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## HIV CO-INFECTION AND HEPATITIS B VIRUSES: PREVALENCE AND PROGRESSION OF HEPATIC DISEASE

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### ABSTRACT

This manuscript is a review of the literature on the prevalence and progression of liver disease. Viral hepatitis B continues to have great incidence and is one of the main problems of Public Health in Brazil and in the world. The World Health Organization (WHO) estimates that approximately 370 million people are chronic carriers of the hepatitis B virus (HBV). In regions with high positive indexes of disease cases, or between groups with a high risk of parenteral transmission, co-infections are common; however, the prevalence of hepatitis B-related comorbidity is not known worldwide because of the scarcity of population-based research. In this way, we will analyze the publications that bring contributions on the issue of co-infections between HIV and hepatitis B virus.

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## INTRODUCTION

In Brazil, viral hepatitis and AIDS are epidemic, dynamic and unstable. In fact, despite significant scientific advances such diseases are a global public health problem. According to an estimate by the World Health Organization - WHO (2011), there are approximately 370 million chronic carriers of hepatitis B virus (HBV). AIDS is a disease characterized by a reduction in the immune system of the individual as a result of HIV infection, resulting in an involvement of the body by various opportunistic diseases. Infections caused by the presence of human immunodeficiency virus type 1 (HIV-1) are characterized by a chronic process in which the virus replicates continuously in the host.

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The high replication rate as well as the high contingent of the viral population results in the production of subpopulations of virus in the same infected individual called quasispecies. HIV-1, hepatitis B virus (HBV) and hepatitis C (HCV) can be diagnosed in the same patient because they share similar transmission routes, inducing a worse prognosis and leading to a rapid evolution of HBV infection and HCV. Despite their impact on the quality of life of HIV-positive patients, information on HIV co-infection and viral hepatitis in some Brazilian hospitals, such as the Clinical Hospital of the Federal University of Paraná, is scarce. In fact, there are no studies describing the demographic characteristics, clinical profile and characterization of HIV-1 in patients co-infected with HIV and hepatitis B or C. Co-infection between human immunodeficiency virus (HIV) and viral hepatitis B or C is explained by the common pathways of virus infection, especially sexual and parenteral. It is estimated that 70.0-90.0% of HIV seropositive patients have serological markers

of previous infection by the hepatitis B virus. Chronic HBV infection occurs in 5.0 to 10.0% of HIV-infected individuals, that is, a proportion ten times that observed in the general population. A study conducted in a hospital in the city of Ribeirão Preto-SP showed a prevalence of HIV / HBV of 20.4%. Epidemiological studies show an association between the occurrence of HIV / HBV in young adults and homosexual men (BELOTO, 2014). The similarity between the transmission of HIV and HCV (parenteral, sexual and vertical) indicates the occurrence of HIV / HCV co-infection. The prevalence of co-infection is highly variable and depends on the occurrence of HCV, HIV and drug users in the populations studied. In the EUROSIDA clinical trial accompanying HIV-positive patients in centers in Europe, the prevalence of HIV / HCV co-infection at the baseline ranged from 5.2% in Israel to 71.3% in Ukraine.

In Brazil, there are few studies that report this prevalence. According to a study conducted in the city of Santos-SP in HIV seropositive individuals, there is an HIV / HCV prevalence of 36.2% (95% IC: 31,9-40,4). Among injecting drug users (IDUs), the percentage reached 84.8% (95% CI: 78.2-91.3). Several factors explain the higher frequency of HCV in HIV-positive individuals, such as illicit drug use, syringe sharing and blood transfusion (FARIAS *et al.*, 2010). Viral hepatitis B and C constitute a mandatory notification. The records mainly represent the capture of cases and the adhesion of the health services to the Notification System of Sinan (Sinan), which increased progressively from the year 2000. Sinan adherences, as well as the exploitation of the data available in official information systems are important for the prevention and control of viral hepatitis, also contributing to the knowledge about the distribution of the various phenomena related to population and health services. (FARIAS, *et al.*, 2010). The AIDS epidemic stands out among infectious diseases because of its complexity, extent of damage to individuals, and changes in the epidemiological characteristics of the disease.

In the current scenario there is a spread of HIV infection in heterosexuals, women and a migration to medium and small cities, thus, the disease is no longer restricted to populations with risk behavior. However, greater survival is observed in patients infected with HIV. The new drugs have reduced the virus-related death rate and HIV-positive people have been living longer. This is due to technological advances, greater knowledge about the disease and the evolution of diagnostic methods. Thus, the disease assumes a chronic character, ceasing to be a disease with a highly lethal outcome. In relation to hepatitis, these diseases are considered a serious public health problem in Brazil. Hepatitis is an inflammation in the liver that can lead to irreversible damage and even death of the individual. They are usually silent diseases that do not always present symptoms, but can appear fatigue, fever, nausea, vomiting, abdominal pain and jaundice. Hepatitis is usually transmitted through unprotected sex, sharing of contaminated needles and syringes, unsterilized manicure objects, among others. Hepatitis C is the disease that causes the highest number of deaths among all types of hepatitis. Since Hepatitis B most cases become acute and can be prevented by means of vaccine.

**Hepatitis B and C Co-infection:** Hepatitis B has a high potential for chronification, which can lead to hepatic diseases such as hepatocarcinoma or hepatic cirrhosis, which

compromises treatment and quality of life and are the main causes of death in these patients. HIV and HBV share the same transmission routes, parenteral and sexual, and there is a high risk of co-infection. It has been shown that 70% to 90% of patients with HIV or AIDS have some serological marker of hepatitis B, evidencing current or former HBV infection, and 10% to 15% are carriers of chronic infection. Studies suggest that the acquisition of B virus by individuals already infected with HIV significantly increases the risk of chronic HBV (BRASIL, 2002). There is a number of evidences that suggest the action of HBV on HIV. In vitro and in vivo studies demonstrate that protein X which is the product of a genomic portion of HBV is able to act concomitantly on HIV, exacerbating its replication. In addition to hepatocytes, HBV has been observed in peripheral T lymphocytes and other lymphoid cells, suggesting that both viruses can infect the same cells. Such a phenomenon seems to indicate that HBV can behave as a cofactor for increasing HIV viral load. However, the subject is still controversial and there is no clear evidence that HBV infection influences the progression of HIV infection (BRASIL, 2002).

In relation to the action of HIV on hepatitis B, it influences the natural history of HBV infection. Recent publications suggest high levels of HBV replication, increased liver injury, and high prevalence of HBV-induced cirrhosis in HIV-positive patients. Reactivation is capable of worsening liver damage, and may progress to fulminant form, acute liver failure and even death. Reactivation of HBV is, however, less frequent in HIV-infected patients than in other procedures leading to immune suppression, such as chemotherapy and liver and bone marrow transplantation (BRASIL, 2002). Knowing the co-infection with HIV and HBV are important since these viruses share the same pathways of contagion, and the fact that liver diseases are referred as one of the main causes of morbidity and mortality in HIV patients, which gives a great clinical importance to cases of co-infection, since it worsens the patient's prognosis and directly interferes with the therapeutic results. Although there is much scientific information about these diseases in Brazil, there is no detailed study in the literature involving the city of Campo Grande, which is also a reference for treatment in the State of Mato Grosso do Sul.

### HIV co- infection and hepatitis virus

In Brazil, the first AIDS cases were confirmed in 1982, in the state of São Paulo. Since then it is estimated that there are more than 600 thousand Brazilians with AIDS. Thus, over the years, the number of infected and sick people shows a tendency to expand, making the situation an icon of great discussions and significant changes in various fields of health. Analyzes identify three important aspects related to the epidemic: the first one called "internalization" of the infection with the increase in the number of cases in medium and small cities. The second refers to the spread of the disease in low-income populations and finally the feminization of the epidemic, with a significant increase in the number of women infected with HIV (Pinto *et al.*, 2007). The HIV/AIDS Epidemiological Bulletin of the Department of Surveillance, Prevention and Control of Sexually Transmitted Infections of the Health Surveillance Secretariat (SVS) of the Brazilian Ministry of Health (MS) has reported that from 2007 to 2016, 136,945 cases of infection by the HIV virus in Brazil were notified by SINAI. The indicators show stabilization in the last 10 years in the AIDS detection rate. The highest concentration

of cases is in individuals aged 25 to 39 years for both sexes, a fact that draws attention is that the rate of detection of AIDS in males aged 14 to 19 years has tripled in the period of 2006 to 2015. Data from SINAN reveal a drop in the detection rate in women except for the age of 15 to 19 years and women over 55 years (BRAZIL, 2016). According to Farias *et al* (2012), viral hepatitis is an important public health problem. The World Health Organization (WHO) estimates that there are about 370 million chronic carriers of the HBV virus. According to the SINAN from 1999 to 2015, the detection rates of Hepatitis B shows a tendency to increase. In this period, 514,678 cases of viral hepatitis were reported in Brazil, of which 196,701 (38.2%) were cases of Hepatitis B. Most of the cases are concentrated in the southeast region (35.5%) and the Central West region has the lowest rate (9.3%). With regard to sex, rates are higher in males, yet the difference in relation to females decreases every year. In the age group the detection rate of Hepatitis B is higher in the age group of 25 to 39 years (BRASIL, 2016).

Co-infection between Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV) has the same transmission factors and as a consequence the associated risk factors explain the high prevalence of these infectious agents. The routes of transmission of HBV and HIV viruses are common and basically sexual, parenteral and vertical. This fact is of clinical importance, since co-infection worsens the prognosis of the patient, since the main complications arise from its high potential of chronification, evidenced by hepatic cirrhosis and hepatocarcinoma (SOUZA *et al*, 2004). Baudi *et al*. (2016) conducted a study involving 176 plasma samples collected from HIV patients to determine the prevalence of co-infection among HIV pretreatment patients in Harare, Zimbabwe. Of the total research sample, 164 were HIV isolates with successful genotyping, 163 (99.4%) were subtype C and only 01 were HIV subtype F1. Regarding the viral mutation, 9.8% presented at least 01 mutation for resistance to treatment drug. This study draws attention to the importance of strengthening HBV screening programs in HIV patients. In Florida *et al* (2017), involving 1,462 HIV-positive pregnant women in Italy, the overall rate of HBV co-infection was 12%. In cases of co-infection there was a median gain of CD4 lower in the first and third trimester of gestation. The study points to a significant reduction in CD4 response in pregnancy in women co-infected with HBV and HIV, particularly with advanced immune deterioration.

According to Cooper *et al*. (2006), in patients with HBV and HIV co-infected, the progression of liver disease appears to be more accelerated with an increased incidence of chronic complications of viral hepatitis such as acceleration of liver injury, increased risk of hepatic toxicity antiretrovirals due to interaction between medications and worse response rates to treatment. Another relevant factor is that the immune recovery after the initiation of Therapy Antiretroviral therapy (ART) appears to be reduced in cases of co-infection. Idoko *et al* (2009) studied 1564 HIV-infected patients in a city in Nigeria called Jos, and obtained a rate of 16.7% of individuals co-infected with HBV. Two-thirds of the patients were women and the median age was 35 years. Co-infected patients had a slower immune response to antiretroviral therapy (ART) and a lower CD4 count at the start of ART. The study demonstrates a hepatotoxicity associated with the use of medication for tuberculosis. Regarding ART, 3.1% of the patients had hepatotoxicity in the initial 24 weeks, compared to 0.5% of

monkey-infected patients with HIV. The rate of hepatotoxicity in co-infected patients decreased to 1% after 48 weeks from the start of ART. In a study conducted in Kolkata, India, in 1331 HIV-positive patients, approximately 10% of the subjects were co-infected with HIV / HBV, of whom 78% were males and the mean age was 35 years. The most likely transmission routes included heterosexual (50%), blood transfusion (25.6%) and 10.3% of patients injecting drug users. In the presence of co-infection the patients had an HIV infection. The results indicate that in co-infection, the course of chronic infection is more aggressive and there is a higher prevalence of cirrhosis, drug toxicity and hepatocellular carcinoma (SARKAR, 2016). Among endemic epidemiological diseases, viral hepatitis and HIV are an important public health problem and remain a challenge for health authorities, despite the fact that in recent years significant progress has been achieved in Brazil. In 2002, the Ministry of Health of Brazil created the National Program for the Prevention and Control of Viral Hepatitis (PNHV) as a way to improve actions and overcome the various variables that hinder prevention and treatment (Ferreira & Silveira, 2004). Studies indicate that HBV / HIV co-infection may be associated with a worse prognosis in the patient and that the progression of hepatic disease seems to be more accelerated, with immunological reduction, increasing the hepatic lesions in the patient, such as the appearance of liver cirrhosis, hepatocarcinoma and toxicity drug therapy. It is known that the transmission pathways between HBV / HIV viruses are common demonstrating the clinical importance of co-infection (Cooper *et al* 2006). Data from SINAN show that from 2007 to 2015, 136,945 new cases of HIV infection were reported in Brazil, 6.7% in the Central West region. In relation to Hepatitis B, 196,701 cases were reported in the period from 1999 to 2015, being 9.3% in the Midwest region (Brasil, 2016).

### Final Considerations

It is fundamental to know regionally the situation of these chronic infections in order to guide the planning of public coping policies, whether in the scope of prevention, treatment or harm reduction. Another issue concerns the clinical and epidemiological importance of these two pathologies, especially when they are associated and also because the fact of co-infection favors a worse prognosis to the patient and interfere in the results of the therapeutic plan. However, the impact of co-infection among patients assisted at referral services in the city of Campo Grande, a major part of HUMAP Day Hospital of the Federal University of Mato Grosso do Sul, was never systematically investigated; reason why it was decided to carry out the present study. It is known that information is a strategic tool and serves as a basis for monitoring, subsidizing and improving health services actions are preventive care or healing and rehabilitation, making it possible to establish goals, analyze strategies and make decisions. Thus, the investigation of HIV and Hepatitis B co-infection in patients treated at HUMAP Day Hospital of the Federal University of Mato Grosso do Sul will provide important data on the prevalence of co-infection of these viruses in the city of Campo Grande, Mato Grosso do Sul, Brazil. The lack of studies reveals the need to delineate the clinical epidemiological profile of co-infected patients. These studies contribute to the knowledge and support of health control strategies and prevention of diseases in cities that refer their clients to treatment in the "Dia Hospital" that is a municipal and regional reference for AIDS / HIV treatment.

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