



# The Brazilian Journal of INFECTIOUS DISEASES

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## Letter to the Editor

# First serological evidence of hantavirus infection in humans from the Orinoquia region of Colombia<sup>☆</sup>



Dear Editor,

Hantaviruses cause a significant number of human illnesses, making them a global public health threat. Approximately 150,000–200,000 patients with hemorrhagic fever with renal syndrome (HFRS) are hospitalized each year throughout the world. On average, approximately 200 cases of hantavirus pulmonary syndrome (HPS) per year are reported in the Americas, and although the number of cases is much smaller in number than that of HFRS, its average case fatality is about 40%.<sup>1</sup>

Hantaviruses are a large group of RNA viruses that belong to the family *Bunyaviridae*. Reservoirs for pathogenic hantaviruses are specific rodent species, suggesting a long history of virus rodent coevolution. Humans are accidental hosts; rodents are generally asymptomatic and may excrete the virus in their urine, saliva, and feces for months.<sup>2</sup> HPS is caused by any of at least 25 hantavirus genotypes distributed throughout the Americas. All hantaviruses that cause HPS are hosted by rodents of the family *Cricetidae*. In general, each hantavirus is associated with a different rodent species or subspecies. However, antigenically and genetically distinct hantaviruses have been recently described from shrews, moles and bats.<sup>3</sup>

HPS is documented in several countries that border Colombia; however, only one HPS case has been reported in the nation, specifically during 2013, in Cordoba Department in the northwestern part of the country.<sup>4</sup>

With the aim of exploring hantavirus infection in other regions of Colombia a laboratory survey was designed enrolling patients with febrile syndromes from the municipalities of Meta Department, in the eastern area (Orinoquia region) of Colombia. Meta is characterized by savannahs and partially covered by dense tropical forest vegetation. Cattle raising and agriculture are among the main sources of employment. Domestic and peridomestic habitats are characterized by poor sanitation and rodents are common.

People enrolled in this study included those attending two hospitals in Meta from May 2013 to June 2014 with a documented temperature  $\geq 38^\circ\text{C}$  for a maximum of seven

days, accompanied by one or more of the following signs and symptoms: headache, myalgia, ocular pain, abdominal pain, arthralgia, generalized fatigue, cough, nausea or vomiting, sore throat, rhinorrhea, dyspnea, diarrhea, jaundice, dizziness, rash, ecchymosis, epistaxis, or gingival bleeding. Patients less than five years old or over 65 years old were excluded, as were individuals with a readily identifiable focus of infection. A total of 100 persons were involved in the study. Paired serum samples (in acute and convalescence phases) were collected from each person and prior individual consent was obtained, in accordance with the World Medical Association Declaration of Helsinki. Each participant completed a questionnaire that included personal data, ethnicity, household and workplace characteristics, occupation, domestic sightings of rodents, recreational activities, duration of residence in the area, and history of travel inside and outside the country. Serum samples were maintained at  $-70^\circ\text{C}$  until tested for hantavirus infection by IgG-ELISA using Sin Nombre virus (SNV) as antigen (Focus Diagnostics, USA) according to manufacturer's instructions; SNV cross reacts with many other New World hantaviruses including Andes virus. Positive samples were also tested for leptospirosis by microagglutination test, dengue using IgM and IgG-ELISA (Focus Diagnostics), Rickettsia by Immunofluorescence (Focus Diagnostics), and thick smears for malaria.

Hantavirus infection was based on United States Centers for Disease Control and Prevention criteria.<sup>5</sup> Accordingly, the infection was confirmed by seroconversion of specific IgG antibodies to SNV in three patients (two females and one male); other confirmatory tests (immunofluorescence assay or Western blot) were not used due to the high cost of these tests in Colombia. In seven other patients, positive IgG serology was obtained in both acute and convalescent phase sera, without rising of IgG values, suggesting previous exposure to a hantavirus.

Review of the clinical histories of the serologically confirmed cases showed common characteristics: five-day mean interval from onset of symptoms, fever  $>39.0^\circ\text{C}$ , myalgia,

<sup>☆</sup> This work was carried out at Instituto de Investigaciones Biológicas del Trópico, Universidad de Córdoba, Colombia.

arthralgia, generalized fatigue, nausea, vomiting, diarrhea, headache, abdominal pain, and rash. Other findings included increased hematocrit, creatinine levels, and leukocyte counts. All patients had thrombocytopenia, significantly low platelet counts (98,000, 24,000 and 29,000), and slightly elevated liver enzymes. Chest radiographs were unremarkable. However, patients had no pulmonary edema; only mild respiratory symptoms.

Similar cases have been reported in Panama where 21% of diagnosed HPS patients did not show pulmonary edema and 44% had mild HPS with mild edema but no respiratory insufficiency. Similarly, the first clinical case of hantavirus infection reported in Colombia had no pulmonary edema.<sup>4</sup>

The mean age of positive cases in this study was 33 years. Briefly, patient 1 was a 32-year-old businesswoman with a history of contact with standing water a month before symptom onset. Patient 2, was an 18-year-old female student with a history of contact with standing water. Patient 3 was a 56-year-old male home builder who had a history of contact with sick animals and rodents.

Interestingly, two of the three positive patients were coinfecting with dengue virus and one of them revealed bleeding in his right knee joint eight weeks later. Pleural effusion was detected in the patient who was negative for active dengue infection. Co-infections are common in the tropics. In Colombia, an endemic country for dengue and leptospirosis, co-infections with flaviviruses and even leptospira are frequent. However, none were found positive for leptospirosis, rickettsia, or malaria.

The serological data and the clinical and epidemiological features presented here are compatible with hantavirus fever. This is the first report of hantavirus infection in the Orinoquia region of Colombia. These findings are important for Colombian public health authorities and medical personnel, and argue for the implementation of clinical and laboratory surveillance for hantavirus infection in patients with previous exposure to rodents, presenting with fever and acute respiratory disorders.

### Conflicts of interest

The authors declare no conflicts of interest.

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