



# Hantavirus infection among children hospitalized for febrile illness suspected to be dengue in Barbados



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## KEYWORDS

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**Summary** Emerging picture of hantavirus infection in the South America is characterized by greater proportion of childhood infection and wider spectrum of disease from mild asymptomatic to lethal cardiopulmonary disease. Barbados is endemic for dengue and leptospirosis, both of which share clinical features with hantavirus infection and in many cases neither of these diagnosis could be confirmed. We investigate whether some of the children hospitalized with suspected dengue could indeed have been hantavirus infections. In this prospective study children hospitalized with suspected dengue were tested for hantavirus infection using ELISA for the IgM antibodies. Thirty-eight children tested positive for hantavirus infection. They presented with fever, headache and mild respiratory and gastrointestinal symptoms and signs. None of them had features suggestive of hantavirus cardiopulmonary syndrome. Blood count values ranged from low to normal to high for their age. There were no deaths. Hantavirus infection is prevalent in this Caribbean country. It predominantly presents with milder disease and is responsible for some of the nonspecific febrile illnesses in children.

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## Background

Hantavirus, a Bunyaviridae, are viral zoonosis transmitted from rodents to humans are known to cause 2 major, sometimes overlapping clinical syndromes [1–3]. In Europe and in Asia several species of

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hantavirus, referred to as the old world hantavirus causes a syndrome characterized by hemorrhagic fever with renal syndrome (HFRS) [2,3]. In 1993, a new syndrome caused by the hantavirus and characterized by a febrile prodrome and rapidly progressive pulmonary edema and shock was recognized [1,3,4]. This syndrome was called the Hanta Pulmonary Syndrome or the hantavirus cardiopulmonary syndrome (HCPS). Since the 1993, similar pulmonary syndromes have been associated with Sin Nombre virus (SN) and other species of hantavirus in many of the North and South American countries [5–8]. With further characterization of the hantavirus infection in the Americas, based on some small studies, certain notable differences in the hantavirus infection in the North and South America have been reported [5–8]. The emerging picture of the hantavirus infection in South America is characterized by possible person to person transmission, greater proportion of childhood infections and wide spectrum of disease from mild asymptomatic diseases to lethal pulmonary disease typical of the HCPS [6,7,9].

Barbados, one of the Caribbean islands, in close proximity to North and South America is endemic for dengue transmitted by *Aedes aegypti* mosquitoes and Leptospirosis transmitted by the rodents [10]. Dengue is known to have nonspecific presentations shared by other infections such as hantavirus, Influenza virus, Leptospirosis and Rickettsia.

## Objectives

In this study we asked the question whether some of the suspected dengue cases where dengue was not confirmed could indeed have been hantavirus infection [11–14]. We also studied the clinical and laboratory features of the confirmed hantavirus infection to see if they can provide clues to the early diagnosis of this infection.

## Methods

### Study design

This is a prospective study. This study was conducted at the Queen Elizabeth Hospital (QEH), which is the only hospital with admitting facility for children in Barbados, from October 2009 to September 2011. This study forms a part of the ongoing Barbados dengue study. The study included all febrile children admitted to the QEH and who

had a positive hantavirus IgM antibody titer. Presence of IgM antibodies in the acute phase serum was considered diagnostic of hantavirus infection [15].

### Study subjects

Children, who are admitted to the QEH with suspected dengue, are attended by pediatricians. They receive standard supportive care. They are routinely tested for dengue IgM titers. Blood samples for serology were obtained on day 3–7 of the illness. All other blood tests are routinely done at the time of admission and repeated as necessary. All treatments, investigation results, discharge date and diagnosis are recorded in the patient's file.

### Laboratory methods

Dengue diagnostic techniques have been discussed in an earlier published study [9]. During the study period, the samples that were submitted for the dengue IgM & IgG titers were also tested for the hantavirus IgM titers if they were found to be negative for the dengue IgM. Not all the dengue IgM negative samples could be tested due to periodic out of stock for the reagents. Hantavirus testing was performed by enzyme linked immunosorbent assay (ELISA) using the Focus Diagnostics kits (IgM and IgG DxSelect® CA, USA). It detects antibodies to five predominant strains including Hantaan (HTN), Puumala (PUU), Dobrava (DOB), Seoul (SEO) and Sin Nombre (SN). The IgM test is reported to have an overall sensitivity of 95.1% (83.5–99.4%) and a specificity of 94.1% (83.8–98.8%) [16]. The testing procedure was performed according to the manufacturer's instructions. Based on the published guidelines from the CDC & PAHO, detection of IgM antibodies in the patient's serum was taken as evidence of recent hantavirus infection [15]. Both the dengue tests and the hantavirus tests were done at the Public Health Laboratory of the Ministry of Health, Barbados. Full blood counts and kidney function tests are routinely done on all admitted febrile children. Other investigations such as leptospira serology, liver function tests and chest radiograph were ordered when indicated.

Files of all the children admitted to the QEH with febrile illness and who tested positive for hantavirus infection were reviewed. Data were extracted into a predesigned structured data collection sheet and included demographic data, date of onset of illness, duration of symptoms at the presentation, symptoms and signs on presentation to the hospital, results from the investigations, course of the illness during the hospital stay, duration of hospital stay and the outcome. Patients name was

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