RESEARCH LETTER

Respiratory Morbidity Following Pediatric Orthotopic Liver Transplantation

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PII: S097475591600048

ABSTRACT

We evaluated the pulmonary complications following orthotopic liver transplantation in children (age <18 y). Twenty-two patients (49%) developed respiratory complications. Pediatric end-stage liver disease (PELD) score >25 and positive fluid balance were independent risk factors. Patients with respiratory complication had significantly higher mortality and intensive care unit stay.

Keywords: *ARDS, Pneumonia, Complications, Biliary atresia*.

Orthotopic liver transplantation (OLT) is the treatment of choice for children with end stage liver disease. Despite advances in intensive care and surgical techniques, respiratory complications are frequently associated with pediatric OLT [1,2]. We retrospectively evaluated medical records of children (age <18 y) who underwent OLT during 2009-14 in a tertiary care referral hospital in Bangalore, Southern India.

Respiratory complications were assessed from clinical and radiological features. Pediatric end-stage liver disease (PELD) score was calculated using online calculators. Fluid balance was calculated as percentage of body weight using formulae: (total fluid in [L] – total fluid out [L] / (admission weight [kg]) × 100%. Patients were dichotomized as those with pulmonary complications and those without. Chi-square test was used to evaluate categorical data and Mann-Whitney U test for continuous data. Statistical significance was defined as $P<0.05$. Univariate analysis was performed and variables with $P<0.05$ were entered into a multivariate logistic regression analysis to determine independent predictors. Odds ratio was calculated for significant factors. Outcome compared included mortality and duration of intensive care unit (ICU) stay.

Forty-five children (28 boys) with median (range) age of 27 (7, 143) months were included. Commonest indication of OLT was biliary atresia (n=23) followed by cryptogenic cirrhosis (n=4). Twenty-two patients (48.9%) developed significant pulmonary complications. Commonest of them was pulmonary edema (n=11; 24.4%) followed by pneumonia (n=10; 22.2%). Although 22 (48.9%) patients

had pleural effusion, 8 (17.8%) were significant enough to required thoracocentesis or intercoastal drainage tube. Five (11.1%) patients developed acute respiratory distress syndrome (ARDS). Seven (15.5%) patients died during the post-operative period; all had pulmonary complications. Operative mortality (7 *vs* 0; *P*=0.003) and mean (SD) length of ICU stay [22.9 (11.8) *vs* 12.7 (52); *P*=0.014] were significantly higher in patients with pulmonary complications. PELD score >25 (*P*=0.001) and positive fluid balance in first 3 post-operative days (*P*=0.001) were independent risk factors (***Table* I**) associated with complications with odds ratio (95% CI) of 11.4 (1.8, 71.6) and 5.7 (1.2, 26.8), respectively.

The rate of pulmonary complications in the early post-operative period is in broad agreement to the range of 13-70% in recent published reports [1-5]. Although all the patients who died had pulmonary complications; not all deaths could be directly attributed to them. Major complication associated with mortality was ARDS which could be a part of severe sepsis. Thus, respiratory complication was the major mode of death rather than cause. Association of different complications with mortality could not be determined because of the small sample size. In our series, patients with pulmonary complications had significantly longer length of ICU stay and mortality. Earlier studies [6,7] also reported higher mortality, and higher ICU and hospital stay in patients with pulmonary complications. Severity of the disease [8,9] and excessive fluid and transfusion requirement [6,8] have also been reported previously as significant risk factors.

We conclude that respiratory morbidity is common in children who undergo OLT. Optimal timing to allow OLT at lower PELD score, and meticulous attention to prevent fluid overload may reduce risk of pulmonary complications and improve outcome.

Contributors: SA and AKS: concept, data collection, statistics, data analysis, drafting of article and critical review; SR and RA: data analysis, drafting of article, and critical review; ALD: drafting of article and critical review. All authors approved the manuscript.

Funding: None; *Competing interest*: None stated.

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TABLE I ANALYSIS OF VARIABLES IN PATIENTS WITH POSTOPERATIVE PULMONARY AND NON-PULMONARY COMPLICATIONS AFTER OLT (*N*=45)

Variable	*Pulmonary Complication (n=22)*	*Non Pulmonary Complication (n=23)*	*P Value*
Age (mo)*	48.7 (45.9)	36.9 (29.8)	0.308
Female gender	11	6	0.098
Weight-for-age *Z* score <-3SD	11	12	0.884
Height-for-age *Z* score <-3SD	12	11	0.652
Preoperative massive ascites	10	8	0.465
Preoperative INR*	2.35 (1.1)	2.02 (0.6)	0.196
Preoperative PELD score >25	20	8	0.000
Preoperative respiratory problem	4	3	0.634
Preoperative sepsis	6	2	0.103
Preoperative ventilation requirement	3	1	0.274
Intraoperative transfusion >40ml/kg	16	14	0.399
Intraoperative positive fluid balance >10% body weight	18	17	0.524
Positive fluid balance in first 3 post-operative days	17	6	0.001
Oliguria in first 7 post- operative day	3	1	0.274
Acute kidney injury in first 7 post-operative day	12	10	0.458
Acute graft rejection	5	2	0.194
Re-laparotomy	8	3	0.069

*Values in numbers on *mean (SD)*