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Liver Transplants from Donors with Schistosomiasis: Clinical and Epidemiological Profile of Patients at Clinics Hospital of São Paulo, Brazil

Transplantes Hepáticos de Doadores com Esquistossomose: Perfil Clínico e Epidemiológico de Pacientes do Hospital das Clínicas, São Paulo, Brasil

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Abstract

Organ transplantation is a surgical procedure that consists of awarding an organ. Considering that the transplantation of an organ or tissue is very competitive, due to the low rate of donors and as the function of the liver is preserved even in controlled schistosomatic fibrosis, it is possible to donate the organ even with the liver infected by verminosis. By analyzing the prevalence and evolution of liver donors with schistosomiasis in liver transplants performed at Hospital das Clínicas, Faculty of Medicine, University of São Paulo - HCFMUSP. This is a descriptive study, consisting of a series of cases, with a retrospective and cross-sectional analysis. The study evaluated the medical records of patients being followed up at the Liver Transplant Outpatient Clinic, at HCFMUSP, from January 2002 to December 2020. The Department of Pathology at USP found 16 patients with records of schistosomiasis reports, of which only one was effective as a donor, since the other patients were excluded due to the state of law of the organ. An analysis showed that almost all donors were men with schistosomiasis with a mean age of 52.55 years. In this context, there was a prevalence of a case of a liver donor with the hepatointestinal form of schistosomiasis, later the organ was transplanted, and the recipient, presented a good evolution until this moment, having been analyzed clinically and laboratory. It is noteworthy that this is the first HCFMUSP study that evaluates liver donors with schistosomiasis mansoni and the evolution of the respective recipient.

Keywords: Schistosomiasis. Liver Transplantation. Epidemiology.

Resumo

O transplante de órgãos é um procedimento cirúrgico que consiste na reposição de um órgão. Haja vista que o transplante de um órgão ou tecido é muito concorrido, em decorrência da baixa taxa de doadores e como a função do fígado está preservada mesmo na fibrose esquistossomatica avançada é possível doador o órgão mesmo com o fígado infectado pela verminose. O objetivo desse estudo foi analisar a prevalência e evolução de doadores fígado, portadores de esquistossomose, nos transplantes hepáticos realizados no Hospital das Clínicas, Faculdade de Medicina da Universidade de São Paulo - HCFMUSP. Trata-se de um estudo descritivo, composto por uma série de casos, sendo a analise retrospectiva e de corte transversal. O estudo avaliou os prontuários de pacientes em seguimento no Ambulatório de Transplante hepático, do HCFMUSP, no período de janeiro de 2002 a dezembro de 2020. O departamento de Patologia da USP constatou 16 pacientes com registros de laudos de esquistossomose, dos quais somente um foi efetivado como doador, uma vez que os outros pacientes foram excluídos em razão do estado de deterioração do órgão. A análise mostrou que quase a totalidade dos doadores eram homens com esquistossomose com idade média de 52,55 anos. Dentro desse contexto, houve a prevalência de um caso de um doador hepático portador da forma hepatointestinal de esquistossomose, posteriormente o órgão foi transplantado, e o receptor, apresentou uma boa evolução até este momento tendo sido analisado clinicamente e laboratorialmente. Vale ressaltar, que este é o primeiro estudo do HCFMUSP que avalia doadores de hepáticos portadores de esquistossomose mansoni e a evolução do respectivo receptor.

Palavras-chave: *Esquistossomose. Transplante de Fígado. Epidemiologia.*

1 Introduction

Organ transplantation is a surgical procedure that involves replacing a diseased person's (recipient) organ (heart, liver, pancreas, lung, kidney) or tissue (bone marrow, bones, corneas) with a normal organ or tissue from a donor, whether living or deceased. There are two types of donors: living and deceased[1]. A living donor can be anyone who agrees to donate, provided it does not harm their own health. They can donate one kidney, a portion of the liver, bone marrow, or a portion of a lung[1].

The removal of organs and tissues must follow legislation that requires a diagnosis of brain death, confirmed and recorded by at least two physicians who are not part of the removal and transplant teams. Additionally, it is necessary to use clinical and technological criteria defined by a resolution of the Federal Council of Medicine, proving brain death conclusively[2].

According to the Brazilian Association of Organ Transplants (ABTO), the total number of transplants performed (cornea, lung, heart, kidney, liver) in 2019 was 23,657 transplants. In descending order of frequency: Cornea (14,943), Kidney (6,283), Liver (2,245), Heart (380), and

Lung (106). The estimated projections were approximately 70% higher than the total number of transplants[3].

Schistosomiasis is considered an endemic disease, transmitted by trematode mollusks of the genus Schistosoma. This parasitic disease is highly neglected in some states and is currently one of the most prevalent parasitic diseases worldwide[4,5].

The clinical manifestations of chronic schistosomiasis include intestinal disease, hepatosplenic disease, and manifestations associated with portal hypertension. During the chronic phase, it is estimated that 50 to 60% of cases are symptomatic, and five to 10% present the most severe forms of the disease with irreversible damage to organs[6].

The hepatosplenic form of the disease manifests early, during the first months of parasitic infection, with involvement and enlargement of the liver due to granulomatous lesions. Hepatomegaly occurs in about 15 to 20% of infected individuals, more frequently in children. In subsequent stages of infection, pre-sinusoidal blockage results in portal hypertension and splenomegaly. Portal hypertension can lead to the development of varices in the lower end of the esophagus and other sites. Liver function usually remains normal for a considerable time; however, in late-stage disease, typical fibrosis changes occur along with deterioration of liver function[6].

As the liver function is preserved even in advanced schistosomiasis fibrosis, liver transplantation will rarely be indicated in schistosomiasis unless complicated by advanced liver cirrhosis or hepatocellular carcinoma of another etiology, such as active chronic viral hepatitis[7].

Schistosoma mansoni is the main causative agent of Schistosomiasis mansoni in Brazil and is found in 18 states and the Federal District. Schistosomiasis is endemic in the North and Northeast regions, although currently, almost all states have reported cases. The Northeast and Midwest regions are the most affected, as they have a high presence of transmitting mollusks. Additionally, poor sanitation and low human development index contribute to the spread of the disease[8].

A cirrose hepática, which is responsible for irreversible damage to liver cells, is the most common indication for liver transplantation in adults and children. Cirrhosis occurs when the organ is damaged and its recovery occurs through anaplastic cells, resulting in scarring and impaired organ functionality due to the new cellular conformation. The main conditions that lead to the need for liver transplantation include: Primary Biliary Cirrhosis, Primary Sclerosing Cholangitis, Cirrhosis, Budd-Chiari Syndrome, Alcoholism, Fulminant Hepatic Failure, Hepatitis, and Liver Tumors[9].

In patients with acute liver failure, the criteria used for transplantation are different. The urgency of liver transplantation in acute form requires that patients receive the organ as quickly as possible. In these cases, there is no need for transplant waiting list scales, as these patients are prioritized. Among the causes that require urgency in liver transplantation are: Fulminant acute liver failure; Primary non-function of the transplanted graft; Anhepatic patients due to trauma.

After the donor's death, the liver enters ischemia within 12 hours, meaning this is its maximum lifespan, which governs the time to find a recipient and transplant it[10].

According to data gathered by ABTO in 2019, there is a significant difference between the estimated need and the transplants actually performed. The estimated need for liver transplants in 2019 was 5,212 transplants, while the actual transplants performed were 2,245. This highlights the significant shortage of organs to meet the number of recipients in need of these organs[3].

Liver transplantation represents the only option to reverse liver failure and its complications in patients with advanced-stage cirrhosis. Although transplantation is a demanding procedure, most patients return to a quality of life close to normal within three to six months. This is made possible mainly by improvements in immunosuppressive therapy in terms of tolerance and effectiveness. However, due to the scarcity of deceased donors, strict criteria are necessary for selecting potential transplant candidates[1].

In a recent study at Hospital AC Camargo / Hospital Sírio-Libanês - São Paulo, 482 pediatric liver transplants were performed, of which six cases of schistosomiasis were identified. Transmission occurred through infected grafts. During the three years of follow-up, there was uncomplicated recovery for the donors. The donors were treated with Praziquantel and were instructed to avoid risk factors for reinfection. No specific treatment for schistosomiasis was given to the recipients. Only the donors should be treated for the infection, due to the parasite's life cycle and the therapeutic target of Praziquantel[11].

The aim of the study was to analyze the prevalence of liver donors with schistosomiasis in liver transplants performed at the Hospital das Clínicas, Faculty of Medicine, University of São Paulo, from January 2008 to December 2020.

2 Material and Methods

It is a descriptive study - a case series, retrospective, and cross-sectional, which evaluated the medical records of patients followed up at the Liver Transplant Outpatient Clinic of HCFMUSP from January 2002 to December 2020. CAEE: 52545421.8.0000.0068.

The data collection was conducted using a standardized form for collecting data from donors and recipients, utilizing the Google Forms platform (Google, Mountain View, California, USA).

After the data collection, the variables investigated in the donor and recipient forms were analyzed and described. For the donor form, these variables included: patient's age; gender; municipality and state of origin; registration number;

transplant date; date of death (if applicable); cause of death diagnosis; description of the report (periportal fibrosis, Schistosoma egg granuloma, *Schistosoma granuloma* without eggs); and treatment. For the recipient form, the variables included: patient's age; gender; municipality and state of origin; registration number; transplant date; date of death (if applicable); whether treatment was needed; and evidence of infection.

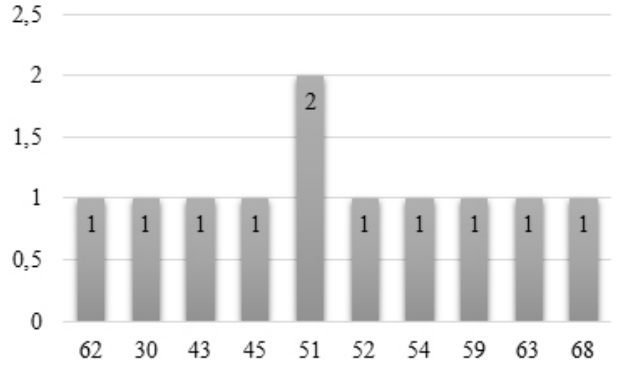
Parallely, an investigation of epidemiological data was conducted in the Notifiable Diseases Information System (SINAN) to analyze regional epidemiology and guide the study from the years 2008 to 2017.

3 Results and Discussion

The liver transplant database of FEMUSP conducted two thousand transplants over 12 years, which constituted the research universe. The analysis of medical record systems from 2008 to 2020 by the Pathology Department of USP identified 16 patients with schistosomiasis reports who were candidates as potential donors. Out of these, only three patients were considered potential effective liver donors. Among these three, only one was confirmed as a donor, as the other two patients were excluded due to organ deterioration.

The analysis showed that potential liver donors with schistosomiasis were men in 94% of cases, with an average age of 52.55 years (Figure 1).

Figure 1 - Frequency of Ages of Donor Candidates



Source: research data.

The analysis of anatomopathological data (Table 1) from the found effective donor revealed some alterations. In the context of this study, the alteration in the examination is the presence of Epithelioid Granuloma with giant cells and non-viable eggs of *Schistosoma Sp*., indicating chronic infection, as there was a cellular immunity response. The organ did not require pre-transplant treatment, as the eggs were not viable. During the analysis of anatomopathological data from the found effective donor, some Macroscopic alterations in the organ were observed, which can be seen in Table 1.

Table 1 - Pathological examination report of the donor

Characteristic		Classification	Conclusion
Macroscopic Analysis	Mild Steatosis	10-15%	Accumulation of fat in hepatocytes.
	Siderosis	Grade I	Accumulation of iron in the organ
	Reperfusion	Grade II	Due to chronic ischemia in the organ
	Evidence of Schistosomiasis	Epithelioid granuloma with giant cells and non-viable *Schistosoma sp.* egg.	Chronic Schistosomiasis infection with cellular immune response

Source: research data.

Upon observing Chart 2, it was possible to notice a decrease in the incidence of schistosomiasis in the Southeast of Brazil over the years, with a significant reduction in disease incidence from 2008 to 2017. During the analysis of the number of schistosomiasis notifications, it was observed that the state with the highest number of notifications is Minas Gerais. Between 2008 and 2017, 88,430 notifications were recorded, with Minas Gerais representing 79% of the total reported cases.

The reduction in the number of cases across the Southeast may have occurred due to various factors, including the population's use of properly treated water sources and improved sanitation over the years. Additionally, increased awareness of the disease and its risk factors likely played a role.

Table 2 - Number of notifications by state and in the Southeast

Year	MG	ES	RJ	SP	Southeast
2008	3.588	2.280	176	1.270	7.314
2009	12.487	1.891	147	1.382	15.907
2010	22.185	1.486	107	1.108	24.886
2011	11.060	664	78	1.126	12.928
2012	5.258	472	73	1.066	6.869
2013	3.815	487	98	894	5.294
2014	3.456	369	87	714	4.626
2015	3.416	411	103	520	4.450
2016	2.741	297	91	523	3.652
2017	1.725	249	74	456	2.504
Total	**69.731**	**8.606**	**1.034**	**9.059**	**88.430**

Source: research data.

The patient who received the liver was under outpatient care before the transplant with a diagnosis of hepatocellular carcinoma, and after the transplant, continued follow-up. Upon observing Table 3, which describes the patient's laboratory tests before and after the transplant, it was possible to verify an improvement in liver enzymes, indicating a good evolution of this recipient over time.

Table 3 – Laboratory tests of the recipient during outpatient follow-up

Criterion	Before Transplant	Last Post-Transplant Outpatient Appointment
Total Bilirubin	18,65 (vr: 1,2 mg/dl)	0,84
Direct Bilirubin	19,09 (vr: até 0,3mg/dl)	0,35
Gama GT	1.960 (Reference range for men: up to 85 U/L; Reference range for women: up to 38 U/L.)	28
Alkaline Phosphatase	409 (Reference range: 46 to 120 U/L)	31
Aspartate Aminotransferase (AST)	64 (Reference range for men: up to 38 U/L; Reference range for women: up to 32 U/L.)	94
Alanine Aminotransferase (ALT)	295 (Reference range for men: up to 41 U/L; Reference range for women: up to 31 U/L.)	59

Source: research data.

4 Conclusion

Analyzing the profile of patients with schistosomiasis who were potential donors, a male patient with an average age of 52.55 years was found. This may indicate the awareness policy targeting younger individuals and that the national policy for combating schistosomiasis has made a difference in reducing the number of cases in the chronic form.

It is possible to infer from the data collected in this study, gathered from SINAN, that schistosomiasis may no longer be endemic in the state of São Paulo. However, the disease remains endemic in the Southeast region, especially in the state of Minas Gerais, which represents the majority of cases in the region. Due to the decreased incidence of schistosomiasis in São Paulo, individuals infected with the parasite are no longer as prone to experiencing serious health complications.

The reduction in the incidence of the disease in the Southeast of Brazil has had a positive impact on the health of the population. As the number of schistosomiasis cases decreases, there are also fewer people experiencing serious complications due to the disease.

The reduction in patients diagnosed with chronic schistosomiasis in the Southeast in recent years may have influenced the results of this study. The research focuses on patients with schistosomiasis who are effective liver donors, which are two very specific variables with reduced numbers, even in a large outpatient clinic like the Liver Transplant Outpatient Clinic of HCFMUSP.

In the analysis of national and international literature, the number of reported cases on the topic addressed is limited. One case of a liver donor with the hepatointestinal form of schistosomiasis was described, and the organ was successfully transplanted. The recipient showed good clinical and laboratory evolution following the transplant.

It is worth noting that this is the first study conducted at HCFMUSP to evaluate liver donors with Schistosomiasis Mansoni and the respective recipient's evolution. Therefore, there is a need for further studies in other transplant centers across Brazil to achieve greater national accuracy.

References

1. Ministério da Saúde. Secretaria de Vigilância em Saúde. Doação de Órgãos: transplantes, lista de espera e como ser doador. Brasília: MEC; 2020.
2. Brasil. Presidência da República. Lei nº 9.434, de 4 de fevereiro de 1997. Dispõe sobre a remoção de órgãos, tecidos e partes do corpo humano para fins de transplante e tratamento e dá outras providências. Diário Oficial da União. Brasília, 5 fev 1997.
3. ABTO. Associação brasileira de Transplante de Órgãos. Dimensionamento dos Transplantes no Brasil e em cada estado (2012-2019). São Paulo: ABTO; 2019.
4. WHO - World Health Organization. Schistosomiasis. Geneve: WHO; 2019.
5. Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. Lancet. 2018; 383(9936):2253-64.
6. King CH, Mahmoud AAF. Esquistossomose e outras infecções por trematódeos. In: Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J. Medicina Interna de Harrison. Porto Alegre: AMGH; 2017. p.1423-9.
7. Richter MN, Jaffe HL. The autoplastic transplantation of tissues into the bone marrow cavity: I. The Thymus. J Exp Med 1928;47(6):981-6. doi: 10.1084/jem.47.6.981
8. Ministério da Saúde. Vigilância em Esquistossomose Mansoni: diretrizes técnicas. Brasília: MS; 2014.
9. Castro-e-Silva Junior O, Sankarankutty AK, Oliveira GR, Pacheco E, Ramalho FS, Dal Sasso K, et al. Transplante de fígado: indicação e sobrevida. Acta Cir Bras 2002;17:83-91. doi: https://doi.org/10.1590/S0102-86502002000900018
10. Ministério da Saúde. Secretaria de Vigilância em Saúde. Portaria n 2.601 de 21 de outubro de 2009 – institui, no âmbito do Sistema nacional de Transplantes, o Plano Nacional de Implantação de Organizações de procura de órgãos e Tecidos - OPO. Brasília: MS; 2020.
11. Vincenzi R, Seda Neto J, Fonseca EA, Pugliese V, Leite KRM, Benavides MR, et al. Schistosoma mansoni infection in the liver graft: The impact on donor and recipient outcomes after transplantation. Liver Transpl 2011;17(11):1299-1303. doi: 10.1002/lt.22316., 2011.