

Seoul hantavirus could be an etiology of acute undifferentiated febrile illness in Colombia?

Carlos Ramiro Silva-Ramos¹  Esp; Álvaro A Faccini-Martínez^{2,3}  Ph.D.

¹Pontificia Universidad Javeriana, Facultad de Ciencias, Departamento de Microbiología, Grupo de Enfermedades Infecciosas, Bogotá, Colombia.

²University of Texas Medical Branch, Pathology Department, Galveston, TX, EE.UU.

³Asociación Colombiana de Infectología, Comité de Medicina Tropical, Zoonosis y Medicina del viajero, Bogotá, Colombia.

*Correspondencia: afaccini@gmail.com

Received: January 2021; Accepted: February 2021; Published: February 2021.

Hantaviruses are classified in two major groups called "Old World" and "New World" hantaviruses due to the geographic distribution of their rodent reservoirs (1). Old World hantaviruses (e.g. Hantaan, Seoul, Puumala viruses among others) cause hemorrhagic fever with renal syndrome (HFRS), whereas New World hantaviruses (e.g. Sin Nombre, Andes viruses among others) mainly target the lung causing hantavirus pulmonary syndrome (HPS) (1).

Seoul virus (SEOV), an "Old World" hantavirus, is moreover the only hantavirus member detected in many countries around the world (2), and infection in urban areas is mainly transmitted to humans by synanthropic rodent species from *Rattus* genus (like *Rattus norvegicus*), however, other forms of infections as intra-laboratory-acquired cases have been reported (3).

SEOV-HFRS is a febrile illness etiology, often misdiagnosed due to its usually mild and atypical clinical presentation, which has a shorter course than other hantavirus-infections and renal dysfunction is associated to oliguria (1,2). Other clinical manifestations like severe abdominal symptoms and hepatic dysfunction may be more common than renal disturbances (3).

Besides Asia continent, molecular and serological evidence of SEOV has been found in pet rats and febrile human patients in Europe, Oceania, Africa and America continents, making SEOV the only hantavirus widely distributed worldwide. In South America, SEOV-positive human sera were found in Brazil during 1994, and evidence of the circulation was also recorded in Argentina and Peru (4,5,6).

Many investigations try to confirm the etiology of acute febrile illnesses worldwide, but usually, in more than the half of cases, it does not have confirmed since diagnostic methods hardly can include all possible pathogens; nevertheless, emerging agents need to be considered, one of them might be SEOV.

How to cite (Vancouver).

Silva-Ramos CR, Faccini-Martínez AA. Seoul hantavirus could be an etiology of acute undifferentiated febrile illness in Colombia?. Rev MVZ Córdoba. 2021; 26(1):e2353. <https://doi.org/10.21897/rmvz.2353>



©The Author(s), Journal MVZ Córdoba 2020. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by-nc-sa/4.0/>), lets others remix, tweak, and build upon your work non-commercially, as long as they credit you and license their new creations under the identical terms.

One of the etiology that causes acute febrile illness and can be confused with SEOV-HFRS is leptospirosis, as both share clinical and epidemiological characteristics: both are febrile illnesses associated with renal damage, both are distributed mostly in tropical and subtropical areas, and both are rodent-borne infections, thus, mistaken diagnosis usually be common. A report in Brazil confirm this concern, in which "Old World" hantavirus cases have been reported clinically as leptospirosis before laboratory-confirmation (5). There are also reports in which both infectious agents, Hantavirus and *Leptospira*, can co-exist in the same host and develop co-infections (7).

In Colombia, serological evidence of hantavirus in humans has been found since 2007, year in which a non-malarial acute febrile illness study at the "Urabá antioqueño" evidenced exposure against Hantavirus in two febrile patients, demonstrating hantavirus circulation between humans (8). Later, between 2012 and 2013, a study made in Córdoba department evidenced Hantavirus infection in six patients, two being co-infections with dengue virus and *Leptospira* and one of them being fatal; none developed clinical or laboratorial characteristics compatible with the typical "New World" HPS (9). In addition, a new case in Montería (capital city of Córdoba) was reported; this patient proved seroconversion to Sin Nombre Virus (SNV), however, only mild respiratory symptoms were present, being initially misdiagnosed as leptospirosis with not clear clinical symptoms of HPS (10).

These preliminary data may suggest that hantavirus disease in this Caribbean department could be mild and not clinically compatible with HPS caused by New World hantaviruses, even positive serological diagnosis for SNV, which can be cross-reactive between hantavirus species (11), being possible that an Old World hantavirus might be involved in these febrile human cases. Interestingly, a study between 2007 and 2009 in Sucre department (north frontier for Córdoba) evidenced seropositivity for SNV in rodents from the families Muridae and Cricetidae, including species from genus *Mus* spp. and *Rattus* spp., demonstrating that at least one hantavirus is circulating in these synanthropic rodents (12).

Finally, in 2013, another study made in the Orinoquía region, in which febrile patients from Meta department were enrolled, three seroconverted to SNV and seven more evidenced seropositive, suggesting previous exposure to Hantavirus. A review of the clinical data of the three patients which seroconverted showed common characteristics of acute febrile illness with general unspecific symptoms and only mild respiratory symptoms; laboratory findings included increased hematocrit, creatinine and leukocyte counts, thrombocytopenia and elevated liver enzymes (13).

The above data reaffirms Hantavirus in Colombia and the importance of consider it into the differential diagnosis of acute febrile illness. However, accurate diagnosis of a typical New World hantavirus is still in doubt, and probably are not involved in these cases as clinical features of HPS are not present; conversely, hantavirus infection in Colombia may be has a milder and atypical course. In this way, adding to the fact that the most widespread Old World hantavirus is SEOV and considering its atypical and mild clinical course, it should be important to consider SEOV as one of the possible etiological agents of hantavirus infections in Colombia, standing out the importance of searching it among febrile patients.

REFERENCES

1. Jonsson CB, Figueiredo LT, Vapalahti O. A Global Perspective on Hantavirus Ecology, Epidemiology, and Disease. *Clin Microbiol Rev*, 2010; 23(2):412-441. <https://doi.org/10.1128/CMR.00062-09>
2. Clement J, LeDuc JW, McElhinney LM, Reynes J, Van Ranst M, Calisher CH. Clinical Characteristics of Ratborne Seoul Hantavirus Disease. *Emerg Infect Dis*. 2019; 25(2):387-388. <https://dx.doi.org/10.3201/eid2502.181643>

3. Kim YS, Ahn C, Han JS, Kim S, Lee JS, Lee PW. Hemorrhagic fever with renal syndrome caused by the Seoul virus. *Nefrón*. 1995; 71(4):419-427. <https://doi.org/10.1159/000188762>
4. García PM, Percy S, Herrera AL, Donaires F, Álvarez C, Arrasco J, et al. Confirmación Etiologic de los dos primeros casos de Hantaviriosis Humana en Perú. *Rev Peru Med Exp Salud Publica*. 2011; 28(3):564-570. <https://doi.org/10.17843/rpmesp.2011.283.542>
5. Hindrichsen S, Medeiros A, Clement J, Leirs H, Mc Kenna P, Matthys P, et al. Hantavirus infection in Brazilian patients from Recife with suspected leptospirosis. *Lancet*, 1993; 341(8836):50. [https://doi.org/10.1016/0140-6736\(93\)92523-V](https://doi.org/10.1016/0140-6736(93)92523-V)
6. Seijo A, Pini N, Levis S, Coto H, Deodato B, Cernigoi B, et al. Study of Hantavirus seoul in a human and rodent population from a marginal area in Buenos Aires City. *Medicina (B Aires)*. 2003; 63(3):193-196. <https://pubmed.ncbi.nlm.nih.gov/12876901/>
7. Clement J, Esbroeck M V, Lagrou K, Verschueren J, Sunil-Chandra NP, Ranst M V. Leptospirosis versus hantavirus infections in the Netherlands and in Belgium, 2000 to 2014. *Euro Surveill*. 2014; 19(38):20912. <https://doi.org/10.2807/1560-7917.ES2014.19.38.20912>
8. Arroyave E, Londoño AF, Quintero JC, Agudelo-Florez P, Arboleda M, Díaz FJ, Rodas JD. Etiología y caracterización epidemiológica del síndrome febril no palúdico en tres municipios del Urabá antioqueño, Colombia. *Biomedica*. 2013; 33(Sup1):99-107. <https://doi.org/10.7705/biomedica.v33i0.734>
9. Mattar S, Tique V, Miranda J, Montes E, Garzón D. Undifferentiated tropical febrile illness in Cordoba, Colombia: Not everything is dengue. *J Infect Public Health*. 2017; 10(5):507-512. <https://pubmed.ncbi.nlm.nih.gov/28162961/>
10. Mattar S, Garzon D, Tadeu L, Faccini-Martínez AA, Mills JN. Serological diagnosis of hantavirus pulmonary syndrome in a febrile patient in Colombia. *Int J Infect Dis*. 2014; 25:201-203. <https://doi.org/10.1016/j.ijid.2014.03.1396>
11. Lederer S, Lattwein E, Hanke M, Sonnenberg K, Stoecker W, et al. Correction: Indirect Immunofluorescence Assay for the Simultaneous Detection of Antibodies against Clinically Important Old and New World Hantaviruses. *PLOS Neglected Tropical Diseases*. 2020; 14(11):e0008864. <https://doi.org/10.1371/journal.pntd.0008864>
12. Arroyo MS, Corrales AH, Perez JJ, Alvarez GL, Castellar MA, Blanco TP. Evidencia serológica de infección por hantavirus (Bunyaviridae: Hantavirus) en roedores del Departamento de Sucre, Colombia. *Rev Salud Pública*. 2012; 14(5):755-764. <https://revistas.unal.edu.co/index.php/revsaludpublica/article/view/22357>
13. Sánchez L, Mattar S, Rodriguez D, Tique V, Rodríguez I. First serological evidence of hantavirus infection in humans from the Orinoquia region of Colombia. *Braz J Infect Dis*. 2016; 20(5):507-508. <https://doi.org/10.1016/j.bjid.2016.05.006>