Hiv And Hepatitis B Virus Co-Infection: Frequency And Presence Of Hepatic Injuries

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Abstract

The clinical importance of HBV-HIV co-infection comes from the fact that both viruses are highly transmissible and share similar routes of transmission. Co-infected individuals are more likely to develop liver cirrhosis and hepatocellular carcinoma. In view of the above, this manuscript is a quantitative, sectional, descriptive study with secondary data obtained from the analysis of medical records of 88 individuals with chronic hepatitis B. Thus, the purpose of this manuscript is to estimate the frequency of HBV-HIV co-infection and to identify the presence of liver damage. The results revealed an HBV-HIV co-infection rate of 9.1% (8//88), with two individuals being infected with the HIV-HBV-HCV virus concurrently. A large percentage of patients are male and heterosexual. There was a relationship between risky sexual behavior (sex without using a condom, multiple sexual partners) and the acquisition of hepatitis B and HIV. Related to the presence of liver lesions, it was observed that only one patient is diagnosed with liver cirrhosis, but there were no cases of hepatocellular carcinoma. Considering the increase in the quality of life and survival of people with HIV, the need to maintain protocols for the investigation of hepatocellular carcinoma is evident, thus seeking early detection and treatment.

Keywords: Co-infection, HIV infections, Hepatitis B, Hepatopathies.

1. INTRODUCTION

Viral hepatitis and AIDS are among the leading causes of death worldwide. Such diseases have an epidemic, dynamic and unstable personality, and despite significant progress they still constitute an important public health problem. The state of HIV immunosuppression increases the risk of the appearance of liver diseases as well as opportunistic diseases (Dong et al., 2015; Peeling et al., 2017; Zenebe et al., 2014).

The prevalence of co-infection between viral hepatitis B (HBV) and HIV is high because both have the same transmission factors and, as a consequence, the associated risk factors. Transmission routes are common, being basically sexual, parenteral and vertical. This fact has clinical importance, since co-infection worsens the patient's prognosis, since the main complications arise from its high potential for chronification, evidenced by liver cirrhosis and hepatocellular carcinoma (CHC) (Baldi, et al., 2016; Bertoletti; Maini; Ferrari, 2010; Chang; Liaw, 2014; Ganesan et al., 2019; Mavilia; Wu, 2018).

Co-infection leads to increased morbidity and mortality compared to HIV or HBV infections, increasing the likelihood of cirrhosis and CHC. In addition, co-infection can complicate the administration of antiretroviral therapy (ART), increasing the risk of using drugs with hepatoxicity and impacting the selection of specific agents with joint action for HIV and HBV (Ioannou et al., 2018; Salmon-Ceron et al., 2005; Singh et al., 2017; Sulkowski, 2008; Zenebe et al., 2014).

This manuscript aims to estimate the prevalence of HIV infection among patients with chronic hepatitis B, as well as to identify the presence of liver damage through the data on liver cirrhosis, CHC, liver failure and drug toxicity associated with ART.

1.1 Methods

This research is a quantitative, sectional, descriptive study based on secondary data from the analysis of medical records of patients seen at the hepatitis outpatient clinic of the Hospital Dia Professora Esterina Corsini of the University Hospital of the Federal University of Mato Grosso do Sul, Brazil. The research was approved by the Research Ethics Committee of the Federal University of Mato Grosso do Sul.

The reference population for the study consists of patients with chronic hepatitis B and HIV who are undergoing outpatient medical follow-up. The medical records analyzed are from patients seen from September 27 to December 20, 2018. Thus, in this study 236 medical records were analyzed, of which 91 patients (38.4%) had chronic hepatitis B and 145 (61, 6%) have hepatitis C.

In this study were excluded the medical records that do not have the results of immunoenzymatic tests for serological markers of hepatitis B (HBsAg, total anti-HBcAg and anti-HBsAg), HIV (anti-HIV), patients with incomplete records or illegible data and patients with hepatitis C. In addition, three records of individuals with hepatitis B were excluded, as well as all records of patients with hepatitis C. Thus, the study population consisted of 88 records referring to chronic HBV patients.

The results of immunoenzymatic tests for hepatitis B serological markers (HBsAg, total anti-HBcAg and anti-HBsAg), HIV (anti-HIV) were researched in the medical records. Data were also extracted to survey the epidemiological profile and the presence of liver injuries. The data were organized, grouped in tables and graphs and later analyzed and discussed. The statistical analysis was performed using Microsoft Excel 2016 16.0.6741.0248, IBM SPSS STATISTICS version 23.

1.1.1 Results

The sociodemographic and epidemiological characteristics that characterize the patients in this study are shown in table 1.

Table 1 - Distribution of patients with hepatitis B and co-infected according to sociodemographic variables and risk factors, Campo Grande - MS, 2018 (n = 88)

Particulars	HBV* (n=80)	%	COIN• (n=8)	%
Sex				
Feminine	28	35.0	03	37.5
Male	52	65.0	05	65.5
Age group (years)				
From 18 to 30	04	5.0	-	-
From 31 to 50	31	38.8	03	37.5
From 51 to 60	31	38.8	04	50.0
From 61 to 69	12	15.0	01	12.5

≥70	02	2,5	-	-
Ethnic groups				
White	44	55.0	06	75.0
Mixed race	27	33,8	02	25.0
Black	09	11.3	-	-
Origin				
Campo Grande	54	67.5	07	87.5
Cidades do interior do Estado de MS	22	27.5	-	-
Outros Estados	04	5.0	01	12.5
Sexual orientation				
Heterosexual	56	70.0	05	62.5
Homosexual	02	2.5	02	25.0
Not declared	22	27.5	01	15.5
Education				
Illiterate	03	3.8	-	-
Incomplete Elementary School	08	10.0	02	25.0
Complete primary education	19	23.8	02	25.0
Incomplete high school	06	7.5	-	-
Complete high school	28	35.0	02	25.0
University education	04	5.0	02	25.0
Ignored	12	15.0	-	-
Marital status				
Married	45	57.5	02	25.0
Single	21	26.3	05	62.5
Widowed	02	2.5	01	12.5
Divorced	04	5.0	-	-
Registered partnership	02	2.3	-	-
Ignored	05	6.3	-	-
Alcoholism				
Yes	34	42.5	03	37.5
Not	46	57.5	05	62.5
Smoking				
Yes	25	31.2	03	37.5
Not	55	68.8	05	62.5

*HBV = hepatitis B Vírus

•COIN = Co-infected

As shown in table 1, with regard to the sexual orientation of the co-infected, it was shown that 62.5% (5/8)

reported being heterosexual and 25.0% (2/8) homosexual. It was not possible to verify their sexual condition in only one medical record of co-infected patients. There were no cases of bisexuality in these individuals.

The data presented in Table 2 corresponds to the serological profile of the study population. The hepatitis B virus serological markers (HBsAg, total anti-HBc, anti-HBs, HBeAg, anti-HBeAg) were analyzed.

Table 2 – Absolute frequency and percentage of patients with hepatitis B and co-infected according to serological markers, Campo Grande - MS, 2018 (n = 88)

Serological markers	HBV* (n=80)	%	COIN• (n=8)	%
HBsAg				
Reagent	76	95.0	06	75.0
Not Reagent	04	5.0	02	25.0
Anti-HBc total				
Reagent	71	88.8	08	100.0
Not Reagent	06	7.5	-	-
Ignored	03	3.7	-	-
Anti-HBs				
Reagent	13	16.3	03	37.5
Not Reagent	62	77.5	05	62.5
Ignored	05	6.2	-	-
HBeAg				
Reagent	12	15.0	01	12.5
Not Reagent	68	85.0	07	87.5
Anti-HBeAg				
Reagent	68	85.0	07	87.59
Not Reagent	12	15.0	01	12.5

*HBV = hepatitis B Vírus

•COIN = Co-infected

As shown in table 3 in the study population, there are no cases of CHC. In co-infected individuals, only one patient already has cirrhosis. It is observed that in the population of monoinfected by HBV, 12.5% (10/80) have cirrhosis, but one patient who had cirrhosis was submitted to liver transplantation. The data reveal that 62.5% (50/80) of the patients have hepatic steatosis and 12.5% (10/80) have already experienced jaundice.

Table 3 – Distribution of patients with hepatitis B and co-infected according to liver injury markers, Campo Grande - MS, 2018 (n = 88)

Variables	HBV* (n=80)	%	COIN• (n=8)	%
Hepatical cirrhosis				
Yes	10	12.5	01	12.5
Not	59	73.8	07	87.5
Ignored	11	13.7	-	-
Liver failure				
Yes	01	1.3	-	-
Not	79	98.7	08	100
Past history of jaundice				
Yes	10	12.5	01	12.5
Not	70	87.5	07	87.5
Report of drug hepatotoxicity				
Yes	01	1.3	-	-
Not	79	98.7	08	100
Presence of Liver Steatosis				
Yes	50	62.5	07	87.5
Not	20	25.0	01	12.5
Ignored	10	12.5	-	-
Internação clínica				
Yes	04	5.0	05	62.5
Not	76	95.0	03	37.5
Carcinoma hepatocelular				
Yes	-	-	-	-
Not	80	100	08	100

*HBV = hepatitis B Vírus

•COIN = Co-infected

According to the table, 4, only 62.5% (5/8) of co-infected patients had sexual orientation as the supposed route of infection, as well as sexual practice without using a condom was the main risk factor present. Of these patients, 4/8 were infected by the sexual partner and this partner was a fixed partner. These patients reported not using a condom with their sexual partner and had no extramarital sex. The other individuals (2/8) acquired the viruses through sexual practice with occasional / sporadic partners and without using a condom.

Table 4 - Risk behavior factors, mechanism of HBV infection and how the patient was diagnosed in the study population (n = 88)

Variables	HBV (n=80)	%	COIN (n=8)	%
History of Syphilis				
Yes	14	17.5	04	50.0
Not	61	76.3	04	50.0
Ignored	05	6.3	-	-
Diagnostic				
Blood Bank Screening	31	38.8	01	12.5%
After manifesting	08	10.0	03	37.5%
symptoms	03	3.8	-	-
At the prenatal consultation	16	20.0	02	25.0%
During routine exams	01	1.2	02	25.0%
After the partner manifests the	21	26.2	-	-
disease				
Ignored				
Infection Mechanism	07	8.8	05	62.5
Suxual	11	13.8	-	-
Vertical	02	2.4	-	-
Blood transfusion	60	75.0	03	37.5%
procedures				
Ignored	03	3.8	03	37.5%
Factors that indicate risky	17	21.3	05	62.5%
behavior	02	2.5	-	-
Multiple sexual partners	01	1.3	-	-
Sexual activity without	57	71.3	-	-
using a condom	-	-	-	-
History of				
Hemostransfusion				
Sharing of manicure /				
pedicure objects				
Ignored				
Injecting drug use				

*HBV = hepatitis B Vírus

*COIN = Co-infected

According to table 4, regarding the form of diagnosis, only 38.8% (31/80) are carriers of HBV (discovered through the screening of blood banks) and 20.0% (16/80) are asymptomatic (discovered through routine

exams, however, 75.0% (60/80) of these patients were unable to report how they were infected with HBV. Table 4 shows that among HIV-infected hepatitis B carriers 37.5% (3/8) had a diagnosis when they presented symptoms related to HIV infection, and the beginning of the development of the signs referring to the virus acting on the body. A percentage of 25.0% (2/8) of the patients discovered that they had HIV-HBV only after their sexual partner showed signs of the disease.

Table 5 shows a frequency of HBV-HIV co-infection of 9.1% (8/88), with the HBV-HIV rate being 6.8% (6/88) and the numbers of HBV-HCV-HIV are 2.3% (2 / 88). In addition, the results showed that 50.0% (4/8) of the coinfected patients had syphilis, that is, the number is 17.5% (14/80) among the population of hepatitis B carriers. In the population of monoinfected by HBV the sexual route corresponded to 8.8% (7/80), the vertical route had the percentage of 13.8% (11/80).

Table 5 – Absolute frequency and percentage of patients with hepatitis B according to the existing co-infection, Campo Grande - MS, 2018 (n = 88)

Variables	Nº	%
Co-infection HBV –HIV	06	6.8
Co-infection HBV- HCV	03	3.4
Co-infection HBV-HCV -HIV	02	2.3
Co-infection HBV - syphilis	08	9.1
Co-infection HBV -HDV	01	1.1
Co-infection HBV –HTLV	01	1.1

2. DISCUSSION

It was observed that among the individuals included in this study, the frequency of HBV-HIV co-infection was 9.1% (8/88), with the HBV-HIV rate being 6.8% (6/88) and the numbers of HBV- HCV-HIV is 2.3% (2/88). In the period from 2007 to 2017, the coinfection rate in Brazil among the notified cases of hepatitis B with HIV was 5.2% (Sulkowski, 2008). In the Midwest region this rate was 3.9% and the highest rate was found in the southeast region of Brazil, being 7.9%. In 2017, the detection rate of hepatitis B was 6.5 cases per 100,000 inhabitants, in this case, the detection rates in the Midwest region were not higher than the national rate only in 2015 (Brazil, 2017).

There were no cases of CHC in the studied population. However, the CHC tumor doubling time varies between 2 to 12 months, so it becomes important that patients with hepatitis B be periodically monitored (Alvariz, 2006; Chang; Liaw, 2014; Fattovich; Bortolotti; Donato, 2008).

Abstinence or limited alcohol consumption is recommended. As described in table 1, it was observed that 37.5% (3/8) of the co-infected consume alcohol and among HBV carriers it is equivalent to 42.5% (34/80). It is important that professionals address the impacts of alcohol consumption on the health of these patients and encourage these patients to stop consuming alcoholic beverages. (Alvariz, 2006).

There is an increase in the survival rates of HIV carriers in Brazil with a significant reduction in mortality (Grego, 2016). In other countries, such as the United Kingdom, more than 25,000 people aged 50 and

over are living with HIV (Catalan et al., 2017). With the increase in life expectancy of people with HIV, there was an increase in the number of individuals co-infected with HBV with fibrosis and liver cirrhosis. In these cases, there is an acceleration of the progression of liver disease as HIV increases the burden of HBV. The risk of dying from some liver disease is multiplied by thirteen among co-infected patients when compared to patients without HIV (Ganesan et al., 2019; Nakagawa; May; Phillips, 2013; Parvez, 2013; Salmon-Ceron et al., 2005; Singh et al., 2017; Vinikoor et al., 2017).

The investigation of CHC is important since HBV is a virus with potential hepatocarcinogen and its presence is one of the main risk factors for the individual to develop hepatocellular carcinoma. CHC is responsible for 70 to 85% of primary liver cancers, however it has a low incidence in Brazil, with the highest incidence rates present in Southeast Asia and sub-Saharan Africa, which are endemic areas of hepatitis B (But; Lai; Yuen, 2008; Chang; Liaw, 2014; Fattovich; Bortolotti; Donato, 2008; Gomes et al., 2013; Papatheodoridi et al., 2015).

A review study revealed that the incidence of CHC in the city of São Paulo is 2.07/100,000 inhabitants and one of the main risk factors described is the presence of chronic HBV infection, having liver cirrhosis and chronic alcoholism. Cirrhosis was present in 80 to 90% of patients with CHC. In a period of five years there is a risk of 5 to 30% for the individual with cirrhosis to develop CHC. (Gomes et al., 2013).

Table 3 shows that in the HBV monoinfected population, only 12.5% (10/80) have cirrhosis, in addition, one patient with cirrhosis has undergone liver transplantation. It is noteworthy that 62.5% (50/80) of patients have hepatic steatosis and 12.5% (10/80) have already experienced jaundice. In addition, among those co-infected with HBV-HIV, only one 36-year-old male patient already has cirrhosis, there are reports of irregular use of ART. The risk of a patient with cirrhosis developing CHC is cumulative over a 5-year period (Fattovich; Bortolotti; Donato, 2008).

CHC is a multifaceted and heterogeneous disease whose main risk factor is cirrhosis. Its diagnosis is a great challenge due to the absence of specific and sensitive immunohistochemical markers, however, histopalology is still an important resource even in the face of new molecular biology techniques and imaging exams (But; Lai; Yuen, 2008; Fattovich; Bortolotti; Donato, 2008; Ganesan et al., 2019; Hsu et al., 2018; Quaglia, 2018; Ioannou et al., 2018).

In conclusion, the HBV-HIV co-infection status is a factor that increases the probability of the evolution of liver diseases such as cirrhosis and HCC due to the increase in the life span of HIV patients. Thus, as explained above, it is essential that the services correctly follow the treatment and investigation criteria of the HCC.

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