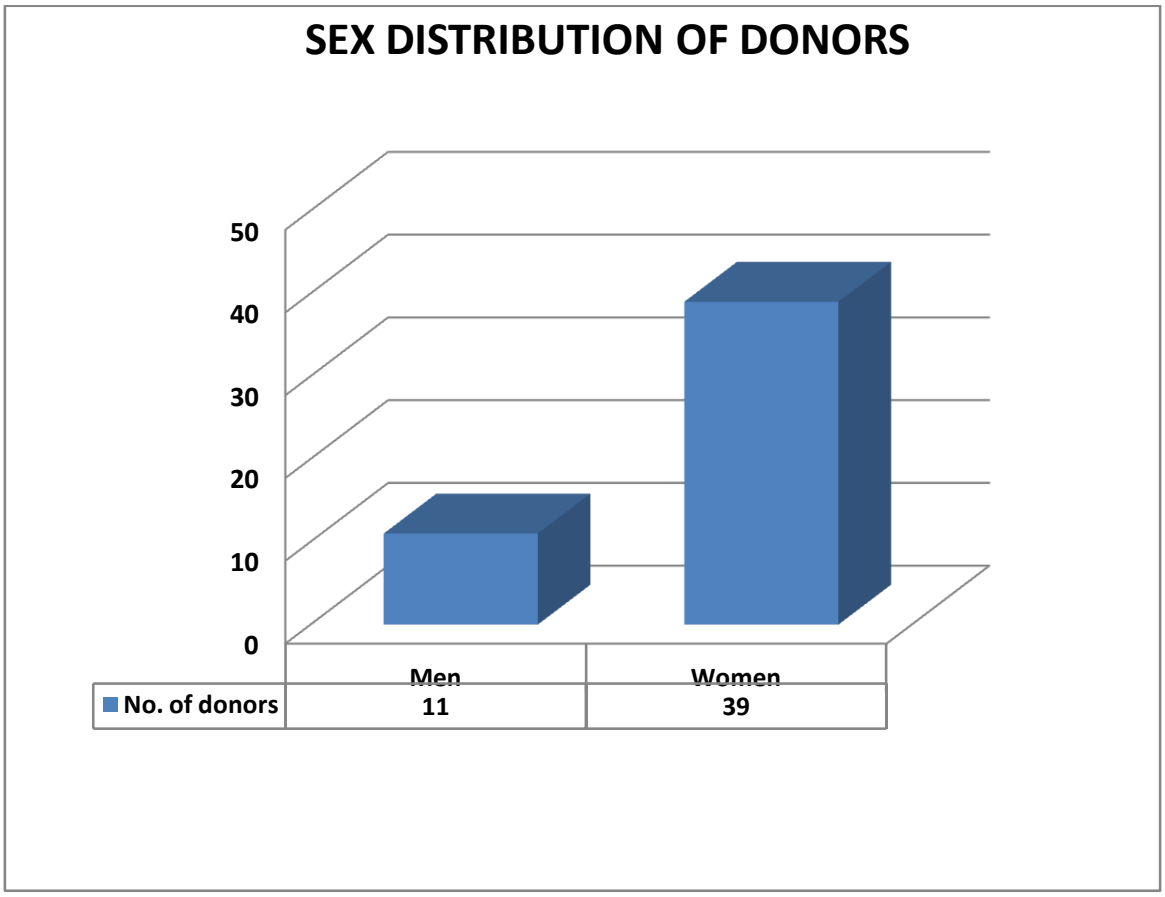
The serum urea measurement was made by the boiling method and creatinine estimated by the jaffe kinetic method in the Department of Biochemistry Laboratory, Thanjavur Medical College Hospital. Urine protein was tested by 2% suphosalicylic acid. The same were used for urine spot protein creatinine ratio estimation.

RESULTS OF THE STUDY

RESULTS

TOTAL NUMBER OF DONORS = 50

SEX	NO. OF DONORS	PERCENTAGE
Male	11	22
Female	39	78



Age characteristics of the donors studied

Youngest donor enrolled	: 32 years
Oldest donor enrolled	: 74 years
Mean donor age	: 49 years

Sex-wise age characteristics

Male donors

Youngest male donor	: 44 years
Oldest male donor	: 60 years
Mean age of male donors in the study	: 54.09 years
Mean age at donation for male donors	: 45.45 years
Mean post nephrectomy follow up period	: 8.63 years

Age of male donors studied		
Age	**No. of donors**	**Percentage**
20-29	**0**	**0**
30-39	**0**	**0**
40-49	**3**	**27.27 %**
50-59	**5**	**45.45 %**
60-69	**3**	**27.27 %**

Age at time of donation – male donors		
Age	**No. of donors**	**Percentage**
20-29	**0**	**0**
30-39	**4**	**36.36 %**
40-49	**2**	**18.18 %**
50-59	**5**	**45.45 %**

Female donors

Youngest female donor : 32 years

Oldest female donor : 74 years

Mean age of female donors in the study : 47.74 years

Mean age at donation for female donors : 41.74 years

Mean post nephrectomy follow up period : 6 years

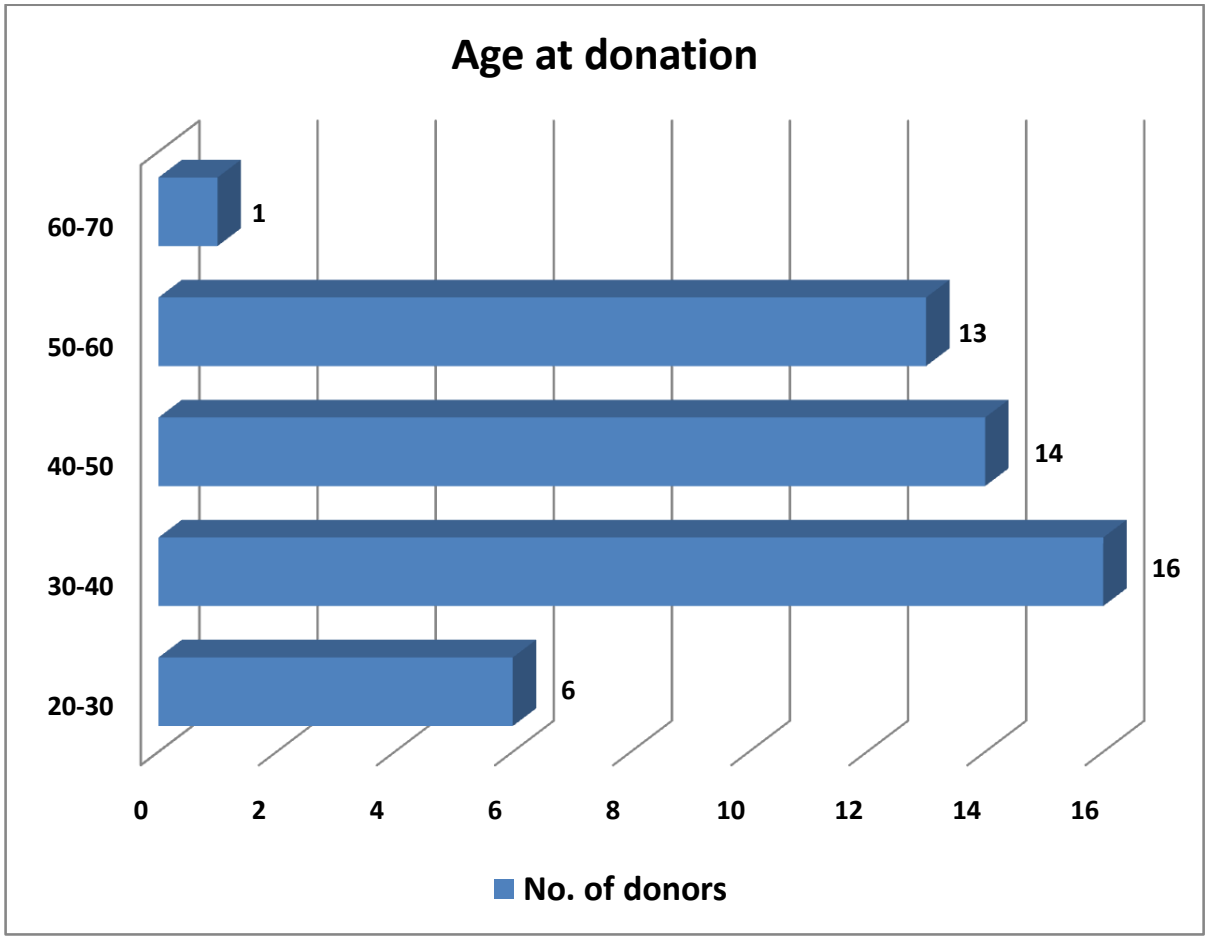
Age of female donors studied		
Age	**No. of donors**	**Percentage**
20-29	**0**	**0**
30-39	**13**	**33.33 %**
40-49	**7**	**17.94 %**
50-59	**12**	**30.76 %**
60-69	**6**	**15.38 %**
70-79	**1**	**2.56 %**

Age at time of donation - female donors		
Age	**No. of donors**	**Percentage**
20-29	**4**	**10.25 %**
30-39	**14**	**35.89 %**
40-49	**10**	**25.64 %**
50-59	**10**	**25.64 %**
60-69	**1**	**2.56 %**

OVERALL STATISTICS		
AGE AT DONATION	**NUMBER OF DONORS**	**PERCENTAGE**
20-30	**6**	**12 %**
30-40	**16**	**32 %**
40-50	**14**	**28 %**
50-60	**13**	**26 %**
60-70	**1**	**2 %**

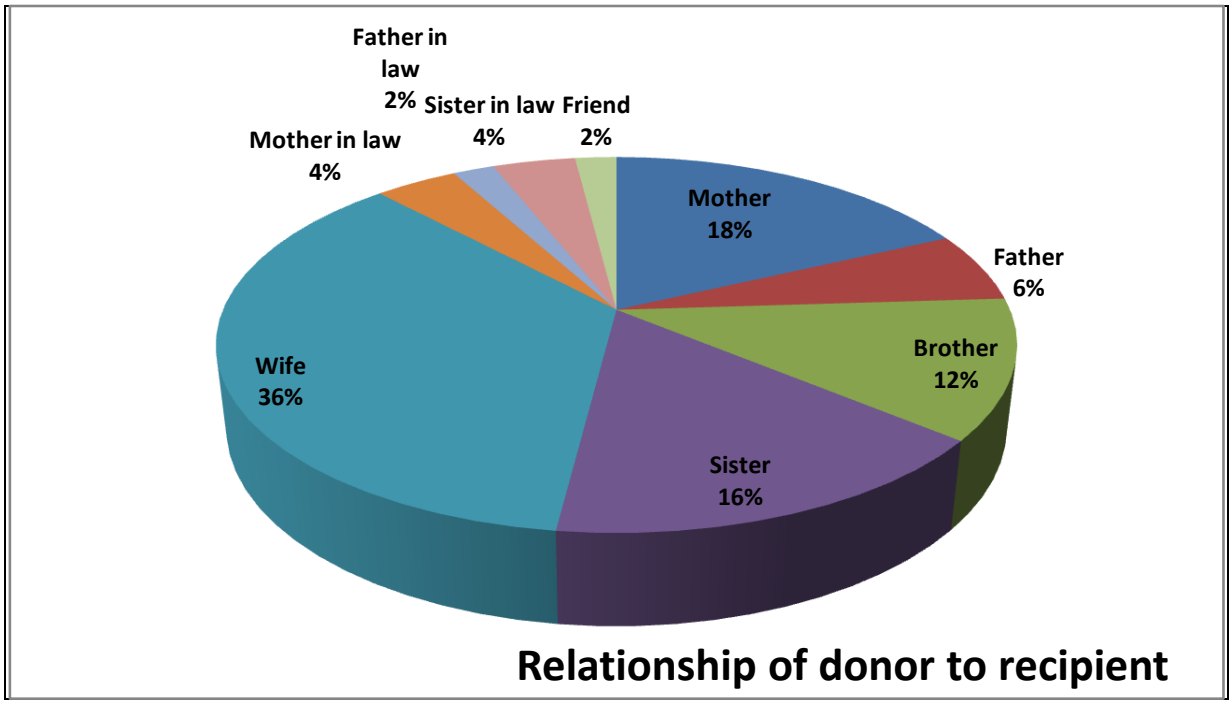
- **Least age at donation – 24 years**

- **Oldest age at donation – 62 years**



Relationship of donor to the recipient

Relationship of donor to recipient	
Mother	9
Father	3
Brother	6
Sister	8
Wife	18
Mother in law	2
Father in law	1
Sister in law	2
Friend	1
Total	50



- Number of related donors : 26
- Shortest post transplant period among related donors : 1 year
- Longest post transplant period among related donors : 27 years
- Mean post transplant follow up period for related donors : 8.42 years

- Number of unrelated donors : 24
- Shortest post transplant period among unrelated donors : 7 months
- Longest post transplant period among unrelated donors : 22 years
- Mean post transplant follow up period for unrelated donors : 4.58 years

Systemic diseases present in donors prior to donation

Number of donors with pre-existent diseases : 3

- Systemic hypertension : 2
- Hypothyroidism : 1

Systemic diseases developed by the donors after donation

Number of donors who developed systemic diseases after donation: 10

- Systemic hypertension : 5
- Diabetes mellitus : 4
- Stroke : 1

Blood pressure

Systolic blood pressure:

Highest systolic blood pressure : 160 mmHg

Lowest systolic blood pressure : 100 mmHg

Mean systolic blood pressure : 122.32±13.65 mmHg

Diastolic Blood pressure:

Highest diastolic blood pressure : 110 mmHg

Lowest diastolic blood pressure : 60 mmHg

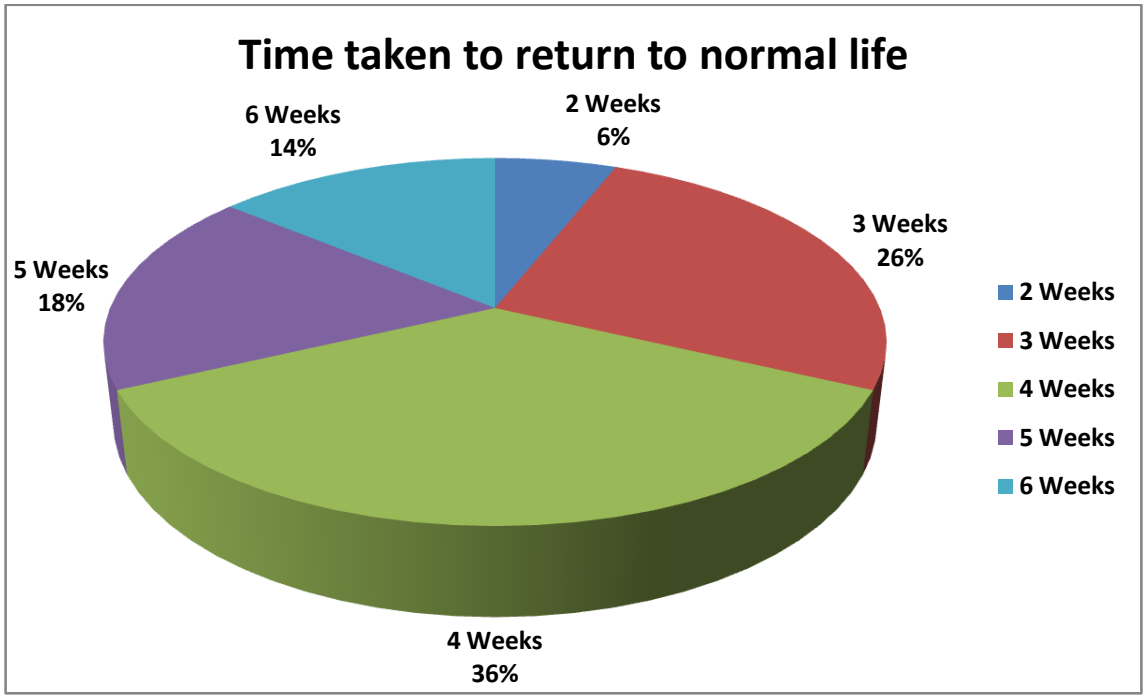
Mean diastolic blood pressure : 79.16±9.85 mmHg

Renal function

- Serum urea >40mg/dl : 4 donors
- Mean serum urea value : 32.12±5.35 mg/dl
- Serum creatinine >1.2mg/dl : 1 donor
- Mean serum creatinine value : 0.91±0.18 mg/dl
- Proteinuria was not noted in any of the donors.
- Maximum value of spot urine protein creatinine ratio: 0.35
- Mean value of spot urine protein creatinine ratio: 0.18±0.08

Time taken to return to normal life after donation

Time taken	No. of donors	Percentage
2	3	6%
3	13	26%
4	18	36%
5	9	14%
6	7	18%



- Minimum time taken to return to normal life: 2 weeks
- Maximum time taken to return to normal life: 6 weeks

- Mean time taken by male donors to return to normal life: 3.63 weeks
- Mean time taken by female donors to return to normal life: 4.20 weeks
- Overall mean time taken by donors to return to normal life: 4.08 weeks

DISCUSSION

Discussion

Living related renal transplantation is the best choice of treatment CKD stage V. Increasing number of patients reaching CKD stage V, has intensified the demand for expanding the kidney donor pool. Although various studies have confirmed the safety of renal donation, it is definitely a major medical, social and psychological issue for the live kidney donor who stands at no direct medical benefit from the procedure. Studies from India have shown that kidney donors had a overall better quality of life after donation[52,53]. So we studied voluntary kidney donors in Thanjavur Medical College to ascertain their physical and psychological status, so that a confident reply can be given to future volunteers for kidney donation.

Among the 50 donors enrolled in the study, 11 were male and 39 were females, constituting 22% and 78% of the study population respectively. Muthusethupathi et al. studied renal donors in a state funded hospital in Tamil Nadu and found that females constituted up to two thirds of the donor study population[54]. The finding of a majority of donors being females was also substantiated by Guleria S[53], in whose study women outnumbered men by a ratio of 6:1. Sale of organs in India is legally banned. All the donors we have studied are

voluntary donors emotionally related to the recipients and none of them were put under pressure to donate a kidney.

The mean age of the donors studied was 49 years. The youngest donor was 32 years old and the oldest 74 years old. This finding is similar to other studies on donors from India by Guleria et al.[52] and Sahay et al.[56]. It was shown kidney donors live a longer and healthier life than the general population, in a Swedish study[55]. Fehrman-Ekholm et al. concluded that renal donors did not have any long term risk compared to the general population and that kidney donors appear to live longer due the fact that only healthy persons are chosen for kidney donation in majority of the circumstances. However, it must be borne in mind that the burden of CKD is growing and all individuals therefore, presently stand at a greater risk of developing CKD than in the past. This can be attributed to the pandemic of diabetes and hypertension, especially so in India which is expected to become the diabetic capital of the world. Thus age at donation appears to be important at present as younger donors are at a greater risk of developing CKD for the reason that they are expected to live longer.

The youngest male donor was 44 years and the oldest male donor in the study was 60 years old. The average age of male donors in the study was 54.09 years. The mean age at donation for the male donors was 45.45 years.

4/11(36.36%) had donated between 30 and 39 years of age. 3/11 (27.27%) were between 60 and 69 years of age.

The youngest female donor was 32 years and the oldest female donor in the study was 74 years old. The average age of female donors in the study was 47.74 years. The mean age at donation for the male donors was 41.74 years. Thus the mean age at donation for female donor was nearly 4 years less, compared to male kidney donors. 14/39 (35.89%) of female donors had donated between 30 to 39 years of age and constituted the majority group. 1/39 (2.56%) had donated between 60 to 69 years of age.

4/39 (10.25%) had donated between 20 to 29 years of age. Thus around 10% of the female donors were in their third decade of their life at the time of donation. There were no male donors in that age group. All the 4 female donors in the 20 to 29 years age at donation were the wives of recipients. Thus it can be surmised that the wives of young men with CKD have opted for transplantation readily. This could be for social and economic benefits for the family. The intention of the young wives has been to help their husbands reach a better state of health and quality of life, who could in turn fend better for the family. Kidney donation at very young and very old ages is happening around the world. Sam Nagy from Britain, at 20 years of age is the youngest voluntary living kidney donor. Britain also houses the oldest donor, Mr. Nicholas Crace at 83 years. A

search on the internet for the oldest donor in India shows Mrs. Shailaja Joshi at 74 years and 7 months as possibly the oldest donor from India. There has also been a donor at 72 years. Both were from Mumbai. There could have been older donors, who were not reported. In our study the oldest donation was at 62 years. Thus it appears that India is trying to match the global scenario for kidney transplantation with more expanded criteria living kidney donors being accepted.

The majority of the donors were wives 18/39 (36%). There were 9 mothers (18%) and 8 sisters (16%) among the donors studied. Thus it is evident that 80% of the donors in the study were females who were emotionally attached to the recipients in the closest order.

Our study included 12 parents and 14 siblings. Thus related donors were 26/50 (52%). Spousal donors were 18 (36%). All were wives. Parents and siblings of wives were 5/50 (10%) and 1/50 (2%) was a long time family friend. Therefore unrelated donors were 24/50 (48%). The finding of lesser male donors in our study is comparable to the findings of Veerappan et al.[57].

The mean post transplant follow up period in the related and unrelated groups were 8.42 years and 4.58 years respectively. This could have reflected a recent increase in unrelated kidney donation. Recently many studies have shown that unrelated kidney transplantation has proved to be very successful despite a

poor HLA match[17]. In an analysis of living related, unrelated and cadaveric transplantations, it was shown that the graft survival rate at 5 years was similar for spousal and living unrelated grafts which stood at 75% and 72% with a half life of 14 and 13 years respectively. For parental living related grafts the 5 year survival of the graft was 74% with a half life of 12 years. These were significantly better than cadaveric grafts which had a 5 year survival of 62% and a half life of 9 years. Thus, a living donor graft performs better then a cadaver graft in any case. It was concluded in the study that promoting spousal transplants could remove as many as 15% of the CKD patients on the UNOS waitlist[17].

Parents of CKD patients are often old and may not be fit to donate their kidneys. The joint family system is gradually vanishing from our society. With shrinking family size, the availability of sibling donors has also come down for obvious reasons. Moreover, siblings are also increasingly unwilling to donate. When a suitable and willing first degree related donor is not available, the patient's wife comes forward[11]. With the Transplantation of human organs act in 1995, spousal donation has become legally permissible in India and has also contributed to increasing number of spousal transplants. In the Indian context, especially in rural India the husband earns for the family, and the wife wants him to live long.

There has been a recent surge to include donors with chronic diseases like hypertension and diabetes which are well controlled and whose kidneys do not

show evidence of injury from the systemic diseases. This is in tune with the ever expanding need for kidney donors. The tendency of diabetes and hypertension to run in family makes it likely that the donor may suffer from CKD in the longer run. Therefore it presently appears reasonable to include these ‘expanded criteria donors’ or ‘marginal donors’ with a stricter age criteria. Likewise, the previous age limits can be relaxed in donors who are otherwise normal and have no systemic diseases when transplantation may offer a better quality of life to the patient, without major medical disadvantages to the donor.

Three of the donors enrolled in the study had systemic diseases prior to donation. Two of them had systemic hypertension and one had hypothyroidism. They were all under appropriate treatment for the same. It was found that one hypertensive donor developed a non fatal cerebrovascular accident one year after donation. He is at present ambulant without support and leads an independent life. He had not been on regular follow up for control of his systemic hypertension after the nephrectomy, till he developed the stroke. We have given appropriate medications and counseling to ensure adherence to antiplatelets and antihypertensive therapy. The other donor with hypertension at the time of donation was a lady 51 years of age at donation and diagnosed with hypertension at the time of pre donation screening. She was on regular follow up and medications. The donor with hypothyroidism was already on thyroxine

supplementation for the past 30 years prior to donation and was in euthyroid state. She is continuing to take the same thyroxine dose.

10 out of the 50 donors studied (i.e. 20%) had present medical ailments. 7 donors had hypertension. 4 had diabetes mellitus. The male hypertensive donor had developed stroke and had a residual hemiparesis with power 4+ and was ambulant. The donor with hypothyroidism continued to take thyroxine and was in euthyroid state.

Prevalence of hypertension is increasing over the years[58]. Nearly 55% of males over the age of 50 years were found to be hypertensive in India[59]. A similar trend is observed in women over the age of 50 years[59]. However, there is a higher prevalence of hypertension in women aged more than 60 years as compared to men[59]. In our study, there were 8/11 (72.72%) male donors over the age of 50 years, and 19/39 (48.71%) female donors were above the age of 50 years. Among the donors with hypertension, 2 were hypertensive prior to donation. One donor was diagnosed with diabetes mellitus and systemic hypertension by his family physician and was on appropriate treatment. He had developed hypertension 5 years ago, 20 years after donation. The donor with hypothyroidism had developed systemic hypertension 1 year back, that is, one year after donation. Another donor had developed hypertension 2 years ago. She was diagnosed with hypertension by her family physician and was on regular follow up. 2 donors were diagnosed with

hypertension for the first time in our study. They were completely asymptomatic after donation and had not attended any medical service for follow up or a periodic medical check up. None of the donors with hypertension had visited a nephrologist after the immediate post transplant follow up. 5 out of the 7 hypertensive donors had already been diagnosed with hypertension and were on treatment for the same. This reflects the importance of the family physician in the follow up of renal donors. All the hypertensive donors were aged more than 55 years. 3 out of the 8 male donors aged more than 50 years were hypertensive. This averages at 37.5%. 4 out of the 19 female donors aged more than 50 years were hypertensive. This averages 21%. The overall average prevalence of hypertension of 7/50 or 14% for the mean age of 49 years and an age adjusted average of 7/27 or 25.92% in donors who were aged more than 50 years is lower, compared with the other community based studies on the prevalence of hypertension[59,60].

There have been studies to show an increase in prevalence of hypertension among kidney donors. Watnick et al [61] showed an increase in the occurance of hypertension in 1988. They also had observed an increase in glomerular proteinuria without a decrement in GFR after up to 18 years post uninephrectomy for renal donation. Talseth T et al.[62] observed a 15% occurrence of hypertension in the post donation follow up study. They however understood the increasing prevalence of hypertension and concluded that the development of hypertension

after donation warrants further observations. Sommerer C et al[63] in 2004 showed that there after age adjustment there was no increase in blood pressure after kidney donation. They also had a significantly fewer number of patients with proteinuria. Manisha Sahay et al[7] observed that 46% of renal donors had developed hypertension. However, the occurance of hypertension in donors enrolled in our study appears to be similar to the general population. All hypertensive donors had a good quality of life and none had proteinuria.

Diabetes mellitus was found in 4 out of the total number of 50 donors enrolled. This averaged at 8% for the mean age of the donor study population at 49 years. There was one male and three female donors with diabetes. The male donor with diabetes also had hypertension and was undergoing treatment for both. One female donor who had never visited a physician after the immediate post transplant follow up was diagnosed with diabetes mellitus for the first time during our study. Two other female donors were already diagnosed and were undergoing appropriate treatment under their family physicians.

Proteinuria has been linked to both increased risk of renal and cardiovascular diseases. It is used as a marker of endothelial dysfunction. The best technique to measure proteinuria is to collect a 24 hour sample and quantify the protein in it. This is due to the fact that protein excretion is not uniform throughout the day and time based variations in spot urine protein estimations are bound to occur.

Creatinine has been used as a marker of clearance since long. It also has variations in the rate of excretion. A 24 hour urine protein estimation is time consuming and cumbersome. It also causes some practical discomfort to the patients undergoing the investigation. To overcome this problem, the estimation of protein to creatinine ratio in a spot urine sample was introduced and widely practiced. The concurrent estimation of protein and creatinine in a spot sample tends to neutralize the variation in excretion of protein. It has been found to be more or less accurate and approximates well with the 24 hour protein quantification. Sometimes a spot albumin creatinine ratio is used, where available. In our study, we chose to use the protein creatinine ratio as a marker of overall proteinuria. The mean protein creatinine ratio 0.18± 0.08 (Range 0.04 – 0.35), this is well within the normal of 0.5 for protein creatinine ratio. None of the donors had demonstrable proteinuria by the standard heat coagulation test.

The mean urea value in our study was 32.12 mg/dl, and the mean creatinine value was 0.91mg/dl. The normal range for serum urea values in our lab is 10 to 40 mg/dl, and for serum creatinine it is 0.6 to 1.2 mg/dl. Concordant higher values for both urea and creatinine in a donor were found in 1 donor, who was the hypertensive donor without regular follow up. He had a serum urea of 43mg/dl and a serum creatinine of 1.5mg/dl. A 74 year old donor 27 years post donation who was a normotensive diabetic had serum urea 42 mg/dl and serum creatinine 1.2

mg/dl. A 60 year old donor, who became a hypertensive after donation, had serum urea 42 mg/dl and serum creatinine 1.1 mg/dl. In all these donors, age, diabetes or hypertension seems to pose a risk for developing a decline in renal function. There was only one donor, a female of age 40 years, who after 1 year of donation had a serum urea of 47mg/dl and serum creatinine of 1.1 mg/dl. She was otherwise normal. She had a systolic blood pressure of 110mmHg and diastolic blood pressure of 70mmHg. She had no proteinuria in heat coagulation and had a spot protein creatinine ratio of 0.08. She has been put on close follow up.

The average time taken for return to normal life was 4.08 weeks. Among female donors it was 4.20 weeks and among male donors it was 3.63 weeks. All the donors in our study had undergone conventional surgical nephrectomy. This could have led to a slightly longer recovery time. The use of laparoscopic nephrectomy, although hastens recovery from the surgery, is associated with a higher chance of early graft dysfunction. This may be due to inexperience, accidental graft damage during the learning curve, compromised renal blood flow due to the prolonged pneumoperitoneum and the chance of having shorter renal vessels and multiple arteries. However, in well experienced centres, the outcomes with surgical and laparoscopic nephrectomy have become somewhat similar.

All the donors had a positive attitude toward donation. They were happy to have been able to help their near ones get a better life. Most of them were unaware

of the need for proper medical follow up. Being asymptomatic, they had continued with their usual life. They were all initiated into the post donation follow up schedule of periodic medial consultation for screening and were happy to enroll in the same. They were willing to advise future prospective donors on the advantages of transplantation for CKD and instill confidence based on their good health after donation.

Limitations of the study

1. Only about 78 transplant recipients are registered in the Department of Nephrology – Transplant OPD in Thanjavur Medical College Hospital. Out of them some were cadaver kidney recipients, some had expired, some recipients had lost to follow up and some of the donors lived in far away places. Only 50 donors could be enrolled in the study. The small number of donors studied limits extrapolation of this study into safety profile of donors.

2. A prospective study would have addressed the donor follow up better. But because Thanjavur Medical College Hospital does not offer renal transplantation facilities, a prospective study could not be conducted.

3. The donors enrolled had undergone the transplantation in various centres. Most of the centres retained their pre-transplant medical records and were not available for comparison with the present values, post donation.

4. There had not been any graft rejection in any of the recipients. Therefore the attitude of all the donors was naturally positive. This may have caused a skewed result.

Strengths of the study

1. Although the study has a small sample size of the donors, it seems to match the characteristics of larger studies from India with regard to the age and sex of the donors.

2. Donors who had a post donation period ranging from few months up to 27 years were studied.

3. The study was conducted in a gentle way, by which the donors understood the importance of post donation follow up without being alarmed that they were at risk of renal failure.

SUMMARY AND

CONCLUSION

Conclusion

1. There were more female donors than males.
2. Female donors had a younger age at donation.
3. A nearly equal number of related and unrelated donors were enrolled.
4. Wives formed the single major group of donors. No husbands were enrolled.
5. The prevalence of hypertension among donors appears similar to normal population.
6. No donor had developed proteinuria.
7. No major deterioration in renal function was noted.
8. Most donors were back to their normal life within a month of donation.
9. The donors were initiated about post donation follow up.
10. All the donors had a positive attitude about donation and would reassure prospective donors in the future.

ANNEXURES

Abbreviations

S.no.	Abbreviations	Expansion
1	CKD	Chronic kidney disease
2	ESRD	End stage renal disease
3	MDRD	Modification of diet in renal disease
4	GFR	Glomerular filtration rate
5	SNGFR	Single nephron glomerular filtration rate
6	BP	Blood pressure
7	SBP	Systolic blood pressure
8	DBP	Diastolic blood pressure
9	PCR	Protein creatinine ratio
10	HD	Hemodialysis
11	PD	Peritoneal dialysis
12	CAPD	Continuous ambulatory peritoneal dialysis

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Proforma

Effects of kidney donation

1. **Name** :
2. **Age** :
3. **Sex** :
4. **Date of donation** :
5. **Pre-existing diseases** :
   (Hypertension / Diabetes Mellitus / Renal disease)
6. **Present co-morbidities** :
7. **Blood Pressure** :
8. **Proteinuria:**
   1. **Qualitative** :
   2. **Spot Protein-Creatinine Ratio** :
9. **Renal function**
   1. **Urea** :
   2. **Creatinine** :
10. **Impact of donation:**
    1. **Returned to daily life in** : **____ weeks**
    2. **Attitude toward kidney donation** :
       (Positive / Neutral / Negative)

MASTER CHART																	
S. No.	Donor Name	Date of Transplant	Age	Sex	Age at donation	Years since Donation	Relationship to recipient	Pre-existing diseases	Present diseases	SBP (mm/Hg)	DBP (mm/Hg)	PCR	Urine Protein	Urea (mg/dl)	Creatinine (mg/dl)	Return to Normal Life (weeks)	Attitude to Donation
1	Kaliyasundaram	28/3/2012	35	F	35	0	Wife	NIL	NIL	100	70	0.29	NIL	26	0.7	2	Positive
2	Vanitha	1/3/2000	36	F	24	12	Wife	NIL	NIL	110	70	0.25	NIL	28	0.7	3	Positive
3	Rani	11/10/2010	64	F	62	2	Mother	Hypothyroidism	SHT/Hypothyroidism	150	100	0.06	NIL	38	0.8	6	Positive
4	Selvakumari	21/11/2007	38	F	33	5	Wife	NIL	NIL	110	70	0.06	NIL	26	0.8	4	Positive
5	Manimegalai	20/7/2006	53	F	47	6	Sister	NIL	NIL	120	70	0.28	NIL	32	0.8	5	Positive
6	Maheswari	10/12/2009	57	F	54	3	Sister	NIL	NIL	120	70	0.15	NIL	32	1	2	Positive
7	Asaithambi	4/8/2010	58	M	56	2	Father	NIL	NIL	120	80	0.16	NIL	36	1	5	Positive
8	Rajeswari	28/10/2010	54	F	52	2	Sister	NIL	NIL	130	80	0.16	NIL	30	1	3	Positive
9	Packiriammal	27/7/2002	65	F	55	10	Mother	NIL	NIL	120	80	0.1	NIL	34	1.2	6	Positive
10	Bhagyavathy	23/3/2010	40	F	38	2	Sister	NIL	NIL	110	70	0.06	NIL	28	0.7	3	Positive
11	Shantha	21/1/2011	36	F	35	1	Sister	NIL	NIL	120	80	0.1	NIL	30	0.6	3	Positive
12	Solayammal	19/07/2005	60	F	53	7	Mother	NIL	SHT	160	90	0.16	NIL	42	1.1	3	Positive
13	Mumtaj	22/4/2010	45	F	43	2	Mother	NIL	NIL	120	80	0.08	NIL	32	0.6	3	Positive
14	Poongothai	25/1/2007	35	F	30	5	Sister	NIL	NIL	140	90	0.24	NIL	30	0.6	4	Positive
15	Balagurusamy	17/1/2011	44	M	43	1	Father	NIL	NIL	120	80	0.15	NIL	36	1	4	Positive
16	Hemamalini	18/5/2010	36	F	34	2	WIfe	NIL	NIL	120	80	0.04	NIL	36	1	5	Positive
17	Vanaja	24/4/1990	51	F	29	22	Wife	NIL	DM	130	80	0.25	NIL	40	1	4	Positive
18	Bhagyam	2/8/1985	74	F	47	27	Mother	NIL	DM	120	80	0.28	NIL	42	1.2	6	Positive
19	Shanmugam	23/7/2010	50	M	48	2	Friend	NIL	NIL	130	80	0.35	NIL	40	1	2	Positive
20	David	2/8/2010	60	M	58	2	Father in law	SHT	CVA/SHT	140	100	0.13	NIL	43	1.5	3	Positive
21	Gomathi	20/8/2010	33	F	31	2	Wife	NIL	NIL	110	70	0.08	NIL	26	0.7	4	Positive
22	Vasuki	12/12/2008	32	F	28	4	Wife	NIL	NIL	116	74	0.1	NIL	30	0.8	5	Positive
23	Pounammal	22/6/2001	55	F	44	11	Sister	NIL	NIL	124	80	0.08	NIL	35	1	4	Positive
24	Selvi	3/3/2008	48	F	44	4	Wife	NIL	NIL	120	80	0.24	NIL	26	0.8	4	Positive
25	Kathiresan	28/11/1987	62	M	37	25	Brother	NIL	SHT	160	110	0.24	NIL	32	1.1	3	Positive
26	Mariyathal	24/6/2008	55	F	51	4	Mother	SHT	SHT	146	100	0.3	NIL	30	1	3	Positive
27	Theivasigamani	6/9/2010	34	F	32	2	Wife	NIL	NIL	108	60	0.1	NIL	26	0.8	4	Positive
28	Sivagami	12/12/2008	55	F	51	4	Mother	NIL	NIL	122	70	0.2	NIL	30	1	6	Positive
29	Rani	23/7/1998	55	F	41	14	Mother	NIL	NIL	120	80	0.27	NIL	29	0.9	4	Positive
30	Kaaja Mohammad	9/8/1987	55	M	30	25	Brother	NIL	DM/SHT	154	90	0.2	NIL	28	0.9	4	Positive

31	Mariammal	25/9/2006	37	F	31	6	Wife	NIL	NIL	116	74	0.25	NIL	30	0.8	5	Positive
32	Shanthi	29/9/2011	35	F	34	1	Wife	NIL	NIL	110	60	0.12	NIL	27	0.7	3	Positive
33	Devaki	2/12/2009	58	F	55	3	Wife	NIL	DM	100	60	0.07	NIL	28	1	4	Positive
34	Rajalakshmi	3/9/2011	40	F	39	1	Wife	NIL	NIL	110	70	0.08	NIL	47	1.1	4	Positive
35	Pushparani	14/2/2006	40	F	34	6	Wife	NIL	NIL	114	80	0.15	NIL	28	0.9	4	Positive
36	Varathan	27/6/2005	60	M	53	7	Brother	NIL	NIL	120	86	0.19	NIL	34	1	4	Positive
37	Kamaraj	4/4/2008	54	M	50	4	Father	NIL	NIL	126	80	0.32	NIL	28	1	4	Positive
38	Valliammai	13/5/2005	50	F	43	7	Wife	NIL	NIL	116	80	0.05	NIL	30	1	4	Positive
39	Chandra	31/1/1996	55	F	39	16	Sister	NIL	NIL	110	70	0.24	NIL	40	1	5	Positive
40	Aleema Beevi	13/4/2011	50	F	49	1	Wife	NIL	NIL	124	80	0.25	NIL	26	0.9	6	Positive
41	Lakshmi	2/9/2009	60	F	57	3	Mother in law	NIL	NIL	110	80	0.26	NIL	36	1	6	Positive
42	Karthikeyan	24/1/2003	59	M	50	9	Brother	NIL	NIL	120	84	0.2	NIL	33	1	5	Positive
43	Pugalesan	27/6/2003	47	M	38	9	Brother	NIL	NIL	126	80	0.26	NIL	32	0.8	3	Positive
44	Jothi	3/5/2000	63	F	51	12	Mother	NIL	SHT	138	86	0.3	NIL	40	1.2	5	Positive
45	Palaniammal	4/10/2004	35	F	27	8	Wife	NIL	NIL	116	80	0.16	NIL	25	0.6	5	Positive
46	Devi	6/10/2005	49	F	42	7	Sister in law	NIL	NIL	110	74	0.2	NIL	32	0.9	4	Positive
47	Alagambal	3/4/2009	45	F	42	3	Sister in law	NIL	NIL	120	80	0.25	NIL	28	0.8	3	Positive
48	Noor Jahan	2/12/2008	60	F	56	4	Mother in law	NIL	NIL	120	80	0.21	NIL	34	1	4	Positive
49	Thiruselvam	22/2/2003	46	M	37	9	Brother	NIL	NIL	120	80	0.24	NIL	28	0.8	3	Positive
50	P.Jagadeeswari	13/5/2009	39	F	36	3	Wife	NIL	NIL	120	80	0.16	NIL	27	0.7	6	Positive
MEAN			49		42.56	6.58				122.32	79.16	0.18	NIL	32.12	0.91	4.08	Positive
	STANDARD DEVIATION		11		9.74189	6.5561624				13.6568	9.85685	0.08		5.3591	0.1821078	1.121951652	