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Living Kidney Transplantation: A Review of Donor Evaluation, Risks and Outcome.

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ABSTRACT:

The number of ESRD patients is rapidly increasing globally. Although the best treatment option for ESRD is kidney transplantation, most patients still have to wait for years for kidney transplant due to shortage of organs. Living kidney transplant gives better recipient and allograft outcomes but donor safety is equally important. To ascertain the safety of donation, living kidney donors undergo extensive evaluation prior to getting accepted for kidney donation. In the long term, donors are at higher risk for hypertension and proteinuria than general population and need close follow up after solitary nephrectomy. This review focuses on donor evaluation, risks, and outcomes of kidney donors.

Key Words: Living donors, Transplant, Kidney, Hypertension, Haematuria

Introduction

The prevalence of End Stage Renal Disease (ESRD) has risen globally over the past decades[1] and ESRD patients have reduced quality of life, increased morbidity, and mortality on dialysis.[2] Although the preferred treatment for ESRD is kidney transplantation as it provides the opportunity to maintain better lifestyle and improve life expectancy [3,4], most patients require dialysis for few months to years prior to transplant. Even with all the efforts to increase the number of kidney transplants in developed countries like the United States, the inadequate pool of donor organs has limited the number of transplants. [5] In developed countries, most patients receive kidney transplant from deceased donors, [6] however, given the limited source of deceased donors and ever growing transplant waiting list, expansion of donor pool is required. In most developing countries, like Nigeria, living kidney donors are the predominant source for kidney transplant and this is due to technological difficulties of cadaveric transplantation. [7] Organ shortage is therefore a major problem in developing countries as well.

Available data clearly suggest that living kidney donors provide the increase in the pool of available organs along with better outcomes for recipient and allograft. [8] However, living donation poses some medical and psychosocial risks to the donors. This review will focus on pros and

cons of living donation including risks and benefits to the donors as well as the evaluation process.

Rationale for living kidney donation.

Live kidney donation rates vary worldwide. In most developing countries few deceased donor transplantations are performed, perhaps because of lack of coordinating organizations like United Network for Organ Sharing (UNOS) and Organ Procurement and Transplantation Network (OPTN), lack of a regulatory and monitoring system, appropriate transport systems, challenges in co-ordinations between different hospitals, cultural and religious beliefs. [7,9] However, in western countries deceased donor transplantation has been the predominant form of kidney transplant. [5,10] In the United States (US), efforts to increase the pool of deceased donor kidneys have led to utilization of expanded donor criteria, donor after cardiac death and high-risk donors with close surveillance. Even with these efforts the waiting list for kidney transplant has continued to grow.[11] Limited and unpredictable supply of deceased donor organs has rekindled great interest in increasing the pool of living donors.

Sufficient evidence exists to show that living kidney donors provide better outcomes for recipient and allograft compared to deceased-donor transplantation. [12] Living donors provide the best opportunity for timely and successful kidney transplant. The allograft in living kidney transplantation is exposed to minimal or no ischemia and is consequently subjected to less ischemic and reperfusion injury compared to deceased kidney. [13] Prolonged cold ischemia time is one of the causes of delayed graft function (DGF),[13] which is a negative risk factor for long-term renal allograft survival. [14,15] Other factors that may contribute to the beneficial effects of living kidney transplant include: (a) The vascular anatomy can be evaluated prior to the donor nephrectomy (b) Elective surgery (c) Lower recipient age and, (d) Recipient's shorter time on dialysis prior to transplantations.

Even with the knowledge of better recipient and allograft outcomes, the number of living kidney donors have not surpassed deceased donors except for in 2001. [2,16] The reasons for decrease in living kidney donation since 2001 are not very clear.

Donor demographics

In the US, majority of living donors are in the age group of 35-49 years (42%) followed by 18-34 years (29%). [6] Among all the ethnicities, white donors dominate in kidney donation. In 2012, 71% of living kidney donors were white, 10% were black and 13% were Hispanic. [6] Spouses are important source of living kidney donation and despite poor human leukocyte antigen (HLA) matching; the graft survival is comparable to that of parental kidney. [17] According to UNOS data more than half of living donors in last 20 years have been female. This trend has continued and among the entire living kidney donors, 62% in 2010 and 60% in 2012 were female donors. [6] Donations by adult offsprings to their parents have increased in last few years. [6] Although small, there has been slight increase in number of emotionally uninvolved donors, also called non-directed donors. [6]

A 16 year review of living kidney donation in a centre in South Africa, revealed a mean donor age of 35.2 $\pm$ 8.3 years, more than half of the donors were females (55%) while only 24% were blacks.[18] These results mirror what obtains in US, one might

suggest that this observation is due to the similarities between both countries in terms of ethnicities (blacks and whites). Possible explanations for these trends include the donor selection protocol that automatically excludes older donors. Exclusion may be strictly due to age or co-morbidities that become more common with increasing age. Females may be more emotionally attached to family members and so may offer to donate more readily than males, however some families may intentionally exempt their male breadwinners from donation in order to 'preserve' the family's source of livelihood. In Nigeria there are scarce data on donor demographics possibly due to the non-existence of a registry. However, a couple of studies that investigated the willingness to donate kidneys amongst a range of respondents (health workers, patient relatives, individuals in rural setting) reported that males and unmarried respondents were more likely to donate kidneys.[9,19,20,21] However, willingness to donate does not always translate to actual organ donation.

LIVING DONOR EVALUATION

To ascertain the safety of living donors prior to proceeding with solitary nephrectomy, potential donors undergo extensive medical evaluation. Since these donors will undergo an elective surgical procedure that will not provide them any health benefit, a thorough psychosocial evaluation is performed in order to ensure that the donors understand the short and long term consequences of solitary nephrectomy. Two international conferences have been held to address the care and evaluation of the living organ donors. [22,23] At The Amsterdam Conference [22], the consensus guidelines for evaluation of potential living kidney donor and care of the donors were developed. Most of the transplant centers follow these guidelines, however there are newer guidelines such as the United Kingdom (UK) guideline, [24] and the European Best Practice (ERBP) guideline on the management and evaluation of the living kidney donor and recipient, [25]

Donor Evaluation Protocol

Kidney donor evaluation has mostly been standardized and it includes thorough medical, surgical, and psychosocial evaluation of the prospective donor to ensure donor safety (Table 1). [22,26] This evaluation includes history, physical exam, chest X-Ray, Urine analysis with microscopic analysis, 24-hour urine for creatinine clearance and albuminuria, electrocardiogram (ECG), and lipid panel. Additional evaluations are indicated after considering age and family history, which include appropriate cardiac stress and cancer screening, thorough infectious disease screening and anatomical studies such as CT angiogram, renal angiogram or Magnetic resonance angiogram (see Table 1). In addition, an assessment of the donor and recipient blood groups and a T and B cell cross match between the individuals is performed. Absolute and relative contraindications for kidney donation are listed in Table 2. Some donors are considered marginal donors and need more than routine evaluation prior to deciding their candidacy for kidney donation. These include donors with obesity, hypertension, proteinuria, nephrolithiasis, and hematuria. This will be discussed in more details below.

Table 1: Evaluation of Living Kidney Donor

Living Kidney Donor Evaluation
Relevant History and Physical Examination: History, Family history, social history and physical exam.
Labs: CBC, Comprehensive metabolic panel, lipid panel. **Urine**: UA with microscopic analysis, 24 hour urine for creatinine clearance and albuminuria, spot ACR **ECG**
Imaging/Anatomical Studies: chest X-Ray, CT angiogram, renal angiogram or Magnetic resonance angiogram.
Special Tests: appropriate cardiac stress and cancer screening results
Infectious Disease Screening: hepatitis C, hepatitis B, HIV, RPR, CMV, EBV serologies, and PPD placement

CBC=complete blood count, UA=Urinalysis, ACR= albumin creatinine ration, ECG=Electrocardiogram, RPR= Rapid plasma reagin, CMV=Cytomegalovirus, EBV= Epstein-Barr virus.

Obese Donors

Obesity is a known risk factor for increased mortality and morbidity in the general population [27] and renal outcome is worse in obese patients as compared to healthy individual. [28] Increased body mass index (BMI) (> or =27 kg/m^2) is associated with increased risk for proteinuria, focal segmental glomerulosclerosis, diabetes, hypertension and metabolic syndrome. [29] Obese donors require longer operative time and higher conversion rates from laparoscopic to open nephrectomy. [30] Higher postoperative complications have been reported in obese donors especially related to open nephrectomy leading to wound complications. [31]

A study from Mayo clinic in Minnesota looked at the outcomes of obese donors. [32] In this study, renal function, blood pressure and proteinuria were compared between obese and non-obese donors. Selected obese donors, prior to donor nephrectomy, had no proteinuria and fasting blood glucose was <126mg/dl. Of more than 100 obese donors (BMI>30 Kg/ M^2) renal function was not significantly different from that of non-obese donors prior to kidney donation. In this study, no change in blood pressure was noted after 12 months of donor nephrectomy. However, in another study with a mean follow up of 13.6+/-8.6 years, Praga et al [33] observed that among the patients with BMI >30 Kg/M^2 at the time of kidney donation, 92% developed proteinuria and/or renal insufficiency.

Median time of developing proteinuria was 6.1 years after nephrectomy; in contrast, among the patients with BMI <30Kg/M^2, only 12% donors developed these complications. [33] Renal biopsy in two obese donors showed focal segmental glomerulosclerosis. These studies show that the obese donors are at higher risk of hypertension and proteinuria after kidney donation and need close follow up, however a meta-analysis showed that most studies of obese donors had short follow up and had conflicting reports on change in GFR. [34]

Most transplant centers exclude donors with BMI >35Kg/m^2 while others will use obese donors
(BMI>30) as long as there are no other co-morbidities. Surveys of US transplant centers [35] showed that 52 percent of the centers use a BMI cut off of 35 and 20% of the centers had BMI cut off of 40. According to Consensus Guidelines from the Amsterdam Conference [22], obese donors should be selected only if they have no hypertension, no proteinuria or have a fasting blood glucose ≤ 126 mg/dl. For fasting glucose between 100-125 mg/dl, a 2-hour glucose tolerance test should be done to rule out glucose intolerance and weight loss/healthy life style encouraged even after donation. The UK guidelines exclude donors with BMI >35kg/m^2 while the moderately obese (BMI 30-35kg/m^2) are to be counseled carefully about the increased risk of perioperative complications, the long-term risk of kidney disease, advised to lose weight prior to donation, and to maintain their ideal weight following donation. [24]

Hypertension

Even mild elevation in blood pressure has been shown to be an independent risk factor for developing ESRD [36], and there is concern that hypertensive donors may be more prone to worsening renal function after nephrectomy secondary to reduction in kidney mass. [37] Data on outcomes of hypertensive donors following nephrectomy is limited and inconclusive. The definition of hypertension (HTN) varies among different studies and most reports have short follow up.[34] A study of 148 white donors, 21 of whom were hypertensive prior to kidney donation, showed that hypertensive donors had slightly lower iothalamate glomerular filtration rate and higher proteinuria compared to non-hypertensive donors at 6 and 12 months post donation (proteinuria could have been higher considering that many of these donors were started on angiotensin receptor blockers). [38] These observed differences were not statistically significant, suggesting that white donors with moderate, essential hypertension and normal kidney function have no adverse effects regarding blood pressure, GFR, or urinary protein excretion during the first year after living kidney donation. [38] The limitations of this study were the inclusion of all Caucasian subjects and a short follow up. Hence the findings of this study cannot be applied to non-Caucasian and younger donors.

In the absence of strong data most US transplant centers have now adopted a flexible approach in excluding patients from living donation. [35] Most centers use less strict blood pressure criteria if the donor is older, or if end organ damage has been excluded. Forty seven percent of transplant centers exclude hypertensive donors on any

antihypertensive medication, 41% exclude donors if they are taking more than one medication, and 8% exclude donors taking more than two medications. [35] Many centers use 24 hour ambulatory blood pressure monitoring especially if the potential donor had high BP in office setting to rule out "white coat" hypertension. The presence of hypertension alone may not be an absolute contraindication for kidney donation in absence of any end organ damage. According to Consensus Guidelines from Amsterdam Conference [22] some patients are considered low risk. These include donors with isolated hypertension, easily controlled hypertension, > 50 years old, GFR of >80ml/minute and urinary albumin excretion of less than 30mg/day. The ERBP and UK guidelines have similar recommendations i.e. the presence of mild-moderate hypertension easily controlled by 1 or 2 antihypertensive is not a contraindication to donation as long as target organ damage is excluded. [24,25] This may apply only to white donors as African American living donors with hypertension are at higher risk of worsening hypertension and ESRD after kidney donation. [39,40,] Therefore, based on the current information it may be appropriate to use the non-African Americans donors with HTN and no other risk factors for kidney disease.

Proteinuria

Persistent proteinuria has been shown to be a strong, independent predictor of ESRD in a mass screening of 106,177 patients in Okinawa, Japan. [41] Urine is usually tested at least on two separate occasions, in the absence of fever, infection or heavy exercise, to differentiate between transient and persistent proteinuria. Dipstick measurements of proteinuria are not adequate for donor evaluation. As laboratories vary in normal values of quantified urine protein, it is recommended to do 24-hour urine collection or spot albumin creatinine ration to evaluate for protienuria. [24] The UK guideline and the ERBP, recommends that potential donors with overt proteinuria (ACR >30 mg/mmol, PCR >50 mg/mmol or 24- hour total protein >300 mg/day) be excluded from donation. [24, 25] Any donor with systemic causes of proteinuria like diabetes, hypertensions, obesity, obstructive sleep apnea amongst others, is also not a candidate for kidney donation.[22] Isolated proteinuria is not an uncommon finding during initial evaluation of donors and there are concerns about worsening proteinuria from hyperfiltration of the remaining kidney after donor nephrectomy. While several studies of patients with solitary kidney have shown no increase in hypertension, chronic kidney disease or proteinuria after unilateral nephrectomy, others have shown slight increase in these outcomes. [40-46] Most of the studies examining the risk of donation in proteinuric subjects are small and the results are inconclusive. [39,40,41] However, there are concerns that the risk of progressing to ESRD in proteinuric person may be even higher with solitary kidneys. Therefore it is imperative to thoroughly screen potential living donors for proteinuria.

In practice, there is no uniform agreement on the acceptance of these marginal donors. The exclusion criteria for kidney donation varies among the transplant centers from >150mg/day to 300mg/day unless the proteinuria is postural. [35] If the potential donors have isolated proteinuria between 250-300 mg/day then urinary albumin excretion rate should be measured and they may be considered for kidney

donation only if urinary albumin excretion is negative. [43]

Haematuria

The incidence of hematuria is about 2.7% among donor screening. [44] Standard donor evaluation includes urine analysis with microscopic exam; dipstick is a very sensitive test and reliable test for haematuria. [45] Persistent haematuria is defined as two or more dipstick positive on separate occasions, at least one month apart. Work up for hematuria in a kidney donor includes detailed family history, urine culture, 24 hour urine collection to estimate calcium and urate, cytology and, renal imaging (Figure 1). If urological work up is negative, donor should have renal biopsy to exclude glomerular pathology. [46] Kidney biopsy is a safe procedure but nevertheless has risk of complications including bleeding (1%), loss of kidney, infections or death. [47,48] Most patients with isolated hematuria (normal GFR and no proteinuria) do not need renal biopsy for diagnosis or treatment and are usually followed closely. However if they choose to be kidney donor, then renal biopsy is necessary to exclude glomerular pathology. The risk of mortality with renal biopsy is 0.02-0.1% in some studies. [47] The risks of complications may be lower in the healthy kidney donors but not completely absent. Given the risk of progression to ESRD, donors with any glomerular pathology are excluded from kidney donation. [24,25] The most common practice (43% of transplant programs in the US) is to only accept the donors if urological work up is negative and renal biopsy is normal.[35] Twenty-one percent (21%) of programs automatically exclude donors with >10 RBC/hpf regardless of work-up. [35]

Nephrolithiasis

In the USA, the prevalence rate of nephrolithiasis has progressively increased from 3.2% in the 1970s to the current rate of 5.2%. [49] The lifetime risk of nephrolithiasis is about 10-15% in developed countries and can be as high as 20-25% in the Middle Eastern and African countries. It can be a recurrent disease and the likelihood of relapse increases with each episode and can be as high as 50% over 10 yrs and 75% over 20 years. [50] Epidemiological data exist to suggest that stone forming populations have slightly increased incidence of chronic kidney disease especially those with BMI> 27 kg/m^2. [51] It is not known whether kidney donation in a stone former, increases risk of renal stone in the remaining kidney compared to stone formers with both kidneys. [52]All potential kidney donors with history of nephrolithiasis are screened for metabolic causes of kidney stones [22,24] and attempts are made to get the results of past stone analysis. Those with a history of cystine stones or struvite stones should not be considered for kidney donation as they are at higher risk of recurrent nephrolithiasis and infections. [53] Asymptomatic potential donors with history of single stone may be suitable for kidney donation provided they have no hypercalciuria, hyperuricemia, cystinuria, hyperoxaluria or metabolic acidosis. [22] They should also not have history of urinary tract infections, nephrocalcinosis or evidence of multiple stones on imaging. Absolute contraindications for kidney donation include systemic disorders such as primary or enteric hyperoxaluria, distal renal tubular acidosis, sarcoidosis, inflammatory bowel disease or history of bowel resection. [22] Persons with recurrence of nephrolithiasis, even while on appropriate treatment, are

also not acceptable as potential donors. According to a survey of the Transplant Centers in US [35] most of the centers accept a potential donor with a history of nephrolithiasis if no current stones are present and metabolic studies are normal. Only a small percent (5%) of programs reported no policy toward stone history in potential kidney donors.

RISKS TO THE DONOR

One of the most important concerns of the living donor kidney transplant procedure is safety of the prospective donor. This includes the physical, psychological and social well being of the donor.[22] The loss of one kidney results in structural compensatory changes in the remaining kidney to compensate for the lost GFR. [54] In addition to structural changes, a vigorous physiological compensatory response occurs (30-40% increase in GFR occurs among young kidney donors). [55-57] In a healthy person with healthy kidneys, these adaptations take place without many negative consequences. Increase in single kidney GFR (SK-GFR), after contralateral nephrectomy, is noted to be higher in younger donors than in older donors. [58] The limited compensatory response in aged kidney is likely due to age related microvascular changes and atrophic renal cortex. [58]

The immediate and long-term risks of kidney donation are discussed below.

IMMEDIATE RISKS TO THE DONOR

Living donors are at peri-operative risks during nephrectomy from general anesthesia and surgical procedure. A survey of 171 UNOS listed kidney transplantation centers [8] comprising 10,828 living donor nephrectomies from1991-2001, revealed that there were 52.3% open, 20.7% hand assisted laparoscopic and 27% total laparoscopic donor nephrectomies. Perioperative mortality in this study was 0.02%, and both deaths were in the laparoscopic group. Twenty-two patients (0.4%) in open nephrectomy group, 1.0% in hand assisted and 0.9% in laparoscopic group needed reoperation for bleeding, bowel obstruction, bowel injury or hernia. Rate of postoperative complications not requiring reoperation were 0.3% and these included bleeding, rhabdomyolysis, deep vein thrombosis/pulmonary embolism, ileus or pneumothorax. Rate of readmission amongst donors was higher for laproscopic nephrectomy vs. open nephrectomy (1.6% vs 0.6%, $p < 0.001$). Reasons for readmission included nausea, vomiting, dehydration, ileus, constipation, diarrhea, wound dehiscence and small bowl obstruction.

Another study from the UK examined morbidity and mortality among 2509 living kidney donors from November 2000 to June 2006. [59] One death occurred three months post-discharge and was that of a 60 yrs old donor who died of myocardial ischemia three months post operatively. The risk of major morbidity was 4.9% in this study. Five other deaths were not related to kidney donation. Review of other published data [60,61] shows that the incidence of development of serious complications including bleeding (0.98–6.3%), infections (wound infection 0.6–21%; pneumonia 2.5–9.8%; urinary tract infection 6.7–7.8%) and pneumothorax (0.6–8.8%) was variable. Overall, the perioperative46 mortality associated with living kidney donation is low (0.02%). [8] Laparoscopic surgery has evolved significantly over the last few years and the complications rates are much lower now. Laproscopic surgery is now considered choice of surgery as it provides several

advantages compared to open nephrectomy including shorter hospital stay, less pain, and better cosmesis; however one of the most common reasons for open nephrectomy remains rightsided nephrectomy because of technical difficulties. [62]

LONG-TERM RISKS TO THE DONOR.

During the early years data on long-term mortality and morbidity of living donors was not available. The physicians relied on the extrapolated data from the follow up of persons with congenital unilateral kidney or who had unilateral nephrectomy for reasons other than kidney donation. [63] These data were used to assess the long-term risks of a solitary kidney. One of the longest follow up of patients with solitary kidney was published in 1993 [64], this study examined consequences of nephrectomy, secondary to trauma, among US Army personnel. There was no increase in glomerular sclerosis or the prevalence of hypertension among the nephrectomy group. In other studies, even patients with diabetes mellitus and polycystic kidney disease with unilateral renal agenesis or unilateral nephrectomy, did not show any accelerated loss of kidney function. [65,66] Conversely another study [67] showed increased incidence of kidney failure, higher blood pressure and increased urinary protein excretion among the patients who had undergone unilateral nephrectomy. Since then there have been several studies published which have shown small increase in blood pressure and increased incidence of proteinuria [42,68,69] after unilateral nephrectomy.

Reports of increased proteinuria and increased incidence of hypertension in patients after unilateral nephrectomy have caused concerns about the fate of the living kidney donors and this has stimulated more research. One study observed that after mean follow up of 12.2+/-9.2 years, the majority of donors had GFR of >60ml/minute/1.73m^2 of body surface area, 32% donors developed hypertension and 12.7% developed albuminuria. [70] However the prevalence of hypertension and albuminuria were similar to the age matched general population. In this study, 99% of the donors were white, 60% were women and average age of donors was 41 years. Thus the outcomes of this study cannot predict outcomes in non-white and older donors. This study also had poor retrieval rates and only a small number (255/3404) had iohexol GFR done. One of the study which had good retrieval rates of the kidney donors [71] showed a 25% decline in GFR after kidney donation over 11 years of follow up. Additionally, 56% of donors developed proteinuria. Abdu et al in South Africa reported a prevalence of hypertension of 24% amongst donors followed up for 8.6$\pm$ 6.4 years. Again this was a short follow-up period and donors were not compared to general population or relatives of donors. [18]

The limitations of the studies on long-term outcomes of the living donors have been poor retrieval rate and comparison of the living kidney donor's outcome with the general population. General population also includes patients who have diabetes, hypertension, obesity and other risk factors for chronic kidney disease. Healthy donors should have better outcomes than general population in long term. The most appropriate and accurate way to compare the outcomes of the living kidney donors will be to compare with the population with same risk profile for chronic kidney disease. An excellent study done using the siblings of the donors as controls found no significant

difference in blood pressure, but a 20% increase in creatinine and increased incidence of urinary protein excretion among donors. [72]

Living kidney donors may be at increased risk of proteinuria and hypertension but there is no increased incidence of ESRD with current screening process. Further studies with long-term follow-ups and better retrieval rates of the living kidney donors are needed. Currently the UNOS require that donors be monitored for at least 2 years after kidney donation. Given the lack of data on long term follow ups it is important to have national and international donor registries.

Pregnancy after Donation

Substantial numbers of donors are young and they are frequently concerned about the effects of unilateral nephrectomy on their future pregnancies. Given that the remaining kidney compensates by hyperfiltrating after contralateral nephrectomy and that hyperfiltration is also an adaptive response to pregnancy, it is conceivable that the risk for development of HTN, proteinuria or worsening renal function among kidney donors may be compounded with pregnancy. Additionally there has been concern about the obstructive nephropathy that occurs with pregnancy. Physiological ureteral dilation occurs in pregnancy and may cause serious obstructive nephropathy in the setting of solitary kidney. A retrospective review of 6275 pregnancies [73] found only 5 cases of ureteral obstruction that required ureteral stent placement. Kidney stone was the cause of obstruction in 4 cases. Overall reported incidence rate of obstruction was only 0.007-0.07%. [73,74]

Only a few studies published have mentioned the outcome of pregnancy in kidney donors. In a study of 39 pregnancies [75], proteinuria was noted in 9 donors (1+ in 2, and trace in 7), which resolved after delivery. No significant changes were noted in renal function or proteinuria after a mean follow up of 7.9 years. Wirenshall et al [76] surveyed 220 women who had donated kidney between 1985-1992. Of the 144 who responded 33 became pregnant with a total of 45 pregnancies. Seventy five percent of the pregnancies had no complications. Overall morbidity was 8.8%; miscarriage (13.3%), preeclampsia (4.4%), gestational hypertension (4.4%), proteinuria (4.4%), and tubal pregnancy (2.2%); there were no deaths or fetal abnormality. Infertility was a problem in 8.3% of respondents, compared with a worldwide incidence of 16.7%. During a long term follow up of kidney donors in University of Minessota, 72 pregnancies were noted among 33 donors, out of which only two donors reported hypertension during first pregnancy and a third donor had preeclampsia. [77] The limitations of these studies are low retrieval rate of the donors.

None of the reported complications of pregnancy among kidney donors exceeded the incidence among general population. Based on the available data it is safe to say that kidney donation during pregnancy does not impose a higher risk compared to general population. However, it is recommended to delay pregnancy until at least 2 months after nephrectomy to assess renal compensation prior to conception. Some transplant centers recommend waiting for 6 months before getting pregnant after kidney donation. Evaluation of blood pressure, GFR, and microalbuminuria [22] is recommended during pregnancy and in the post partum period.

Table 2: Contraindications for Living kidney Donation

Absolute Contraindication	Relative Contraindication
Age <18yrs	Age >65 yrs
Uncontrolled hypertension or cardiovascular disease	Hypertension
Hypercoagulable State, Bleeding Disorder	History of Thrombotic events
Uncontrolled Psychiatric Illness	History of Gestational DM
Morbid Obesity	More than one first degree relative with DM, renal disease
Chronic Moderate to severe Lung, liver Disease	Family history of renal cell cancer
History of Melanoma or metastatic cancer	Renal Anomaly
Bilateral or recurrent nephrolithiasis	Nephrolithiasis
CKD stage 2/3	Collagen vascular disease
Proteinuria >300 mg/day	Social: Tobacco use, Inadequate financial or social support
Active infections: HIV, Hep B, Hep C	
Pregnancy	
Diabetes mellitus	
Social: Incarceration, undue pressure, financial gain, Substance abuse	

Donor's Quality of Life

The quality of life (QOL) among the kidney donors has been shown to be equal or better than the general population in USA. Using a QOL assessment tool (SF-36) on 972 US donors, Johnson et.al observed that donors scored better than general population in 7/8 categories. [78] Only 4% regretted the donation, another 4% found the experience extremely stressful and 8% very stressful. Donors who had perioperative complications (odds ratio=3.5, P=0.007) and female donors (odds ratio=1.8, P=0.1) were more likely to find the overall experience more stressful. Vast majority of donors had a positive experience and would readily donate again if it were possible. Parents who donated to offspring had the best scores and donors unrelated to the recipient, the worst; however, all scores were still the same or better than for the US general population.

Overall, among the surveys in US and Japan only <5% donors were dissatisfied after donation and a small number of the donors experienced depression, anxiety and rare cases of suicides. [78,79] The quality of life of a donor can be affected by the long-term outcome of the allograft and the relationship of the donor to the recipient. Donors are less likely to say that they would donate again (if it were possible) if they are donating to a person who is not a close blood relative or if the recipient of their kidney died in the first year after transplant. Recipients also have more feelings of guilt if transplant came from living donor than deceased donor. [80] The results of the US study are overwhelmingly positive and

encourage the continuation of living donor kidney transplants.[78] However there are psychological issues associated with living donation and appropriate counseling should be provided after nephrectomy.

Summary

The best treatment option for patients with ESRD is kidney transplant and the living kidney donation provides the best patient and allograft outcome. Potential living kidney donors should be well informed of the risks associated with donation and undergo thorough medical and psychosocial evaluation before being acceptance for organ donation. The risks of kidney donation are small but not completely absent. Donors should be encouraged to maintain healthy lifestyle and regular access to health care even after donation. Available data suggest that with the current screening processes, living kidney donors may be at increased risk of proteinuria and hypertension but not ESRD. However, most data are short term and have poor retrieval rates underscoring the need for longer prospective studies with better retrieval rates. Finally, formation of national and international registries on living donors will be a significant step towards achieving such a goal.

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Figure 1: Algorithm to investigate microscopic haematuria in donors (46)