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# Hepatitis C virus infection among pregnant women in Central-Western Brazil, 2005-2007

# **ABSTRACT**

The study was aimed at estimating the prevalence of infection with and the genotype of hepatitis C virus (HCV), and to determine the extent of underreporting of HCV cases. A total of 115,386 pregnant women seen by the Program for Protection of Pregnancy [*Programa Estadual de Proteção à Gestante*] of the state of Mato Grosso do Sul, Central-Western Brazil, were tested for anti-HCV antibodies between 2005 and 2007. Prevalence of HCV infection was 1.07 cases per thousand. Positive samples were tested for HCV RNA and genotyped. Genotype 1 was detected in 73% of samples, genotype 3 in 24.3%, and genotype 2 in 2.7%. Underreporting of hepatitis C cases was 35.5%.

DESCRIPTORS: Pregnant Women. Hepatitis C, epidemiology. Hepacivirus, genetics. Seroepidemiologic Studies.

## **INTRODUCTION**

The hepatitis C virus (HCV) infects 130 million people worldwide, most of which become chronic carriers. Hepatitis C is an important public health problem: 50% to 80% of infections become chronic, which can lead to the later development of cirrhosis and hepatocellular carcinoma.<sup>1</sup>

HCV is divided into six genotypes (1-6) and multiple subtypes, with variable geographical distribution. Genotypes 1, 2, and 3 are spread throughout the entire world. Subtypes 1a, 1b, 2a, 2b, and 3a are found in Brazil, Western Europe, and the United States. In India, Bangladesh, and other parts of Asia, genotype 3 is most common. In Northern Africa and the Middle East, especially Egypt, genotype 4 is predominant. Genotypes 5 and 6 are found in specific geographical regions, such as South Africa and Asia, respectively.<sup>1,2</sup>

In Brazil, prevalence of HCV infection among pregnant women appears not to differ from that of the general population, ranging from 0.9% to 1.5%. Despite the relatively low risk of vertical transmission, the lack of specific prophylactic measures justifies routine screening of pregnant women for hepatitis C.<sup>3</sup>

The aim of the present study was to estimate the prevalence of HCV infection among pregnant women, to identify major viral genotypes and subtypes circulating in this population, and to estimate the degree of underreporting of hepatitis C.

## **METHODS**

We carried out a descriptive cross-sectional study including 115,386 pregnant women seen by the State Program for Protection of Pregnancy of the state of Mato Grosso do Sul, Central-Western Brazil, from January 2005 to December

2007. This number represents 97% of the pregnant women in Mato Grosso do Sul, based the number of live births registered in the same period. Subjects underwent their first serological test during antenatal care at the *Instituto de Pesquisa*, *Ensino e Diagnóstico – Associação dos Pais e Amigos dos Excepcionais* (IPED-APAE, Institute for Research, Education, and Diagnosis – Association of Parents and Friends of Children with Special Needs).

Blood samples were obtained in health care units of all municipalities in the State by finger puncture on previously identified filter paper. All samples were tested for antibodies (ELISA) against the hepatitis C virus (anti-HCV). Subjects whose samples tested positive or indeterminate were subjected to further blood collection by venous puncture for molecular testing. Anti-HCV-positive samples were tested for of viral RNA by real-time polymerase chain reaction (real-time PCR) using primers complementary to the 5' noncoding region of the HCV genome. Samples positive for HCV RNA were genotyped using the line probe assay (INNO-LiPA, Versant HCV Genotype Assay, Innogenetics, Belgium), which uses biotinylated primers complementary to the 5' noncoding region of the HCV genome.

Other infections such as syphilis, toxoplasmosis, hepatitis B, HIV, human T cell leukemia virus (HTLV), herpes simplex, cytomegalovirus, rubella, chlamydia, and Chagas' disease were investigated simultaneously to HCV.

Subjects positive for anti-HCV in the IPED/APAE screening were compared to those notified in the database of the *Sistema de Informação de Agravos de Notificação* (SINAN, Notifiable Disease Surveillance System) as an attempt to estimate the degree of underreporting of hepatitis C cases.

Data were analyzed using EpiInfo 3.4.1 and SPSS 13.0 software. We used the chi-square test to compare calculated prevalences, assuming a significance level of p<0.05.

The study protocol was approved by the Ethics Committee for Research on Human Subjects of the Universidade Federal do Mato Grosso do Sul (CEP/UFMS protocol no. 488/2009).

# **RESULTS**

Of all subjects tested, 124 were positive for anti-HCV, a prevalence rate of 1.07 cases per thousand (Table). Prevalence rates were distributed unevenly within the state, ranging from 0.45/1000 in the city of Nova Andradina to 6.25/1000 in the city of Novo Horizonte do Sul. The cities with the highest prevalences of anti-HCV were located in the center-south of the state, and all have populations of less than 10 thousand.

Prevalence tended to increase with age (p < 0.001). More than half the pregnant women assayed were in the 20-29 years age group, in which prevalence was 1.05/1000. Prevalence was 1.94/1000 among subjects aged 30-39 years, and 2.97/1000 among the 40-49 years age group.

The majority of subjects positive for anti-HCV (53.2%) underwent antenatal screening in the first trimester of pregnancy, 28.22% did so in the second trimester, and 5.6% in the third trimester. This information was not available for 12.9% of cases.

Of the 124 samples positive for anti-HCV, 81 (65.3%) were positive for 5' noncoding RNA. Of these, 74 (91.3%) were genotyped. Genotype 1 (73.3%) was predominant, followed by genotypes 3 (24.3%) and 2 (2.7%). Of the 46 samples subtyped (62.2%), 75.1% were subtype 1a (25/33), 21.2% were subtype 1b (7/33), and 3% were subtype 1d (1/33); subtype 2a was detected in only a single sample; and 91.7% (11/12) were subtype 3a and 8.3% (1/12) were subtype 3d.

Co-infections were detected in 13.7% of cases of HCV, the most prevalent of which was syphilis (8.1%), followed by HIV (2.5%). Underreporting of hepatitis C cases in SINAN was 35.5%, ranging from 23.1% in 2007 to 40.3% in 2006.

## **DISCUSSION**

The present study is the first epidemiological survey of HCV infection in pregnant women in the state of Mato Grosso do Sul to include viral genotyping. Global prevalence of the anti-HCV marker was 1.07 cases/1000, similar to estimates calculated for three municipalities of the state of Goiás (1.50 cases/1000).<sup>3</sup> On the other hand, prevalence in the present study was lower to that found in subjects 19 years or older in a population-based survey of the Central-West Region (19.0 cases/1000).<sup>5</sup>

Similarly to a previous study carried out in the Central-West,<sup>3</sup> prevalence of HCV in the present study increased with age, the highest prevalence being detected in the 40-49 years age group (2.79 cases/1000).

**Table.** Prevalence of infection by hepatitis C virus among pregnant women in the State Program for Protection of Pregnancy. Mato Grosso do Sul, Central-Western Brazil, 2005–2007.

Year	Subjects tested	Positive	Cases/1000
2005	39,204	46	1.17
2006	39,118	52	1.33
2007	37,064	26	0.70
Total	115,386	124	1.07

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Genotyping revealed a predominance of genotype 1, followed by 3 and 2, and subtypes 1a (54.3%) and 3a (23.9%). These results are in agreement with the findings of studies of the geographical distribution of HCV genotypes in Brazil.<sup>2</sup>

Co-infection with HIV was observed in 2.5% of cases, which is lower than the worldwide prevalence of co-infection, which is as high as 6.5%.<sup>4</sup>

Prevalence of underreporting in our survey was of 35.5%. This indicates the presence of shortcomings in routine HCV surveillance, which hinder the development

of measures aimed at controlling the disease.

The low prevalence (1.07 cases/1000) of HCV infection in the present study does not argue against the possibility of vertical transmission, and must therefore be monitored during routine antenatal care. Moreover, the high rate of underreporting of HCV suggests that the sensitivity of surveillance systems is low. Such deficiencies must be promptly corrected so as to improve the foundations of programs for the prevention and control of hepatitis C among pregnant women in the state of Mato Grosso do Sul.

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