Original Research Article

Setting up of Renal Transplant Program in private setup: our experience

Abstract: Renal diseases especially CKD(chronic kidney diseases) & ESRD(End stage renal diseases) incidence & prevelance is increasing day to day in developing as well as developed countires of world.Many modalities of treatment havebeen developed all over the world in the management of CKD. Developed countries have modern medical facilities especially renal replacement therapy like HD,CAPD & renal transplantation which befine ESRD patients a lot. however in developing countries & poor countries patients have to struggle a lot to get such facilities and ultimately suffer with complications related to uremia. Renal transplantation brings significant improvement in quality of life.1Unfortunately, renal transplantation has not flourished in many countries, especially in developing countries. Very low percentage of ESRD patients gets transplanted. There may be so many factors affecting renal transplantation.2-4 This article focuses on setting up KTprogramme at Sumeru kidney hospital. The aim of this study is to highlight all the challenges faced to set up renal transplant programmae. Total of 8 kidney transplants were done at this center with in 6month of time frame. Renal graft as well as patient survival was 100%.The complications recorded included fungal infection 1 out of 5, surgical re-exploration and acuterejection episodes remains nil. We can conclude that renal transplantation can lead to improved survival. But due to lack of awareness,donor accessibility, affordability, poor financial as well as legislative support, immunosuppression availability, government help in funding renal transplantation is unable to flourish to its full extent in private

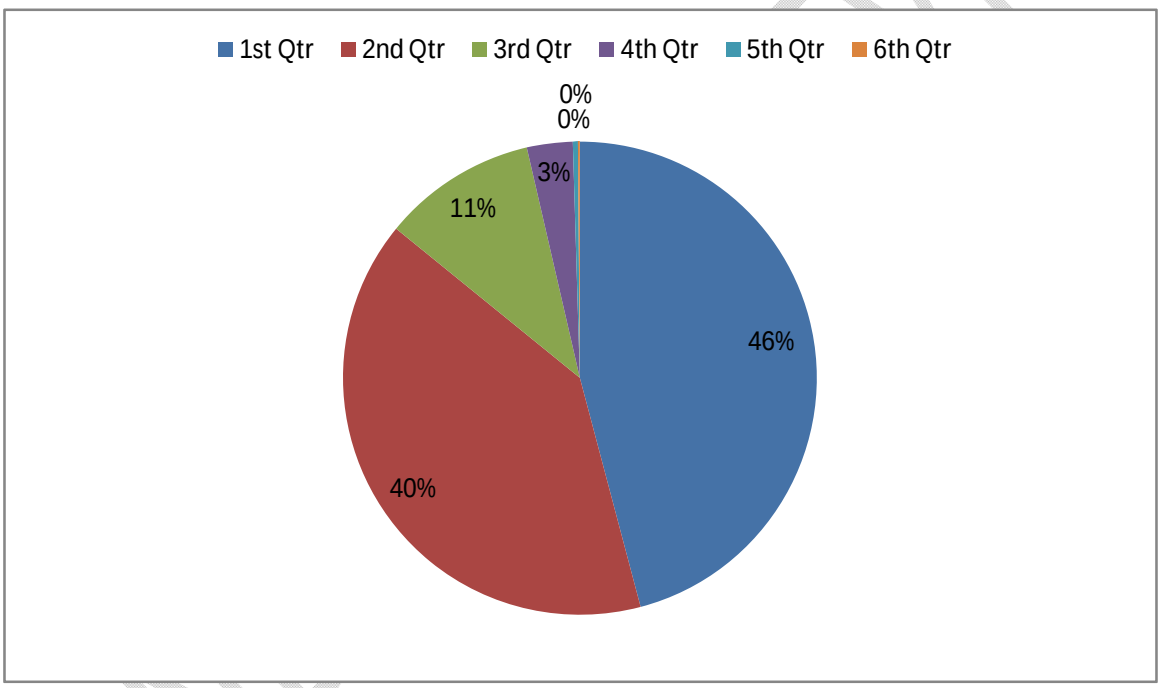
settings.Formulation of proper government legislation with proper funding at private setting will help to improve transplant utilization and better outcome.

Key Words: Renal failure, Kidney transplant(KT),CKD Chronic kidney disease,ESRD end stage renal disease, HD heamodialysis.

INTRODUCTION:

kidney transplantation is one of the best treatment option for patients with ESRD. It bring patients renal function homeostasis to normal level & hence inhancese quality of life.it is the most cost effective therapy. Especially in case rural area of Nepal, where maintenancedialysis is beyond the reach of most of the population. Nepal is multiethnic country with an estimated population of 29.14million(2020). Nepal is located in Asia, with surface area being 147 181 sq km2. It has aliteracy of 64.7% and life expectancy of 67.7 years.5The per capita income(gross) isUS$775.5. Governemnet of Nepal provides PHC (Primary health care) facilities at free of the cost to its all provincial, municipality, village health posts. However secondary & tertiary health centers provides servies with minimal cost. Total expenditure on health per capita in 2019 was US$53, is equal to 4.45% of GDP.6 Nepal is a developing country. There is significant number of communicabe as well as non-communicable diseases that badly affects its economy. Renal diseases like AKI,CKD is increasing day by day. There are so many factors contributing it as, Hypertension, DM (Diabetic nephropathy), chronic glomerulonephritis,Poor dietry habit,genetic diseses of kidney etc. It is estimated that about 10% of population is suffering from CKD annually,out of which 3 lakh develops into ESRD and need renal replacement therapy. Ironically, hemodialysis is only available at tertiary centers of Nepal.Studies shows that around 4500 patients gets maintainceHD anually. And around 3 thousands patients get on adding per year.6–8

The diagnosis of CKD is made by recurrent urinary proteinuria, decrease in GFR and radiological ecogenic poor CMD kidney.There is exponential increase in number of patients with CKD.(figure 1).The ratio of young age between 20 -50years patients with CKD is increasing in higher rate than other age group.9,13 this might be due to infection related chronic glomerulonephritis & hypertension induced renal damage in young age group. In one hand there is increasing rate in CKD patients and in other hand there is limited availability of resources in management of it has lead into health crisis especially regarding renal replacement therapy in our setting.



Human organ transplant center- 45.80% Tribhuan university teaching hospital 39.94%,Bir hospital10.47%, Grande hospital3.14%,Sumeru hospital0.34%, Nidhan hospital0.13%, college of medical science chitwan 0.13%,Chitwan medical college 0%.

Figure 1. Percentage of End-stage renal disease (ESRD) patients (NEPAL)

ESRD mortality is a very high about 50% ESRD. Hemodialysis remains the most prescribed modality of treatment of ESRD in our setting, reason being easily available, affordable and

temporary measure of treatment. Around 70 % of patients preffered HD, 5% Peritoneal dialysis, <1% were positive for reanl transplantation surgery, others refused renal replacement therapy in our setting. Out of 70 % those who selected HD were unable to maintain HD more than 12 weeks because of lack of availability of HD centre in rural areas of Nepal. Only less than 0.5 % selected Continuous ambulatory peritoneal dialysis. Kidney transplantation(KT) was started in TUTH, Nepal since 2008, after then total 7 centers started KT. In total, 8 recognized centers for KT, 3 are government hospitals, 5 are private hospitals. In last 11 years total 1436 KT has been done successfully. Out of total KT , less that 5% were done in private settings. Kidney transplantation is considered as gold standard modality of renal replacement therapy for ESRD patients. The reason for its superiority is become of its cost effectiveness, improving quality of life and increase in duration of life after KT.

KT is recognized as one of the best modality of treatment for ESRD patients. As renal transplantation warrants normal quality of life and cost effective it dominates all other forms of renal replacement therapies. Moreover, it reduces total hospital visit & stay.1–4,13 however renal transplantation has its own limitation, like high financial cost, increase in number ofpatainet but shortage for donor, immunosuppression availability, organ trafficking. This article is aimed in reviewing the setting up for transplant programmae in private set up of Nepal,with the objective of highlighting the outcome and challenges. So that ethically & culturally acceptable solution can be identified and shorted out without compromising the standard.

METHODS

- Retrospective analysis for the eight renal transplant cases were done.all the cases were operated from the 8th july 2019-jan 2020 in sumeru hospital dhapakhel, which is dedicated hospital for treatment for kidney diseases. Informed consent was taken from

all our patients before study. Donor selection were to those who were compatible blood group with recipient. Through history & examination was made, cardiovascular, gynecological, ENT, dental & psychiatric ftinesswere taken. For all the female patients, pap smear & mammography was done. PSA was done in male aged greater than 50 years old.. To assess cardiovascular status of patients coronary angiography was performed in all the recipients aged greater than 50 years& DM. To assess donor renal status, 24 hour urine protein, DTPA renal scintigraphy was done.Diabetics with creatinine level >1.5 mg/dl & 24hr urinary protein >500 mg were excluded as donor. CT angiography was done to assess the renal anatomy of donor for donor nephrectomy. Serology for hepatitis B,C,HIV,CMV(IgG, IgM),EBV was done in all the cases. Tuberculosis screening was done by chest x-ray & AFB staining. Imunological work up includes; HLA(Human leucocyte antigen), PRA(panel reactive antigen),DSA(Donor specific Antibodies),CDC(Complement dependent cytotoxicity). Open donor nephrectomy was done in all the cases. Renal vessels were anastomosed in end to side manner. And uretero-neocystostomy was carried out over 6fr COOK DJ stent in modified liche-Gregoir technique. On average donor was discharged on 5^{th} day , and recipient on 8^{th} days after surgery. DJ stent was removed after 2 wks. Recipients were administered with inj. Methylprednisolone 500 mg on the day of surgery. In all reciepients, Inj.ATG at dose of 1.5 mg/kg of body wt with three doses given on the 0, 1 and 2^{nd} post operative day was preferred. Apart from that, Tab. Tacrolimus (TAC, 0.1 mg/kg in BID dose) were initiated. Tab Mycophenolate Mofetil Sodium (500mg BD) and Methylprednisolone (20mg OD) was added in immunosuppresive regime. The dose of Tacrolimus was adjusted as per TAC level. For first 2 weeks, 8–10 ng/mL; 2–6 weeks

6–8 ng/mL; 6–24 weeks, 5–7 ng/mL; beyond six months and 3–5 ng/mL. To prevent from oral thrush all recipient received cotrimazole mouth drops, similary oral valgancyclovir for three was given to prevent from cytomegalovirus infection and oral Trimethoprim-sulfamethoxazole (80 mg–400 mg) was given for three months as prophylaxix of Pneumocystis pneumonia infection.. Both donor and recipient were closely followed through out patient department.Patients were monitiored through renal function, complete blood count,urine analysis & sonography as per Kidney Disease Improving Global Outcomes (KDIGO) guideline. Outcomes was measured as postoperative base line creatinine and estimated glomerular filtration rate (eGFR) .14

RESULTS Eight kidney transplants were performed in sumeru hospital (Fig. 2). All patients were first-degree relatives (husband, wife, siblings, father, mother, children). Human leucocyte antigine(HLA)Tissue typing was performed in Arogya foundation in all patients. In our all cases cost for per-operative, operative and post operative expenses were beared by patients themselves. 100% (Table 1). Initial immunosuppression consisted of INJ. ATG (@1.5 mg/kg) 3 dose, tacrolimus, mycophenolate sodium, methylprednisolone. Antibiotic (Meropenem). Transplant outcome for graft and patient survival was 100% .

Funding for transplantation in Nepal

Funding of kidney transplant pre operative investigations , surgery & postoperative maintaince is beared by patients or their relatives in private settings, while in government settings, all expenses are sourced from ministry of health & population Nepal. But because of long queue in government set up, patients have to wait long before they get transplanted (average waiting 6 month to 1 year)

Immunosuppressive regime

Immunosuppressive regime include induction with polyclonal antibody INJ. ATG total 3 dose and Calcineurin inhibitor-based triple drug therapy as tacrolimus(3.5mg BID), mycophenolate sodium(30 mg/kg TDS), methylprednisolone as maintenance regime.

Transplant outcome

Patient & graft survival was100%. Invasive candidaisis was seen in 1 patient which was treated successfully.

Table 1Baseline demographic and clinical characteristics of the recipient

Variables n= 8	**Frequency**	**Percent**
Age = 34.3 years (range 23–45yrs)		
Gender		
Male	6	75.0
Female	2	25.0
Cause of ESRD		
Chronic glomerulonephritis		
Hypertension	6	75.0
IgA Nephropathy	1	12.5
Pre-emptive transplant	1	12.5
CMV (IgG) positive		
Yes	8	100.0

Table 2Baseline demographic and clinical characteristics of the donors,

Variables n= 8	**Frequency**	**Percent**
Age = 34.3 years (range 23–45yrs)		
Gender		
Male	6	75.0
Female	2	25.0
Cause of ESRD		
Chronic glomerulonephritis		
Hypertension	6	75.0
IgA Nephropathy	1	12.5
Pre-emptive transplant	1	12.5
CMV (IgG) positive		
Yes	8	100.0

Table 3: Laboratory Parameters

	Mean $\pm$ SD
Duration of haemodialysis	
Laboratory parameters	

Haemoglobin(gm/dl)	9.9
Albumin (gm/dl)	
Calcium 2.5 _ 1.7 mmol/L	
Phosphorus 5.7 _ 2.1 mg/dl	
Alkaline phosphatase 168.7 _ 80.2 IU/L	
iPTH 190.6 _ 165.7 pg/mL	

DISCUSSION

In Nepal, Human organ transplant act 2055 BS(1998 AD) was passed to regulate activities pertaining to the extraction of an organ from human body. According to this act only closely related relatives were allowed to donate their organ. First kidney transplantation was successfully done in 2008 at TUTH (Tribhuvan University Teaching Hospital).7Although renal transplantation are successfully conducted there are some many limitation related to HLA laboratory and Immunflourescence staining for renal biopsies arestill not available in many hospitals.

To prevent the commercialization & monetary involvement in organ transplantation,human organ transplant act was re-modified in 2073BS Nepal. The outcome of transplantation is soley based on immunological status of receipient,HLA tissue-typying,Cross matching, Donor specific antibodies & panel-reactive antibodies.50 % matching at locai A,B DR is accepatble and catorised as low immunological risk.patients with hepatitis B,C,HIV positive are not acccepted at our setting. Preparation of recipient included; controledl hypertension, optimized diabetes

mellitus, and overall good cardiovascular status. Recipients must be adequately dialyzed (3 times a week). All the transplant centers generally investigate donors and recipient at its own center. Moreover , HLA typing is not available at all the centers, many centers have to rely on other centers for it. Immunosuppressive regime include triple drug induction regimes that includes: Tacrolimus alone with Mycophenolate mofetil-Sodium (MMF-s) and Prednisolone. These regimes were used in our cases, while induction was made by administration of polyclonal antibodies(ATG).

Challenges of KT in private hospitals

Kidney transplant was first undertaken in august 2008 in a TUTH hospital Kathmandu.

Till now, eight units have sucessfully carried out renal transplantation in Nepal. Transplant program has been successfully done in government hospital with good financial, manpower & legislative support but in private setting beause of the lack of financial support it have not achieved remarkable outcome. 17

Major challenge related to transplantation in our setting is financial & donor availablity .Majority of patients belongs to poor class & hardly afford transplant cost. Voluntary donation of organ from relative is not easy for every family & becomes really hard to convience for it. Moreover donor has poor knowledge regarding donation & its outcome.5,16 In a number of instances, long duration of waiting list in government hospitals is another important factor that patients are bound to search for other transplant centers. Imunnological as well as some viral markers done at other center with heavy cost is another challenging part. This delays the surgical preparation.

Dvelopment of laboratories by government sector will reduce cost as well the time.

Moreover Induction agents(ATG),Immunosuppressant & Antiviral drugs are also imported from other countries this increases the cost more than the expected. Surgical and medical experties are required to develop transplant center,but relatively low number of cases may decrease the over all sustanability of any transplant programme. Governement development of national transplant centers with free of cost transplant services is good initiative. But establisment of private hospital centers & allowing transplantation programmae supported by government in establishment of private transplant centers to run at cost synonymous to government setting that would not only improve the outcome rather decrease burden on government hospitals , which may be counter productive.

This will bring a better exposure of medical professional in all the transplant centers.It will inhance the quality and quantity of transplant as a whole.It will bring easy access to poor patients to benefit from transplant service in emerging country like Nepal.

Conclusion:

Kidney transplantation has improved a lot in private hospitals of Nepal. It is cost effective & easily accessible to all. Transplantation has increasd tha survival of ESRD patients. But, financial support and availability of laboratory needs to be improved. National Health insurance coverage for renal transplantation should be improved. It is important to speed up the process of enactment of relative kidney transplant legislation in Nepal in conjunction with the Deceased donation act to increase the transplantation rate, but also to prevent commercialism and organ trafficking. Formation of private transplant centers; allowing transplant program to run at cost synonymous

to government setting that would not only improve the outcome rather decrease burden on government hospitals , which may be counter productive.

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