

Renal Transplantation GEZIRA Hospital FOR Renal Disease and Surgery (GHRDS)

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Abstract

Background: Recent years have witnessed an explosive growth in the number of patients experiencing end stage renal disease (ESRD), as well as number of centers providing therapeutic modalities such as hemodialysis, peritoneal dialysis and renal transplantation.

Algorithm: 1. To audit the practice of renal transplantation in Gezira hospital for renal disease and surgery (GHRDS). 2. To recommend and contribute in some aspects that may reduce surgical complications and transplant-related deaths, and improve the outcome. 3. To assess the impact of preoperative co-morbid medical conditions of the recipient on the frequency of surgical complications of renal transplantation in GHRDS

Patients and Methods: This is non-interventional descriptive retrospective review was made of all patients transplanted in the period June 2001-June 2008 in GHRDS. A total of 82 renal transplants were performed at GHRDS in our study period, all were adults and they are representing our study population group. Data was analyzed by computer program the SPSS. To determine the statistical significance of differences, the Pearson test was used and probability test (P. value) with $p < 0.05$ considered as significant. The incidence of surgical complications was correlated with several pretransplant, technical and post-transplant risk factors

Results: Among the 82 patients underwent living donor renal transplantation in the GHRDS in the period 2001-2008 some surgical complications were occurred. These complications included hemorrhage in 9 patients, hematoma necessitating surgical exploration in 5 patients, urinary leakage in 7 patients, ureteric obstruction with clots in 3 patients, significant hematuria in 5 patients, wound dehiscence in 4 patients. The incidence of urological complications (ureteric obstruction and urinary leakage) was 8.5% and vascular complications 4.9%. There were 3 gastrointestinal complications (3.7%). We lost 10 grafts (12.2%) and 9 recipients (10.9%).

Conclusion: The practice of renal transplant in GHRDS was found to be sound and comparable to the learning curve of the literature. The numbers of patients transplanted not yet paralleling the increasing numbers of patients with ESRD.

Key words: Gezira hospital, renal transplant, renal failure, ESRD.

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INTRODUCTION

Recent years have witnessed an explosive growth in the number of patients experiencing end stage

renal disease (ESRD), as well as number of centers providing therapeutic modalities such as hemodialysis, peritoneal dialysis and renal transplantation⁽¹⁾.

Fifty-two years ago, on December 23, 1954, a kidney was transplanted from one healthy identical twin to his twin who was dying of renal disease. The surgery was performed at the Peter

Bent Brigham Hospital in Boston, and John Merrill, Joseph Murray, and Hartwell Harrison led the clinical team (2). This was the first successful transplantation, performed against a background of failure. For this reason, it created enormous excitement, both in the media and among medical professionals, at a time when the pioneers of kidney transplantation were despondent about the possibility of any real clinical application. This successful transplantation occurred some 50 years after Emerich Ullmann (1861-1937) performed the first experimental transplantation of a kidney between dogs in Vienna in 1902 (3).

As a result of economic considerations, quality of life, and outcomes, renal transplantation has emerged as the preferred treatment modality for most patients with ESRD (4). However, the number of transplants performed has not kept pace with the ESRD population growth, and more than 42,000 patients are now awaiting transplantation (5).

Surgical problems following renal transplantation are predominantly related to either vascular or urologic complications. Improvement in surgical technique and meticulous attention to both the donor and the recipient operations has led to a significant decrease in surgical complications rate. Equally important in minimizing the morbidity associated with renal transplantation are anticipation of surgical complications and their prompt treatment when they occur (6).

Surgical complications continue to occur in 10% of transplant recipients, but, fortunately are rarely the cause for allograft loss today (7).

The incidence of graft loss due to acute rejection is now less than 1% (8), and the incidence of graft loss due to chronic rejection is decreasing. Therefore, somewhat ironically, surgical complications remain an important cause of graft loss after kidney transplants.

The initial presentation of surgical problems may be very similar to and must be differentiated from non-surgical problems such as rejection or drug toxicity (8).

The overall incidence of surgical complications after kidney transplant is low, especially when compared to extra-renal transplants such as liver or pancreas. Many centers report an incidence in the 5 -30% range (8) (9).

The objectives of this work are: 1. To audit the practice of renal transplantation in Gezira hospital for renal disease and surgery (GHRDS). 2. To recommend and contribute in some aspects that may reduce surgical complications and transplant-related deaths, and improve the outcome. 3. To assess the impact of preoperative co-morbid medical conditions of the recipient on the frequency of surgical complications of renal transplantation in GHRDS. 4. To identify factors that related to frequency of immediate surgical complications of renal transplantation in GHRDS. 5. To evaluate graft and recipient survival after the occurrence of surgical complications of renal transplantation in GHRDS.

PATIENTS AND METHODS

This is non-interventional descriptive retrospective review was made of all patients transplanted in the period June 2001-June 2008 in Gezira hospital for renal disease and surgery (GHRDS).

GHRDS is specialized renal complex peculiarly unique in its infrastructures, consists of 36 dialysis machines with all subsets and water treatment system. With 50 beds, 30 for urology and others in nephrology, with standard well equipped theatre and well learned personnel. At 2001 the proposal of the hospital was endorsed and it was inaugurated in 2004-2005. Renal hospital is provided by joint work from Egypt, KSA, and other national rivals. The catchment area of this specialized hospital is ultimately the whole country, because it is the only hospital provides urology and nephrology at tertiary level.

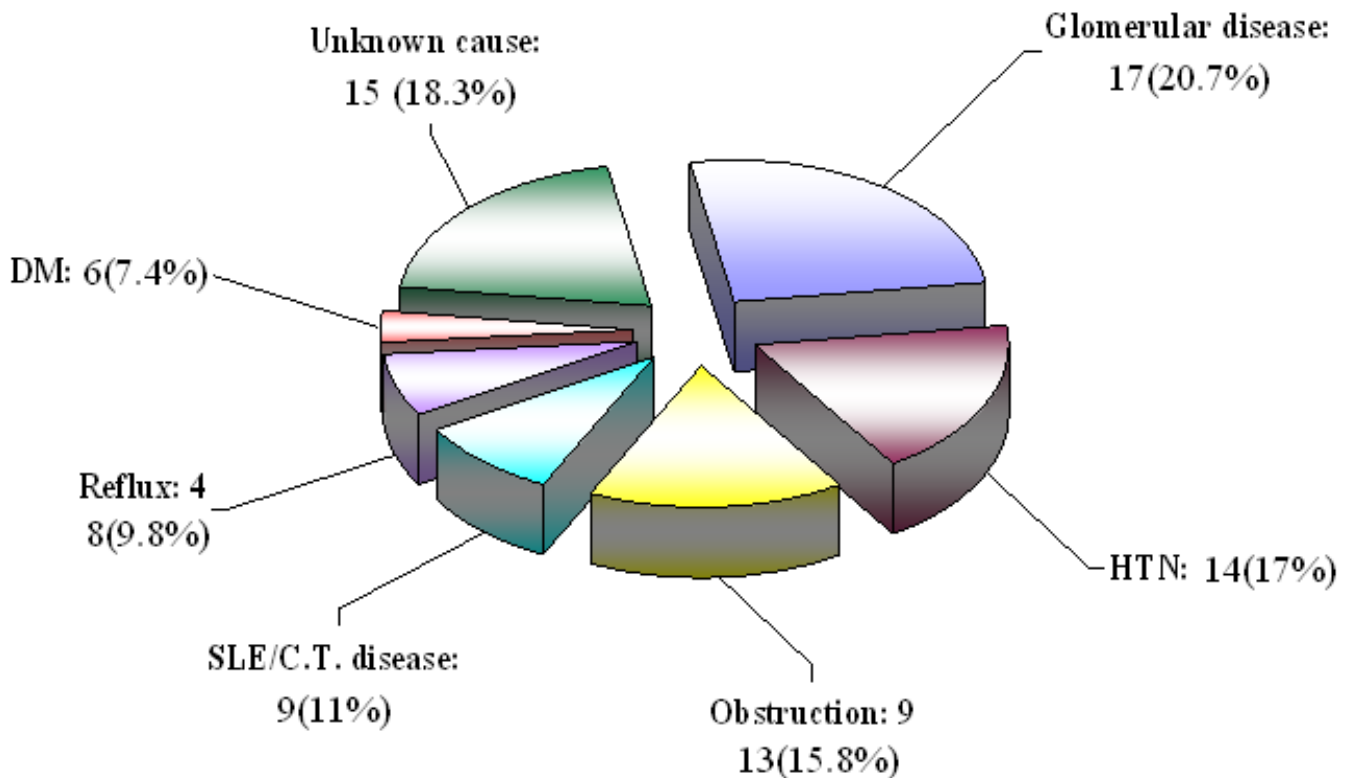
Data was collected from hospital records of transplant cases. Independent variables selected for study included preoperative serum albumin, hemoglobin, pretransplant creatinine, weight, height, body mass index (BMI), time on dialysis, donor type, age, and gender. Dependent variables included postoperative creatinine, urine output, wound infection, wound dehiscence, presence of lymphocele, acute tubular necrosis (ATN), bleeding and other immediate complications, length of stay in the hospital, postoperative weight, loss of kidney, and patient survival.

A total of 82 renal transplants were performed at GHRDS in our study period, all were adults and they are representing our study population group.

The 82 recipients were evaluated and selected guided by the "European guideline for renal transplantation" (10).

Data was analyzed by computer program the SPSS. To determine the statistical significance of differences, the Pearson test was used and probability test (P. value) with $p < 0.05$ considered as significant. The incidence of surgical complications was correlated with several

Number of patients underwent renal transplant in this period was 82 patients, with 3:2 male to female ratio. Beside the Gezira, they were coming from different directions e.g.: Sinnar, Khartoum, Singah, Portsudan, and Obied. The causes of renal failure were glomerular disease in majority, followed by unknown cause, HTN, obstructive uropathy, reflux disease, SLE, and diabetes mellitus. All of our patients were under



pretransplant, technical and post-transplant risk factors

RESULTS

This presents the initial experience with living kidney transplantation in the Gezira - Sudan.

Figure (1): causes of ESRD in 82 renal transplant recipients in GHRDS

Among the 82 patients underwent living donor renal transplantation in the GHRDS in the period 2001-2008 some surgical complications were occurred. These complications included hemorrhage in 9 patients, hematoma necessitating

surgical exploration in 5 patients, urinary leakage in 7 patients, ureteric obstruction with clots in 3

hemodialysis with variable durations.

The causes of the ESRD and their frequency in patients coming for transplantation in GHRD were demonstrated in figure (1).

patients, significant hematuria in 5 patients, wound dehiscence in 4 patients. The incidence of urological complications (ureteric obstruction and urinary leakage) was 8.5% and vascular complications 4.9%. There were 3 gastrointestinal complications (3.7%). We lost 10 grafts (12.2%) and 9 recipients (10.9%) as seen in table (1). Ureteric leakage was observed in 7 patients. The interval to diagnosis was <1 wk in four patients and the second wk in three patients. Symptoms

generally included sudden oliguria or anuria, an increasing serum creatinine level with or without external leakage and with or without graft or abdominal tenderness or distension. Small ureteric leakage (five patients) was treated by stenting and prolonged bladder catheterization (for 3 weeks). Leaks associated with ureteral necrosis (two patients) required repeat uretero-neocystostomy. Early ureteric obstruction was present in 3 patients. Diagnosis was usually suspected by a progressive increase of the serum creatinine level and dilatation of the graft pelvicalyceal system by routine U/S.

Oliguria following good primary graft function was observed in 11 patients. 4 of them were due to clot obstruction in cases of significant hematuria, 6 of them due to acute rejection episode, 1 due to hypotension and vascular thrombosis.

Early vascular complications occurred in 4 patients: one patient developed arterial kink, tow disruption of the arterial anastomosis accompanied by massive bleeding, and the fourth was thrombosis of the graft vessels.

Symptomatic lymphocele was diagnosed in two patients. Symptoms included compression to the graft ureter one patient and localized abdominal distention in the other. The diagnosis was made by U/S and confirmed by needle aspiration of the lymphocele content and estimation of the creatinine concentration. Treatment was initiated by percutaneous drainage that succeeded the two patients.

Five patients had a significant hematoma, which presented in the immediate postoperative period with a decreasing hematocrit and hypotension requiring blood transfusion. Exploration and drainage were carried out and no active bleeding site could be identified. Four patient experienced wound dehiscence following wound infection which necessitated secondary closure. On univariate analysis the factors that might affect the incidence of surgical complications were analyzed.

TABLE (1): Frequency of Surgical and Urological Complications in 82 renal transplant recipients in GHRDS:

COMPLICATION	Frequency	%
Delayed graft function	6	7.3
Hemorrhage	9	11
Oliguria	11	13.4
Vascular catastrophe*	4	4.9
Significant hematuria	5	6.1
Urine leakage	7	8.5
Haematoma	5	6.1
Wound infection	8	9.8
UTI	8	9.8
Wound dehiscence	4	4.9
Lymphocele	2	2.4
GI complications	3	3.7
Graft loss	10	12.2
Recipient death	9	10.9
*One kink, one thrombosis and two major anastomotic bleeding.		

We noticed that there were 56.4% of our renal transplant recipients had concurrent medical problems apart from the renal failure. The most frequent medical problem was hypertension followed by cardiac problems, connective tissue disease (SLE), DM, and viral hepatitis. The frequency is demonstrated below in figure (2).

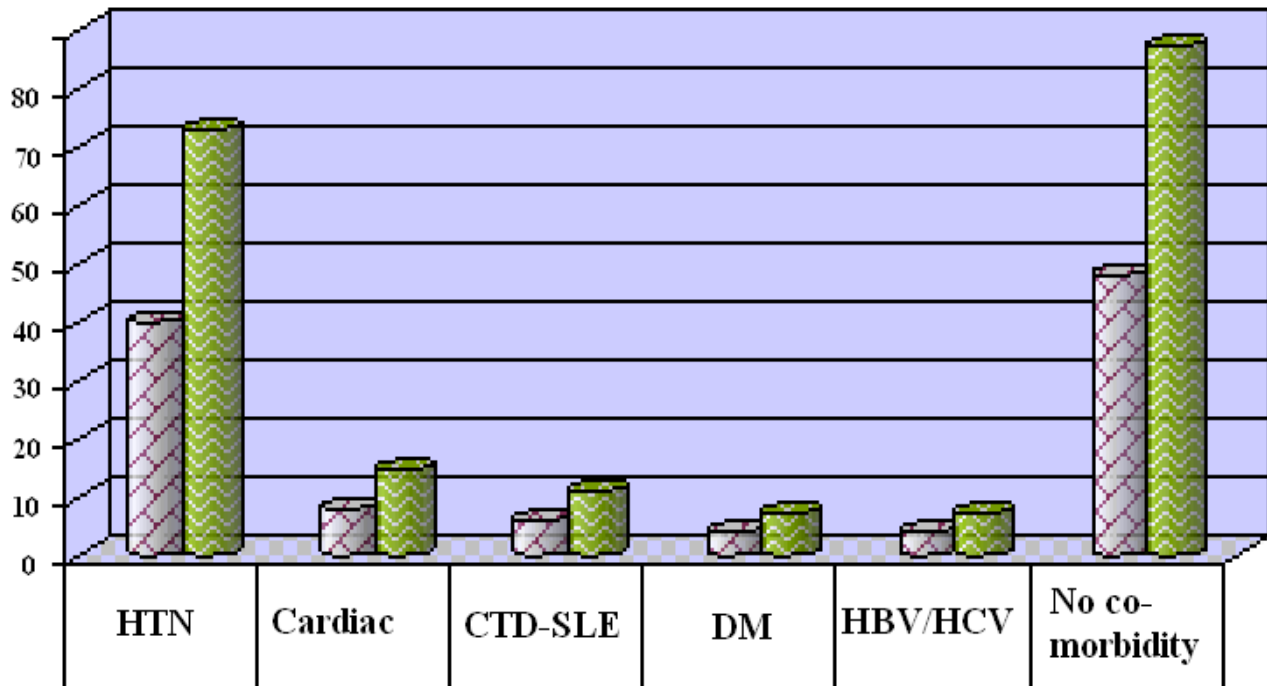


Figure (2) co-morbid medical condition in 82 renal transplant recipients in GHRDS

The time spent on dialysis in transplanted patients prior to transplantation was 2-48 months with mean duration of 18.95 months. Most of the transplanted patients stayed 6-12 months on dialysis before transplantation. There is no significant relation was demonstrated statistically between dialysis duration and frequency of surgical complications (P.value was more than 0.05).

We have 6 cases of delayed graft function that were found to be obviously related to the length of both cold ischemic time and warm ischemic time. The latter was influenced by the number of the graft arteries. It is found that the arterial multiplicity is a genuine factor for prolonged operative time and hence acute tubular necrosis (ATN) and delayed graft function (P.value < 0.05)

Statistical analysis of the occurrence of urinary leakage and ureteric complications did not show any differences in the results between removing the ureteric stent in 3 and 6 weeks. Occurrence of urinary leakage is not affected by the time of removing the stent. Wound complications, infection (in 8 patients) and dehiscence (in 4 patients). Wound infection was significantly resulted in high rate of dehiscence, and perhaps

the presence of intended immunosuppression was also a factor.

The frequency of wound dehiscence with antirejection drugs is seen in table (2).

		wound dehiscence		Total
		yes	no	
Immuno-suppression	cyclosporine	1	18	19
	prograf	3	60	63
Total		4	78	82

Table (2): Relation: immunosuppression and wound dehiscence in 82 renal transplant recipients in GHRDS

We found that early graft losses occurred in 15 cases in our study. 8 (9.8%) were lost due to acute rejection, 2(2.4%) with vascular complications, and 5(6.1%) due to death of recipient. ATN as a cause of delayed graft function did not result in any of the graft losses. Table (3) is showing

significant relation between occurrence of acute rejection and graft loss (P.value < 0.05).

Graft Loss		
Acute rejection	Pearson Correlation	-.515
	Sig. (2-tailed)	.000
	N	82
ATN	Pearson Correlation	.202
	Sig. (2-tailed)	.139
	N	82
(Sig. more than 0.05 is not significant)		

Table (3): Correlation: Acute rejection, ATN and graft loss in 82 renal transplant recipients in GHRDS:

Three patients (3.7%) developed gastrointestinal complications. Patients that developed foregut complications were two, one patient developed

	number	Percent
Intact graft	72	87.8
Lost graft	10	12.2
Total	82	100
Cause of graft loss		
Acute rejection	8	9.8
Vascular catastrophe	2	2.4

Table (4): graft status after 6 months

gastroduodenal ulceration with perforation, required laparotomy, and he was ended by infectious complication and died. The second one developed oesophageal candidiasis and he responded to antifungal treatment. The third one

	number	Percent
Alive	73	89.1
Died	9	10.9
Total	82	100
Cause of recipient death		
Drug toxicity	2	2.4
Infectious complication	3	3.7
Bleeding	1	1.2
PE*	1	1.2
DIC**	2	2.4
* PE: pulmonary embolism		
**DIC: disseminated intravascular coagulation		

Table (5): The recipient status in 6 month time.

was colitis with severe diarrhea. There was no significant difference in the frequency of complications between patients that received tacrolimus (2/63, 3.1%) and those on cyclosporine (1/19, 5.3%) based immunosuppression regimes.

	number	Percent
Intact graft	72	87.8
Lost graft	10	12.2
Total	82	100
Cause of graft loss		
Acute rejection	8	9.8
Vascular catastrophe	2	2.4

Table (6): Early complications occurred in 82 kidney transplant donors in the GHRDS

The over all early graft and recipient status is accepted. Table (4) is showing number of graft losses and their cause. Table (5) is showing the

recipient transplant-related death in the early post-transplant period (6months).

Donor morbidity was 3.6% (3cases): namely, two primary bleeding resulted from insecure vascular ligature that were immediately discovered and managed. The third one was superficial wound infection improved with simple dressing. There was no donor mortality as is shown in table (6).

DISCUSSION

It is known that the ultimate modality of treatment for patients with ESRD is renal transplantation, and should any ESRD patient be offered this kind of treatment. Today it can be truly said that there are no absolute contraindications to renal transplantation, and all patients with end-stage renal failures are potential candidates for renal transplantation.

Frequency of renal transplant operations in GHRDS in 2001-2007

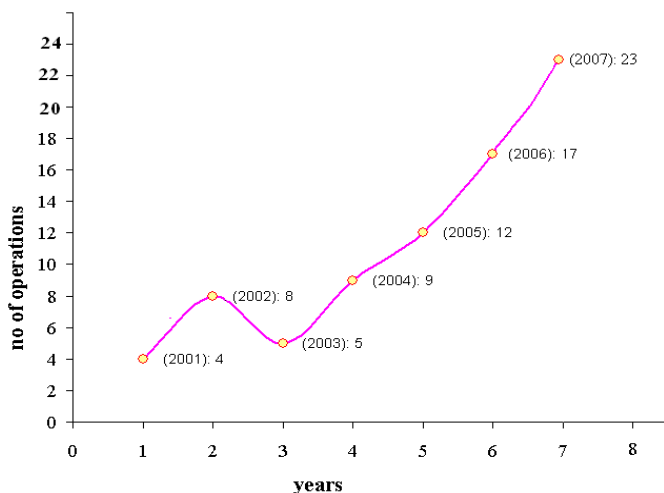


Figure 3: showing the frequency of renal transplantation in GHRDS till the end of the year 2007

Some factors influence patient's processing into the transplant program in our hospital. The financial aspect is the most important part in some CRF patients.

The impact of the original disease causing the renal failure on the selection of any patient to fulfill the criteria of acceptance for transplantation is known. Internationally of the metabolic disorders causing end-stage renal failure type I diabetes is by far the most common, ranging from

10 to 25 per cent of all patients coming to transplantation⁽¹¹⁾. In our situation it was that

patients with glomerular disease were the most, and represented about 25% of transplant recipients, followed by hypertension, obstructive uropathy, connective tissue disease, reflux disease, and diabetes mellitus represented only 3.6% as shown in figure (1) above.

The vast majority of our CRF patients under follow up and dialysis in GHRDS and their families are highly convinced by the transplantation, and they are willing to be included in the future as transplant recipients. Donors usually are family members either first or second degree relatives, and yet no spouses were appear in the field of transplantation in our area. In addition to living donors as the only source of kidneys for procurement, it also provide to the patient a safe, long-lasting graft with significantly increased potential for HLA matching in particular with related donor, and the opportunity to initiate and optimize immunosuppression therapy preoperatively⁽¹²⁾. That also beside avoidance of prolonged waiting in the cadaveric donors' waiting list. It is reported by the "United Network for Organ Sharing" (UNOS) the average waiting time for renal transplant is 36months⁽¹³⁾⁽¹⁴⁾, a period long enough for the patient on dialysis to develop a lot of complications. All of these advantages contribute to a lower incidence of early acute rejection and to improved graft and patient survival rates. While there is significant benefit for the recipient, there is no physical or medical benefit for the living donor⁽¹⁵⁾⁽¹⁶⁾⁽¹⁷⁾⁽¹⁸⁾.

The donors after assessing their general health and renal functions, radiological evaluation of renal outline and vasculature (IVU\renal angiography) was also done which was crucial to select the graft⁽¹⁹⁾.

It is found that operative morbidity and mortality are increased in patients who have had a myocardial infarction within 6 months before surgery⁽²⁰⁾. So optimization of the cardiovascular status of the patients was achieved before transplantation.

Open donor nephrectomy carries a significant rate of morbidity as compared with laparoscopic and laparoscopy-assisted techniques which have proven to be a major improvement to living donation⁽²¹⁾⁽²²⁾⁽²³⁾.

The left side was used in 65 donors with 8 cases discovered intraoperatively to have two renal arteries and one case with 4 renal arteries which were not reported in the angiography. This confirms the need for updated modalities of vascular studies (such as CT angiography) (24) than conventional angiography. The right side was used in 17 cases and no vascular multiplicity was encountered.

The immediate graft function in our transplanted patients was achieved in 76 patients (approximately 92.7%). This is by far, one of the advantages of living donation over cadaveric donation. Other advantages reported in the literature include: significantly decreased incidence of acute tubular necrosis (ATN); with careful planning, the total ischemic time between clamping the kidney's arterial supply in the donor and restoration of blood flow in the recipient can be less than 1 hour. It also significantly increased potential for HLA matching and the opportunity to initiate and optimize immunosuppression therapy preoperatively (12).

Six of our patients developed delayed graft function. Delayed graft function was defined as: need for at least one dialysis session after transplant, before establishing good graft function (25). Delayed graft function was relatively more frequent among grafts with multiple arteries, but without statistically significant difference, and this fact can be explained by the manipulation necessary for vascular reconstruction in these grafts, causing an increase in warm ischemia period. Although we did not analyze this aspect in this study, it is clear that warm ischemia time was longer in transplants with multiple arteries and this may influence the immediate function of the graft.

There were 12 cases of acute rejection (14.6%); histological confirmation by renal biopsy was done in only two of them. Only 4 of them were successfully reversed and 8 grafts were lost due to acute rejection. The diagnosis of rejection is needed to be more objective. It must be diagnosed after clear histological and immunological picture rather than clinical or being diagnosed by exclusion of other problems.

The problem of arterial multiplicity was managed by ex vivo pinch technique with side to side anastomosis of the two arteries to create a single ostium (25)(26). This was done in two cases. The

others were directly anastomosed with external iliac and hypogastric arteries. Multiple arteries appeared to prolong the operative time and resulted in acute tubular necrosis and delayed graft function in three cases. It also was a cause of bleeding and hematoma formation in one of the patients. Shokeir et al from Mansoura urology and nephrology center stated that: hemorrhagic crises are as serious as the stenotic and thrombotic complications affecting patient and graft survival. Because they are a significant factor in the development of hemorrhagic complications, grafts with multiple renal arteries should be managed critically (27).

We reported 9 cases of bleeding (14.5%). The principal tool in their diagnosis was the Doppler ultrasound. In 5 cases there were no major bleeders were found in exploration, and the bleeding was attributed to the use of heparin in cases during early post transplant dialysis needed for delayed graft function. In the other four cases of bleeding, in three the source was arterial anastomotic leakage. One of them was caused by straining and coughing, in whom the graft was lost. The other two were repaired by simple suturing without any harm to the graft. Ureteric complications occurred in our study in two forms; immediate ureteric obstruction by a clot was in three cases (3.7%). Although this type of complication is commonly encountered with Politano-Leadbetter uretero-neocystostomy when used, more than Lich or direct implantation procedure (28). Other type of ureteric complications we encountered was urinary leakage. It occurred in 7 patients (8.5%). All of them within the first post transplant week. Although rejection has been implicated as a possible mechanism in the development of ureteral leaks (29), analysis of the data in our study failed to confirm this view. Wound infection was 9.8% in this study (8cases). Ranges between 2% and 43% were reported by Eduardo M. et al. (25) and it was associated mainly to diabetes, urinary leakages, hematomas and after graft nephrectomy. Also prolonged wound drainage is an important risk factor for wound infection and dehiscence (30). The role of immunosuppression is known in the increasing the wound complications (31). But in this study the relation was not statistically significant. Factors mentioned above were actually the predisposing for wound complications.

Over all, there were 9 recipients' mortalities (10.9%) in first 6 months post-transplant. The problem that followed the use of prograf, new immunosuppressive drug, and the monitoring of its blood levels, resulted in loss of two recipients as a result of drug toxicity. Three recipients were lost due to infectious complications. Two of them were following acute rejection process and graft loss. It is recognized that patient mortality due to infections is relatively high after graft loss following acute rejection⁽³²⁾.

The third infectious death occurred in a recipient who had positive HCV serology with evidence of very mild disease in liver biopsy. In the 6th post transplant day he developed perforated peptic ulcer. After laparotomy was being done for him, he developed increasing jaundice and died of hepatic coma 5 days later. It is known that existence of HBV or HCV infection is not a contraindication for renal transplant unless evidence of active disease by viral antigens profile or by liver biopsy. Some people use the U/S findings plus previous history of liver decompensation as a contraindication for renal transplantation⁽³³⁾. In this patient no one of the above was found during pretransplant workup and he was offered renal transplantation accordingly.

The last death was a 34 years old non obese lady with body mass index of 21.3 kg/m² (height: 1.65m – weight: 58 kg) the cause of her renal failure was SLE and she was on hemodialysis with left radial A-V fistula for 8 months before transplant. She succumbed in the morning of the 2nd post transplant day. Her workup did not show any evidence of thrombophilic problem and she was not on heparin, because it is not routine post-transplant in our hospital. Autopsy was not done for this patient. The cause of her death was attributed to either acute myocardial infarction or massive pulmonary embolism.

Regarding the donors the morbidity was 3.7% (3cases): namely, two primary bleeding resulted from insecure vascular ligature which were immediately discovered and managed, and the third one was superficial wound infection that was responded to simple daily dressing and was not resulted in wound dehiscence or hernia. There were no differences between the preoperative and the postoperative mean serum creatinines and systolic blood pressure values. All living donors are in good health with a mean serum creatinine

of 0.80 mg/L at a mean follow-up of 6 months. There was no donor mortality. Cardiac disease, which is chief among these co-morbidities, can be exacerbated by complications of immunosuppression. Therefore, special attention should be paid to cardiac risk factors following transplantation, including hypertension, hyperlipidemia, and diabetes⁽¹⁶⁾.

CONCLUSION

The practice of renal transplant in GHRDS was found to be sound and comparable to the learning curve of the literature. The numbers of patients transplanted not yet paralleling the increasing numbers of patients with ESRD although the curve of progress is significantly uprising. Surgical complications of renal transplantation in the GHRDS though at the learning curve pattern, but it was found to be comparable to other similar institutes.

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