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**Current state of medical tourism involving liver transplantation-the risk of infections and potential complications**

Neupane R *et al*. Transplant tourism

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**Abstract**

Liver transplant has been shown to significantly improve mortality and quality of life in various liver diseases such as acute liver failure, end-stage liver disease, and liver cancer. While the organ transplant demand is continuing to rise, the organ donation supply remains unmatched. The organ shortage, high cost, and long waiting lists have stimulated a desire for routes that may be unethical. This process which is named transplant tourism is the term used to describe traveling to another country to purchase an organ for transplant. Liver transplant tourism has been associated with post-transplant complications and higher mortality compared to a domestic liver transplant. Improper pre-and post-transplant infectious screening, inadequate opportunistic infection prophylaxis, and loss to follow-up were noted in patients who travel abroad for a liver transplant. It is crucial to understand the risk of transplant tourism to prevent morbidity and mortality.

**Key Words:** Commercial transplant; Liver transplant; Organ tourism; Transplant tourism

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**Core Tip:** Liver transplant tourism can be associated with higher post-operative infections, biliary complications, and mortality compared to a domestic liver transplant. Pre-transplant education about the risk of liver transplant tourism and post-transplant management is essential to improve the patients' outcomes.

**INTRODUCTION**

***Liver disease and the role of transplantation***

Acute liver failure, a rare and rapid deterioration of liver function in patients without pre-existing liver disease, is commonly caused by drug-related hepatotoxicity and viral hepatitis[1,2]. Without the transplant, mortality ranges from 26.7%-80%[3,4]. Chronic liver disease is frequently caused by non-alcoholic steatohepatitis, alcoholic and viral hepatitis, leading to cirrhosis and impaired function[5]. The immense morbidity and mortality of end-stage liver disease place a significant healthcare burden causing the liver transplant–its only ‘cure’–the second most common transplanted organ globally[6-9].

Liver transplant has been shown to improve mortality and quality of life in various liver diseases such as acute liver failure, end-stage liver disease, liver cancer, liver disease with hepatopulmonary syndrome, and Porto-pulmonary hypertension[10,11]. Moreover, patients with metabolic disorders such as alpha 1-antitrypsin deficiency, familial amyloidosis, glycogen storage disease, hemochromatosis, and Wilson disease are also considered liver transplant candidates[11].

According to the United States Department of Health and Human Services, about 180000 liver transplantations were performed until 2020. While the organ transplant demand is continuing to rise, the supply remains unmatched. In 2018, the number of new registrants for the liver transplant waitlist in the United States was 11844, while 8250 liver transplants were performed[12]. The European Union has also stated a similar predicament with a severe donor shortage. This problem has been a constant stimulus for alternative–not so legal–pathways to obtain organ transplants.

**Transplant tourism**

According to World Health Organization, transplant tourism is the term used to describe traveling to another country to purchase an organ for transplant[13]. Travel for transplantation was defined by the 2018 edition of the Declaration of Istanbul on Organ Trafficking and Transplant Tourism as the movement of the person across jurisdictional borders for transplant purposes and considered transplant tourism if it is related to trafficking humans for organ removal intention or trafficking in human organs, or if the resources dedicated to providing transplants to non-resident patients undermine the country’s ability to supply transplant for people in its own country[14]. Transplant tourism can be divided into four models (Figure 1). First, the donor and recipient who are from the same country travel to another country for transplantation. Second, the donor travels to the country where the recipient resides. Third, the recipient travels to the country that the donor resides. Forth, the donor and recipient from different countries travel to the third country for transplantation[15]. Transplant tourism is a rampant phenomenon that needs more undivided attention. It accounts for approximately 10%-20.6% of global transplantation[16,17].

According to a national United States survey, many foreign transplants included young and male gender Asians with non-resident alien status[18]. Most of the countries that patients traveled to for transplant tourism were China, the Philippines, or India[18]. An interesting study from Syria pointed out the effects of a law passed in 2003 which legalized the use of organs from deceased donors, benefited patients, and increased commercialization as the poor used it as a means for monetary gain[19]. The formulation of law cannot be completed without enacting the regulation. The exploitation of the poorer population who give up organs for monetary benefit cannot be ignored. Although reports on tourism related to transplant have continued to decrease after great interest in the initial decade at the start of the 21st century, the lack of data is obvious as there is zero probability of anything remotely illegal to be documented. There is a great paucity of data involving liver transplantation pursued through illegal means and international travel for medical tourism for organ procurement. Most of the current data available is on renal transplantation. There has been a report of end-stage liver disease patients who traveled from Saudi Arabia and Egypt to China for liver transplantation due to lower associated financial burden and shorter waiting time[20]. From 2000 to 2016, a total of 1229 Korean patients traveled overseas for liver transplants based on the Korean Network for Organ Sharing. Of these, 98% of the patients underwent liver transplants in China[21]. In Taiwan, 5%-24.5% of patients who underwent liver transplants came from abroad[22,23].

From 2013 to 2016, 2806 patients who were non-United States citizens/non-United States residents registered for an organ transplant in the United States[24]. Of these patients, 1149 patients were foreigners who traveled to the United States for transplantation purposes. Deceased donor liver transplants were conducted in more than 5% of non-United States citizen/non-United States resident patients[24]. Liver transplant tourism is not limited to adult patients and can also be found in the pediatric population. In a study from Taiwan, pediatric cases comprised 79% of all foreign living donor liver transplant cases[22]. Liver transplant tourism can be costly. The price of liver transplants ranges from $40000 to $300000 which is higher than kidney transplants[17].

**Outcome**

The transmission of infectious diseases is one of the problems related to liver transplant tourism (Table 1) that can occur due to the lack of proper evaluation and management before and after the transplant for both donor and recipient[25]. Donor risks have been studied in detail and associated morbidity and mortality have been established. The people who remain vulnerable to trafficking, putting themselves at increased risks of surgical complications, infections, and increased mortality with ‘less intensive’ and ‘poorly regulated’ protocols need to be protected. Most of the time, this certain group of people appears vulnerable due to the existing inequities in health care. The financial drain resulting from this is bound to impact subsequent health care post-transplant, which carries significant importance. There have been reports of a lack of screening for even general pathogens like hepatitis-causing viruses. Thus, it compromises the general principles and practices which are crucial for such a sensitive procedure.

According to questionnaires from severe United Kingdom liver transplant centers, the top destinations for patients who traveled abroad for liver transplant were China, Egypt, India, followed by South Africa, France, and the United States[26]. This report showed that patients underwent liver transplants without or with unknown screening for hepatitis B and C viruses in some places. Unknown screening is also noted for carbapenemase-producing Enterobacteriaceae, cytomegalovirus, varicella-zoster virus, and Epstein-Barr virus. The majority of intraoperative and post-transplant prophylaxis in these patients is even unknown[26]. Indigenous infections such as malaria, Zika, rabies may be able to transmit through commercial transplant. Compared to domestic transplants in Saudi Arabia, overseas transplants in China showed a higher rate of sepsis (9.5% *vs* 0.83%) and acquired hepatitis B infection (5.4% *vs* 0%) following transplantation[20]. Surgical procedure complications can be difficult to manage by the new surgeon who did not perform the transplant for the patient in the first place. Compared to domestic transplantation, patients who received transplants abroad in China had significantly higher biliary complications (32.4% *vs* 11.7%) and significantly higher post-transplant interventions[20].

An eleven-year retrospective study from Taiwan demonstrated significant discrepancies between domestic and foreign liver transplants and their outcomes, with the latter faring worse mainly attributed to malignancy and liver disease. Survival rates within the 1st, 5th, and 10th year of the Taiwanese patients who received liver transplants domestically *vs* abroad were 89.2%, 79.5%, 75.2% *vs* 79.8%, 62.3%, and 49.9%, respectively[23]. An unfavorable outcome of transplant tourism was also noted in China. One- and three-year survival rates of liver transplants were 83% and 62% for Saudi and Egyptian patients who received a liver transplant in China while 92% and 84% were reported for domestic transplants in Saudi Arabia[20]. In the United States, post-liver transplant outcomes of non-United States citizen/non-United States resident were comparable to those of a United States citizen/United States resident, except the former group which had an increased risk of being lost to follow-up[27]. The significant influx of Taiwanese people to China appeared to decrease after the Human Organ Transplant Act was passed in 2007. This followed suit by Taiwan in 2015 when they passed amendments to the act by punishing organ brokers, and those patients received illegal transplants[23].

**Clinical Implications**

This article provided an overview of liver transplant tourism and outcomes.

**CONCLUSION**

Liver transplant has been shown to improve mortality in various advanced liver diseases. However, due to the shortage of organ donations, patients may seek liver transplant tourism. To prevent liver transplant tourism and its ongoing complications, it is crucial to educate patients regarding the risks of transplant tourism, the importance of proper screening, transplant center follows ups and liver transplant tourism morbidity and mortality. While efforts have been made at innumerable national and international platforms, more aggressive implementations to raise the awareness of organ donations are needed to overcome the rise in liver transplant tourism.

**REFERENCES**

1 **European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu.;** Clinical practice guidelines panel, Wendon, J; Panel members, Cordoba J, Dhawan A, Larsen FS, Manns M, Samuel D, Simpson KJ, Yaron I; EASL Governing Board representative, Bernardi M. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. *J Hepatol* 2017; **66**: 1047-1081 [PMID: 28417882 DOI: 10.1016/j.jhep.2016.12.003]

2 **Grande RG**. Liver Transplantation in Acute Liver Failure: Indications and Outcome. *Liver Res Clin Manag* 2018; **8** [DOI: 10.5772/intechopen.72664]

3 **Hey P**, Hanrahan TP, Sinclair M, Testro AG, Angus PW, Peterson A, Warrillow S, Bellomo R, Perini MV, Starkey G, Jones RM, Fink M, McClure T, Gow P. Epidemiology and outcomes of acute liver failure in Australia. *World J Hepatol* 2019; **11**: 586-595 [PMID: 31388400 DOI: 10.4254/wjh.v11.i7.586]

4 **Marudanayagam R**, Shanmugam V, Gunson B, Mirza DF, Mayer D, Buckels J, Bramhall SR. Aetiology and outcome of acute liver failure. *HPB (Oxford)* 2009; **11**: 429-434 [PMID: 19768148 DOI: 10.1111/j.1477-2574.2009.00086.x]

5 **Asrani SK,** Devarbhavi H, Eaton J, Kamath PS. The burden of liver diseases in the world. *J Hepatol* 2019; **70**: 151–171 [PMID: 30266282 DOI: 10.1016/j.jhep.2018.09.014]

6 **Moon AM**, Singal AG, Tapper EB. Contemporary Epidemiology of Chronic Liver Disease and Cirrhosis. *Clin Gastroenterol Hepatol* 2020; **18**: 2650-2666 [PMID: 31401364 DOI: 10.1016/j.cgh.2019.07.060]

7 **Vardell E**. FastStats: a public health statistics database. *Med Ref Serv Q* 2014; **33**: 195-201 [PMID: 24735268 DOI: 10.1080/02763869.2014.897520]

8 **Centers for Disease Control and Prevention.** National Center for Health Statistics. Underlying Cause of Death, 1999-2019 on CDC WONDER Online Database [Internet]. 2020. [cited 6 February 2021]. Available from: https://wonder.cdc.gov/controller/datarequest/D76;jsessionid=0994DFC00C5AFF6DCC7962AE88A6#Citation

9 **GODT.** Organ donation and transplantation activities 2016. [cited 7 February 2021]. Available from: http://www.transplant-observatory.org/download/2016-activity-data-report/

10 **Hager A**, Mager D, Robert C, Nicholas D, Gilmour S. Health-Related Quality of Life 10 Years after Liver Transplantation: A Longitudinal Retrospective Review. *Diagnostics (Basel)* 2021; **11** [PMID: 33445652 DOI: 10.3390/diagnostics11010111]

11 **Martin P**, DiMartini A, Feng S, Brown R Jr, Fallon M. Evaluation for liver transplantation in adults: 2013 practice guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. *Hepatology* 2014; **59**: 1144-1165 [PMID: 24716201 DOI: 10.1002/hep.26972]

12 **Kwong A**, Kim WR, Lake JR, Smith JM, Schladt DP, Skeans MA, Noreen SM, Foutz J, Miller E, Snyder JJ, Israni AK, Kasiske BL. OPTN/SRTR 2018 Annual Data Report: Liver. *Am J Transplant* 2020; **20 Suppl s1**: 193-299 [PMID: 31898413 DOI: 10.1111/ajt.15674]

13 **Shimazono Y**. The state of the international organ trade: a provisional picture based on integration of available information. *Bull World Health Organ* 2007; **85**: 955-962 [PMID: 18278256 DOI: 10.2471/blt.06.039370]

14 **The declaration of Istanbul on organ trafficking and transplant tourism.** About "The Declaration of Istanbul". [cited 7 February 2021]. Available from: https://www.declarationofistanbul.org/the-declaration

15 **Hindi Z**, Congly S, Tang E, Skaro A, Brahmania M. Liver Transplant Tourism. *Liver Transpl* 2020; **26**: 276-282 [PMID: 31765044 DOI: 10.1002/lt.25692]

16 **WHO.** WHO proposes global agenda on transplantation [Internet]. [cited 7 February 2021]. Available from: http://www.who.int/news/item/30-03-2007-who-proposes-global-agenda-on-transplantation

17 **Ambagtsheer F,** de Jong J, Bramer WM, Weimar W. On Patients Who Purchase Organ Transplants Abroad. *Am J Transplant* 2016; **16:** 2800–2815 [PMID: 26932422 DOI: 10.1111/ajt.13766]

18 **Merion RM**, Barnes AD, Lin M, Ashby VB, McBride V, Ortiz-Rios E, Welch JC, Levine GN, Port FK, Burdick J. Transplants in Foreign Countries Among Patients Removed from the US Transplant Waiting List. *Am J Transplant* 2008; **8**: 988-996 [PMID: 18336701 DOI: 10.1111/j.1600-6143.2008.02176.x]

19 **Saeed B.** The impact of living-unrelated transplant on establishing deceased-donor liver program in Syria. *Exp Clin Transplant* 2014; **12:** 494-497 [PMID: 25299377]

20 **Allam N**, Al Saghier M, El Sheikh Y, Al Sofayan M, Khalaf H, Al Sebayel M, Helmy A, Kamel Y, Aljedai A, Abdel-Dayem H, Kenetman NM, Al Saghier A, Al Hamoudi W, Abdo AA. Clinical outcomes for Saudi and Egyptian patients receiving deceased donor liver transplantation in China. *Am J Transplant* 2010; **10**: 1834-1841 [PMID: 20353478 DOI: 10.1111/j.1600-6143.2010.03088.x]

21 **Ahn HJ**, Kim HW, Han M, Jeon HJ, Kwon OJ, Ahn C. Changing Patterns of Foreigner Transplants in Korea and Overseas Organ Transplants Among Koreans. *Transplantation* 2018; **102**: 310-317 [PMID: 28863044 DOI: 10.1097/TP.0000000000001935]

22 **Kabiling CS**, Chen CL, Concejero A, Wang CC, Wang SH, Lin CC, Liu YW, Yong CC, Jawan B, Cheng YF. Section 18. Professional framework for liver transplantation for overseas patients: traveling for living donor liver transplantation. *Transplantation* 2014; **97 Suppl 8**: S75-S79 [PMID: 24849841 DOI: 10.1097/01.tp.0000446282.66675.24]

23 **Tsai DF**, Huang SW, Holm S, Lin YP, Chang YK, Hsu CC. The outcomes and controversies of transplant tourism-Lessons of an 11-year retrospective cohort study from Taiwan. *PLoS One* 2017; **12**: e0178569 [PMID: 28575014 DOI: 10.1371/journal.pone.0178569]

24 **Delmonico FL**, Gunderson S, Iyer KR, Danovitch GM, Pruett TL, Reyes JD, Ascher NL. Deceased Donor Organ Transplantation Performed in the United States for Noncitizens and Nonresidents. *Transplantation* 2018; **102**: 1124-1131 [PMID: 29329187 DOI: 10.1097/TP.0000000000002086]

25 **Buchan CA**, Kotton CN; AST Infectious Diseases Community of Practice. Travel medicine, transplant tourism, and the solid organ transplant recipient-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant* 2019; **33**: e13529 [PMID: 30859623 DOI: 10.1111/ctr.13529]

26 **Kerr Winter B**, Odedra A, Green S. A questionnaire based assessment of numbers, motivation and medical care of UK patients undergoing liver transplant abroad. *Travel Med Infect Dis* 2016; **14**: 599-603 [PMID: 27640117 DOI: 10.1016/j.tmaid.2016.09.004]

27 **Ferrante ND**, Goldberg DS. Transplantation in foreign nationals: Lower rates of waitlist mortality and higher rates of lost to follow-up posttransplant. *Am J Transplant* 2018; **18**: 2663-2669 [PMID: 29981179 DOI: 10.1111/ajt.15005]

**Footnotes**

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**Figure Legends**



**Figure 1 Transplant tourism models.** 1: Donor and recipient from the same country travel to another country for transplantation; 2: Donor travels to the country where the recipient resides; 3: Recipient travels to the country that the donor resides; 4: Donor and recipient from different countries travel to the third country for transplantation.

**Table 1 Problems related to liver transplant tourism compared to domestic transplant[20,25,26]**

|  |  |
| --- | --- |
|  | **Previous reported problems related to liver transplant tourism**  |
| 1 | Higher surgical procedure complications |
| 2 | Inadequate pre-operative infection screening, prophylaxis documentation and higher post-operative infections rate |
| 3 | Higher mortality |



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