Travel Medicine and Infectious Disease 64 (2025) 102800

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Hantavirus and Leptospira are important causes of nonspecific acute febrile syndrome, Meta, Colombia

Liliana Sánchez-Lerma [a], Salim Mattar [b,*], Verónica Contreras [b], Jorge Miranda [b], Vaneza Tique [b], Virginia Rodríguez [c], Derly Rodriguez [d], Sonia Lopez [a], Andrés Rojas-Gulloso [a,**]

[a] Universidad Cooperativa de Colombia, Facultad de Medicina. Grupo de investigación de Villavicencio-GRIVI, y Centro de Investigación en Salud para el Trópico, Colombia
[b] Universidad de Córdoba, Instituto de Investigaciones Biológicas del Trópico, Montería, Córdoba, Colombia
[c] University of Cordoba, Faculty of Health Sciences, Department of Bacteriology, Research group GIMBIC. Monteria, Cordoba, Colombia
[d] Hospital Departamental de Villavicencio, Meta-Colombia, Colombia

ARTICLE INFO

Keywords:
Emerging infectious diseases
Environment
Preventive medicine public health
Dengue fever
Tropical climate
Disease vector infectious

ABSTRACT

Introduction: Acute undifferentiated febrile illnesses are fevers lasting less than fourteen days without an evident focus of infection on the initial physical examination or with inconclusive laboratory tests.
Objective: Carry out epidemiological surveillance of the etiology of acute undifferentiated febrile syndrome in the Meta department.
Methods: A descriptive, prospective cross-sectional study was carried out between February 2021 and June 2023 in a first-level hospital in the department of Meta, Colombia. All enrolled patients underwent routine hematology and blood biochemistry examinations. RT-qPCR was performed for Dengue and serology for laboratory diagnoses using ELISA and MAT for Hantavirus and Leptospirosis, respectively. A descriptive and bivariate analysis was performed using SPSS vr 23.0.
Results: Of the study's total of one hundred patients, 14 % showed antibodies against hantavirus IgG, of which two were seroconverted. In addition, a risk factor OR = 8.3 (CI = 1.8–38.4) for Hantavirus was found in those patients who had contact with farm animals. Regarding leptospirosis, 3 % of the sera agglutinated with titers greater than 1:400, resulting in a primary infection; 11 % of the sera presented agglutination with titers no greater than 1:200 as exposure to leptospirosis. The bivariate analysis showed an OR = 2.4; CI = 0.75–7.4 with water recreational activities in the last 30 days before the onset of symptoms.
Conclusions: Our study demonstrates the importance of Hantavirus, Dengue, and leptospirosis as a cause of acute undifferentiated febrile illnesses. Coinfections are frequent in one of the tropical areas of Colombia, so it is crucial to establish a more precise diagnosis.

1. Introduction

During the last two decades in tropical countries, acute undifferentiated febrile illnesses (AUFI) have increased, caused mainly by emerging or re-emerging pathogens [1]. AUFI is a fever lasting less than fourteen days without an obvious source of infection on the initial physical examination or with inconclusive laboratory tests. AUFI can be a self-limiting disease but can progress to severity and be potentially lethal [2]. Different factors contribute to the appearance of these diseases, such as climate change, forced displacement, tourism, migration, urbanization, and unplanned human activities. The above affects wildlife, which can cause high morbidity and mortality in humans and animals, leading to a significant economic burden in developing countries [1,3–6].

There are approximately 60 etiologies that are part of the AUFI, which have a similar clinical presentation. Furthermore, diagnostic tests are scarce, so the diagnosis is based on the patient's clinical history and the endemicity of the agents in each region [2,7,8]. As a tropical country, Colombia is endemic in many tropical diseases, which for decades has had a high prevalence of dengue and malaria cases. However,

* Corresponding author.
** Corresponding author.
E-mail addresses: smattar@correo.unicordoba.edu.co (S. Mattar), andres.rojasgu@campusucc.edu.co (A. Rojas-Gulloso).

https://doi.org/10.1016/j.tmaid.2025.102800
Received 18 March 2024; Received in revised form 26 November 2024; Accepted 10 January 2025
Available online 17 January 2025

there is serological and molecular evidence of the circulation of other etiological agents that produce clinical symptoms like Dengue, encephalitis, yellow fever, malaria, brucellosis, rickettsiosis, leptospirosis, lymphocytic choriomeningitis, Mayaro fever, Oropuche, and hantaviruses among others [1,2,9–14]. Despite efforts to develop clinical algorithms that allow healthcare personnel to make the possible etiological diagnosis, about 40 % of cases remain undiagnosed. Therefore, making a clinical diagnosis without laboratory confirmation is almost impossible [2,7].

Hantavirus fever is an underdiagnosed disease and is little known by healthcare personnel. It sometimes presents as a mild illness with fever, myalgia, arthralgia, and other characteristic symptoms of nonspecific acute febrile syndrome [10]. The first serological evidence of hantavirus circulation in Colombia was reported in 2004 in the department of Córdoba [15,16]. In 2016, hantavirus infection was diagnosed through seroconversion in three patients with febrile syndrome in the department of Meta [9]. A coinfection of Hantavirus and malaria was recently reported in the department of Córdoba [12].

On the other hand, leptospirosis is an acute septicemic febrile disease transmitted by direct or indirect contact with rodents and other animals and affects humans and animals. Leptospirosis has been underestimated compared to other febrile diseases, such as Dengue, masking its true incidence [13,17]. In humans, signs and symptoms of leptospirosis range from subclinical infection to severe manifestations beginning with a septicemic phase followed by a severe presentation with vascular, hepatic, renal, pulmonary, and skeletal muscle injury, or Weil syndrome [18].

Both hantavirus fever and leptospirosis can be transmitted by rodents, which allows infection by these agents to be present enzootically in rodents or domestic animals. This could increase the risk of coinfection in humans and make diagnosis difficult, which allows notification to entities in charge of public health [17]. In developing countries, laboratory diagnosis resources are insufficient; epidemiological surveillance is scarce in these endemic regions, so the incidence of etiologies and the diagnosis of fatal cases are unknown [13].

This study aimed to carry out epidemiological surveillance of the etiology of acute undifferentiated febrile syndrome in the department of Meta.

2. Methods

2.1. Study design, location, samples, patients, inclusion, and exclusion criteria

A descriptive, prospective cross-sectional study was conducted between February 2021 and June 2023. The study was conducted in the main hospital of the department of Meta, located in the capital of Villavicencio. The department is in the East of Colombia, and it is characterized by a tropical climate with an average temperature of 24 °C, a humidity of 95 %, and an altitude of 467 m above sea level (Fig. 1). Paired serum samples were obtained; in the acute phase, they were taken in the first five days of the appearance of symptoms. Convalescent phase sera were obtained between 15 and 20 days after the appearance of symptoms. The definition of cases of acute febrile syndromes was taken according to the guidelines of the CDC and the Ministry of Health of Colombia [19]. The inclusion criteria were fever, myalgia, arthralgia, headache, asthenia, chills, jaundice, dyspnea, and rash. Patients with malaria, upper urinary tract infections, bronchitis, otitis media, tuberculosis, and diarrhea as primary symptoms were excluded from the study, as were patients with autoimmune diseases and chronic liver disease.

2.2. Epidemiological, clinical, and laboratory data information

Sociodemographic data were obtained from the patients, including age, sex, geographic origin, travel outside the city of residence, date of admission, date of onset of prodrome, symptoms, clinical findings, and ownership of domestic animals at home. At admission, all patients

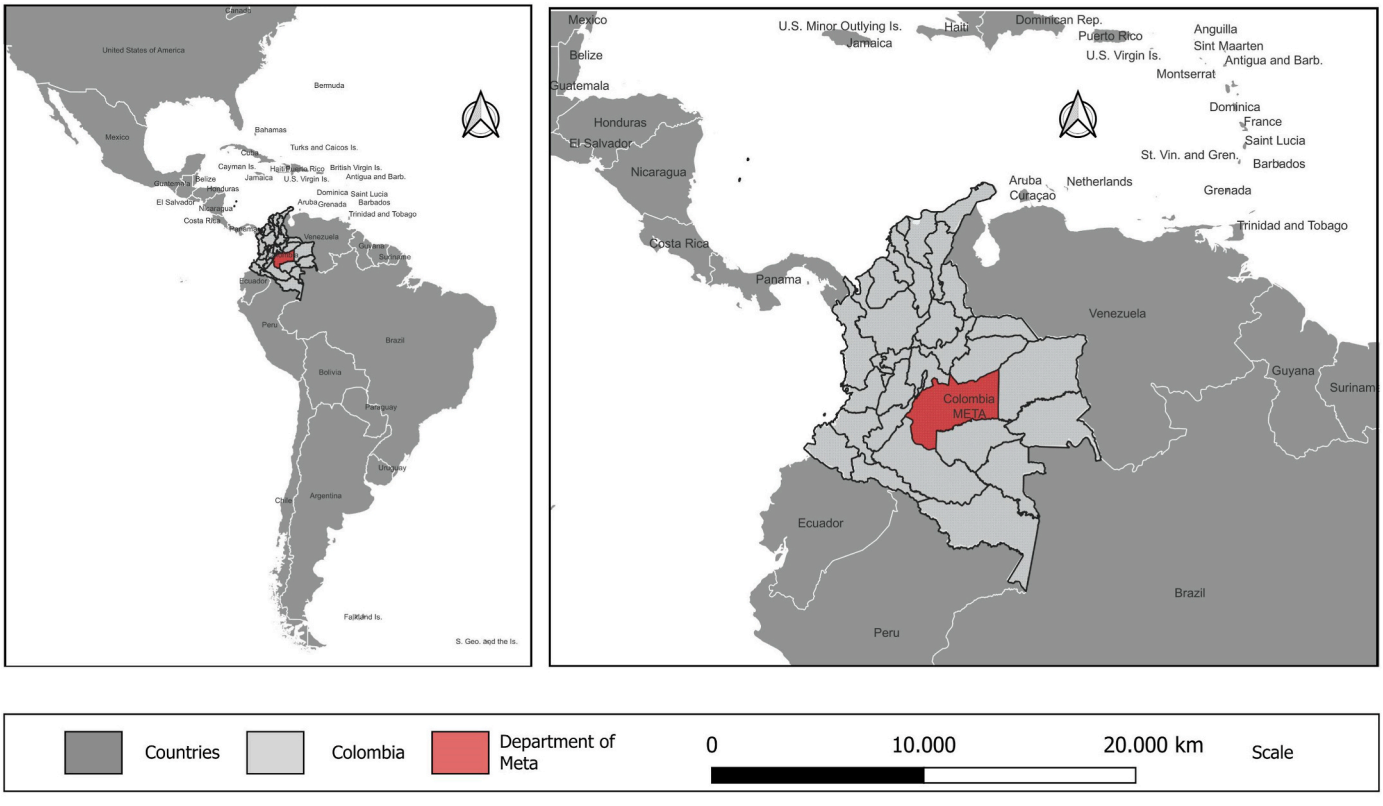

Fig. 1. Map of Colombia and location of department of Meta.

underwent routine hematology and blood biochemistry examinations, such as blood cell count, prothrombin time, platelet number, blood glucose, and liver biochemical profile. According to the clinical presentation, some patients underwent clinical studies such as X-rays, electrocardiograms, and pulse oximetry.

2.3. Serological and molecular diagnosis

The serological detection of Hantavirus was carried out using an ELISA Anti-Hantavirus pool 2 America (Euroinmun, Ref EI 278h-9601-2-G), is designed with a high specificity due to the quality of the recombinant antigen used. The manufacturers have standardized the kit, including subjects with different infectious diseases [20], and none showed a cross-reaction with the recombinant hantavirus antigen. The ELISA kit also includes a negative control of human origin, which is instrumental in establishing a defined cut-off. Samples with a ratio of $\geq$1.1 were considered as seropositive, those with a ratio of $\geq$0.8 to $<$1.1 were regarded as borderline, and those with a ratio of $<$0.8 were considered as negative. The ELISA kit detects IgG antibodies against the Andes and sin Nombre virus (SNV) virus (New world). The serological detection of Leptospira spp was carried out with the MAT microagglutination technique, using 16 serovars of Leptospira (L. interrogans: Autumnalis, Australis/Bratislava, Canicola, Icterohaemorrhagiae/Copenhageni, Grippotyphosa, Hardjoprajitno, Hebdomadis, Djasiman, Pomona, Pyrogenes/Zanoni. L. borgpetersenii:/Ballum, Mini/Sari, Tarassovi. L. weilii: Celledoni, L. weilii/Javanica/Coxi/Cox; and L. noguchii/Panama). Confirmed cases of acute leptospirosis were based on micro-agglutination testing (MAT) criteria. Titers $>$1:400 were considered positive; those patients with a four-fold or more significant increase in MAT titers between acute and convalescent-phase samples were confirmed [13,19,21]. A negative control consisting of the antigen and PBS diluent was included to verify that there was no autoagglutination. Because the department of Meta is an endemic area for Dengue, an RT-qPCR for DENV was performed, which amplified the regions of the NS1 gene [22,23]. RNA was extracted from sera using the Magnetic Beads Viral RNA Extraction Kit (Bioland Scientific).

2.4. Analysis of data

Data from medical records, paraclinical examinations, and laboratory results were analyzed using the SPSS statistical program (version 23.0). The descriptive and bivariate analysis was carried out, considering the dependent variables. (seropositive or seronegative results to Hantavirus and Leptospira) and independent variables such as sociodemographic and epidemiological data of the patients. with a significance $<$ *0.05* (P value) and a Confidence Interval (CI) of 95 %.

2.5. Ethics

This study was approved by the ethical committee of the Institute of Biological Research of Tropics (IIBT), University of Cordoba. A written informed consent was obtained from each patient, and in the case of pediatric patients, it was obtained from an accompanying family member. The study was carried out under principles of the Declaration of Helsinki and ethical considerations of research in Colombia, resolution number 008430 of 1993 of the Ministry of Health.

3. Results

A comprehensive study was conducted, including a significant number of patients-one hundred in total. There were no differences between the gender of the patients; 84 % came from urban areas and 16 % from rural regions. Fourteen percent of patients had IgG antibodies corresponding to the acute and convalescent phases. However, in two of these cases, a four-fold increase in IgG titers was observed, which is evidence of acute infection and seroconversion in these patients. The clinical and epidemiological characteristics of the two patients with acute Hantavirus infection are shown in Table 1. The bivariate analysis of these one hundred patients is shown in Table 2; a vital risk factor was found between the seroprevalence of Hantavirus and contact with animals of the farm with an OR = 8.3 (CI = 1.8–38.4) and origin from an urban or rural area with an OR = 4.27 (CI = 1.2–14.3).

Regarding leptospirosis, 3 % of the sera agglutinated with titers greater than 1:400 against the serovar *L. interrogans*: *Australis/Bratislava*. Eleven percent of the sera presented agglutination with titers no greater than 1:200 with the serogroups *L. interrogans: Australis/Bratislava, L. interrogans: santarosai/Batavie, L. interrogans: Canicola/Canicola, L. interrogans: Grippotyphosa/Grippotyphosa, L. interrogans: Sejroe/Hardjo/Hardjoprajitno and* L. *interrogans: Pyrogenes/Zanoni.* The bivariate analysis showed a risk factor for Leptospira infection with an OR = 2.4; CI = 0.75–7.4 with water recreational activities in the last 30 days before the onset of symptoms. Furthermore, the results were compatible with their clinical and epidemiological data (Tables 1 and 2).

The diagnosis of Dengue by RT-qPCR was positive in only 4 % of patients; coinfection of Dengue with Hantavirus (ELISA-seroconversion) was found in patient number seven.

4. Discussion

Dengue is remarkable since the Department of Meta is endemic for this flavivirus, and the frequency of infection was expected to be much higher. This could be because the vectors and the etiological agents of the acute febrile syndrome are displaced or asymmetrically circulated.

Colombia is an endemic country to Dengue and other emerging and re-emerging diseases. However, other etiological agents can cause coinfections, such as Hantavirus and leptospirosis. These pathologies are essential in acute febrile syndromes in the department of Meta [24].

In the present study, 14 % of the patients showed antibodies against Hantavirus (Hantan/Sin Nombre Virus), and two (2 %) showed seroconversion by ELISA tests. In Colombia, Hantavirus seroprevalence studies in rodents have been described [16,25,26]. In humans, the first serological evidence of Hantavirus was reported in 2004 in Córdoba and 2007 in two febrile patients from Uraba near the border with Panama [14]. Between 2012 and 2013, Hantavirus infections were reported in six patients from the department of Córdoba; two of them had coinfections with Dengue and Leptospira, and another died [27]. Subsequently, a case of Hantavirus infection was reported in Monteria, Córdoba. This patient presented seroconversion against the Sin Nombre virus, with mild respiratory symptoms [28]. In the department of Meta, between 2013 and 2014, three febrile patients presented seroconversion against Hantavirus using ELISA; all had low platelet counts, and none presented respiratory difficulty; two were coinfected with dengue [9].

There are studies in several South American countries where a less virulent variant of Hantavirus has been reported, especially in Panama [29], close to the area of the present study Mattar et al., with Serological diagnosis of hantavirus pulmonary syndrome in a febrile patient in Colombia [30]. ii) the antigen used in the ELISA is a mixture of recombinant antigens of the nucleocapsid protein of the Andes hantavirus and Sin Nombre Virus, which guarantee a high specificity. iii) Since seroconversion only occurred in two patients, it indirectly confirms the specificity of the hantavirus test; otherwise, more seropositive sera would have been presented due to possible cross-reactions. Regarding the use of PCR, it is known that viremia in patients with Hantavirus occurs in the prodrome, so molecular techniques can rarely detect active viremia. This is because when patients require medical attention in the emergency room, several days have already passed.

The results obtained in the present work are similar to the previously mentioned studies; two of our patients presented seroconversion of IgG antibodies against Hantavirus using an ELISA test, and one of these showed coinfection with Dengue, presenting mild clinical manifestations, with headache, vomiting, and fever. The patient did not present findings of thrombocytopenia or renal or respiratory symptoms

Table 1
Clinical and epidemiological findings in patients confirmed by Laboratory with Hantavirus, Dengue virus and Leptospira.

Patient	Age/ Gender	Area	Clinical presentation and Symptoms	Paraclinic findings	Presuntive Diagnosis	Laboratory diagnosis
5	14/M	Rural	Headache, vomiting and fever	Normal	Undifferentiated febrile syndrome	Hantavirus (ELISA)
7	10/M	Urban	Vomiting and fever	Normal	Undifferentiated febrile syndrome	Hantavirus (ELISA) Dengue (RT-qPCR)
8	10/F	Urban	Fever, headache, myalgia, arthralgia, Nausea, Abdominal pain, diarrhea, retroocular pain, rash,	Thrombocytopenia Lymphocytopenia	Dengue	Dengue (RT-qPCR)
34	8/M	Urban	Fever, headache, vomiting, abdominal pain,	Leukocytopenia, lymphocytopenia Hepatomegaly	Dengue	Dengue (RT-qPCR
56	13/M	Urban	Fever, headache, chills, general malaise, myalgia and arthralgia	Trombocitopenia Linfocitopenia	Dengue	Dengue (RT-qPCR
25	63/M	Urban	Headache, chills, myalgia, arthralgia, dizziness, vomiting, abdominal pain, diarrhea and fever	Occult blood in stool	Undifferentiated febrile syndrome	*L. interrogans: Australis/ Bratislava.* (MAT)
68	26/M	Urban	Headache, abdominal pain, fever	ND	Undifferentiated febrile syndrome	*L. interrogans: Australis/ Bratislava.* (MAT)
118*	27/F	Rural	Chills, myalgia, arthralgia, nausea, jaundice, fever	High transaminases,	Undifferentiated febrile syndrome	*L. interrogans: Australis/ Bratislava.* (MAT)

M = male; F = female; *patient with diagnosed with lupus; ND = no done.

Table 2
Bivariate analysis of the epidemiological characteristics of one hundred patients with positive results for Hantavirus and Leptospira.

	Leptospira		Hantavirus	
Sociodemographic data	P-value	RP (IC)	P-value	RP (IC)
Age	0,239	0,98 (0,94-1,01)	0.445	1.07 (0,89-1,28)
Gender				
Female	0,488	0,668 (0,214-2,09)	0,074	0,325 (0,095-1,12)
Area				
Urban	0,787	0,826 (0,206-3,31)	0,019	0,234 (0,069-0,78)
Rural	0,787	1,21 (0,302-4,84)	0,019	4.27 (1,2–14,3)
Epidemiological data				
Presence of rodents at home	0,15	0,317 (0,06-1,51)	0,337	1,76 (0,55-5,5))
Contact with rodents	NS	NS	0,662	1,44 (0,27-7,51)
Contact with farm's animals	0.908	0,87 (0,09-7,74)	>0,05	8,3 (1,8–38,4)
Domestic animals at home	0,377	2,3 (0,4–9,8)	0,825	1,17 (0,29-4,6)
Aquatic recreational activities in the last 30 days	0,144	2,4 (0,75-7,4)	0,344	0,5 (0,13-2)
Floods in the housing area in the last 30 days	0.56	0,53 (0,06-4,5)	0,77	1,3 (0,25-6,6)

characteristic of Hantavirus. The findings suggest that the clinical characteristics are mild and atypical or that there is the circulation of a Hantavirus variant that is less virulent than those circulating in Argentina. Chile, Brazil, and USA [10].

Furthermore, considering the bivariate analysis in Table 2, a significant risk factor can be observed between the seroprevalence of Hantavirus and contact with farm animals, with an OR = 8.3 (CI = 1.8–38.4) and origin from rural areas, with an OR = 4.27 (CI = 1.2–14.3). In previous studies, the interaction between wild rodents and synanthropic rodents was evidenced, which allows the maintenance of the enzootic cycle of the virus in rodents that have more significant contact with humans and domestic animals in rural areas.

Leptospirosis was reported as the second cause of acute febrile syndrome in the Colombian Orinoquia. However, it is considered an underdiagnosed disease that may be overlapped by dengue [9]. MAT remains the gold-standard method; however, its sensitivity depends on the serovars evaluated, so it is necessary to include local native strains to improve their effectiveness [14,31].

Rodents can transmit leptospirosis and hantaviruses, coexist in the same host, and cause human coinfections [10,30]. However, there were no cases of coinfection between these two etiological agents in our study; 14 % of the patients presented antibodies against Leptospira spp. Of these, three patients presented antibody titers >1:400 with clinical characteristics compatible with the disease (Table 1).

In Colombia, since 2007, leptospirosis has been declared notifiable; however, there is a large number of underreports in many regions, mainly due to the difficulty of obtaining paired samples during the convalescent phase. There is also no adequate diagnostic equipment, and maintaining viable Leptospira serovars requires much time and laboratory personnel trained in the MAT technique. Furthermore, in endemic areas, the nonspecific symptoms of acute febrile syndrome confuse the diagnosis with other tropical diseases, making etiological diagnosis difficult [17].

Considering that nearly 60 etiologies are part of the AUFI and have similar clinical presentations, diagnostic tests to confirm the disease represent a real challenge. Furthermore, 40 % of cases of acute febrile syndrome are underdiagnosed or never have a definitive diagnosis, which represents a challenge for health institutions and government institutions [1,2,7,8,14,15,18,32]. One of the limitations of the present study was the need for more funds to search for more etiological agents and thus try to reduce the percentage of underdiagnosis.

In conclusion, our study demonstrates the importance of Hantavirus, Dengue, and leptospirosis as a cause of AUFI. Coinfections are frequent in one of the tropical areas of Colombia, so it is crucial to establish a more precise diagnosis.

CRediT authorship contribution statement

Liliana Sánchez-Lerma: Writing – original draft, Project administration, Investigation, Data curation. **Salim Mattar:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis. **Verónica Contreras:** Writing – original draft, Methodology, Investigation. **Jorge Miranda:** Writing – review & editing, Writing – original draft, Methodology, Investigation. **Vaneza Tique:** Writing – original draft, Methodology, Investigation, Data curation. **Virginia Rodríguez:** Methodology, Investigation, Formal analysis, Data curation. **Derly Rodriguez:** Supervision, Methodology, Investigation, Data curation. **Sonia Lopez:** Methodology, Investigation, Data curation. **Andrés Rojas-Gulloso:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation.

Funding/support

This work was funded by Universidad Cooperativa de Colombia. Number project INV2983.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Mattar S, Tique V, Miranda J, Montes E, Garzon D. Undifferentiated tropical febrile illness in Cordoba, Colombia: not everything is dengue. J Infect Public Health 2017;10:507–12. https://doi.org/10.1016/j.jiph.2016.09.014.
[2] Silva-Ramos CR, Gil-Mora J, Serna-Rivera CC, Martínez Díaz H-C, Restrepo-López N, Agudelo-Flórez P, et al. Etiological characterization of acute undifferentiated febrile illness in Apartadó and Villeta municipalities, Colombia, during COVID-19 pandemic. Le Infez Med 2023;31:517–32. https://doi.org/10.53854/liim-3104-11.
[3] Rojas-Gulloso A, Sánchez-Lerma L, Montilla M, Morales-Pulecio F, Sarmiento-Rudolf E, Tapia-Reales R. Infectious diseases in migrant pregnant women from an area of the Colombian Caribbean. Trav Med Infect Dis 2023;55:102629. https://doi.org/10.1016/j.tmaid.2023.102629.
[4] Camprubí-Ferrer D, Cobuccio L, Van Den Broucke S, Genton B, Bottieau E, D'Acremont V, et al. Causes of fever in returning travelers: a European multicenter prospective cohort study. J Trav Med 2022;29. https://doi.org/10.1093/jtm/taac002.
[5] Murray KA, Daszak P. Human ecology in pathogenic landscapes: two hypotheses on how land use change drives viral emergence. Curr Opin Virol 2013;3:79–83. https://doi.org/10.1016/j.coviro.2013.01.006.
[6] Hess J, Boodram L-LG, Paz S, Stewart Ibarra AM, Wasserheit JN, Lowe R. Strengthening the global response to climate change and infectious disease threats. BMJ 2020:m3081. https://doi.org/10.1136/bmj.m3081.
[7] Mørch K, Manoharan A, Chandy S, Singh A, Kuriakose C, Patil S, et al. Clinical features and risk factors for death in acute undifferentiated fever: a prospective observational study in rural community hospitals in six states of India. Trans R Soc Trop Med Hyg 2023;117:91–101. https://doi.org/10.1093/trstmh/trac091.
[8] Wangdi K, Kasturiaratchi K, Nery SV, Lau CL, Gray DJ, Clements ACA. Diversity of infectious aetiologies of acute undifferentiated febrile illnesses in south and Southeast Asia: a systematic review. BMC Infect Dis 2019;19:577. https://doi.org/10.1186/s12879-019-4185-y.
[9] 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;20:507–8. https://doi.org/10.1016/j.bjid.2016.05.006.
[10] Silva-Ramos CR, Faccini-Martínez ÁA. Podría el hantavirus Seúl ser una etiología de la enfermedad febril aguda indiferenciada en Colombia? Rev MVZ Córdoba 2021;26. https://doi.org/10.21897/rmvz.2353.
[11] Cabrera R, Mendoza W, López-Mosquera L, Cano MA, Ortiz N, Campo V, et al. Tick-Borne-agents detection in patients with acute febrile syndrome and ticks from magdalena medio, Colombia. Pathogens 2022;11:1090. https://doi.org/10.3390/pathogens11101090.
[12] Tique-Salleg V, Chevel-Mejia J, Miranda J, Mattar S. Unusual coinfection of malaria and hantavirus in the Colombian caribbean region. Trav Med Infect Dis 2023;55:102631. https://doi.org/10.1016/j.tmaid.2023.102631.
[13] Parra Barrera EL, Reales-González J, Salas D, Reyes Santamaría E, Bello S, Rico A, et al. Fatal acute undifferentiated febrile illness among clinically suspected leptospirosis cases in Colombia, 2016–2019. PLoS Neglected Trop Dis 2023;17:e0011683. https://doi.org/10.1371/journal.pntd.0011683.
[14] Arroyave E, Londoño AF, Quintero JC, Agudelo-Florez P, Arboleda M, Díaz FJ, et al. Etiología y caracterización epidemiológica del síndrome febril no malárico en tres municipios del Urabá antioqueño, Colombia. Biomedica 2012;33. https://doi.org/10.7705/biomedica.v33i0.734.
[15] Máttar S, Parra M. Serologic evidence of hantavirus infection in humans, Colombia. Emerg Infect Dis 2004;10:2263–4. https://doi.org/10.3201/eid1012.040821.
[16] Alemán A, Iguarán H, Puerta H, Cantillo C, Mills J, Ariz W, et al. First serological evidence of Hantavirus infection in rodents in Colombia. Rev Salud Publica (Bogota) 2006;8(Suppl 1):1–12.
[17] Arboleda M, Mejía-Torres M, Posada M, Restrepo N, Ríos-Tapias P, Rivera-Pedroza LA, et al. Molecular diagnosis as an alternative for public health surveillance of leptospirosis in Colombia. Microorganisms 2023;11:2759. https://doi.org/10.3390/microorganisms11112759.
[18] Tique V, Mattar S, Miranda J, Oviedo M, Noda A, Montes E, et al. Clinical and epidemiological status of leptospirosis in a tropical caribbean area of Colombia. BioMed Res Int 2018;2018:1–8. https://doi.org/10.1155/2018/6473851.
[19] Centers for Disease Control and Prevention. Viral hemorrhagic fever (VHF) 2022 case definition. https://ndc.services.cdc.gov/case-definitions/viral-hemorrhagic-fever-2022/. [Accessed 13 January 2024].
[20] Salehi-Vaziri M, Sarvari J, Mansurnejadan M, Shiri A, Joharinia N, Khoshbakht R, et al. Evidence of Hantavirus circulation among municipal street sweepers, southwest of Iran. VirusDisease 2021;32:251–4. https://doi.org/10.1007/s13337-021-00694-3.
[21] Ministerio de Salud. Lineamientos para la preparación y respuesta ante la eventual introducción de casos de enfermedad por el virus del ébola (EVE) en Colombia 2014. https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/VSP/LineamientosEVE.pdf. [Accessed 10 January 2024].
[22] CDC. Guidelines for the control of leptospirosis. WHO Offset Publ; 1982. p. 1–171.
[23] Chadsuthi S, Bicout DJ, Wiratsudakul A, Suwancharoen D, Petkanchanapong W, Modchang C, et al. Investigation on predominant Leptospira serovars and its distribution in humans and livestock in Thailand, 2010-2015. PLoS Neglected Trop Dis 2017;11:e0005228. https://doi.org/10.1371/journal.pntd.0005228.
[24] Waggoner JJ, Gresh L, Mohamed-Hadley A, Ballesteros G, Davila MJV, Tellez Y, et al. Single-reaction multiplex reverse transcription PCR for detection of zika, chikungunya, and dengue viruses. Emerg Infect Dis 2016;22:1295–7. https://doi.org/10.3201/eid2207.160326.
[25] Maggi RG, Birkenheuer AJ, Hegarty BC, Bradley JM, Levy MG, Breitschwerdt EB. Comparison of serological and molecular panels for diagnosis of vector-borne diseases in dogs. Parasites Vectors 2014;7:127. https://doi.org/10.1186/1756-3305-7-127.
[26] Sanchez L. Dengue, Leptospirosis, Hantavirosis y Rickettsiosis en Pacientes con Síndrome Febril Agudo no Paludico en el Meta, Colombia (2013-2014). Instituto de Medicina Tropical Pedro Kouri; 2017.
[27] Blanco P, Arroyo S, Corrales H, Pérez J, Álvarez L, Castellar A. Evidencia serológica de infección por hantavirus (Bunyaviridae: Hantavirus) en roedores Serological evidence of hanta virus infection (Bunyaviridae: Hantavirus) in rodents from the Sucre Department in Colombia Artículos Originales/Original Articles. Rev Salud Pública 2012;14:755–64.
[28] Montoya-Ruiz C, Diaz F, Rodas J. Recent evidence of hantavirus circulation in the American tropic. Viruses 2014;6:1274–93. https://doi.org/10.3390/v6031274.
[29] Armien B, Pascale JM, Muñoz C, Mariñas J, Núñez H, Herrera M, et al. Hantavirus fever without pulmonary syndrome in Panama. Am Soc Trop Med Hyg 2013;89:489–94. https://doi.org/10.4269/ajtmh.12-0334.
[30] 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;25:201–3. https://doi.org/10.1016/j.ijid.2014.03.1396.
[31] Guzmán TC, Calderón RA, González Tous M, Mattar VS. Infecciones por hantavirus. Rev MVZ Córdoba 2017;22:6101–17. https://doi.org/10.21897/rmvz.1079.
[32] Budihal SV. Leptospirosis diagnosis: competancy of various laboratory tests. J Clin DIAGNOSTIC Res 2014. https://doi.org/10.7860/JCDR/2014/6593.3950.