

Frequency of Acute Kidney Injury Following Liver Transplant and Factors Associated With AKI

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Abstract

Objective: This study aimed to determine AKI frequency in post-liver transplant patients and the factors associated with AKI. **Methodology:** A cross-sectional study was conducted in the Department of Nephrology, Shifa International Hospital, Islamabad. Permission was obtained from the hospital ethics committee and written informed consent was administered to all 367 study patients. Information during surgery (blood loss, cold and warm ischemia time) was recorded. Serum creatinine was measured 24 hourly in all recipients during their postoperative hospital stay. All the data collection was conducted by the researcher himself to maintain data quality and compliance with the study protocol. The data was analyzed in SPSS software version 20.0.

Results: The mean age was 51.5 ± 9.6 years. There were 213 (58%) males and 154 (42%) females cases. After liver transplant, 10 (2.7%) cases had acute kidney injury. There were 128 (34.9%) cases who had the presence of comorbidity, 122 (33.2%) cases had blood loss > 2500 ml, 125 (34.1%) cases had warm ischemia time >10 minutes and 110 (30%) cases had cold ischemia time >7 hours. AKI was associated with comorbidity, blood loss >2500 ml, warm ischemia time >10 min, and cold ischemia time of >7 hours (p-value <0.05).

Conclusion: The frequency of AKI following post-liver transplant was less though, but it was higher in factors that can be controlled before, during, or after the liver transplant. Hence, by managing the preoperative morbidities, controlling blood loss, and warm and cold ischemia time we can prevent post-liver transplant acute kidney injury.

Keywords: Liver transplant, risk factors, warm ischemia time, acute kidney injury, cold ischemia time, comorbidity.

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Introduction

Acute kidney injury (AKI) is a common postoperative complication after liver transplantation (LT). The occurrence of postoperative AKI after LT is associated with inferior patient and graft outcomes. The predisposing factors & long-term consequences of AKI are not well understood. The first human liver transplant was performed by Thomas Starzl in 1963. Currently, liver transplantation programs have been expanded to more than 80 countries, with reported 1-year patient survival rates over 80%.¹ Acute kidney injury is a commonly observed complication after orthotopic liver transplantation (OLT) and is considered the main cause of severe morbidity and mortality. The reported incidence

rates of AKI after OLT ranges from 5% to 94% and about 8% to 17.0% need renal replacement therapy.²⁻⁵

The development of ARF after LT surgery has been linked to several factors, like pre-LT status of health; type & volume of fluid transfused; surgery time; use of medications during the surgery; harmful free radicals are released; and ischemia time tis are warm & cold.^{4, 6} The proper selection of LT candidates is one of the most effective step in lowering the risk of developing ARF after LT. During surgery, medicine doses must be carefully adjusted and electrolyte balance must be maintained or patients may require intensive care admission due to high risk of ARF post - LT.⁷

Yin Zongyi et al determined the risk factors for acute kidney injury following orthotopic liver transplantation

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across multiple transplant centers in China and witnessed post - OLT AKI in 3.9% of their patients. Blood loss was an independent factor for post - OLT AKI, (32.9% in AKI vs 4.52% in the non-AKI group; $P < 0.05$), cold ischemia time (5.0-10.5 hours in AKI vs 4.5-6.3 hours in non-AKI group, $p < 0.05$), warm ischemia time (3.2-14.3 min in AKI vs 2.0-8.0 min in the non-AKI group, $p < 0.05$), preoperative serum creatinine (Mean of $85 \mu\text{mol/L}$ in AKI vs 74.6 mol/L in the non-AKI group, $P < 0.05$), the treatment period with dopamine (Mean of 5.4 days in AKI vs 3.2 days in the non-AKI group, $P < 0.05$), overexposure to calcineurin inhibitor, and combined mycophenolate mofetil use ($P < 0.05$).⁸

Since post liver transplant, acute kidney injury is quite frequent and an avoidable incident, there is a need of taking all precautionary measures and proper selection and management of patients before, during and after the transplant procedure. Identification of all the factors related to post - LT AKI can help transplant doctors assess the risks for comorbidities in their prospective LT recipients & optimize pre-operative & peri-operative care to reduce the risk for post - LT complications. This can eventually develop clinical outcomes in those patients. The aim of this study was to determine the frequency of AKI in post-liver transplant patients and also to assess the factors associated with AKI.

Material and Methods

This cross-sectional study was conducted from September 2018 to March 2019 in the Nephrology Department, Shifa International Hospital, Islamabad. The study was conducted after permission from hospital's ethical review board and a written informed consent was obtained. The sample of 367 cases was calculated with a 5% level of significance, 80% power of the study, and taking expected anticipated population proportion of 3.97%.

All patients between the ages of 18 and 65 who were scheduled for orthotopic liver transplantation were included. Patients planned for re-transplantation, H/O renal replacement therapy before transplantation were excluded.

Information during surgery (blood loss, cold and warm ischemia time) was noted. Serum creatinine was measured 24 hourly in all recipients during their postoperative hospital stay. All the data collection was

conducted by the researcher himself to maintain data quality and compliance with the study protocol.

Data was entered in SPSS version 20.0. Quantitative data like age, baseline serum creatinine & post-surgery serum creatinine were presented as mean \pm SD. Gender, risk factors (male gender, age > 40 years, presence of comorbid, blood loss > 2500 ml, warm ischemia time > 10 min, cold ischemia time of > 7 hours), and acute kidney injury was presented as percentage and frequency. The data was stratified for risk factors and preoperative serum creatinine. The study factors were associated with AKI using chi-square test considering a p-value of ≤ 0.05 as significant.

Results

In this study, 367 patients were included, the average age was 51.5 ± 9.6 years. There were 41 (11.2%) cases aged ≤ 40 years while 326 (88.8%) cases were > 40 years old. There were 213 (58%) male and 154 (42%) female cases. The mean serum creatinine before and after treatment was 0.80 ± 0.20 (0.5 – 1.10) and 0.89 ± 0.64 (0.5 – 4.7) respectively. (Table I)

	No of cases	%age
Age (yrs)		
Mean \pm SD	51.5 \pm 9.6	
Age categories (yrs)		
<40 years	41	11.2%
>40 years	326	88.8%
Gender		
Male	213	58.0%
Female	154	42.0%
Serum creatinine		
At baseline	0.80 \pm 0.20	
Post-transplant	0.89 \pm 0.60	

Out of total 367 cases, 10 (2.7%) patients developed acute kidney injury while the rest of 357 (97.3%) cases remained intact with normal serum creatinine levels. There were 128 (34.9%) cases with presence of a comorbidity.

There were 122 (33.2%) cases with blood loss of > 2500 ml, 125 (34.1%) had warm ischemia time > 10 minutes whereas 110 (30.0%) cases had cold ischemia time > 7 hours. (Table II)

Age more than 40 years was found associated with AKI, however, it was not statistically significant (p-value, 0.06). Male gender was more likely to have AKI compared to females, however, the difference between those with and

without AKI was not significant (80.0% vs 57.4%). Comorbidity (80.0% vs 33.6%) was significantly associated with AKI (p-value, 0.002). Similarly, blood loss of > 2500 ml (80.0% vs 31.9%), warm ischemia time >10 minutes (90.0% vs 32.4%) and cold ischemia time of >7 hours (80.0% vs 28.5%) were all found associated with AKI (p-value, <0.001). (Table III)

Table II: Distribution of blood loss, Warm Ischemia time>10 min & cold ischemia time of >7 hours		
	Distribution	
	Yes	No
Blood loss >2500ml	122 (33.24%)	245 (66.67%)
Warm Ischemia time >10min	125 (34.05%)	242 (65.94%)
Cold Ischemia time of >7 hours	110 (29.97%)	257 (70.03%)

Table III: Associated factors of Acute Kidney injury in the study			
	Acute Kidney Injury		P-value
	Yes (n=10)	No (n=357)	
Age (years)			
<40 years	3 (30.0%)	38 (10.6%)	0.06
>40 years	7 (70.0%)	319 (89.3%)	
Gender			
Male	8 (80.0%)	205 (57.4%)	0.154
Female	2 (20.0%)	152 (42.5%)	
Comorbidity			
Yes	8 (80.0%)	120 (33.6%)	0.002
No	2 (2.0%)	237 (66.3%)	
Blood loss>2500ml			
Yes	8 (80.0%)	114 (31.9%)	<0.001
No	2 (2.0%)	243 (68.0%)	
Warm Ischemia time>10 min			
Yes	9 (90.0%)	116 (32.4%)	<0.001
No	1(0.4%)	241 (67.6%)	
Cold Ischemia time of > 7 hours			
Yes	8 (80.0%)	102 (28.5%)	<0.001
No	2 (20.0%)	255 (71.5%)	

Discussion

In the present study, post orthotopic liver transplantation, the frequency of AKI was found quite low with only 3.0% cases. Many previous reports have witnessed variable findings regarding this, ranging between 4.5% to up to 60.0% patients requiring renal transplant replacement therapy due to severe AKI.^{9,10,11} OLT AKI also impacts the long-term survival of the grafts & recipients.

According to the Scientific Registry of Transplant Patients, CKD following a non-renal transplant was linked to a more than 4 times increased risk of death.¹² In Charlton's study, post-transplant kidney disease, both

chronic & acute kidney disease is associated with decreased short or long-term survival.¹³

The MELD (Model of End-Stage Liver Disease) scale is based on blood creatinine, bilirubin, and the international normalized ratio and is used to predict the survival in patients with disease of the liver.¹⁴ Patients with a high level of creatinine are given higher priority in OLT treatment than those who have normal kidney function.¹⁵ As a result, the number of individuals with renal failure who receive transplants has increased significantly.¹⁶ A thorough evaluation of OLT patients with kidney dysfunction is essential to determine who may benefit from a combined kidney or liver transplant & who will most likely recover from renal dysfunction spontaneously after transplantation.¹⁷

In the current study older than 40 years male patients who were comorbid were found more prone to AKI. Moreover, in this study blood loss of > 2500 ml, warm ischemia time >10 minutes and cold ischemia time of >7 hours were all found associated with AKI. A study from China reported AKI in 3.9% of their cases and majority of them was males. In their study, blood loss was an independent factor with post-OLT AKI, time for warm ischemia time, time for cold ischemia, creatinine level in the blood before surgery, the dopamine therapy phase, and Use of mycophenolate mofetil in combination (P 0.05).¹⁸

Another study was conducted for predisposing factors for early post-transplant AKI witnessed AKI in 52.0% cases, and weight > 100 kg, liver disease severity, prior diabetes, amount of components of blood or frozen plasma transfusion during surgery & the etiology of last stage liver disease were all predisposing factors for the development of AKI (p-value, 0.005).⁶

Another study witnessed that intra-operative blood transfusion volume (P=0.0041) & operation length (P=0.0051) were significantly associated with AKI after liver transplantation. They also found that intraoperative blood transfusion volume and operation length were both contributing factors to post - OLT ARF.¹⁹

The above evidence regarding rates of AKI and its associated factors is comparable to the findings of the current study. Comorbidity, has a significant role in the incidence of AKI and before hand if these patients are monitored well during the transplant, the occurrence of AKI may be reduced. Moreover, the factors like blood volume, as well as warm and cold ischemia time can be

controlled to prevent AKI and resultantly acute replacement therapy.

This study has many advantages, firstly, a large group of liver transplant patients was selected and analyzed. Secondly, local evidence on this topic is rare and this is one of the very first attempts. The advantages of the study outweigh the few limitations in terms of the observational study design and its weaknesses.

Conclusion

In this study the frequency of (AKI) acute kidney injury following post-liver transplant was less though, but it was higher in factors that can be controlled before, during, or after transplantation. Hence by managing the preoperative morbidities, controlling blood loss, and warm and cold ischemia time we can prevent post-liver transplant acute kidney injury.

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