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# Respiratory Complications in Chronic Liver Disease Patients Before and After Liver Transplantation at Al Sahel Teaching Hospital<sup>☆</sup>

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## Abstract

**Background:** Chronic liver diseases and disorders has been accompanied by pulmonary complications and dysfunction that occur before and/or after hepatic transplantation. Detection of these lung complications is necessary for therapeutic interventions. This is a prospective cohort study that analyzes the pulmonary complications before and after liver transplantation.

**Results:** In patients suffering from hepatopulmonary syndrome who were subjected to liver transplantation there was a high statistically significant improvement in PaO<sub>2</sub> from 58.41 ± 4.00 to 87.12 ± 12.02 mmHg (room air) (*P* < 0.001). There were no differences found when comparing hepatic hydrothorax patients and their controls as regards mechanical ventilation days spent after the surgery, the requirements for transfusion, postoperative mortality or long term survival. 27% of patients with portopulmonary hypertension received no treatment for pulmonary hypertension and were not subjected to hepatic transplantation, of these patients, 40% are alive. 54.0% of patients with portopulmonary hypertension received treatment for pulmonary hypertension and were not subjected to liver transplantation, a 45% of them had survived. 19% of the patients with portopulmonary hypertension underwent liver transplantation, of these, 57.14% survived liver transplantation. The most evident complications after liver transplantation were pneumonia, pulmonary edema, atelectasis and pleural effusion.

**Conclusions:** Awareness of the pulmonary complications before and after liver transplantation and their diagnosis and specificities, exhibit high evidence of suspicion and initiate therapy within a perfect time consequently a major number of patients subjected to liver transplantation can succeed post liver transplant.

**Keywords:** Hepatic hydrothorax, Hepatopulmonary syndrome, Liver transplantation, Portopulmonary hypertension, Pulmonary complications

## 1. Introduction

Chronic hepatic disease has been accompanied by pulmonary complications before and after hepatic transplantation.<sup>1</sup> Transplantation of the liver is the ultimate intervention for particular patients who had either acute liver failure or complicated cirrhosis. Pulmonary complications that occur initially after LT may additionally affect and deteriorate morbidity, and mortality of liver transplant

recipients. However, these problems may be to some degree controlled, prohibited or treated and consequently result in clinical improvement of the outcomes, and adjust the usage of resources and budgets.<sup>2</sup>

Limited information built on a literature analysis and a previous prospective multicenter research recommends that portopulmonary hypertension (POPH) is accompanied by a reduced prognosis. This information was created only from particular cases, minor series of studies and institute specific

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procedures that actually did not document variations in the pulmonary vascular hemodynamic prior to liver transplant.<sup>3</sup>

Hepatic transplantation (LT) is the paramount management option for decompensated liver cirrhosis, and is consequently considered to be the greatest management for patients with hepatic hydrothorax. However, there are no comprehensive studies evaluating the survival and advancement of these hepatic patients next to liver transplantation. Actually, there is few stated series about liver transplantation in patients with hepatic hydrothorax.<sup>4</sup>

Delineating each one of these respiratory complications in addition to their risk elements comes to be vital to guide definite therapeutic approaches.<sup>5</sup>

The backbone of the management of end stage hepatic illness is hepatic transplantation. In spite of the improvements in medicinal, and surgical treatments, post hepatic transplant respiratory complications remain to be a chief reason of illness and mortality among recipients of solid organ transplantation, lung complications specifically have a tendency to ensue more commonly after liver transplantation compared to renal transplantation.<sup>6</sup> Though, these complications ensue at an identical rate when compared to heart and lung transplants. Numerous risk elements in enhancing posttransplant pulmonary complications have involved both preoperative factors (i.e., the severity of hepatic dysfunction, recipient age, and any previous pulmonary illness) and perioperative factors (i.e., intra operative hemorrhagic volumes, fluid balances, and fluid volumes). The down-stream results of impairing lung function include a prolonged time of airway intubation and mechanical ventilation with consequent augmented risk of infective complications.<sup>7</sup>

The aim and purpose of the present study was to detect and analyze the utmost clinically significant pulmonary complications distressing patients in the peri-liver transplant period. For achievement a favorable outcome and higher survival rates after liver transplantation.

## 2. Material and methods

This prospective cohort study analyzes pulmonary complications before and after hepatic transplantation in hepatic transplant recipients. From March 2013 to March 2020 at Al Sahel Teaching Hospital where liver transplantation was performed.

All patients involved in this work were applicants for liver transplantation owing to end stage hepatic disease or even hepato-cellular cancer. Department of the liver transplantation formerly confirmed the need and indication for liver transplantation. All

cirrhotic liver disease patients had predicted by typical clinical, biological signs or both and significant portal hypertension, ascites, varices, splenomegaly or findings of liver biopsy. Patients evaluated for liver transplantation listing were subjected to transthoracic echocardiography screening for diagnostic criteria for POPH of Doppler echocardiography.<sup>8</sup> If there were any suspicions of pulmonary hypertension with no signs of left cardiac disease, patients consequently referred to specialized center for pulmonary hypertension. Occurrence of pre-capillary pulmonary hypertension detected via existence of at rest mean pulmonary arterial pressure of 25 mmHg or even more, also, presence of pulmonary arterial wedge pressure equal 15 mmHg or lesser, these were confirmed by performing right cardiac catheterization in pulmonary hypertension center.

Exclusion criteria were pulmonary hypertension which accompanied by significant pulmonary diseases, chronic thrombo-embolic pulmonary hypertension, left cardiac diseases associated with pulmonary hypertension and PAH accompanied by additional disorders, including congenital left to right shunts, human immunodeficiency virus infection, exposure to drugs known to induce pulmonary hypertension, and connective tissue diseases, also active smokers were excluded.

HPS identification was established upon clinical examination and radiological signs of hepatic disorder and dysfunction with or without the presence of portopulmonary hypertension, presence of intrapulmonary dilatation of the vasculature by chest HRCT,<sup>9</sup> and signs of abnormal gas exchange (alveolar-arterial oxygenation gradient >20 mmHg on room air or the partial pressure of arterial oxygen <70 mmHg).<sup>10</sup>

All patients involved in the research were subjected to a complete clinical history comprising personal, smoking, alcohol intake, familial, drug therapy, environmental risk factors and past history, also a history of chest conditions including symptoms and signs of asthma.

Thorough clinical examination including general and local examination. Ventilatory function test and arterial blood gas analysis. Laboratory investigations comprising complete blood count, fasting blood glucose, ESR, liver functions tests (bilirubin both total and direct, serum albumin, prothrombin time, ALT, AST, gamma-glutamyl transferase, and alkaline-phosphatase), kidney function tests, HCV Ab, HBsAg, ASMA, ANA, serum alfa fetoprotein. Also, all patients were subjected to chest high-resolution computed tomography, abdominal ultrasound examination, ECG, CT liver angiography and psychological evaluation and assessment.

The research was permitted by the local principles and ethics commission of GOTHI. Written learned and informed consent was gotten from each patient. Most of the patients had a steady and regular monitoring and follow up for medical evaluation and laboratory investigations till death or till March 2020.

### 2.1. Statistical analysis

Data and information were composed, reviewed, coded, and go into version 23 IBM SPSS. The quantifiable information was offered as mean, standard deviation and range once parametric. Furthermore, qualitative variables were offered as numerals, ratios and fractions. The evaluation and comparison between two groups with qualitative information were completed by means of the Chi square test. The contrast among two groups with quantitative information and parametric spreading was completed via independent-t-test whereas extra than 2 groups were completed via One Way ANOVA test. Additionally, paired *t*-test was used in comparing two paired readings. Usage of Spearman correlation coefficients to evaluate the association and correlation among two quantitative parameters in the similar groups. The confidence interval was established at 95% in addition the border and margin of error accepted was established at 5%. Consequently, the *P* value was considered important and significant at the level of <0.05.

## 3. Result

### 3.1. Pulmonary complications before liver transplantation

A total of 95 patients were included, 71 of them were diagnosed with pulmonary complications, in whom 37 patients were diagnosed with Portopulmonary hypertension, 22 patients were diagnosed with hepatopulmonary syndrome and 12 patients with hepatic hydrothorax and comparing

those 12 patients with a control group of 24 patients transplanted in close time previously and after each case.

#### 3.1.1. Patients with portopulmonary hypertension

We recognized and identified 37 patients who fulfilled the modified analytic criteria of POPH, 19 (51.3%) were females and 18 (48.6%) were males. (Table 1). The mean age per year was 46.0. (range 34–57) in addition the mean MELD score was 12.0 (range from 6 to 20). 7 patients (19%) submitted to LT and 30 patients were possible LT applicants (81%) who were not transplanted. Thirteen subjects were registered for LT in whom 9 (69.2%) died while on the waiting list. Seventeen patients were deprived of LT owing to many co-morbid disorders (morbid obesity, alcoholic dependency, poor obedience or compliance). Two of these 17 were deprived for the reason of severe PH, which might not be sufficiently controlled in spite of the oral sildenafil treatment.

As regards the 37 patients, MPAP was  $49.73 \pm 6.97$  mmHg (range 33–62). (Table 1). MPAP were not considerably altered in patients subjected to LT in comparison with individuals who did not. 20 (54%) of the 37 patients with POPH had died. Eleven (55%) deaths were associated with hepatic disease, five (25%) due to PH, three in perioperative time, and one from acute myocardial infarction.

### 3.2. Treatment subgroups

(1) Patients not obtain medical treatment for pulmonary hypertension and are not subjected to liver transplantation:

Ten of the 37 (27%) patients did not receive treatment for PH but did not submit to LT. The disease courses of these patients characterize the natural and usual history of POPH from the identification. The average survival of this group of patients were 14 months and of these patients, 4 are successful and 6 were dead, 3 within 1 year of the identification and nobody registered for LT. The

Table 1. Starting point characteristics and hemodynamic parameters of patients with Porto pulmonary hypertension.

Subgroup parameter	Total Number = 37	No treatment Number = 10	Medical treatment only Number = 20	LT ± medical treatment Number = 7	Test value	<i>P</i> Value
Males	18 (48.6%)	5 (50.0%)	9 (45.0%)	4 (57.1%)	3.986 <sup>a</sup>	0.136
Females	19 (51.3%)	5 (50.0%)	11 (55.0%)	3 (42.9%)		
MPAP						
Mean ± SD	49.73 ± 6.97	51.60 ± 8.32	50.85 ± 5.41	43.86 ± 6.67	3.154 <sup>b</sup>	0.140
Range	33–62	33–60	37–62	36–55		

Non-Significant: *P* > 0.05, Significant: *P* < 0.05, Highly Significant: *P* < 0.01.

<sup>a</sup> Chi Square Test.

<sup>b</sup> One Way ANOVA test.

mean starting point of PAP was not statistically different among patients who were successful or dead ( $45.75 \pm 9.22$  mmHg vs.  $55.50 \pm 5.28$  mmHg,  $P = 0.062$ ). Pulmonary hypertension severity did not seem to affect or expect survival. Of the 6 deaths, three were linked to hepatic disease, two to pulmonary hypertension and one to, acute myocardial infarction.

(2) Patients take medical treatment for pulmonary hypertension and are not subjected to liver transplantation:

Twenty of the 37 (54.0%) patients took medical treatment for PH and did not subject to LT. A total of eleven patients had died, two patients in one year of identification and the other nine died after that. Five patients were ready and registered for LT and altogether died while on the waiting list, four owing to hepatic associated reasons and one from PH. There were no important differences in baseline mean PAP among patients alive and dead ( $48.33 \pm 7.11$  vs.  $52.91 \pm 2.21$  mmHg). Twenty patients were started on oral sildenafil (9 alive; 11 died mean PAP  $50.85 \pm 5.41$  mmHg). Follow-up in 9 patients (follow-up extended from 3 to 48 months), by echocardiography established that medical treatment for PH improved mean PAP ( $48.33 \pm 7.11$  vs.  $41.44 \pm 6.25$  mmHg;  $P < 0.01$ ).

(3) Liver transplantation:

Seven (19%) of the 37 patients submitted to LT, of these, three died. One death was intraoperative. This patient not obtained medical treatment for PH previous to LT and died intraoperatively through tried LT. The patient had moderate PH at baseline. 6 patients received oral sildenafil as a medical treatment for PH previous to LT, with 2 patients who died within one month of LT one suffered from VAP and the other suffered from pulmonary edema in ICU. Four patients on oral sildenafil treatment stay alive after LT and were capable to withdraw medication post LT. Two patients discontinued sildenafil within 7 months and one patient at one year. The last one was transitioned to oral amlodipine.

### 3.2.1. Patients with hepatopulmonary syndrome

A total of twenty-two patients were identified with HPS over this work period. Seventeen patients (77.2%) were subjected to LT. Five patients (22.8%) did not obtain LT as they were either rejected for LT (2/22, 9%) or died while awaiting liver transplantation (3/22, 13.6%). Pretransplant arterial blood gases were accomplished within six months of

transplant in all 17 patients. Twelve patients (70.5%) were on oxygen therapy during the period of liver transplantation. There was no statistically significant association between baseline ( $\text{PaO}_2$ ) and MELD score.

Patients were monitored for a median of 22 months (range 3–44 months) after liver transplantation and mortality was; 1/17 (5.9%). The only patient who died in the research period ensued about seven months next to liver transplantation. All patients survived the transplantation hospitalization and 16 patients are now still alive.

4 of 17 patients (23.5%) developed pneumonia and hypoxic respiratory failure in the posttransplant period (range 9–28 days).

Few drawbacks were detected throughout the initial and late postoperative phases. 4 of 17 (23.5%) patients had hemorrhage or vascular drawbacks in addition 7 (41.1%) had biliary complications.

One patient suffered from postoperative respiratory failure, VAP, and sepsis. After 79 days in the hospital, he was discharged and continued on  $\text{O}_2$  therapy through nasal prongs 2 L/min, (it was on six L/min pre-operatively). 4 months late, the patient established pneumonia with consequent ARDS, needing intubation and mechanical ventilation. He died from respiratory failure, after a few days (213 days posttransplant) and the death was not linked to his basic HPS directly which had significantly better in the completion of the time of his transplantation hospitalization. Nevertheless, his elongated post-transplant retrieval may have rendered him more vulnerable to the upcoming complications.

Follow-up of patients with HPS after LT on room air evaluation of oxygen levels was accessible in all 17 patients after LT. We compared the last preoperative to the utmost new postoperative results in all patients, with a minimum three months posttransplant. All patients had  $\text{PaO}_2$  or saturation improvement, (17 of 17).  $\text{PaO}_2$  increased from  $58.41 \pm 4.00$  to  $87.12 \pm 12.02$  mmHg (room air) ( $P < 0.001$ ). (Table 2) (Fig. 1).

Ten of twelve patients (83.3%) who were on ambulatory  $\text{O}_2$  pre-operatively had a normal room air partial pressure of  $\text{O}_2$ , and were off oxygen by 4 months posttransplant, and two patients (16.6%) by 6 months after transplant.

To define the extent of postoperative elevation of  $\text{PaO}_2$ , we measured only patients whose first postoperative ABGs revealed a  $\text{PaO}_2$  value that was lower than the normal range (six patients), assumed that oxygen level and gas exchange of patients who had previously returned to the normal by the time of first oxygen detection would not be likely to increase additionally.

Table 2. Arterial oxygen pressure before and after liver transplantation.

	Range	Mean $\pm$ SD	Test value	P value	Sig.
PaO <sub>2</sub> pre	55–66	58.41 $\pm$ 4.00	10.387	<0.001	H S
PaO <sub>2</sub> post	68–97	87.12 $\pm$ 12.02			

Non-Significant:  $P > 0.05$ , Significant:  $P < 0.05$ , Highly Significant:  $P < 0.01$ .

Through 4–24 months of surveillance and observation postoperatively, one patient died and five patients showed an improvement in PaO<sub>2</sub>, starting from a mean of  $63.20 \pm 1.10$  to  $91.00 \pm 3.54$  mmHg on room air. The mean degree of improvement and rising was  $2.20 \pm 0.32$  mmHg/month (Table 3 and Fig. 2).

### 3.2.2. Patients with hepatic hydrothorax

Patients suffering from hepatic hydrothorax, and their control group, were similar as regards age, sex, cause of hepatic disease, and the presence of hepato-cellular carcinoma. Although liver function defined by Child Pugh index was significantly worse in patients who had hepatic hydrothorax. There were no variances among the hepatic hydrothorax group of patients and their control group as regard duration of surgery; intensive care unit admission days after surgery, days of mechanical ventilation, or necessities of transfusion (Table 4). There were no alterations in long term survival (70.8% vs. 66.6%) at 7 years follow up,  $P = 0.98$ .

8 patients required thoracic tube next to surgical intervention for about two to ten days. 2 patients developed hospital acquired pneumonia. One month after LT pleural effusion continued in 4 patients, though 3 months later the pleural effusion

continued in merely one patient, due to heart failure. Only one patient established novel hydrothorax 6 years after LT, due to deterioration of the hepatic cirrhosis. In the course of follow up four patients died, within 7 years.

### 3.3. Pulmonary complications after liver transplantation

Among 69 patients who followed up after LT, 8 patients (11.6%) developed hospital acquired pneumonia in the ICU, mean age:  $50.36 \pm 7.32$  years.

Late onset pneumonia that was established after the first month after liver transplantation till the completion of the first year was identified in ten patients (14.50%) and was complicated by a forty percent mortality rate. The causal organisms were bacterial agents followed by fungi. Only one patient was identified as pleural tuberculosis after liver transplantation.

Among 69 patients who underwent LT, 10 patients (14.5%) had pulmonary edema during ICU stay and they have relatively prolonged ICU stay and ventilator dependency. 17 patients (24.6%) developed pleural effusion within three days after surgery. 37 patients (53.6%) experienced atelectasis radiologically within 10 days after LT. One patient had hypoxemia compatible with TRALI throughout the surgery and had relatively long ventilator dependence and ICU stay.

## 4. Discussion

The current study confirmed and established the poor prognosis and outcomes of untreated portopulmonary hypertension patients (POPH). POPH is

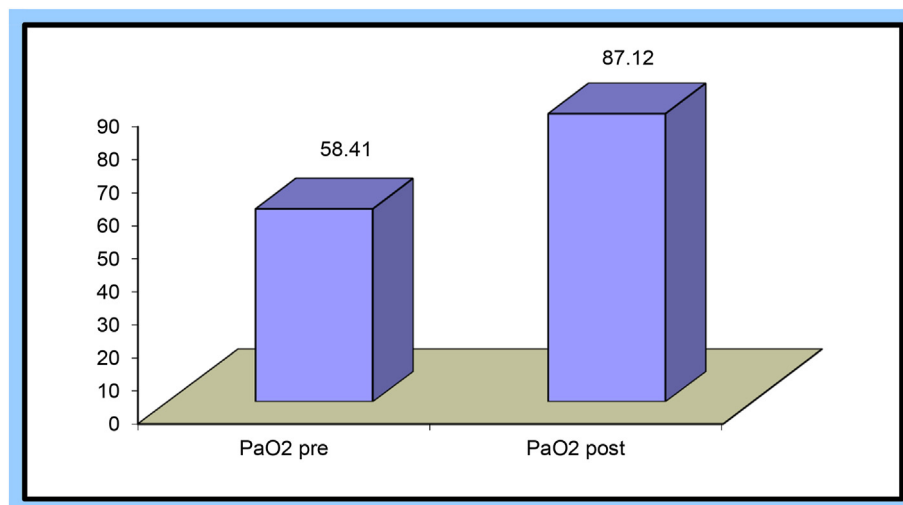


Fig. 1. Arterial oxygen pressure before and after liver transplantation.

Table 3. Follow up the patient's partial pressure of arterial oxygen from 4 to 24 months postoperatively.

	PaO <sub>2</sub> at 4 months	PaO <sub>2</sub> at 24 months	Rate of increase/month	Test Value <sup>a</sup>	P Value	Sig
Mean ± SD	63.20 ± 1.10	91.00 ± 3.54	2.20 ± 0.32	16.213	<0.001	H S
Range	62–65	85–94				

Non-Significant:  $P > 0.05$ , Significant:  $P < 0.05$ , Highly Significant:  $P < 0.01$ .

<sup>a</sup> Paired T Test.

a significant subclass of Pulmonary arterial hypertension, constituting about nearly 7–10% of PAH patients.<sup>11</sup> Transthoracic echocardiography is a suggested investigation for the detection of the occurrence of POPH in liver transplantation applicants.<sup>12</sup> Assessed and estimated pulmonary arterial systolic pressure were frequently used variables to identify pulmonary hypertension.<sup>13</sup> The aim of therapy for portopulmonary hypertension is to increase survival, improve the quality of lifespan, and facilitate safe and effective liver transplantation.<sup>14</sup> Liver transplantation is the greatest accessible interventional and beneficial therapeutic choice for patients suffering from an advanced and progressive hepatic disease. Liver transplantation resolves and improves portal hypertension, and is considered an efficient intervention for POPH. Nevertheless, without pulmonary arterial hypertension specific treatment, patients suffering from POPH still have a worse outcome after liver transplantation.<sup>3</sup> Moreover, failure of resolution of POPH with liver transplant supposing the occurrence of permanent remodeling of the pulmonary vasculature formerly to the beginning of PAH-specific treatment. The complete hemodynamic picture is obviously significant not only before liver transplantation but moreover throughout the LT technique particularly at the stage of allograft recirculation. It is likely that a previous right

ventricular non-hypertrophied dilatation, cannot tolerate and accommodate acute blood products volume additions or the vaso-constrictive properties of pulmonary vasculature inflammatory cytokines interactions, that may arise at the recirculation of allograft.<sup>15</sup>

In current years many researches have established that patients with POPH might benefit from vasodilators medications,<sup>3,15,16</sup> and patients who had POPH and treated by vasodilator treatment may have the best outcome and longtime survival after LT Vasodilator treatment for POPH. Further prospective researches are required for confirmation of the mechanism of vasodilators medications in the enhancements of the hemodynamic and results in patients suffering from POPH. The ideal pre-liver transplantation therapeutic program, time to when to accomplish liver transplantation and detecting the applicable hemodynamics profile in POPH patients for liver transplantation has inadequate support in the previous research and literature. Although many liver transplant centers attempt to improve and advance the hemodynamics (find mean arterial pulmonary pressure <35 mmHg prior to liver traant), and features of right cardiac functions probably show a major role.<sup>17–19</sup>

Particular patients may be capable to stop the pulmonary hypertension treatment after a liver

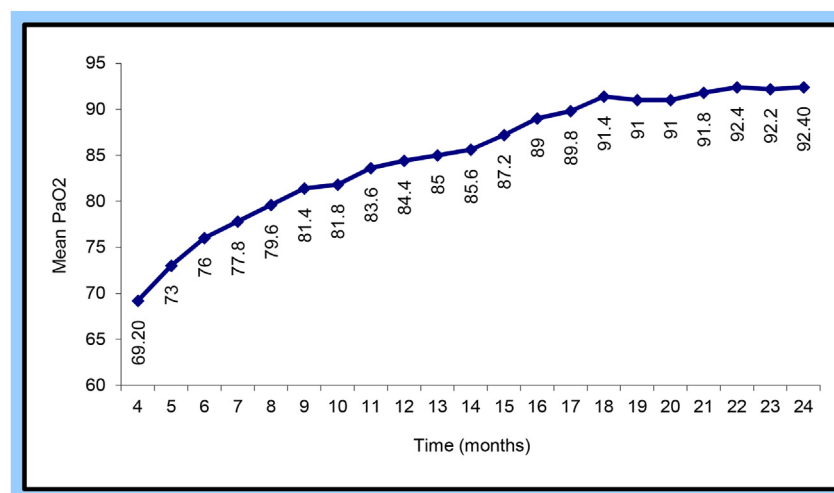


Fig. 2. Follow up the patient's partial pressure of arterial oxygen from 4 to 24 months postoperatively.

Table 4. Comparison between hepatic hydrothorax patients and their controls.

	Control group Number = 24	Hepatic Hydrothorax Group. No = 12	Test value	P value	Sig
Age					
Mean $\pm$ SD	53.33 $\pm$ 6.34	50.00 $\pm$ 8.02	1.360 <sup>b</sup>	0.183	N S
Range	43–63	36–62			
Sex					
Female	4 (16.7%)	2 (16.7%)	0.00 <sup>a</sup>	1.00	N S
Male	20 (83.3%)	10 (83.3%)			
Child grade					
B	17 (70.8%)	4 (33.3%)	4.629 <sup>a</sup>	0.031	S
C	7 (29.2%)	8 (66.7%)			
Child score					
Mean $\pm$ SD	9.20 $\pm$ 1.32	10.42 $\pm$ 1.44	2.513 <sup>b</sup>	0.017	S
Range	8–12	8–12			
Length of surgery (min.)					
Mean $\pm$ SD	425.42 $\pm$ 89.93	436.92 $\pm$ 81.78	–0.372	0.712	NS
Range	275–560	285–560			
Ventilation (days)					
Mean $\pm$ SD	4.00 $\pm$ 0.78	4.42 $\pm$ 0.99	–1.377	0.178	NS
Range	3–5	3–7			
ICU stay (days)					
Mean $\pm$ SD	6.54 $\pm$ 1.22	7.58 $\pm$ 2.27	–1.802	0.080	NS
Range	5–9	5–12			
Hospital stay (days)					
Mean $\pm$ SD	28.79 $\pm$ 8.23	30.83 $\pm$ 3.83	–0.812	0.422	NS
Range	11–41	26–37			
Blood units					
Mean $\pm$ SD	9.00 $\pm$ 2.27	10.25 $\pm$ 2.53	2.258	0.142	NS
Range	5–14	6–13			

Non-Significant:  $P > 0.05$ , Significant:  $P < 0.05$ , Highly Significant:  $P < 0.01$ .

<sup>a</sup> Chi Square Test.

<sup>b</sup> Independent T- Test.

transplant. liver transplantation may be beneficial and even beneficial and curative in some patients suffering from POPH, however it is not generally the rule. It is essential to know that in the present study nine hepatic patients who were being received therapy for Pulmonary hypertension died during waiting for liver transplantation.

The sequential treatment with sildenafil and bosentan has been described to intensely improve and recover pulmonary hemodynamics through two months duration to link a patient to effective and successful liver transplantation.<sup>20</sup>

In the present work, most of the involved hepatic patients have an extended course of hepatic disease. The advancement of POPH in these patients results in right sided cardiac dysfunction and worsens hepatic congestion, which aggravates the original hepatic disease.

In the current study, POPH patients were 18 (48.6%) males and 19 (51.3%) females. A previous study found high prevalence of portopulmonary hypertension in females.<sup>21</sup>

In the current study, we have shown a 100% survival rate in peri-transplant within six months, and a 94% survival rate within one year for liver

transplantation in hepatopulmonary syndrome. This information is similar to general survival statistics and information for both DDLT and LDLT in the United States.<sup>22</sup>

In our center there was no obvious choice preference that preferred patients who had less HPS severity for a liver transplant, as non-transplanted patients had a greater mean PaO<sub>2</sub> than the patients who were transplanted. Dissimilarities in the severity of HPS might not also be a cause for better survival as compared to previous researches, for instance the results of our study enclosed many patients suffered from severe HPS and had the lowermost mean PaO<sub>2</sub> = 55 mmHg. There were definitely no apparent dissimilarities in standard features and characteristics linked to survival, in comparison to former research.<sup>22</sup> The mean age of the current study group (50.6 years) was the uppermost, also spreading and distribution of recipient hepatic diseases was comparable to that in the previous studies by the exclusion of a high and low incidence and prevalence of alcoholic cirrhosis of the liver which found in Taille et al. study (52%)<sup>23</sup> and Swanson et al. study (8%),<sup>24</sup> respectively.

The severity and extent of hepatic disease in the current work were similar and comparable to that



found in the previous studies with which it might be compared, no information is available on the severity of hepatic disease from the study of Krowka et al.<sup>25</sup> But patients in the current work had a similar mean MELD scores (MELD = 14) to that of the study of Swanson et al.'s results (MELD = 13).<sup>24</sup>

Though nobody of the previous studies stated MELD score, the fraction of patients with HPS in Child's Pugh class A was comparable and similar to our results 29%, in Taille and his associates' research was 30%<sup>23</sup> and in the study of Krowka et al.'s research was 24%<sup>25</sup> Only study of Arguedas et al.<sup>26</sup> had a greatly low fraction of Child's Pugh (class A) patient were 12%. Nevertheless, this current work noted indistinguishable mean Child's Pugh score in survivors ( $9 \pm 2$ ) and non-survivors ( $9 \pm 1$ ) proposing no statistically significant association among CP classes, and the mortality in this population an observation confirmed by the study of Swanson et al.<sup>24</sup>

Our study may propose that liver transplantation is efficient in adult patients who had severe HPS. liver transplantation may be a principally essential intervention to be considered in patients with HPS. The main medical implications of the current work are that even the utmost severe HPS patients should be subjected to liver transplantation consideration and when there are additional comorbidities that do not rule out liver transplantation, the stage and severity of HPS would not be a cause for liver transplantation rejection.

Hepatic hydrothorax takes place as a consequence of the passing of ascetic fluid through a defect in the diaphragm, and ascites is due to the occurrence of portal hypertension and retaining of salt by the kidney. Consequently, management can be focused to decrease salt retention by medications like diuretics to diminish portal hypertension and TIPS or to close the diaphragmatic defects through VAT.<sup>4</sup>

In the current study, patients who suffered from hepatic hydrothorax, as well as their controls, were comparable in the basic characters, like age, sex, etiology of the hepatic disease, and presence of hepatocarcinoma. Although liver function measured by Child Pugh score showed significant worsening in patients who suffered from hepatic hydrothorax. There were no variances among hepatic hydrothorax individuals and controls as regard interval of operation, intensive care unit admission days after the surgery, mechanical ventilation duration, or requirements for blood transfusion. There were no variances in long time survival.

Xavier et al. stated that, there were no studies that discussed the survival of patients who had non-complicated hydrothorax, however can be assumed it would be comparable to that of patients suffering

from cirrhotic liver and ascites. Survival after liver transplantation of patients with non-complicated hydrothorax is 90% at one year and 80% at five years, obviously superior to the survival of non-transplanted cirrhotic liver patients suffering from ascites. Liver transplantation is in terms of survival the greatest management option for patients with non-complicated hydrothorax, consequently any patient suffering from hepatic cirrhosis developing hepatic hydrothorax must be taken into consideration a potential applicant for liver transplantation. A prospective research of thoracentesis in patients suffering from cirrhosis and hepatic hydrothorax presented 8% prevalence of pneumothorax post thoracentesis. The possibility is higher when continuing taps. Though insertion of a chest tube was required in 50% of patients with pneumothorax, there was definitely no mortality accompanying this technique. Consequently, patients who had a probable short duration delay (<3–6 months) were able to be achieved via interventional thoracentesis. Hepatic hydrothorax Patients who required recurrent intervention with thoracentesis, have good risk considered by MELD score, as well as a probable elongated waiting list time can be managed by TIPS such as a bridge to liver transplant.<sup>4</sup> Briefly, hepatic transplant is an admirable beneficial intervention for patients who had hepatic-hydrothorax. Occurrence of hepatic-hydrothorax does not add additional peri-operative and postoperative complications, or differences in long duration survival.

The incidence of pneumonia post-liver transplantation ranges from 4.6% to 57.8% with severe cases occurring in 18.2% of patients. Development of pneumonia following liver transplantation was closely associated with prolonged use of mechanical ventilation, prolonged ICU stay, the need for tracheostomy placement, primary graft dysfunction, and the need for renal replacement therapy.<sup>1</sup> In the current work, among 69 patients who followed up after LT, 8 patients (11.6%) developed hospital-acquired pneumonia in the ICU. Late onset pulmonary infections that were established after one month afterwards transplantation till the finish of the first year were found in ten patients 14.50% and were complicated, by a 40% mortality rate. The utmost common source of pneumonia was bacterial agents followed by fungal infection. Merely one patient was detected as tuberculous pleural effusion in the late period of 8 months. The current study results in this concern are in accordance with those in the preceding literature. In the previous study found that among patients who underwent liver transplantation, 15.5% developed HAP in the ICU, (17.4%) of them died whereas in the ICU.<sup>27</sup> In an

additional cohort study, 8.3% were detected with HAP in the ICU,<sup>28</sup> pneumonia required longer ICU stay and accompanied by a greater mortality percentage in the hospital. Furthermore, lung infection has similarly been detected as the main reason for ICU readmission during the time of hospital stay duration after hepatic transplantation.<sup>28</sup>

Pulmonary edema is defined by the accumulation and addition of fluid in the alveoli and the interstitium of the lung, while pleural effusion is the accumulating fluid inside the pleural sac. Atelectasis is defined as loss of volume in the anatomical area of the lung. Pleural effusion and atelectasis are the utmost common chest problems after LT. Pleural effusion is generally found on the right side and is usually self-limiting it decreases through time postoperatively. Surgical intervention, hypoalbuminemia, elevated fluid inputs during surgery, long surgery time, insufficient deep inspiration due to a major incision, and postoperative pain are the main causes that result in early postoperative atelectasis and pleural effusion.<sup>29</sup>

Pleural effusions have been found to be the most common post-liver transplantation pulmonary complications. Although the exact etiology is unclear, a number of mechanisms have been proposed including injury to the right hemidiaphragm that can lead to transection of the hepatic lymphatics, perioperative infusion of blood products, hypoalbuminemia, and atelectasis.<sup>1</sup> Atelectasis is a noninfectious post-liver transplantation pulmonary complications with an incidence ranging from 17% to 87.6%. It is often directly related to surgical technique (i.e., diaphragmatic dissection, caval anastomosis) which can result in injury to the right phrenic nerve.<sup>1</sup>

In the present work, a total of 69 patients who submitted to LT, 10 (14.5%) experienced pulmonary edema through ICU stay and they have relatively prolonged ventilator dependency and ICU stay. 17 patients (24.6%) developed pleural effusion within three days following surgery. 37 patients (53.6%) experienced atelectasis radiologically within 10 days after LT. In a new cohort study, among ninety patients who submitted to LT, (17.8%) had pulmonary edema throughout the ICU stay, (37.4%) experienced pleural effusion up to two days after surgery.<sup>2</sup> In another cohort study, (64.3%) developed atelectasis one week after LT.<sup>29</sup>

Transfusion-related acute lung injury (TRALI) is a serious complication of blood transfusion and is among the leading causes of transfusion-related morbidity and mortality in most developed countries.<sup>30</sup> In the current study one patient had suffered from hypoxemia compatible with TRALI throughout

the surgery and had a relatively long ventilator dependency and ICU stay. In a recent cohort, 1.4% of patients had hypoxemia of TRALI intraoperatively.<sup>31</sup>

Transfusion related ALI is not easy to avoid, but some approaches may be worth-while to think through; for instance, understanding the patient's exact clinical risk factors for TRALI, optimizing and managing the patients before LT in terms of preoperative haemoglobin, haematocrit, preoperative platelet count, and fibrinogen levels.<sup>32</sup>

#### 4.1. Conclusions

Pulmonary complications before and after hepatic transplantation are public, miscellaneous, and actually have a deleterious effect on patient consequences and outcomes. Considered by a variable clinical appearance, and in the majority of cases, specific symptoms are absent. Assiduous selection of liver transplant candidates for hepatopulmonary syndrome and portopulmonary hypertension is fundamental for their best management and accomplishment of higher rates of survival after liver transplant. Also, the occurrence of hepatic hydrothorax does not indicate more postoperative complications of liver transplantation.

#### Authors contributions

T.S.G.: concept, acquisition of data, writing, reviewing, and publishing. M.W.E.: acquisition of data and reviewing. The authors have read, reviewed, and approved the final manuscript. E.A.: concept, and acquisition of data.

#### Conflict of interest

There are no conflicts of interest.

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