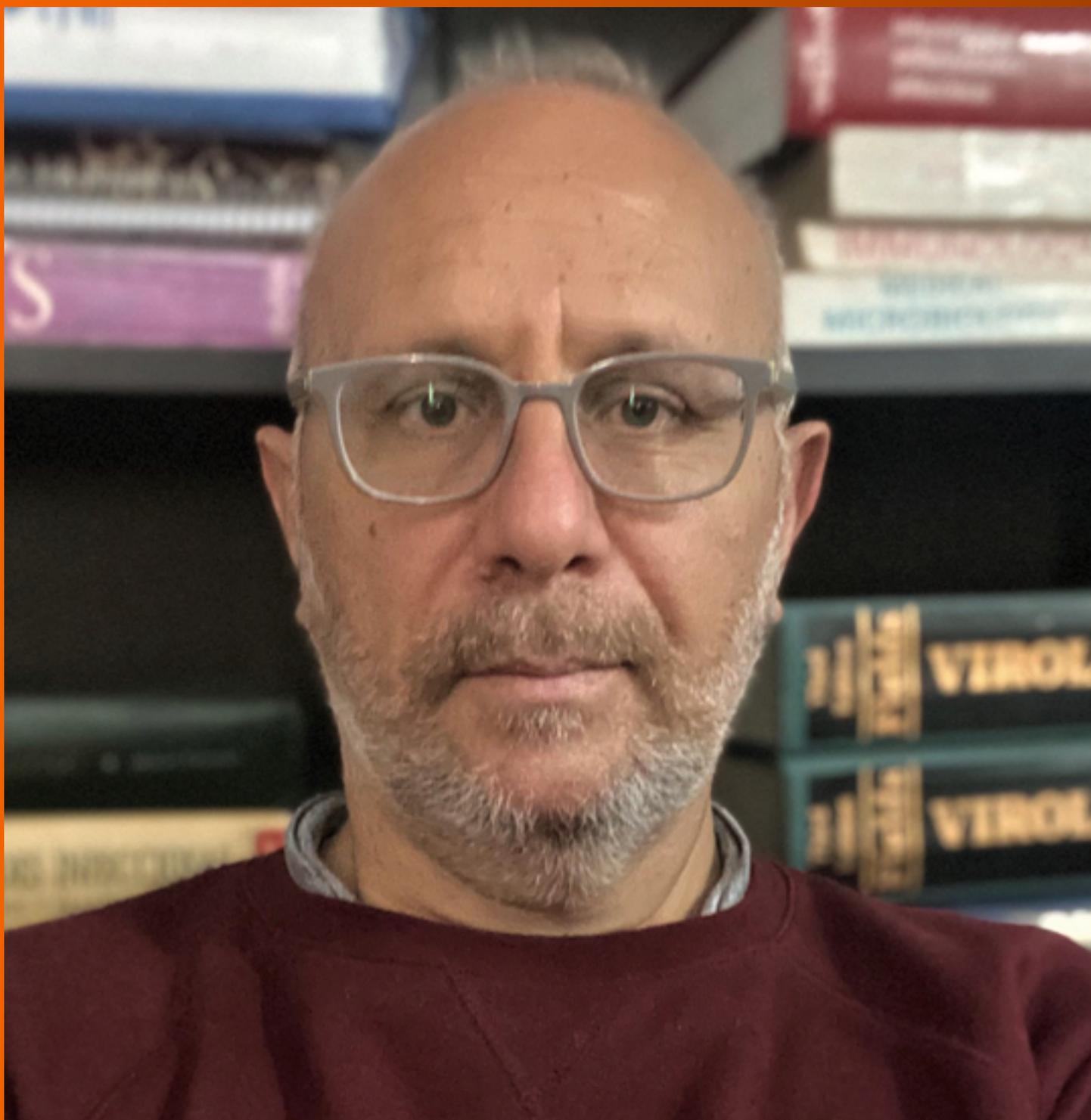


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EDITORIAL

- 717 Current state of medical tourism involving liver transplantation-the risk of infections and potential complications
Neupane R, Taweeseed PT, Anjum H, Surani S

OPINION REVIEW

- 723 Hepatitis E virus in professionally exposed: A reason for concern?
Mrzljak A, Balen I, Barbic L, Ilic M, Vilibic-Cavlek T

REVIEW

- 731 Clinical algorithms for the prevention of variceal bleeding and rebleeding in patients with liver cirrhosis
Pfisterer N, Unger LW, Reiberger T
- 747 Liver injury associated with drug intake during pregnancy
Kamath P, Kamath A, Ullal SD

MINIREVIEWS

- 763 Racial differences in prevalence and severity of non-alcoholic fatty liver disease
Bonacini M, Kassamali F, Kari S, Lopez Barrera N, Kohla M
- 774 Torsion of spleen and portal hypertension: Pathophysiology and clinical implications
Jha AK, Bhagwat S, Dayal VM, Suchismita A
- 781 Impact of coronavirus disease 2019 on prevention and elimination strategies for hepatitis B and hepatitis C
Rehman ST, Rehman H, Abid S

ORIGINAL ARTICLE**Retrospective Study**

- 790 Prevalence and risk factors of steatosis and advanced fibrosis using transient elastography in the United States' adolescent population
Atsawarungruangkit A, Elfanagely Y, Pan J, Anderson K, Scharfen J, Promrat K

SYSTEMATIC REVIEWS

- 804 Safety of liver resection in patients receiving antithrombotic therapy: A systematic review of the literature
Fujikawa T

META-ANALYSIS

- 815** Effects of intragastric balloon placement in metabolic dysfunction-associated fatty liver disease: A systematic review and meta-analysis

de Freitas Júnior JR, Ribeiro IB, de Moura DTH, Sagae VMT, de Souza GMV, de Oliveira GHP, Sánchez-Luna SA, de Souza TF, de Moura ETH, de Oliveira CPMS, Bernardo WM, de Moura EGH

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WJH mainly publishes articles reporting research results and findings obtained in the field of hepatology and covering a wide range of topics including chronic cholestatic liver diseases, cirrhosis and its complications, clinical alcoholic liver disease, drug induced liver disease autoimmune, fatty liver disease, genetic and pediatric liver diseases, hepatocellular carcinoma, hepatic stellate cells and fibrosis, liver immunology, liver regeneration, hepatic surgery, liver transplantation, biliary tract pathophysiology, non-invasive markers of liver fibrosis, viral hepatitis.

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

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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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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.

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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

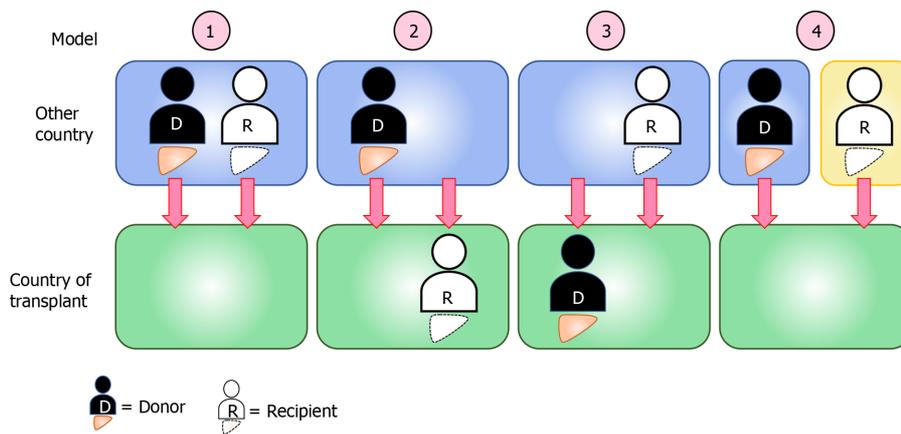


Figure 1 Transplant tourism models. 1: Donor and recipient from the same country travel to another country for transplantation; 2: Donor travels to the country where the recipient resides; 3: Recipient travels to the country that the donor resides; 4: Donor and recipient from different countries travel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

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

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

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.

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