Research Article Open Access

Journal of Preventive Medicine, Infectious Diseases & Therapy

ISSN: 3071-0588

DOI: doi.org/10.63721/26JPMIDT0131

Serological Evidence for Laboratory Diagnosis of Hantavirus Infection in Humans: Future Potential

Hewa Babarandage Chathurika Harshani, Weerasangalige Charith Rangana, Niranjala Weerasinghe, Buddhini Samaraweera and Janaki I Abeynayake*

Medical Research Institute, Colombo-08, Sri Lanka

Citation: *Hewa Babarandage Chathurika Harshani, Weerasangalige Charith Rangana, Niranjala Weerasinghe, Buddhini Samaraweera and Janaki I Abeynayake (2026) Serological Evidence for Laboratory Diagnosis of Hantavirus Infection in Humans: Future Potential. J of Preventive Medi, Infec Dise & Therapy 2(3), 1-7. WMJ/JPMIDT-131*

Abstract

This study evaluated serological evidence of hantavirus infections in patients with acute febrile illnesses (AFI) at the Medical Research Institute (MRI) in Sri Lanka, with a concurrent assessment of dengue virus infections. By analyzing both pathogens within the same population, the study aimed to enhance diagnostic accuracy and elucidate the clinical relevance of hantavirus infections.

A retrospective analysis was performed on 58 patients aged 0.5 to 71 years (mean age ± SD: 29.8 ± 26.27), including 37 males, 18 females, and 3 individuals with unreported gender. Data extracted from samples collected between January and May 2024 from diverse regions of Sri Lanka were analysed. Hantavirus infection was identified through IgM antibody detection via ELISA, while dengue virus diagnosis relied on NS1 antigen testing, IgM assays, and PCR.

Serological evidence confirmed hantavirus infection in 12% of cases, with no co-infections observed. Dengue virus was detected in 13.7% of cases. Hantavirus infections were associated with severe systemic complications, including cardiac issues (e.g., pericarditis), renal failure, and pulmonary conditions such as acute respiratory distress syndrome (ARDS) and pulmonary hemorrhage. In contrast, dengue infections presented distinct clinical features, including dengue hemorrhagic fever (DHF) with hepatomegaly, neurological involvement (e.g., viral encephalitis), and typical dengue fever without severe systemic impact.

The findings highlight the utility of serological testing, particularly IgM ELISA, for diagnosing hantavirus infections in AFI. The study underscores the need for routine inclusion of hantavirus diagnostics in endemic regions and calls for further research to refine diagnostic strategies for co-circulating febrile illnesses.

***Corresponding author:** Janaki I Abeynayake, Medical Research Institute, Colombo-08, Sri Lanka.

Submitted: 26.05.2026 **Accepted**: 01.06.2026 **Published**: 15.06.2026

Keywords: Hantavirus, Dengue, Acute Febrile Illness (AFI), Serological Testing, Diagnostic Accuracy

Introduction

Acute febrile illness (AFI) is characterized by a sudden onset of fever, typically ≥38.0 °C, accompanied by non-specific symptoms such as headache, rash, and myalgia, often without an identifiable source of infection [1]. In Sri Lanka, the limited studies on the Serological evidence for laboratory diagnosis of hantavirus infection in humans.

Hantavirus infections are caused by a group of RNA viruses belonging to the family *Hantaviridae*, with over 40 species identified, 22 of which are known to cause disease in humans [2,3]. The clinical syndromes associated with hantavirus infections include Hantavirus Pulmonary Syndrome (HPS), caused by New World hantaviruses such as the Sin Nombre virus in the Americas, and Hemorrhagic Fever with Renal Syndrome (HFRS), caused by Old World hantaviruses in Asia and Europe [4]. Transmission predominantly occurs through inhalation of aerosolized rodent excreta, although rare cases of human-to-human transmission, such as with the Andes virus in South America, have been documented [5]**.**

Clinically, HPS is characterized by flu-like symptoms progressing to severe respiratory distress, while HFRS presents with fever, hemorrhagic manifestations, and renal dysfunction [6]. These overlapping symptoms often lead to diagnostic confusion with other febrile illnesses, such as leptospirosis or dengue.

The presence of hantavirus in Sri Lanka was first documented in 1988, with serological evidence of antibodies in humans and rodents indicating local transmission, particularly among individuals with leptospirosis-like symptoms [7,8]. Although a 1991 nationwide survey confirmed human exposure, cases of hantavirus infections have remained sporadically reported and under-investigated, with limited studies conducted since 1994 [9,10]. Notably, cases misdiagnosed as leptospirosis or dengue but later identified as hantavirus have underscored the diagnostic overlap and need for targeted surveillance [11,12].

In Sri Lanka, AFI diagnostics primarily focus on leptospirosis and dengue, leaving hantavirus as an underrecognized pathogen despite its potential for severe complications. The availability of serological assays, such as IgM antibody detection via ELISA, presents a valuable tool for improving the diagnosis of hantavirus infections. Incorporating serological testing into routine diagnostic workflows could help identify undetected cases, particularly in patients with atypical presentations or refractory febrile illnesses.

Materials and Methods

This study employed a retrospective study design to evaluate the positivity rates of hantavirus and dengue virus infections among patients presenting with symptoms received at Medical Research Institute in Sri Lanka during January to May 2024. This convenient sample consisted of 58 patients aged 0.5 to 71 years (mean age ± SD = 29.8 ± 26.27), comprising 37 males, 18 females, and 3 individuals with unreported gender. Seven autopsy samples were also included in this study. Records of patient samples were analyzed for both dengue and hantavirus.

Laboratory tests included the detection of hantavirus was diagnosed using ELISA (Euroimmun, Germany, Lot no: E200826Bx) test assays while dengue through NS1 antigen testing (BIO RADP\ Platelia Dengue NS1 Ag kit, Lot: 4D0076) and serotyping PCR (altona RealStar Dengue type RT-PCR Kit 1.0, Germany, Lot: 042328) where necessary and followed relevant procedure provided by the manufacturer. Ethical clearance was not required for this study as it was retrospective in nature and involved the analysis of anonymized samples that had been originally received for routine hantavirus and dengue virus testing.

For data analysis, the collected data were processed using statistical software SPSS.23 and Microsoft Excel 2016 version. Descriptive statistics were employed where necessary.

Results

Table 1: Hantavirus-Positive, Dengue-Negative Cases among Patients with Acute Febrile Illnesses

Case No	Gender	Age	Hanta IgM	Dengue NS1	Dengue Serotyping	Clinical History
1	M	30	Positive	Negative	Not Detected	Atypical chest pain, pericardial effusion, pericarditis
2	M	38	Positive	Negative	Not Detected	Fever, elevated serum creatinine, renal involvement
3	M	40	Positive	Negative	Not Detected	Gastrointestinal sepsis, septic shock, AKI, pulmonary hemorrhage, myocarditis, persistent hypocalcemia
4	M	27	Positive	Negative	Not Detected	Fever, arthralgia, myalgia, jaundice, AKI, sepsis, ARDS, myocarditis
5	F	64	Positive	Negative	Not Detected	AKI, acute lung injury, sepsis with shock, heart failure, multiple abnormalities
6	M	39	Positive	Negative	Not Detected	Fever, bloody diarrhea, vasculitis, hematological changes
7	M	39	Positive	Negative	Not Detected	Fever for 5 days, renopulmonary syndrome, history of residence in the Middle East

Table 2: Dengue-Positive, Hantavirus-Negative Cases Hantavirus-Positive, Dengue-Negative Cases among Patients with Acute Febrile Illnesses

Sample ID	Gender	Age	Hanta IgM	Dengue NS1	Dengue Serotyping	Clinical History
8	F	3	Negative	Positive	Not Detected	Dengue Fever, Day 4
9	M	40	Negative	Positive	Not Detected	NS1 Antigen Positive
10	F	78	Negative	Positive	Not Detected	No fever, NS1 Antigen positive, Dengue Encephalitis excluded
11	F	79	Negative	Positive	Not Detected	Dengue Fever, Day 4
12	M	NM	Negative	Positive	Not Detected	High-grade fever for 5 days, confusion, viral aetiology in CSF, treated with antivirals
13	M	11.91	Negative	Positive	Not Detected	Dengue Fever, Day 2

14	F	19	Negative	Positive	Not Detected	Dengue Haemorrhagic Fever, persistent fever, liver enlargement, hyperbilirubinemia
15	F	58	Negative	Negative	Dengue Type 4	Fever for 4 days, autopsy performed

NM- Not Mentioned

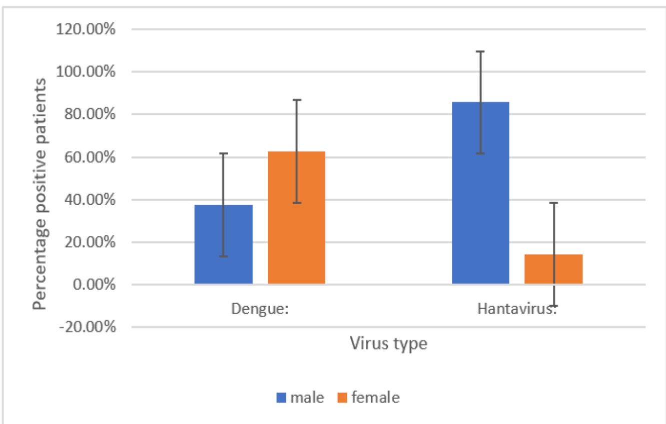

Figure 1: Gender distribution of dengue and hantavirus positive patients among patients with acute febrile illnesses.

Table 1 shows a cohort exclusively positive for hantavirus IgM antibodies and negative for dengue NS1 antigen and serotyping, indicating infections consistent with HPS or HFRS. In contrast, Infection patterns observed in Table 2 reveal that all patients, except for Case No 15, tested positive for dengue NS1 antigen, while Hantavirus results were negative. Most of these patients were diagnosed with dengue fever, and several presented severe complications, including DHF. Case No 15 exhibited a negative NS1 result but was later confirmed as Dengue Type 4 via serotyping after autopsy.

In hantavirus positive patients (Table 1), the age range is narrower, from 27 to 64 years, with patients suffering severe systemic complications such as renal, pulmonary, and cardiovascular issues, which are consistent with hantavirus infections. Disease severity also varies between the two groups of patients. Age demographics in dengue positive patients (Table 2) range from 3 to 79 years, with patients mostly experiencing classical dengue symptoms, though some displayed neurological involvement.

Hantavirus cases (Table 1), exhibited more severe systemic issues, including cardiac complications like pericarditis, renal failure, and pulmonary complications such as ARDS and pulmonary hemorrhage. Notably, cases of sepsis and renopulmonary syndrome point toward a more life-threatening clinical course associated with hantavirus. Dengue complications (Table 2) included DHF with liver enlargement, neurological involvement such as viral encephalitis, and several cases of typical dengue fever without severe systemic effects. However, Case No 15 highlighted a diagnostic challenge, with a false-negative NS1 result.

Regarding multi-organ involvement, hantavirus patients (Table 1), show a higher frequency of multi-organ involvement, with combined renal, pulmonary, cardiovascular, and gastrointestinal issues. Dengue cases (Table 2), however, generally exhibit single-organ effects, with a few exceptions like liver damage and neurological complications.

Hantavirus-positive cases were reported from samples submitted by DGH Negombo, DGH Kegalle, TH Karapitiya, CSTH Kalubowila, and Kalutara while dengue-positive cases were identified in samples submitted by CNTH Ragama, DGH Kegalle, TH Kandy, and TH Jaffna.

Gender-based comparisons across both hantavirus and dengue patients reveal notable differences in the representation and clinical outcomes of dengue and hantavirus infections. In hantavirus positive patients (Table 2, Figure 1**),** females accounted for only 14.3% of cases, suggesting that women may either be less affected by hantavirus infections or face different exposure risks or immune responses compared to men. The lone female Case No (5) involved severe multi-organ involvement, including renal and pulmonary complications, though this is the exception rather than the norm in the sample. On the other hand, males dominated the hantavirus cases, representing 85.7% of the total hantavirus positives. Male patients were more likely to suffer from severe systemic involvement, including renal failure, pulmonary hemorrhage, sepsis, and cardiac complications, pointing to a higher propensity for developing HPS or HFRS.

Among dengue positives, females represent 62.5% of the cases, indicating a higher prevalence of dengue among women in dengue positive cohort. These female patients exhibited a broad spectrum of symptoms, ranging from mild dengue fever to severe forms like DHF. In contrast, males made up 37.5% of dengue cases, with some presenting unique complications. In terms of disease severity by gender, both males and females with dengue showed a mix of mild to severe symptoms.

Discussion

This study highlights a crucial challenge in infectious disease diagnosis: the clinical overlap between hantavirus infections and other febrile illnesses, such as dengue fever. The acute febrile phase of these infections often presents with non-specific symptoms, making differentiation difficult without comprehensive diagnostic testing. Our findings emphasize the need for a dual-pathogen approach to diagnosis, particularly in regions where both hantavirus and dengue virus are endemic.

The detection of hantavirus in 12% of patients and dengue virus in 13.7% of patients with acute febrile illness (AFI) underscores the importance of multi-pathogen testing. This aligns with previous studies highlighting the prevalence of hantavirus infections in areas traditionally associated with dengue. For instance, identified hantavirus in 4% of suspected dengue cases, emphasizing the need for inclusion of hantavirus in the differential diagnosis of AFI [13]. Similarly, documented the concurrent presence of hantavirus alongside other febrile pathogens in diverse geographic contexts [14,15].

Our findings also suggest that while dengue may dominate the spectrum of AFI in tropical and subtropical areas, hantavirus infections are not insignificant, particularly in rural and semi-urban populations. Although co-infections with hantavirus and dengue virus have been reported in studies such as those by no such cases were observed in this study. This lack of co-infections may reflect regional variations in transmission dynamics, diagnostic practices, or sample size limitations [16,17].

The overlapping symptoms of hantavirus and dengue virus, such as fever, headache, myalgia, and gastrointestinal distress, present significant diagnostic challenges. Single-pathogen testing may lead to misdiagnosis, delaying appropriate treatment and skewing epidemiological data. The use of serological assays, such as IgM antibody detection via ELISA, offers a reliable tool for identifying hantavirus infections and complements molecular diagnostic methods for dengue.

A multi-pathogen diagnostic strategy is essential for improving clinical outcomes, enabling timely and accurate treatment. demonstrated that testing for hantavirus in children suspected of dengue revealed a subset of hantavirus cases, illustrating the importance of incorporating hantavirus into standard diagnostic panels in endemic areas [15].

This study is limited by its small sample size and restricted geographic scope, which may constrain the generalizability of the findings. The cross-sectional design also precludes analysis of causative factors or long-term health outcomes. Larger, multi-center studies with longitudinal follow-up are needed to better understand the epidemiology and clinical impact of hantavirus infections.

Future research should explore the potential interactions between hantavirus and other pathogens, including socio-environmental factors such as urbanization and climate change that influence their prevalence. Studies should also assess the clinical outcomes of co-infections, which may differ from single-pathogen cases.

To address diagnostic gaps in regions where hantavirus and dengue are endemic, public health initiatives should focus on promoting awareness among healthcare providers about the clinical overlap between these infections. Enhancing laboratory capacity for multi-pathogen testing is essential to improve diagnostic accuracy and facilitate timely interventions. Additionally, the development of rapid, cost-effective diagnostic tools capable of simultaneously detecting multiple pathogens is crucial. Integrated surveillance systems that consider various pathogens could provide more accurate epidemiological data, guiding targeted prevention and control strategies. The advancement of serological and molecular diagnostic tools tailored to endemic regions has the potential to transform the management of acute febrile illnesses, reducing misdiagnosis-related complications and improving patient outcomes.

Conclusion

This study underscores the complexity of managing febrile illnesses in dual-endemic regions and highlights the need for multi-pathogen diagnostic approaches. Our findings emphasize the importance of a comprehensive surveillance system to inform public health policy and improve patient care in settings where hantavirus and dengue co-circulate. Addressing these challenges will require collaborative efforts across healthcare systems, research institutions, and public health bodies to mitigate the impact of these pathogens on vulnerable populations [18].

Conflicting Interest (If present, give more details): All authors declare there is no conflict of interest

Acknowledgement: We would like to express our sincere gratitude to the department Virology, Medical Research Institute, Sri Lanka. We are also thankful to Medical Research Institute, Sri Lanka.

Funding: No

Ethics Approval: Ethical approval was not required for this study due to retrospective nature and as it did not involve human or animal interventions, and data were anonymised.

Author Contribution: Study concept and design: JIA, HBCH; data analysis: HBCH, JIA; Laboratory analysis: CR, NW; Manuscript writing and reviewing: HBCH, JIA, BS.

References

1. Tun ZM, Moorthy M, Linster M, Su Y CF, Coker R J, et al. (2016) Characteristics of Acute Febrile Illness and Determinants of Illness Recovery among adults Presenting to Singapore Primary Care Clinics. BMC Infectious Diseases 16: 612.
2. Bi Z, Formenty PB, Roth CE (2008) Hantavirus Infection: A Review and Global Update. Journal of Infection in Developing Countries 2: 3.
3. Chandy S, Mathai D (2017) Globally Emerging Hantaviruses: An Overview. Indian Journalof Medical Microbiology 35: 165-175.
4. Peters CJ, Simpson GL, Levy H (1999) Spectrum of Hantavirus Infection: Hemorrhagic Fever with Renal Syndrome and Hantavirus Pulmonary Syndrome. Annual Review of Medicine 50: 531-545.
5. Padula P, Figueroa R, Navarrete M, Pizarro E, Cadiz R, et al. (2004) Transmission Study of Andes Hantavirus Infection in Wild Sigmodontine Rodents. Journal of Virology 78: 11972-11979.
6. Toledo J, Haby MM, Reveiz L, Sosa Leon L, Angerami R, et.al (2022) Evidence for Human-to-Human Transmission of Hantavirus: A Systematic Review. The Journal of Infectious Diseases 226: 186-194.
7. Vitarana T (1994) Hantavirus Disease. Ceylon Medical Journal 39: 63-66.
8. Dalugama C, Nanayakkara M, Rathnayaka N, Medagama A (2020) Atypical Case of Hantavirus Infection in Sri Lanka Mimicking LeptospirosIS: A Case Report. Journal of Medical Case Reports 14: 71.
9. Sunil-Chandra NP, Clement J, Maes P, De Silva H J, Van Esbroeck M, Van Ranst M (2015) Concomitant Leptospirosis-Hantavirus Co-Infection in Acute Patients Hospitalized in Sri Lanka: Implications for a Potentially Worldwide Underestimated Problem. Epidemiology and Infection 143: 2081-2094.
10. Dahanayaka NJ, Agampodi SB, Bandaranayaka AK, Priyankara S, Vinetz JM (2014) Hantavirus Mimicking Leptospirosis in Sri Lanka. Journal of Infection in Developing Countries 8: 1072-1075.
11. Ehelepola NDB, Basnayake BMLS, Sathkumara SMBY, Kaluphana KLR (2018) Two Atypical Cases of Hantavirus Infections from Sri Lanka. Case Reports in Infectious Diseases Article 4069862 https://doi.org/10.1155/2018/4069862.
12. Pattiyakumbura TT, Pathirathne SH, Muthugala MARV (2024) Hantavirus Infection in Central Sri Lanka - An Unusual Clinical Presentation: A Case Report. Access Microbiology 6: 000554.
13. Lima DM, Sabino Santos Junior G, Oliveira ACA (2011) Hantavirus Infection in Suspected Dengue Cases from State of Ceará, Brazil. Revista da Sociedade Brasileira de Medicina Tropical 44: 795-796.
14. Suharti C, Van Gorp ECM, Dolmans WMV, et al. (2009) Hantavirus Infection During Dengue Virus Infection Outbreak in Indonesia. Acta Medica

Indonesiana 41, 75-80.

15. Kumar A, Krishnamurthy K, Nielsen A L (2016) Hantavirus Infection among Children Hospitalized for Febrile Illness Suspected to be Dengue in Barbados. Journal of Infection and Public Health 9: 81-87.
16. Dos Santos VM, De Sá DA, Martins RR, Paz B C, De Oliveira E R, Barcelos M Dos (2010) Hantavirus Pulmonary Syndrome Coexistent with Dengue. The Indian Journal of Chest Diseases & Allied Sciences 52: 249-251.
17. Mattar S, Tique V, Miranda J, Montes E, Garzon D (2017) Undifferentiated Tropical Febrile Illness in Cordoba, Colombia: Not Everything is Dengue. Journal of Infection and Public Health 10: 507-512.
18. Kularatne, SA, DalugamaC (2022) Dengue Infection: Global Importance, Immunopathology and Management. Clinical Medicine (London) 22: 9-13.