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ORIGINAL ARTICLE

Anaesthetic challenges in the management of renal transplant recipients - An institutional review.

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ABSTRACT... Objective: To provide an overview of our institutional experience with anaesthetic management of renal transplant data in terms of demographics, preoperative status, anaesthesia management, and postoperative care. **Study Design:** Descriptive study. **Setting:** Pakistan Kidney and Liver Institute and Research Center, Lahore. **Period:** January 2022 to June 2022. **Material & Methods:** This descriptive study included 203 cases of renal transplant. We reviewed the medical records of these patients for demographics, preoperative anaesthetic assessment, intraoperative anaesthesia records, and postoperative care unit notes. Data was analyzed using SPSS Version 25. **Results:** The mean age of the patients was 35.75 $\pm$ 10.1 years, and most of the patients had co-morbidities. The preoperative echocardiographic findings were significant in 52.7% of the patients, and 87.2% were on dialysis preoperatively. General anaesthesia was used in 99.5% of cases. Mean volume of intravenous fluid was 5.8 L, and 9.35% required ionotropic support, 9.9% received transfusion intraoperatively while 3.9% required postoperative mechanical ventilation. **Conclusions:** Renal transplant recipients have significant co-morbidities and require a meticulous approach for successful perioperative anaesthetic management.

Key words: Chronic Kidney Diseases, End-Stage Renal Disease, General Anesthesia, Kidney Transplantation, Living Donors, Perioperative Period, Preoperative Care, Renal Transplantation.

INTRODUCTION

Chronic kidney disease (CKD) is associated with a wide range of complications affecting almost all body organs.[1] The reported prevalence of CKD in Pakistan ranges from 12.5% to 31.2%, and the estimated incidence of End-stage renal disease (ESRD) is 100 per million of the population.[2,3] The disease burden of CKD is quite significant and there is a paucity of resources and dialysis centers which leads to significant morbidity and mortality in Pakistan.[4] Kidney transplantation is the preferred treatment for these patients as they have a better quality of life and a higher chance of survival than those who continue to have dialysis alone.[5] Moreover, a live donor kidney transplant is associated with increased graft survival and is preferred over a cadaveric transplant.[6]

Renal transplant recipients suffer from multiple underlying problems, attributable to their CKD as well as complications of long-term dialysis.[7] Hypertension and diabetes mellitus are present in 30% to 90% of cases as a contributing factor to and a result of chronic renal disease.[8] Cardiovascular manifestations of CKD such as coronary artery diseases, myocarditis, Valvular lesions and pericardiac effusion make these patients at high risk for perioperative morbidity and mortality. The European Society of Anesthesiology stratifies renal transplantation as an intermediate-risk surgical procedure.[9] Patients on intermittent hemodialysis have acid-base disturbances, electrolyte imbalance, hypo or hypervolemia and anaemia. History of prior central venous cannulation for hemodialysis catheter makes central venous access difficult due to stenosis

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and thrombus in major vessels.[10]

Perioperative anaesthetic management of renal transplantation requires preoperative assessment to identify risk factors that affect the postoperative complications, risk stratification and development of a perioperative anaesthetic plan according to the patient's clinical condition. Intraoperative monitoring of hemodynamics, fluid status, acid-base management, postoperative management of pain and other complications. The focus of management is multifactorial, including, anxiolysis before the procedure; maintaining stable hemodynamics; eliminating surgical stress response while maintaining renal blood flow, maintaining urine output; and ensuring adequate postoperative analgesia which may require regional block.[11] The purpose of this study is to provide an overview of challenges in the anesthetic management of renal transplant recipients in terms of demographics, preoperative status, anesthesia management, and postoperative care.

MATERIAL & METHODS

This was a descriptive study which reviewed renal transplant recipients operated at Pakistan Kidney and Liver Institute and Research center, Lahore Pakistan from May 2018 to December 2021. Adult patients of age 15 years and above were included. Paedrictic living related renal transplant and patients with incomplete medical record were excluded from this study. Following institutional review board approval (PKLI-IRB/AP/47), preoperative anesthesia assessment, intraoperative anesthesia record and postoperative care unit record on hospital approved forms was retrieved from patient medical record. We recorded gender, age, type of transplant, comorbidities, history of dialysis, echocardiographic findings, in preoperative assessment. Anesthetic management such as type of anesthesia, documentation about fluid and blood transfusion and vasopressor used was retrieved from intraoperative record while post anesthesia care unit documentation was also reviewed. The data was entered in electronic database and analyzed using SPSS Statistics for Windows, Version 25.0 (SPSS Inc., Chicago, USA). Continuous variables were presented as mean and standard deviation while categorical variables were analyzed as frequency and percentage.

RESULTS

Demographics

Medical records of 227 cases operated from May 2018 to December 2021 were reviewed. One pediatric renal transplant and 23 incomplete records were excluded from this study, so thus the final analysis included 203 patients. The kidney transplant program is mainly operated as living related renal transplant. Most of the patients were in the age group of 16 to 64 years and were predominantly male. The demographics are shown in Table-I.

Characteristics	
Age (years)**	35.75 $\pm$ 10.1
Gender** Female Male	 25 (12.3) 178 (87.7)
Weight (Kg)*	61.77 $\pm$ 14.5
Height (cm)*	165.56 $\pm$ 9.2
BMI (Kg/m^2) *	22.49 $\pm$ 5.1
Type of transplant** Living related Cadaveric	 202 (99.5) 1 (0.5)
Duration of surgery (min)*	265 $\pm$ 54
*Mean + SD, ** n (%)	

Table-I. Demographics

Preoperative Status

Preoperative anaesthesia assessment records showed that 193 patients (95.1%) were associated with at least one comorbid condition. Out of these, hypertension was present in (189) and diabetes mellitus (20) patients. One patient had undergone mitral valve replacement before the renal transplant. Other coexisting medical conditions were valvular lesions, COPD/asthma, epilepsy, hypothyroidism, poliomyelitis, and peripheral vascular disease.

All the recipients had echocardiography preoperatively and 52.7% of the patients had abnormal findings. These abnormalities in echocardiography included segmental wall motion abnormalities (7.4%), left ventricular

hypertrophy (28.6%), left ventricle dilatation and dysfunction (4.9%), dilated atrium (12.8%), diastolic dysfunction (17.7%), pulmonary hypertension (15.3%) and pericardiac effusion (4.9%). One patient had a mitral valve replacement. Estimated ejection fraction was > 60% in 70.1%, between 40-60% in 28.4% and < 40% in 1.47% of the patients. One hundred and seventy-seven (87.2%) patients presented with ESRD and were on dialysis before the transplant whereas 12.8% were CKD-V and were booked for a preemptive kidney transplant. In patients with ESRD, fistula (78.8%) was a primary route of hemodialysis in most of the patients and remaining through permcatheter (4.4%) or dialysis catheter (3.4%).

Anesthesia Management

General anaesthesia with endotracheal intubation was the technique of choice in 202 (99.5%) patients and one case (0.5%) was carried out in combined spinal epidural (CSE) with intermittent intravenous sedation. All the living-related renal transplant patients were electively operated while the cadaveric case was done semi-electively. To reduce the risk of hyperkalemia and fluid overload, all patients of ESRD had a session of hemodialysis within 24 hours of the surgery and preemptive transplant patients were dialyzed only if clinically indicated such as hyperkalemia. All the routine medications of the patients were continued until the day of surgery.

Patients were monitored with electrocardiogram, oxygen saturation, non-invasive blood pressure and waveform capnography. Following induction of anaesthesia, a radial arterial line (96.1%) was passed in the radial artery opposite the fistula arm. A central venous line (Multicath 4, VYGON, France) was passed in 89.2% of cases on right or left internal jugular vein depending on the patency of the vein on ultrasound (LOGIQ P6, GE Healthcare, USA) while the remaining 10.2% of cases, in-situ available permcath or hemodialysis catheter was used as central venous line Swan-Ganz catheter was used in patients with severe pulmonary hypertension in 4 cases.

All patients were premedicated with midazolam (1-2 mg), and routine induction of anaesthesia was performed with propofol (1-2 mg/Kg) followed by non-depolarizing muscle relaxant cisatracurium (0.2 mg/kg) or atracurium (0.5mg/kg) to facilitate endotracheal intubation. Anaesthesia was maintained with 50% oxygen-air with 1-2% isoflurane (77.8%) or 1-2% sevoflurane (22.2%) at a fresh gas flow of 2L/min. All the patients received an infusion of non-depolarizing muscle relaxant cis- atracurium (2ug/kg/min) or atracurium (0.01 mg/kg/min) which was discontinued at the end of surgery. Intraoperative analgesia was achieved with fentanyl (2-4 mcg/kg), paracetamol (1g) and ultrasound-guided transversus abdominis plane (TAP) Block on the side of surgery with bupivacaine 0.25% 20-30 ml.

Crystalloid fluid was the fluid of choice in 92.61% of patients whereas 7.39% of patients received a combination of crystalloid and colloid. Normal saline was the intravenous fluid of choice and the mean volume of crystalloid given was 5806 + 1305 ml whereas the mean volume of colloid was 40.64 + 152 ml. Packed cell transfusion was done intraoperatively in 9.9% of the patients at a transfusion trigger of 6-7 mg/dl. Following reperfusion, patients received furosemide 1-2 mg/kg.

Figure-1 shows heart rate, systolic and diastolic and mean arterial blood pressure at baseline, at 1 hour, 2 hour, 3 hour, 4 hour and at the time of reperfusion intraoperatively.

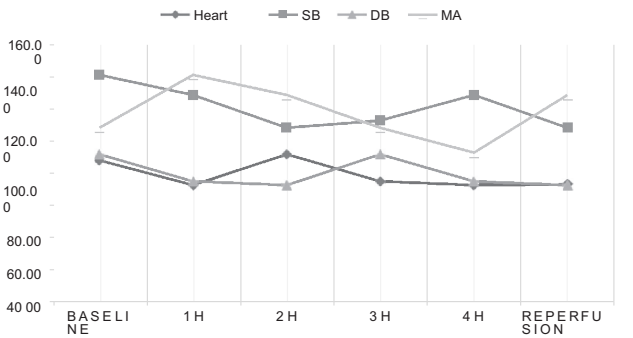

Figure-1. Intraoperative Hemodynamics

Nineteen patients (9.35%) required ionotropic support to maintain intraoperative blood pressure. These included norepinephrine (12 cases), phenylephrine (3 cases), epinephrine (2 cases), dopamine (1 case) and milrinone (1

case). After the surgery, neuromuscular blockade was reversed with neostigmine-glycopyrrolate (0.05mg/kg) intravenously and extubated.

Postoperative Care

Eight (3.9%) patients required postoperative mechanical ventilation due to slow initial kidney function after reperfusion, and acidosis. These patients were extubated on subsequent day. The postoperative analgesia regimen included fentanyl as needed and paracetamol 8 hourly. Perioperative anaesthesia-related events are shown in Table-II

Events	Frequency
Post Extubation Hypertension	44
Postoperative Hypotension	19
Arrythmia	15
Difficult Central Venous Access	8
Fluid Overload	3

Table-II. Perioperative events

DISCUSSION

Pakistan Kidney and Liver Institute and Research Center Lahore is a specialized center for kidney and liver transplants. The institute carries out living-related transplants routinely, but one case of the cadaveric transplant was performed with special permission from the government. Anaesthesia for renal transplant is planned after assessing patients in a pre-anaesthesia clinic and preparation to optimize the patients before anaesthesia.

Standard ASA monitoring has been used in the patients along with routine use of invasive arterial blood pressure which facilitates better hemodynamic stability in hypertensive patients. Several centers use continuous arterial pressure monitoring for these cases.[12] In addition, CVP was also passed for monitoring and administration of anti-thymocytes Immunoglobulin which requires IV infusion using a high-flow vein.

Intraoperatively fluid management is one of the key challenges in renal transplant anaesthesia. A balanced approach is required for volume loading for adequate perfusion of the graft following reperfusion and simultaneously avoiding volume overload after the surgery and delayed graft dysfunction.[13] We use goal-directed fluid therapy for intraoperative fluid management, targeting pulse pressure variation (PPV) less than 10% from the arterial line. The average volume of crystalloid infused in our patients was 5.8 litres, like Anand et al[14] who reported 6 litres in 350 cases. Cavaleri et al[15] showed a significant reduction in cardiovascular complications, delayed graft dysfunction and surgical complications using stroke volume variation (SVV) for goal-directed therapy ($p < 0.05$). De Cassai et al[16] used pulse pressure variation (PPV) for intraoperative fluid management and reported improved urea and creatine levels postoperatively. We mainly used normal saline as intravenous fluid. The choice of fluid for these cases remains controversial and normal saline is commonly used crystalloid in these patients as anesthesiologists avoid potassium-containing fluid such as ringer's lactate due to the risk of hyperkalemia.[17]

Intraoperative hypotension causes hypoperfusion of the graft and may lead to delayed graft function (DGF) because of anaerobic glycolysis & lactic acidosis.[18] Factors such as volume depletion due to excessive ultrafiltration in preoperative dialysis, Autonomic dysfunction, decreased cardiac reserve due to poor left ventricular systolic function, overzealous use of antihypertensive drugs, tissue ischemia induced release of vasodilators, such as nitric oxide and adenosine lead to hypotension in recipients. Correction of precipitating factors and adequate volume replacement improves blood pressure intraoperatively, however, some patients require the administration of vasopressors. About 9.35% of patients in our institutes received inotropic support to maintain blood pressure > 95 mmHg despite adequate volume replacement. Potura et al[19] reported that 22.6% of patients required catecholamines to maintain a mean arterial pressure above 60 mm Hg in deceased donor renal transplant. There are no clear guidelines or recommendations for the use of inotropic-vasoactive drugs during renal transplant and clinical judgement is required.[20]

In the present study, 10 patients (9.9%) received

packed red blood cell transfusion during the surgery if haemoglobin < 6 mg/dl to maintain adequate tissue oxygen delivery. Although there is a risk that perioperative blood transfusion might induce anti-HLA antibodies which is associated with antibody-mediated rejection, studies have found the risk of rejection is not significantly increased in patients with perioperative blood transfusion.[21]

Eight patients (3.9%) in our study required postoperative controlled ventilation because of fluid overload due to low urine output in the first hour (5 cases) following reperfusion and acidosis (3 cases). Postoperative mechanical ventilation because of delayed recovery has been reported by Jain et al and Sidi et al due to prolonged neuromuscular blockade. However, they used vecuronium (4 out of 29 cases) and atracurium (4 out of 36 cases) during the maintenance of anaesthesia. Atracurium and cis-atracurium undergo Hofmann degradation and do not accumulate in blood in such patients.[22] We used cis-atracurium infusion during surgery and no such case was reported. Shaheen et al[23] used atracurium in 124 cases without major complication.

There are certain limitations to our study. Firstly, this is a retrospective study where living-related renal and liver transplant is the main transplant program. Recipients of living-related transplants are well optimized before surgery, so anaesthesia challenges of cadaveric transplants which are performed semi-electively or emergently are not clear. Secondly, the surgical complications and outcomes have not been discussed.

CONCLUSION

Our study reveals that a significant proportion of the patients with end-stage renal disease have associated comorbidities and most of the patients have cardiac manifestations on echocardiography before the transplant. These patients require meticulous anaesthetic management for intravascular volume maintenance and hemodynamic optimization for successful perioperative care. Anesthesiologists should have a thorough understanding of end-stage renal disease including its implications, team approach for proper patient selection. A team approach for proper patient selection, preparation for surgery and intraoperative care is necessary for renal transplantation.

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3	Tahira Younas	Data analysis, data interpretation.	
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