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Hepatic alterations in kidney transplant recipients from the largest kidney transplant center in Brazil

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ABSTRACT – Background – Kidney transplant is the treatment of choice for patients with end-stage renal disease and is associated with lower mortality when compared to dialysis methods. Brazil is the country with the second largest number of kidney transplants in the world and among these patients it has been observed that liver abnormalities are common. The frequency of liver abnormalities ranges from 20–50% post-transplantation, and have an important impact on the survival and quality of life of these patients. There are scarce data about the frequency, causes and characteristics of these alterations. **Objective –** To determine the prevalence of the different causes of hepatic abnormalities in kidney transplant recipients, to associate the characteristics of these abnormalities with demographic, epidemiological and clinical variables, to compare the characteristics of hepatic alterations between different etiologies, and to evaluate possible changes in diagnosis over two different periods of time. **Methods –** Descriptive, cross-sectional observational, epidemiological study was conducted at the outpatient "Hepato-Rim"clinic of Hospital São Paulo (EPM/UNIFESP), a center providing specialized care for patients with hepatic abnormalities and underlying kidney diseases. **Results –** Five-hundred eighty-one transplant patients were evaluated. The most prevalent etiologies of liver abnormalities were hepatitis C and B, iron overload, nonalcoholic fatty liver disease (NAFLD), and drug-induced liver injury (DILI). The most common cause – hepatitis C – was analyzed in greater detail. Compared to the other causes, this infection was more frequent in older patients, female patients, and patients with a longer time since transplantation and hemodialysis. Analysis of the two periods showed that patients of period 1 (P1 – 1993 to 2005) were older and were more frequently referred because of positive serology; referral due to aminotransferases abnormalities predominated during period 2 (P2 – 2006 to 2018). The predominant diagnoses were hepatitis C and B during P1 and NAFLD and DILI during P2. **Conclusion –** Assessment of the main hepatic alterations in kidney transplant recipients is important because it permits better management of these patients in terms of diagnostic investigation and treatment and contributes to the prevention of complications in this special population.

Keywords – Kidney transplant, hepatic alterations, liver disease.

INTRODUCTION

Kidney transplant is the treatment of choice for patients with end-stage renal disease (ESRD) and is associated with lower mortality when compared to dialysis methods[1]. Infections have been the main causes of mortality during early kidney transplantation worldwide. These complications have been controlled over time and the life expectancy of kidney transplant recipients (KTR) started to increase progressively. Other causes of mortality such as cardiovascular complications, acute rejection, complications of immunosuppressive therapy and decompensation of comorbidities have also declined, especially because of advances in diagnostic and therapeutic methods[2].

Acute and chronic hepatic abnormalities have been recognized in KTR since the 1970s[3] and have contributed to the increasing morbidity and mortality of these patients. It is well known that KTR are at increased risk for viral liver diseases caused by parenterally transmitted viruses, especially because of the previous period of hemodialysis[4] when the patients were exposed to contamination with hepatitis B (HBV) or C virus (HCV) through blood transfusion or, more frequently, environmental contamination. Furthermore, in KTR the liver damage caused by these viruses is frequently aggravated by the immunosuppression[5].

Several other potential causes of liver disease are also present among KTR, such as the use of a large spectrum of medications including immunosuppressive drugs, comorbidities (diabetes, hypertension, dyslipidemia) frequently associated with non-alcoholic fatty liver disease, iron overload remaining from the dialysis period, and even alcohol abuse.

Kidney transplants are the most frequent organ transplantation in Brazil, and 95% of kidney transplants are performed within the Brazilian Unified Health System (SUS)[6]. Brazil is nowadays the country with the second largest number of kidney transplants in the world, surpassed only by the United State[7]. In 2019 6.283 kidney transplants were performed in Brazil and the largest transplant center in that year was *Hospital do Rim e Hipertensão*[8].

This hospital is the largest kidney transplant center in the world, performing up to 900 procedures annually[9]. This is more than dou-

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ble the number of procedures performed by the best international institutions of this specialty. Founded in 1998 and administrated by the *Fundação Oswaldo Ramos*, the hospital performs 20% of all kidney transplants in the country. In view of the attendance of this large number of patients, hepatic abnormalities are frequently detected, including altered liver enzymes, positive viral serology, or altered liver imaging findings. These cases are referred to hepatology specialists for investigation. The present study was undertaken to better understand the causes and characteristics of these hepatic alterations.

Therefore, the objectives of the present study were 1) to determine the prevalence of the different causes of hepatic alterations in KTR; 2) to associate the characteristics of hepatic abnormalities with demographic, epidemiological and clinical variables; 3) to compare the characteristics of the hepatic abnormalities between hepatitis C and other etiologies, and 4) to evaluate possible changes in the causes of hepatic alterations of KTR over two different periods of time.

METHODS

This is a descriptive, cross-sectional, observational, epidemiological study conducted at the outpatient "Hepato-Rim" clinic of Hospital São Paulo (EPM/UNIFESP), a center providing specialized care for patients with hepatic abnormalities and underlying kidney diseases.

Characteristics of the sample

Kidney transplant patients referred mainly by the kidney transplant outpatient clinic of *Hospital do Rim e Hipertensão* were evaluated retrospectively and prospectively.

Patients of both genders older than 18 years were included, regardless of the disease that led to kidney failure. All patients who had at least one medical consultation at the Hepato-Rim outpatient clinic between January 1993 and March 2018 were included. For the evaluation of changes over time, the characteristics of patients referred during two different periods were analyzed: P1 – from 1993 to 2005 and P2 – from 2006 to 2018.

Patients younger than 18 years, patients who lost the graft, and patients without exams defining the diagnosis in the medical record were excluded.

This study was approved by the Research Ethics Committee the from *Universidade Federal de* São Paulo with the number 3.006.733 of November 7th, 2018.

Method

The cause for referral was evaluated in all patients: positive serology, (anti-HCV, HBsAg, anti-HBc), altered enzymes (aminotransferases, alkaline phosphatase, bilirubin, and gamma-glutamyl transferase – GGT), or altered imaging findings (ultrasonography, tomography, or magnetic resonance).

Demographic, epidemiological, clinical and laboratory data were obtained from the standard medical records used for consultation at the outpatient clinic.

Variables evaluated for final diagnosis

Demographical: sex, age, naturalness; epidemiological: etiology of kidney disease, dialysis time before transplantation (in years), transplant time (in years), type of kidney graft (living or deceased donor); clinical: main comorbidities; laboratorial: alanine aminotransferase (ALT) (normal values for women <33U/L and men <41U/L), aspartate aminotransferase (AST) (normal values for women <32U/L and men <40U/L), alkaline phosphatase (FA) (normal values for women <105U/L and men <130U/L) and gamma glutamyl transferase (GGT) (normal values for women <40U/L and men <60U/L). Enzymes were expressed as an index (times upper limit of normality – ULN), iron profile (serum iron, ferritin and transferrin saturation), autoantibodies (anti-nucleus (ANA), anti-smooth muscle (AML), anti-mitochondria (AMA), Other laboratory measurements: blood count, blood glucose, bilirubin, creatinine, albumin, prothrombin time/INR, copper ceruloplasmin, TSH, immunoglobulins, Serologies (HBsAg, anti-HBc, anti-HBs and anti-HCV).

Diagnosis of hepatitis C was determined by the presence of anti-HCV positive and/or viral load or genotype detected. (Hepatitis B: presence of reagent HBsAg and/or detectable viral load, ferric overload: presence of ferritin ≥500 ng/dL and/or transferrin saturation ≥50%, non-alcoholic fatty liver disease: ultrasound alteration, liver biopsy and other etiologies ruled out, drug-induced liver injury: alteration of liver enzymes, drug use during the period of alteration and excluding other causes) The evaluation also included image exams (ultrasonography, computed tomography, magnetic resonance imaging and upper digestive endoscopy) immunosuppressive regimen; evaluation of the main immunosuppression regimens was made.

Fibrosis degree was established by liver biopsy, transient liver elastography or APRI calculation (AST to platelet ratio index – AST in times the upper limit of normal divided by the number of platelets).

Statistical analysis

Categorical variables are expressed as frequency. Numerical variables are reported as mean and standard deviation. Normality was analyzed using measures of skewness and kurtosis. The chi-squared test was used for the comparison of categorical variables. Normally distributed variables were compared by the Student *t*-test and non-normally distributed data by the nonparametric Mann-Whitney test. A level of significance of 0.05 was adopted. Descriptive levels (*P*) less than this value were considered significant. The collected data were stored and managed using the SPSS 20 program.

RESULTS

Between January 1993 and March 2018, 1558 patients were evaluated at the Hepato-Rim outpatient clinic. Of these, 964 (62%) had CKD and received conservative or dialysis treatment and 594 (38%) were KTR. Thirteen of these 594 patients had no exams reported and were excluded from the study. Thus, 581 patients were eligible for analysis (FIGURE 1).

Among the 581 patients, 383 (66%) were male and 198 (34%) were female. The mean age was 56.9±10.8 years. The patients were mainly from the southeastern region (n=282, 48.5%), followed by the northeastern region (n=152, 26.2%). Transplantation was performed with grafts of deceased donors in 52.8% and with grafts from living donors in 40.4%; no information about the type of graft was observed in 6.7% of the cases.

The etiologies of CKD were indeterminate causes in 41.7%, systemic arterial hypertension in 29.8%, nephritis in 12.9%, and diabetes mellitus in 4.3%. The mean time since transplantation was 9.7±7.05 years. These data are shown in TABLE 1.

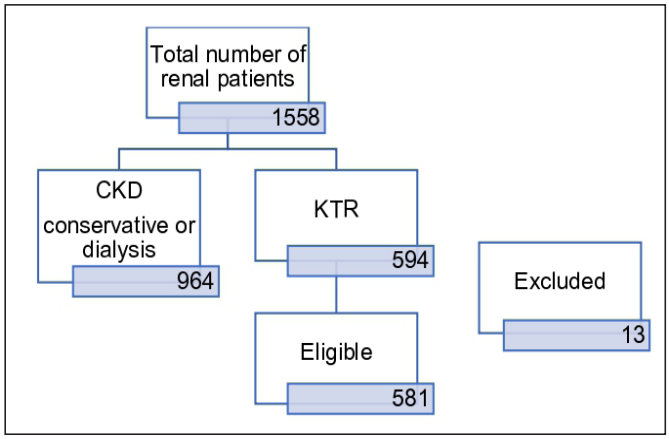

FIGURE 1. Patients eligible for the study.
CKD: chronic kidney disease; KTR: kidney transplant recipients.

TABLE 1. Demographic and epidemiological characteristics of the patients studied (n=581).

Variable	
Age in years (mean ± SD)	57.0±10.8
Male gender	66%
Origin	
Southeast	48.5%
Northeast	26.2%
Others	25.3%
Etiology of kidney disease	
Indeterminate	41.7%
Arterial hypertension	29.8%
Nephritis	12.9%
Diabetes mellitus	4.3%
Polycystic disease	3.4%
Systemic lupus erythematosus	1.2%
Recurrent urinary tract infection	1.5%
Donor type	
Deceased	52.8%
Living	40.4%
Time since transplantation in years (mean ± SD)	9.7±7.05
Duration of hemodialysis in years (mean ± SD)	5.3±4.43

Analysis of the present sample showed 17 different etiologies of hepatic abnormalities, with a higher frequency of HCV, HBV, iron overload, NAFLD, and DILI. The most frequent etiology was hepatitis C, as can be seen in TABLE 2.

Hepatitis C was the most frequent diagnosis. Alone or associated with other liver diseases hepatitis C was observed in 310 (53.3%) cases. HCV genotyping was performed in 161 (51.9%) cases and the most frequent genotypes were: genotype 1a in 60 (37.2%) cases, genotype 1b in 46 (28.5%), indeterminate genotypes in 29 (18%), genotype 1a/1b in 15 (9.3%), genotype 3 in 10 (6.2%), and genotype 4 in 1 (2.4%) case.

TABLE 2. Diagnoses in the kidney transplant recipients studied (n=581).

Final diagnosis	Number of patients with the diagnosis
Hepatitis C	310
Hepatitis B	133
Iron overload	107
Nonalcoholic fatty liver disease	54
Drug-induced liver injury	50
Alcohol	35
Schistosomiasis	14
Cholestasis	8
Hepatocellular carcinoma	3
Polycystic disease	3
False-positive HCV	2
Primary biliary cholangitis	1
Primary sclerosing cholangitis	1
Amyloidosis	1
Cured hepatitis B	1
Liver hemangioma	1
Benign cholestasis of pregnancy	1
Total	725

HCV: hepatitis C virus.

Hepatitis C was associated with other diagnoses in 118 cases: iron overload (n=46), HBV (n=24), NAFLD (n=22), DILI (n=9), alcoholic liver disease (n=8), schistosomiasis (n=4), cholestasis (n=3), and HCC (n=2).

Patients with hepatitis C (n=310) were compared to patients with other etiologies (n=271) and the following differences were: patients with HCV were older than those without HCV (57.8±10.4 vs 55.9±11.1 years; P=0.04). In addition, the duration of hemodialysis (5.7±4.3 vs 4.8±4.4 years; P=0.005) and the time since kidney transplantation (10.7±7.4 vs 8.6±6.4 years; P<0.001) were longer in patients with HCV. Laboratory parameters [ALT (1.3±1.4 vs 1.8±2.5; P=0.15), alkaline phosphatase (1.6±2.2 vs 1.4±1.2; P=0.62) and GGT (4.2±8.9 vs 5.2±8.4; P=0.17)] did not differ significantly between patients with and without HCV. Liver fibrosis evaluated by APRI (aspartate aminotransferase-to-platelet ratio index) was significantly lower in KTR with HCV compared to the other patients (0.8±0.9 vs 0.9±1; P=0.005). TABLE 3 shows the comparison of these parameters between KTR with and without hepatitis C.

The proportion of type 2 diabetes mellitus as etiology of pre-transplant CKD was similar in KTR with and without HCV (4.5% vs 4.1%; P=0.84). The same was observed for hypertensive nephrosclerosis (13.5% vs 12.7%; P=0.71) and nephritis (27.4% vs 32.5%; P=0.20).

Regarding immunosuppression, the main immunosuppressors used were azathioprine (AZA; 38%), cyclosporine (CYA; 42%), mycophenolate sodium (MMF; 35.8%), tacrolimus (FK; 41.3%), and prednisone (98.3%). The most frequent combinations were AZA, CYA and prednisone (n=132, 22.7%); MMF, FK and prednisone (n=113, 19.4%); AZA, FK and prednisone (n=57, 9.8%); CYA, MMF and prednisone (n=53, 9.1%); CYA, FK and pred-

TABLE 3. Epidemiological and laboratory parameters of kidney transplant recipients with and without hepatitis C virus.

Parameter	HCV + (n=310)	HCV – (n=415)	*P*
Age in years	57.8±10.4	55.9±11.1	0.04
Male gender	61.9%	70.5%	0.03
Etiology of CKD			
DM2	4.5%	4.1%	0.84
SAH	13.5%	12.7%	0.71
Nephritis	27.4%	32.5%	0.20
Time since transplantation in years	10.7±7.4	8.6±6.4	<0.001
Duration of hemodialysis in years	5.7±4.3	4.8±4.4	0.005
APRI	0.8±0.9	0.9±1	0.005
ALT	1.3±1.4	1.8±2.5	0.15
AP	1.6±2.2	1.4±1.2	0.62
GGT	4.2±8.9	5.2±8.4	0.17

HCV: hepatitis C virus; CKD: chronic kidney disease; APRI: aspartate aminotransferase-to-platelet ratio index; ALT: alanine aminotransferase; AP: alkaline phosphatase; GGT: gamma-glutamyl transferase; DM2: type 2 diabetes mellitus; SAH: systemic arterial hypertension; *P*: level of statistical significance.

nisone (n=1, 0.2%), and AZA, MMF and prednisone (n=1, 0.2%). The use of AZA (44.5% vs 45.4%; *P*=0.87) and MMF (37.3% vs 35.4%; *P*=0.66) was similar in patients with and without HCV. On the other hand, CYA was more frequently used by patients with HCV (47.2% vs 39.2%), but the difference was not statistically significant (*P*=0.06).

Comparison of the older (P1 – 1993 to 2005) and more recent periods (P2 – 2006 to 2018) revealed differences in the causes of liver abnormalities of the patients studied, which are shown in TABLE 4 and 5. Patients of P2 were younger, most of them were from the Southeastern and Northeastern regions, and had a shorter time since kidney transplantation. Twenty-seven patients were excluded from this analysis because of the lack of data of the first consultation.

During P1, the main etiologies were HCV infection (59.5%) and HBV infection. (23.4%). On the other hand, during P2, HCV decreased to 38.8%, HBV to 12.9% and there were more cases referred to investigate abnormal liver enzymes, corresponding to iron overload, NAFLD and DILI (7.7% in P1 and 26.3% in P2). The differences between periods were significant in all cases (*P*<0.001).

DISCUSSION

Literature data show that almost 25% of renal transplant patients (KTR) have evidence of hepatic disfunction[10]. In the present study 581 renal KTR referred to a hepatology specialized center to investigate liver abnormalities (positive viral serology, abnormal liver enzymes or image exams showing hepatic damage) were analyzed. The main diagnoses were hepatitis C, hepatitis B, iron overload, NAFLD and DILI.

HCV was the most prevalent condition, detected in 310 (53.3%) cases. Hepatitis C is common in KTR and its prevalence is higher than in the general population, ranging from 3 to 80% depending on the country and sample studied[11-12]. This high prevalence is the result of the acquisition of infection during the period of dialysis, with high prevalence rates that range from 3 to 10% in developed countries and from 15 to 80% in developing countries. These rates are much higher than those found in the general population of each region[13]. Genotype 1a predominated in the present population, as also observed in another series[14].

Hepatitis C is an important condition in KTR because it is one of the causes of nephropathy (generally associated with cryoglobulinemia causing membrane-proliferative glomerulonephritis) or, more frequently, a consequence due to the prolonged period of dialysis in CKD patients[15,16]. Infection with HCV is associated with post-transplant diabetes and chronic allograft nephropathy and is also a risk factor for acute rejection, although not a very common cause[13].

Treatment of HCV in KTR is no longer based on interferon-containing regimens whose efficacy ranged from 18 to 34%. In addition to its low response, this therapeutic regimen resulted in a risk of rejection of 12.5 to 51% and was therefore previously used

TABLE 4. Demographic and epidemiological characteristic of the patients studied divided into two periods [P1 (1993–2005) and P2 (2006–2018)] (n=554).

Variable	P1 (n= 299)	P2 (n=255)	*P*
Age in years (mean ± SD)	58.4±10.8	55.2±10.7	<0.001
Male gender	62.4%	68.6%	0.18
Origin			
Southeast	41.5%	57.6%	<0.001
Northeast	24.1%	27.8%	<0.001
Others	34.4%	14.5%	<0.001
Etiology of kidney disease			
Diabetes mellitus	3.3%	5.5%	0.24
Arterial hypertension	28.8%	30.6%	0.64
Nephritis	12.4%	13.3%	0.8
Donor type			
Deceased	52.8%	51%	0.59
Living	41.1%	40.8%	0.59
Time since transplantation in years (mean ± SD)	10.3±6.9	8.8±7.1	0.05

SD: standard deviation; *P:* level of statistical significance.

TABLE 5. Final diagnoses of kidney transplant recipients in periods [P1 (1993–2005) and P2 (2006–2018)] (n=554).

Diagnostic	P1 (n=299)	P2 (n=255)	*P*
HCV	64.9%	40.9%	<0.001
HBV	68.5%	49.5%	<0.001
Iron overload	55%	49%	0.31
NASH	37.3%	55.7%	<0.005
DILI	33.3%	55.8%	0.005

HCV: hepatitis C virus; HBV: hepatitis B virus; NASH: nonalcoholic fatty liver disease; DILI: drug-induced liver injury.

only in higher-risk KTR[13,17]. In 2013, a new class of drugs, direct-acting antivirals, were approved and became the best option for treating HCV in KTR, with a cure rate higher than 90%[13]. Most patients of the present series were treated or are being treated with these drugs.

The duration of hemodialysis was longer in KTR with hepatitis C compared to the other etiologies. Studies have shown that the prevalence of hepatitis C increases progressively with increasing dialysis duration due to the higher risk of contracting the infection. This risk has been declining over time due to improved cleaning processes during hemodialysis and the use of adequate screening tests for the disease and strategies to reduce transmission[13]. Furthermore, patients with HCV were older than those with other etiologies. This finding can be explained by the fact that patients with hepatitis C generally contracted the disease in the past and are therefore older.

Laboratory parameters (ALT, alkaline phosphatase and GGT) did not differ between KTR with HCV and those with other diagnoses. There was also no difference in diabetes mellitus or nephritis. A higher frequency of these two conditions might be expected as they can be consequences of the direct action of HCV[18], but this was not observed in the present study. Analysis of fibrosis by the noninvasive APRI method showed a lower degree of fibrosis in patients with HCV compared to the other etiologies, suggesting that the evolution of hepatitis C might be slower in KTR when compared to patients with NAFLD, DILI or iron overload. On the other hand, when compared to the non-immunosuppressed population, the progression of liver disease seems to be faster in KTR[19]. However, this disease progression during immunosuppressive therapy may be related to the use of high doses of corticosteroids and "old" immunosuppressants, which can increase viral replication[12,20,21,22].

The use of immunosuppressive drugs did not differ between KTR with HCV and patients with the other etiologies, regardless of the immunosuppressant used (AZA, MMF or CYA). However, there was a greater tendency to use CYA, probably because the patients were older and had a longer time since transplantation and this drug was more frequently used in the past.

Comparison of the two periods showed a larger number of patients with HCV during P1 (1993–2005). This finding reflects a higher frequency of HCV at hemodialysis services during this period as a result of environmental transmission of the virus[23,13]. HBV infection was also frequent, identified in almost 25% of the cases.

In the more recent period (2006–2018) HCV showed a decrease in frequency, but still the main reason for referral and HBV reduced its frequency by 50%. However, patients referred due to abnormal liver enzymes were more frequent, corresponding to iron overload, NAFLD and DILI. Iron overload is observed in 10% of KTR patients, as observed in other studies[24], as a consequence of iron administration during hemodialysis period that persists after transplantation[25].

Non-alcoholic fatty liver was also more frequent in P2, resulting from metabolic abnormalities, such as diabetes, dyslipidemia, hypertension and overweight. Furthermore, prolonged immunosuppression with corticosteroids and calcineurin inhibitors can also contribute to the development of NAFLD[26].

DILI was also frequent among referred patients and similarly to the present study, Guo (2012) identified this condition in 10% of KTR. The main drugs associated with this finding were azathioprine and sulfamethoxazole-trimethoprim[27].

In conclusion, the present study could evaluate hepatic laboratory and clinical abnormalities of several causes in a large casuistic of kidney transplant recipients, who require a more in-depth assessment because of their complexity. Early evaluation of possible hepatic alterations in these patients is important in order to prevent complications, acute liver failure and even progression to chronic liver disease.

Over time, the distribution of the various etiologies of liver disorders has changed, with a lower proportion of hepatitis B and C and a higher proportion of diagnoses of non-alcoholic fatty liver disease and drug-induced injury, showing the impact of control over time of viral infections in dialysis units.

Authors' contribution

Vieira GA: study design, data analysis, article writing. Amaral ACC: data collection, patient care. Carvalho-Filho RJ: data collection, patient care. Souza ALS: data collection, patient care. Medina-Pestana JO: provision of data relating to the casuistry. Ferraz MLG: study design, data analysis, article writing.

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RESUMO – Contexto – O transplante renal é o tratamento de escolha para pacientes com doença renal terminal e está associado a menor mortalidade quando comparado aos métodos dialíticos. O Brasil é o país com o segundo maior número de transplantes renais do mundo e, entre esses pacientes, observa-se que as alterações hepáticas são comuns. A frequência das alterações hepáticas varia de 20 a 50% pós-transplante e tem importante impacto na sobrevida e qualidade de vida desses pacientes. Existem poucos dados sobre a frequência, causas e características dessas alterações. **Objetivo –** Determinar a prevalência das diferentes causas de anormalidades hepáticas em receptores de transplante renal, associar as características dessas anormalidades a variáveis demográficas, epidemiológicas e clínicas, comparar as características das alterações hepáticas entre diferentes etiologias e avaliar possíveis alterações no diagnóstico em dois períodos diferentes de tempo. **Métodos –** Estudo epidemiológico descritivo, transversal, observacional, realizado no ambulatório "Hepato-Rim" do Hospital São Paulo (EPM/UNIFESP), centro de atendimento especializado a pacientes com anormalidades hepáticas e doenças renais de base. **Resultados –** Quinhentos e oitenta e um pacientes transplantados foram avaliados. As etiologias mais prevalentes de anormalidades hepáticas foram hepatite C e B, sobrecarga de ferro, doença hepática gordurosa não alcoólica e lesão hepática induzida por drogas. A causa mais comum – hepatite C – foi analisada em maiores detalhes. Em comparação com as outras causas, essa infecção foi a mais frequente em pacientes mais velhos, pacientes do sexo feminino e pacientes com mais tempo de transplante e hemodiálise. A análise dos dois períodos mostrou que os pacientes do período 1 (P1 – 1993 a 2005) eram mais velhos e encaminhados com maior frequência devido à sorologia positiva; encaminhamento devido a anormalidades de aminotransferases predominou durante o período 2 (P2 – 2006 a 2018). Os diagnósticos predominantes foram hepatite C e B durante P1 e doença hepática gordurosa não alcoólica e lesão hepática induzida por drogas durante P2. **Conclusão –** A avaliação das principais alterações hepáticas em receptores de transplante renal é importante, pois permite melhor manejo desses pacientes na investigação diagnóstica e no tratamento e contribui para a prevenção de complicações nesta população especial.

Palavras-chave – Transplante renal, alterações hepáticas, doença hepática.

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