



Diagnostic Preparedness and Biosafety Measures for Hantavirus Infections in Clinical Laboratories: A Systematic Review

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Abstract

Background: Hantavirus infections are potentially severe zoonotic diseases whose effective laboratory management requires timely clinical recognition, reliable diagnostic testing, appropriate biosafety practices, and surveillance of animal reservoirs. In the Philippines, evidence of human exposure and hantavirus circulation in wildlife exists, but contemporary information on hantavirus-specific diagnostic and biosafety preparedness remains limited.

Methods: This systematic review evaluated evidence on hantavirus epidemiology, clinical recognition, laboratory diagnosis, reservoir surveillance, occupational exposure, and biosafety, with particular emphasis on implications for Philippine clinical laboratories. PubMed, Scopus, Web of Science, Google Scholar, and supplementary sources were searched. Of 304 records initially identified, 18 studies met the eligibility criteria. Because of substantial heterogeneity in study designs, populations, diagnostic approaches, and outcomes, findings were synthesized narratively and thematically.

Results: Philippine evidence demonstrated 6.1% hantavirus antibody prevalence among 461 asymptomatic participants and molecular detection of Quezon virus in local wildlife. International studies demonstrated that hantavirus infection may be clinically misrecognized, including as dengue, and severe HPS was associated with substantial mortality. Molecular diagnostic studies showed that RT-qPCR can facilitate early detection, with one study reporting 94.9% sensitivity and 100% specificity. Serological and molecular methods were complementary, while reservoir studies demonstrated considerable hantavirus diversity. Occupational investigations documented laboratory-associated infections and highlighted aerosol exposure, infected animals, and potentially infectious specimens as important biosafety risks. Philippine studies demonstrated existing biosafety training capacity but identified broader gaps in biorisk management and pathogen-specific preparedness.

Conclusion: Evidence of human exposure and wildlife-associated hantavirus circulation supports strengthened preparedness in the Philippines. A risk-based, tiered, and One Health approach integrating clinical recognition, serological and molecular testing, specimen-referral systems, quality assurance, biosafety training, occupational protection, and human-animal surveillance is warranted. Contemporary Philippine studies are needed to define current exposure, circulating viruses, and laboratory readiness.

Keywords: Hantavirus, laboratory preparedness, biosafety, molecular diagnosis, serological diagnosis, One Health, surveillance, Philippines.

INTRODUCTION

Hantaviruses are enveloped, negative-sense, single-stranded RNA viruses of the family *Hantaviridae* that are maintained primarily in rodent and other small-mammal reservoirs and transmitted to humans mainly through inhalation of aerosolized virus-contaminated urine, feces, or saliva [1]. Medically important hantaviruses cause two major clinical syndromes: hemorrhagic fever with renal syndrome (HFRS), occurring predominantly in Europe and Asia, and hantavirus pulmonary syndrome (HPS) or hantavirus cardiopulmonary syndrome (HCPS), reported mainly in the Americas [2, 3].

The potentially severe clinical course of these infections makes early laboratory recognition and appropriate biosafety practices essential [4].

Laboratory assessment of hantavirus infection relies principally on serological and molecular methods [5]. Detection of hantavirus-specific IgM and IgG antibodies using enzyme-linked immunosorbent assays (ELISA) is widely employed, while reverse-transcription polymerase chain reaction (RT-PCR) enables detection of viral RNA, particularly during the acute phase [2]. Immunofluorescence, immunoblotting, neutralization assays, and immunohistochemistry may provide supplementary or confirmatory evidence [6].

The effectiveness of hantavirus diagnosis depends not only on the analytical performance of serological and molecular assays but also on the broader laboratory system in which testing occurs [7]. Essential components include appropriate laboratory infrastructure, trained personnel, early recognition and notification of suspected cases, safe specimen collection and transport, functional referral pathways to authorized reference laboratories, and quality-assurance procedures that support reliable and timely results [8].

Diagnostic preparedness must therefore be accompanied by appropriate biosafety and biorisk-management measures to protect laboratory personnel, prevent laboratory-associated transmission, and ensure that testing can be performed safely and reliably [9]. Laboratory personnel may encounter potentially infectious clinical specimens before hantavirus infection is recognized, creating occupational risks from aerosol-generating procedures, accidental percutaneous inoculation, mucous-membrane exposure, and contamination of work surfaces [10]. Risk-based precautions include appropriate personal protective equipment, biological safety cabinets, safe centrifugation, specimen inactivation where appropriate, decontamination, waste management, exposure-response procedures, and higher containment for activities involving propagation or concentration of live virus [11]. These measures are particularly important in laboratories with limited experience handling uncommon or emerging zoonotic pathogens, where agent-specific training, documented risk assessment, competency verification, and access to expert or reference-laboratory support may be limited [9].

At the population level, hantavirus infection remains an important zoonotic and public-health concern, with transmission shaped by rodent abundance, occupational and recreational exposure, climatic variability, urbanization, agricultural activity, and environmental disturbance [12]. Agricultural and forestry workers, military personnel, wildlife handlers, sanitation workers, and laboratory personnel may experience increased occupational exposure to hantaviruses through activities that bring them into contact with infected rodents, their excreta, contaminated environments, or potentially infectious specimens [13]. A recent global review reported that hantavirus seroprevalence among several occupational populations exceeded background population levels, emphasizing the importance of integrated surveillance, prevention, and occupational protection [3, 14]. These findings demonstrate that laboratory preparedness forms part of a broader One Health response connecting human health, reservoir surveillance, and environmental risk.

In the Philippines, hantavirus remains underrecognized despite ecological conditions favorable to rodent-borne zoonoses and historical evidence of human exposure. Earlier seroepidemiological research demonstrated hantavirus antibodies among Filipino populations [15].

Philippine evidence indicates that hantavirus exposure has occurred in human populations, while studies of rodents and other wildlife suggest possible viral circulation in animal reservoirs. However, the available evidence remains limited by geographically restricted studies, incomplete surveillance, insufficient characterization of occupational and environmental risk factors, and constrained diagnostic capacity [15, 16]. The review emphasized the need for strengthened One Health surveillance, improved diagnostic capability, ecological monitoring, and occupational biosafety [17]. Evidence from other Asian countries, Europe, and the Americas is nevertheless essential because established diagnostic and biosafety systems internationally may provide approaches that can be adapted to Philippine and other resource-limited laboratory settings [18].

Despite growing research on hantavirus epidemiology, reservoir ecology, occupational exposure, and diagnostic techniques, important gaps remain in the integration of clinical laboratory preparedness and biosafety within hantavirus response systems [12]. Current international guidance emphasizes that laboratory confirmation requires appropriate serological or molecular testing, while potentially infectious specimens must be handled, packaged, transported, and processed under risk-appropriate containment conditions [1]. However, preparedness also depends on trained personnel, quality-management systems, validated procedures, referral networks, and sufficient resources. A recent Asia-Pacific assessment involving substantial participation from Philippine laboratories identified staff-training and budget limitations among the major barriers to strengthening laboratory quality and competence, indicating broader system-level constraints that may also affect preparedness for uncommon emerging pathogens [19].

These limitations are particularly relevant to hantavirus preparedness in the Philippines. In June 2026, the Research Institute for Tropical Medicine issued specific instructions for the collection, handling, packaging, transport, and referral of specimens from suspected hantavirus cases, emphasizing personnel safety, specimen integrity, coordination with designated reference laboratories, and compliance with biosafety and biosecurity standards [18]. Nevertheless, the existence of national referral guidance does not necessarily indicate that hantavirus testing and biosafety procedures are routinely implemented across hospital and clinical laboratories. Thus, limited evidence regarding decentralized diagnostic capacity, laboratory personnel competency, quality assurance, containment practices, and functional referral pathways represents an important knowledge gap. Systematically evaluating these areas is necessary to determine how effectively Philippine laboratories could recognize suspected hantavirus infections and safely manage and refer to associated clinical specimens, while drawing lessons from laboratory systems in other countries.

Therefore, this systematic review aims to evaluate diagnostic preparedness and biosafety measures for hantavirus infections in clinical laboratories, with particular consideration of their applicability to the Philippines. Specifically, it seeks to identify and compare diagnostic methods used for hantavirus detection; assess laboratory preparedness, testing capacity, quality assurance, and specimen-referral systems; evaluate biosafety measures for specimen collection, processing, transport, storage, and disposal; compare practices across countries and resource settings; identify major diagnostic and biosafety gaps; and determine evidence-based strategies that may strengthen hantavirus laboratory preparedness in the Philippines and comparable resource-limited settings.

METHODOLOGY

2.1 Study Design and Reporting Framework

This study employed a systematic review design to identify, evaluate, and synthesize available evidence on hantavirus infection, with particular attention to epidemiology, human exposure, clinical manifestations, laboratory diagnosis, reservoir surveillance, biosafety, and implications for public health and laboratory preparedness in the Philippines. The review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [20]. A structured approach was applied to literature identification, screening and eligibility assessment, data extraction, methodological appraisal, and evidence synthesis. The review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) [39] under registration number CRD420261485094. Given the heterogeneity of the included evidence in terms of study design, geographical setting, study populations, diagnostic approaches, exposure measures, and reported outcomes, a meta-analysis was not considered appropriate. Instead, findings were synthesized using a narrative and thematic approach, allowing evidence to be organized and interpreted across the major domains addressed by the review.

2.2 Literature Search Strategy

A comprehensive literature search was conducted to identify studies relevant to hantavirus infection and its epidemiological, clinical, laboratory, ecological, and public health dimensions. The principal electronic databases searched were PubMed, Scopus, Web of Science, and Google Scholar. Supplementary searches were undertaken through manual screening of reference lists and relevant institutional and research repositories. Grey literature and technical documents from recognized public health organizations and national agencies were also considered when they contributed directly to the objectives of the review.

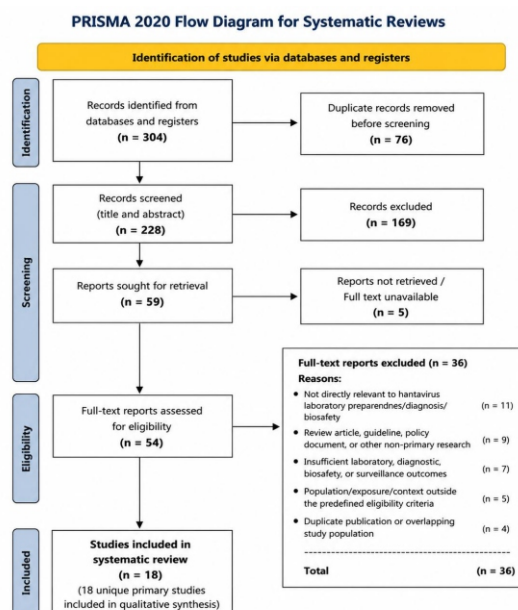
Search terms were combined using Boolean operators and included terms related to *Hantavirus*, *Orthohantavirus*, human–rodent interaction, zoonotic transmission, occupational exposure, seroprevalence, reservoir surveillance, laboratory diagnosis, and public health. An example of the search strategy was: (Hantavirus or Orthohantavirus) and (occupational exposure or human–rodent interface or zoonotic transmission) and (seroprevalence or reservoir surveillance or public health) Search terms were modified where necessary to accommodate the indexing systems and search functions of individual databases.

2.3 Eligibility Criteria

Studies were considered eligible when they provided evidence relevant to hantavirus infection or transmission, including human exposure, seroprevalence, clinical disease, laboratory diagnosis, occupational or environmental risk, rodent reservoirs, ecological or molecular surveillance, outbreaks, biosafety, or public health implications. Eligible evidence included observational studies such as cross-sectional, cohort, and case-control studies, as well as outbreak investigations, seroepidemiological studies, ecological and molecular surveillance studies, and other relevant primary investigations. Selected authoritative technical and public health documents were considered when they provided information directly relevant to laboratory diagnosis, surveillance, biosafety, or preparedness. Studies were excluded when they were unrelated to the objectives of the review, provided insufficient information for meaningful interpretation, represented duplicate publications, consisted primarily of opinion or editorial material, or could not provide adequate information for eligibility assessment. Duplicate records identified during the search and screening process were retained only once.

2.4 Study Selection and Screening

All records retrieved from the literature search were compiled and screened systematically. The initial search identified 304 records. Duplicate records were removed before screening, after which titles and abstracts were evaluated against the predetermined eligibility criteria. Potentially relevant publications were subsequently assessed through full-text review. Studies that did not satisfy the eligibility criteria at the full-text stage were excluded, with the principal reasons for exclusion documented. Following completion of the screening and eligibility assessment, 18 studies met the inclusion criteria and were retained for the final systematic review. The study-selection process was documented using a PRISMA flow diagram showing the progression of records through identification, duplicate removal, title and abstract screening, full-text assessment, exclusion, and final inclusion.



2.5 Data Extraction

Relevant information was systematically extracted from each included study using a structured data-extraction approach. Extracted variables included, where applicable, the author and year of publication, country or geographical setting, study design, study population or sample, sample size, hantavirus species or strain, diagnostic or laboratory method, exposure or reservoir characteristics, principal findings, and implications for clinical practice, laboratory diagnosis, surveillance, or public health. Particular attention was given to findings relevant to human exposure, seroprevalence, clinical manifestations, laboratory detection, rodent reservoirs, molecular characterization, occupational and environmental risks, and biosafety or laboratory preparedness. The extracted information was organized to permit comparison across the 18 included studies and formed the basis of Table 1, which summarizes the characteristics of the included evidence.

2.6 Methodological Quality and Risk-of-Bias Assessment

The methodological quality of the included studies was assessed with consideration of their respective study designs. The appraisal focused on the clarity of the study objectives, appropriateness of study design and participant or specimen selection, adequacy of sample size and methodology, reliability of diagnostic or laboratory procedures, completeness of outcome reporting, and potential sources of selection, measurement, and reporting bias. Quality assessment was used primarily to determine the strength and reliability of the evidence and to guide interpretation of the findings rather than as the sole basis for study exclusion. The results of the methodological appraisal are summarized in Table 2.

2.7 Data Synthesis

Because the included studies differed substantially in their populations, study designs, geographical settings, diagnostic techniques, exposure measurements, and reported outcomes, a narrative

and thematic synthesis was undertaken. The evidence was organized according to major themes reflecting the objectives of the review, including the epidemiology and human exposure to hantavirus, clinical manifestations and diagnostic challenges, serological and molecular laboratory diagnosis, rodent reservoirs and molecular or ecological surveillance, biosafety and laboratory preparedness, and evidence gaps and implications for the Philippines. Findings were compared across studies to identify areas of consistency, variation, and uncertainty. Greater interpretive weight was given to findings supported by methodologically stronger studies, while the limitations of individual studies were considered when interpreting the evidence and drawing conclusions.

2.8 Philippine Context and Evidence Integration

Because a central objective of the review was to determine the relevance of the international evidence to the Philippines, Philippine studies were examined alongside evidence from other geographical settings. Particular consideration was given to documented hantavirus exposure in Filipino populations, the availability of laboratory diagnostic capacity, possible rodent-associated transmission, biosafety preparedness, and gaps in contemporary local surveillance. International evidence was used to contextualize potential risks and preparedness needs but was not assumed to represent the epidemiological situation in the Philippines directly. This distinction was maintained throughout the synthesis to avoid extrapolating prevalence estimates, circulating strains, or clinical patterns from other countries to the Philippine population without supporting local evidence.

2.9 Ethical Considerations

Ethical approval was not required because this systematic review analyzed information derived from previously published studies and publicly available reports and did not involve direct recruitment of human participants, collection of identifiable personal information, or experimental procedures involving humans or animals. Ethical principles relating to accurate representation of published evidence, appropriate citation, and transparent reporting were observed throughout the review.

RESULTS

Overview of the Evidence

The included studies demonstrated that hantavirus laboratory preparedness is multidimensional, encompassing recognition of human exposure, clinical identification, availability of serological and molecular diagnostic methods, surveillance of potential animal reservoirs, occupational biosafety, and laboratory workforce preparedness. The evidence was geographically diverse, with studies from the Philippines, other parts of Asia, Europe, Oceania, and the Americas. Philippine evidence was particularly relevant because it demonstrated previous human exposure to hantaviruses, molecular detection of a hantavirus in local wildlife, and existing institutional experience with laboratory biosafety training.

For synthesis, the findings were organized into six interrelated domains: human exposure and epidemiological evidence; clinical recognition and diagnostic challenges; serological and molecular diagnostic capacity; reservoir and molecular surveillance; occupational laboratory exposure and biosafety; and Philippine biosafety and laboratory preparedness.

Characteristics of the Included Studies

The 18 studies included in the systematic review represented a diverse body of evidence relevant to hantavirus epidemiology, clinical presentation, laboratory diagnosis, reservoir surveillance, and biosafety preparedness. The studies varied in geographical setting, study design, population or sample characteristics, diagnostic approaches, and primary outcomes.

Collectively, they provided evidence ranging from human seroepidemiological investigations and clinical case assessments to molecular detection, rodent reservoir studies, and laboratory or biosafety-related evaluations.

The included literature also reflected differences in the geographical distribution and clinical manifestations of hantavirus infection. Studies from endemic and emerging settings contributed evidence on hemorrhagic fever with renal syndrome (HFRS), hantavirus pulmonary syndrome (HPS), serological exposure, and diagnostic approaches, while Philippine evidence provided important local context regarding hantavirus exposure and laboratory preparedness. These variations were considered during the synthesis to avoid directly equating findings obtained from substantially different populations, disease presentations, and laboratory settings. The principal characteristics and contributions of the 18 included studies are summarized in Table 1.

Table 1: Characteristics of Studies Included in the Systematic Review

No.	Study	Country	Study design / population	Sample	Laboratory / assessment method	Key findings	Relevance to laboratory preparedness
1	Quelapio et al. (2000)	Philippines	Cross-sectional seroepidemiological study; asymptomatic community participants	461	High-density particle agglutination (HDP-A) antibody test	Hantavirus antibodies detected in 6.1%; prevalence was 7.6% rural, 5.6% urban, and 5.1% urban-poor populations.	Provides direct evidence of previous human hantavirus exposure in the Philippines and supports diagnostic and serological surveillance capacity.
2	Arai et al. (2016)	Philippines	Molecular surveillance of fruit bats	376 bats	RT-PCR, sequencing and phylogenetic analysis	Hantavirus RNA detected in a Geoffroy's rousette; molecular characterization identified Quezon virus (QZNV).	Demonstrates local hantavirus circulation in wildlife and supports molecular and One Health surveillance.
3	Medina et al. (2017)	Philippines	Biosafety training program evaluation among infectious-disease/laboratory personnel	NR	Training evaluation/awareness assessment	Three-level biosafety program established at RITM; approximately 30% improvement in biosafety awareness reported following initial training components.	Demonstrates existing Philippine capacity for structured laboratory biosafety training.
4	Destura et al. (2021)	Philippines	Assessment of biosafety/biorisk-management preparedness	38	Institutional/biorisk assessment	Identified gaps involving implementation, coordination, facilities, biosafety training and professionalization of biosafety officers.	Identifies systemic weaknesses relevant to preparedness for handling emerging pathogens such as hantaviruses.
5	Vial et al. (2016)	Chile	Diagnostic accuracy study; laboratory-confirmed Andes hantavirus cases and controls	78 cases; 166 controls	Quantitative RT-PCR	RT-qPCR showed 94.9% sensitivity and 100% specificity and could detect viral RNA before antibody detection.	Supports molecular testing for early diagnosis and demonstrates the importance of RT-qPCR capacity.
6	Geeraedts et al. (2024)	Netherlands	Retrospective diagnostic evaluation of clinically suspected cases	85 patients	Real-time RT-PCR plus serology	PUUV RNA is detected in ~11% of all specimens and 50% of anti-PUUV/TULV IgM-positive specimens.	Supports integration of molecular and serological assays into diagnostic algorithms.
7	Lee & Johnson (1982)	South Korea	Investigation of laboratory-acquired Hantaan virus infections	9 cases	Clinical/serological and occupational investigation	Nine clinically apparent laboratory-acquired infections were documented; aerosol exposure from infected rodents was considered probable.	Demonstrates occupational infection risk and the importance of containment and aerosol-control procedures.
8	Wong et al. (1988)	Singapore	Laboratory-animal and occupational serological investigation	329 rats; 74 personnel	Serology	Antibodies detected in 143/329 laboratory rats and 2/74 laboratory personnel.	Supports animal surveillance, biological safety cabinet use, occupational monitoring and infection-control measures.
9	Costa et al. (2013)	Brazil	Occupational seroepidemiological investigation among personnel handling rodents	63	Hantavirus serology	Hantavirus antibodies were detected among personnel involved in field/laboratory rodent handling despite absence of recognized occupational illness.	Demonstrates potential asymptomatic occupational exposure and supports surveillance of high-risk laboratory/field workers.
10	Nolte et al. (1996)	United States	Investigation/recommendations concerning autopsy and laboratory handling of HPS specimens	NR	Pathological/laboratory biosafety assessment	Identified occupational hazards associated with handling potentially infectious HPS specimens and aerosol-generating procedures.	Supports respiratory protection, biological safety cabinets and biocontained centrifugation.
11	Chow et al. (2005)	Taiwan (Kinmen)	Retrospective investigation of patients negative for scrub typhus	85 patients	Serology and molecular testing	Evidence of hantavirus infection identified in 7/85 (8.23%) patients; Seoul-type virus was implicated.	Shows potential for hantavirus to be missed during differential diagnosis of febrile illness.

12	Blasdel et al. (2011)	Cambodia, Lao PDR and Thailand	Multi-country rodent reservoir surveillance	NR	Serology, RT-PCR and sequencing	Hantavirus-reactive antibodies detected in several rodent species; molecular testing identified Thailand and Seoul viruses.	Demonstrates value of combined serological and molecular reservoir surveillance in Southeast Asia.
13	Xu et al. (2019)	China	Bat hantavirus molecular and serological surveillance	1,419 bats	Serology, RT-PCR and sequencing	Laibin and Xuan Son viruses identified; antibodies detected in 131/709 (18.5%) tested sera.	Supports surveillance beyond conventional rodent reservoirs and demonstrates molecular characterization capacity.
14	Lozynskiy et al. (2020)	Ukraine	Human seroepidemiological surveillance	966 healthy individuals	Serology	Hantavirus antibody cross-reactivity detected in approximately 1.6% of participants.	Demonstrates that exposure may occur despite limited recognition of clinical disease and supports population surveillance.
15	de Oliveira et al. (2017)	Brazil	Case/outbreak and human-rodent epidemiological investigation	45 human contacts; 72 rodents	ELISA, RT-PCR and sequencing	A fatal HPS case was initially misdiagnosed as dengue; antibodies occurred in 10/45 (22%) contacts and 6.9% of sampled rodents. Juquitiba virus was characterized.	Demonstrates consequences of diagnostic misrecognition and importance of integrated clinical, molecular and reservoir surveillance.
16	Matheus et al. (2023)	French Guiana	Clinical investigation/series of confirmed HPS	9 cases	Clinical and laboratory confirmation	All nine developed respiratory failure and five died (55.6% case fatality).	Highlights need for early clinical recognition, rapid diagnostic confirmation and laboratory preparedness.
17	Nguyen et al. (2025)	Vietnam	Occupational serosurvey among wildlife farmers	210	IgG/IgM serology (ELISA)	Apparent IgG seroprevalence was 8.7%, with IgM detected in 1.9%.	Demonstrates occupational exposure risk and supports surveillance among persons with frequent wildlife contact.
18	Smith et al. (2025)	Australia	Molecular surveillance of flying foxes	495 bats	RT-PCR, sequencing and phylogenetic analysis	Robina virus RNA prevalence was 4.2% (95% CI 2.8 - 6.4%); virus was closely related to Philippine Quezon virus.	Supports genomic and wildlife surveillance and provides regional context for Philippine bat-associated hantaviruses.

Abbreviations: ELISA, enzyme-linked immunosorbent assay; HPS, hantavirus pulmonary syndrome; IgG, immunoglobulin G; IgM, immunoglobulin M; NR, not reported/confirmed in the extracted material; PUUV, Puumala orthohantavirus; QZNV, Quezon virus; RITM, Research Institute for Tropical Medicine; RT-PCR, reverse-transcription polymerase chain reaction; RT-qPCR, quantitative reverse-transcription polymerase chain reaction; TULV, Tula orthohantavirus.

Quality Assessment of Included Studies

The methodological quality of the 18 included studies was assessed using appraisal criteria appropriate to their respective study designs. Overall, the evidence base demonstrated varying levels of methodological quality, reflecting differences in study design, sample size, participant or specimen selection, diagnostic methods, and reporting completeness. Particular attention was given to the clarity of study objectives, appropriateness of the methodology, reliability of laboratory and diagnostic procedures, adequacy of outcome reporting, and potential sources of bias. Studies were retained in the synthesis when they provided relevant and sufficiently credible evidence addressing the epidemiological, clinical, diagnostic, laboratory, or biosafety dimensions of hantavirus infection. The quality assessment was used to guide interpretation of the findings rather than as the sole basis for study exclusion. A summary of the methodological appraisal of the included studies is presented in Table 2.

Table 2: Quality and Risk-of-Bias Assessment of the Included Studies

No.	Study	Study type	Key methodological strengths	Main limitations / risk-of-bias concerns	Overall risk of bias
1	Quelapio et al. (2000)	Cross-sectional seroepidemiological study	Stratified multistage sampling; clearly defined population; reported prevalence by sex and residential setting; laboratory antibody testing performed	Older study; particle agglutination assay may have lower specificity than contemporary confirmatory methods; no molecular confirmation reported	Moderate
2	Arai et al. (2016)	Molecular wildlife surveillance	Large multispecies bat sample; RT-PCR detection; sequencing and phylogenetic analysis; clear specimen and host characterization	Only one positive Geoffroy's rousette; wildlife detection does not establish human pathogenicity or human infection risk	Low-Moderate
3	Medina et al. (2017)	Training/program evaluation	Structured three-level intervention; conducted in a national infectious-disease reference institution; measurable pre/post awareness outcome	Limited information on participant number and evaluation design from the extracted source; awareness is a surrogate rather than direct biosafety-performance outcome	Moderate
4	Destura et al. (2021)	National biorisk-management assessment/framework development	Multi-component assessment; examined national biosafety/biosecurity systems; included tabletop exercises and policy-gap analysis	Framework-oriented rather than disease-specific; outcome measures not directly linked to hantavirus diagnostic performance	Moderate
5	Vial et al. (2016)	Diagnostic accuracy study	Included confirmed cases and negative controls; quantitative RT-PCR evaluated; sensitivity and specificity reported; very low detection limit	Conducted for Andes virus in a specific epidemiological context; applicability to other hantavirus species may be limited	Low
6	Geeraedts et al. (2024)	Retrospective diagnostic study	Routine clinically suspected samples; molecular testing combined with serology; clinically relevant diagnostic algorithm proposed	Retrospective design; relatively small sample; conducted primarily in a PUUV-endemic European setting	Low-Moderate
7	Lee & Johnson (1982)	Occupational case investigation	Direct documentation of laboratory-acquired infections; detailed exposure context; biologically plausible aerosol pathway identified	Historical study; small number of cases; limited modern laboratory confirmation/occupational exposure quantification	Moderate
8	Wong et al. (1988)	Occupational/laboratory serosurvey	Included both laboratory animals and personnel; quantified seropositivity; direct occupational relevance	Historical study; small personnel sample; serology alone limits attribution of occupational transmission and timing	Moderate

9	Costa et al. (2013)	Occupational seroprevalence study	Direct assessment of workers handling rodents; laboratory serology performed; relevant occupational exposure group	Small number of seropositive individuals; limited evidence regarding infection timing and causal occupational exposure	Moderate
10	Nolte et al. (1996)	Laboratory/autopsy biosafety assessment	Directly addresses aerosol-generating procedures, respiratory protection and containment	Primarily recommendations/observational biosafety evidence rather than comparative empirical study; older safety context	Moderate-High
11	Chow et al. (2005)	Retrospective clinical and reservoir investigation	Human serology accompanied by rodent surveillance and molecular analysis; etiological evidence for Seoul virus	Retrospective design; relatively small patient sample; selected scrub-typhus-negative population limits generalizability	Moderate
12	Blasdel et al. (2011)	Multicountry rodent surveillance	Multiple Southeast Asian sites; several rodent species; serology supplemented with RT-PCR and sequencing	Unequal/site-specific sampling; human disease was not directly assessed; reservoir prevalence may not reflect human risk	Low-Moderate
13	Xu et al. (2019)	Bat molecular/serological surveillance	Large bat sample; combined RT-PCR, ELISA, Western blot and neutralization approaches; viral characterization performed	Bat serology and cross-reactivity complicate inference; direct human pathogenicity not established	Low-Moderate
14	Lozynski et al. (2020)	Human seroprevalence study	Large population sample; laboratory serological testing; assessment of demographic/exposure variables	Cross-reactive antibody findings; no strong molecular confirmation reported; cross-sectional design prevents timing of infection from being established	Moderate
15	de Oliveira et al. (2017)	Case/outbreak investigation	Integrated human serology, rodent sampling, RT-PCR and sequencing; molecular characterization of circulating virus	Investigation arose from a single index case; contact seroprevalence may not represent the general population	Low-Moderate
16	Matheus et al. (2023)	Clinical case series	Laboratory-confirmed cases; detailed clinical severity and outcomes reported	Only nine cases; no control/comparator group; strong risk of selection effects inherent to severe hospital-based cases	Moderate-High
17	Nguyen et al. (2025)	Cross-sectional occupational serosurvey	Defined wildlife-farmer population; IgG and IgM assessment; risk factors analyzed using multivariable methods	Cross-sectional design; antibody detection cannot precisely establish timing or source of exposure; some behavioral variables were self-reported	Low-Moderate
18	Smith et al. (2025)	Molecular wildlife surveillance	Large follow-up bat sample; qRT-PCR; epidemiological modelling and phylogenetic analysis; multi-year surveillance	Experimental assay; animal infection does not establish zoonotic pathogenicity; findings are indirectly relevant to human laboratory preparedness	Low-Moderate

Fernandes et al. [25] tested 206 rural settlers in the Western Brazilian Amazon and detected antibodies to mammarenavirus in six participants (2.91%) but found no serological evidence of orthohantavirus infection. Collectively, these studies demonstrate substantial geographical variability in hantavirus exposure and reinforce the importance of locally generated surveillance data rather than extrapolating prevalence estimates between populations.

Clinical Recognition and Diagnostic Challenges

The included evidence demonstrated that hantavirus infection may be difficult to recognize clinically because its early manifestations overlap with those of other febrile and infectious diseases. This diagnostic ambiguity may contribute to delayed recognition, particularly in settings where hantavirus is not routinely considered in the differential diagnosis. De Oliveira et al. [26] investigated a fatal case of hantavirus pulmonary syndrome (HPS) in Rio de Janeiro State, Brazil, that had initially been misdiagnosed as dengue. Subsequent epidemiological investigation detected hantavirus antibodies in 10 of 45 (22%) household and occupational contacts, while antibody prevalence among sampled rodents was 6.9%. Molecular testing and sequencing identified Juititaba hantavirus in local rodent reservoirs. This investigation demonstrated the importance of combining clinical suspicion with serological testing, molecular confirmation, and reservoir surveillance when investigating unexplained febrile or respiratory illnesses.

The potential consequences of delayed clinical recognition were further demonstrated by Matheus et al. [27], who described nine confirmed HPS cases in French Guiana. All nine patients developed respiratory failure, and five died, corresponding to a case fatality of 55.6%.

These findings emphasize the importance of considering hantavirus during the nonspecific early phase of compatible illness and strengthening surveillance for potentially unrecognized clinical presentations.

Serological and Molecular Diagnostic Capacity

The diagnostic evidence demonstrated complementary roles for serological and molecular methods, with their usefulness varying according to the stage of infection. Vial et al. [28] evaluated quantitative reverse-transcription polymerase chain reaction (RT-qPCR) for early diagnosis of Andes hantavirus infection using peripheral blood cells from 78 laboratory-confirmed patients and 166 negative controls. RT-qPCR demonstrated 94.9% sensitivity and 100% specificity, with an analytical detection limit of approximately 10 viral genome copies. Importantly, viral RNA could be detected before symptom onset, when anti-hantavirus antibodies may still be negative. These findings demonstrate the potential value of molecular testing for early laboratory confirmation.

Similarly, Geeraedts et al. [29] evaluated the incorporation of real-time RT-PCR into routine orthohantavirus diagnostic practice. Serum specimens from 85 patients with clinically suspected infection were retrospectively tested for Puumala, Tula, and Seoul orthohantavirus RNA. Puumala virus RNA was detected in approximately 11% of all tested specimens and in 50% (8/16) of anti-PUUV/TULV IgM-positive specimens, whereas Tula and Seoul virus RNA were not detected. The investigators proposed diagnostic algorithms combining real-time RT-PCR with conventional serological testing, illustrating the potential value of integrated diagnostic approaches for earlier confirmation and virus identification.

Collectively, these findings indicate that molecular and serological testing should be regarded as complementary rather than competing approaches.

Molecular assays may offer particular advantages during early acute infection, whereas serological methods remain important for identifying antibody responses and documenting previous exposure. The evidence therefore supports diagnostic strategies that consider the timing of specimen collection and stage of infection when selecting and interpreting laboratory tests.

Reservoir and Molecular Surveillance

Studies examining animal reservoirs demonstrated substantial hantavirus diversity and highlighted the importance of molecular and ecological surveillance in identifying circulating and potentially emerging viruses. Of particular relevance to the Philippines, Arai et al. [30] examined lung tissues from 376 fruit bats representing six genera collected in the Philippines between 2008 and 2013. RT-PCR detected hantavirus RNA in one of 15 Geoffroy's rousettes (*Rousettus amplexicaudatus*) captured in Quezon Memorial National Park, Luzon. Molecular and phylogenetic characterization identified a genetically divergent hantavirus designated Quezon virus (QZNV). This finding expanded the recognized host range of hantaviruses and provided direct molecular evidence of hantavirus circulation in Philippine wildlife. Smith et al. [31] subsequently investigated Robina virus (ROBV), initially detected in a black flying fox in Australia. Surveillance of 495 bats between 2018 and 2023 detected ROBV RNA at an overall prevalence of 4.2% (95% CI: 2.8–6.4%). Phylogenetic analyses demonstrated that ROBV was closely related to the Philippine Quezon virus, further illustrating the value of molecular wildlife surveillance for identifying emerging hantaviruses and understanding their evolutionary relationships. Additional studies from Asia demonstrated broader reservoir diversity. Xu et al. [32] screened 1,419 bats in China and identified Laibin virus and Xuan Son virus, while hantavirus antibodies were detected in 18.5% (131/709) of tested bat sera. Similarly, Blasdell et al. [33] detected hantavirus-reactive antibodies among several rodent species in Cambodia, Lao PDR, and Thailand, with site-specific seroprevalence ranging from 0% to 5.6%. RT-PCR and sequencing confirmed Thailand and Seoul viruses and provided the first reported molecular evidence of hantavirus from Lao PDR. Together, these studies demonstrate that reservoir surveillance provides information beyond the detection of human disease. Molecular characterization of viruses in wildlife can contribute to identification of circulating strains, clarification of host associations, assessment of geographical distribution, and recognition of potentially emerging hantaviruses.

Occupational Laboratory Exposure and Biosafety

The included evidence identified occupational exposure as an important component of hantavirus laboratory preparedness, particularly among personnel handling infected animals, animal tissues, or potentially infectious clinical specimens. Lee and Johnson [34] documented nine clinically apparent laboratory-acquired Hantaan virus infections among personnel associated with the Korea University Virus Institute between 1971 and 1979.

The infections were associated with exposure to wild rodents or naturally or experimentally infected laboratory rodents rather than accidental parenteral inoculation. Aerosol exposure from infected rodents was considered the probable occupational transmission mechanism.

Wong et al. [35] similarly investigated laboratory rats and personnel in Singapore. Hantavirus antibodies were detected in 143 of 329 laboratory rats (44%) and 2 of 74 laboratory personnel. The investigators recommended replacement of infected laboratory-animal colonies with hantavirus-free stocks, regular serological surveillance of laboratory animals, use of biological safety cabinets for aerosol-generating procedures, surveillance of personnel, and prompt investigation of suspected infections. Nolte et al. [36] addressed occupational risks associated with autopsy procedures and laboratory examination of specimens from patients with HPS. Their recommendations emphasized respiratory protection, biocontained centrifugation, and opening potentially infectious specimen containers within Class II biological safety cabinets. Collectively, these findings identify aerosol generation and contact with infected animals or potentially infectious materials as important occupational hazards and underscore the need for appropriate engineering controls, personal protective equipment, safe specimen-handling procedures, and risk-based biosafety practices.

Philippine Biosafety and Laboratory Preparedness

Evidence from the Philippines indicates that broader biosafety infrastructure and institutional experience already exist and could provide a foundation for strengthening hantavirus-specific laboratory preparedness. Medina et al. [37] described the implementation of a three-level biosafety training program at the Research Institute for Tropical Medicine. The program consisted of Biosafety 101 for new employees, applied biosafety training for laboratory personnel, and advanced training intended for biosafety officers and infectious-disease outbreak responders. Implementation of the first two components was associated with a reported 30% improvement in biosafety awareness, demonstrating the potential value of structured, competency-oriented biosafety training.

Conversely, Destura et al. [38] identified broader weaknesses within the Philippine biorisk-management environment, including limitations in the implementation of existing protocols, emergency-response coordination, facility capacity, biosafety training, and professionalization of biosafety officers. These findings suggest that the existence of general laboratory regulations and biosafety structures does not necessarily translate into pathogen-specific diagnostic and response readiness. In the context of hantavirus, preparedness would therefore require not only general biosafety systems but also appropriate diagnostic pathways, referral mechanisms, specimen-handling protocols, trained personnel, and surveillance capacity.

Synthesis of Major Findings

Overall, the evidence demonstrates that hantavirus laboratory preparedness requires an integrated approach involving epidemiological surveillance, clinical recognition, diagnostic capacity, reservoir monitoring, occupational protection, and laboratory biosafety. Philippine evidence establishes both previous human exposure to hantaviruses and molecular detection of hantavirus in local wildlife, indicating that the country has epidemiological and ecological evidence relevant to preparedness. International evidence further demonstrates that clinical recognition can be complicated by nonspecific presentations and that delayed diagnosis may have serious consequences.

The diagnostic evidence supports complementary use of serological and molecular methods, with molecular assays providing particular value during early infection and serological methods remaining important for detecting immune responses and documenting previous exposure. Reservoir studies demonstrate considerable hantavirus diversity and highlight the contribution of molecular characterization to understanding host associations and viral circulation. Occupational evidence further indicates that personnel working with infected animals or potentially infectious specimens may be exposed to preventable risks, particularly during aerosol-generating procedures.

Taken together, the findings support a preparedness framework incorporating clinical awareness, appropriate serological and RT-PCR testing or referral capacity, standardized specimen collection and handling, laboratory quality systems, trained personnel, appropriate personal protective equipment and engineering controls, occupational risk management, and integrated human-animal surveillance. For the Philippines, the available evidence provides a basis for preparedness but also reveals an important gap between evidence of hantavirus exposure and wildlife circulation and the availability of contemporary, hantavirus-specific information on human disease burden, diagnostic readiness, and surveillance capacity.

DISCUSSION

Principal Findings

This systematic review demonstrates that laboratory preparedness for hantavirus infection extends beyond the availability of individual diagnostic assays. Effective preparedness requires the integration of epidemiological surveillance, clinical recognition, serological and molecular diagnostics, laboratory biosafety, workforce competency, occupational protection, and reservoir surveillance. This integrated approach is particularly relevant in settings where clinically recognized hantavirus disease is uncommon but serological or ecological evidence indicates previous exposure or viral circulation.

Three findings are particularly important for the Philippines. First, Quelapio et al. [15] demonstrated measurable hantavirus antibody prevalence among Filipino populations, providing evidence of previous human exposure.

Second, Arai et al. [30] molecularly identified Quezon virus in a Philippine bat species, demonstrating the presence of hantavirus diversity in local wildlife. Third, Medina et al. [37] showed that structured biosafety capacity-building has been implemented within a major Philippine infectious-disease reference institution. Taken together, these findings suggest that the central preparedness question is not simply whether hantaviruses are relevant to the Philippines, but whether existing clinical, diagnostic, surveillance, and biosafety systems are sufficiently prepared to recognize and safely investigate suspected infections.

Hantavirus Exposure and Its Significance for the Philippines

The 6.1% seroprevalence reported by Quelapio et al. [15] is particularly relevant because antibodies were detected among asymptomatic individuals from rural, urban, and urban-poor communities. Although seropositivity does not establish the incidence or current burden of clinically significant hantavirus disease, it provides evidence of previous exposure and indicates that hantavirus circulation should not be dismissed solely because recognized HPS or HFRS cases are uncommon. This interpretation is supported by evidence from other geographical settings. Chow et al. [22] retrospectively identified hantavirus infections among patients initially investigated for another febrile illness, while Lozynskyi et al. [21] demonstrated serological evidence among apparently healthy individuals. These findings illustrate an important epidemiological challenge: limited recognition of clinical disease does not necessarily indicate an absence of underlying exposure or viral circulation. The possibility of underrecognition may be especially important in settings where hantavirus manifestations overlap with more commonly suspected infectious diseases. De Oliveira et al. [26] reported a fatal HPS case initially diagnosed as dengue, demonstrating how nonspecific early manifestations may complicate clinical recognition. This observation has potential relevance to the Philippines, where acute febrile illnesses have numerous possible infectious causes. Nevertheless, the available Philippine evidence does not establish the frequency of hantavirus misdiagnosis or underdiagnosis. This should therefore be regarded as an important area for investigation rather than evidence of an established national diagnostic problem.

Implications for Serological and Molecular Diagnosis

A major finding of this review is that hantavirus diagnostic preparedness should incorporate complementary serological and molecular approaches. Vial et al. [28] demonstrated high diagnostic performance of RT-qPCR for Andes hantavirus, reporting 94.9% sensitivity and 100% specificity, while also showing that viral RNA could be detected before antibodies became detectable. Geeraedts et al. [29] similarly demonstrated the usefulness of incorporating real-time RT-PCR into routine diagnostic algorithms.

These findings have practical implications for laboratory preparedness. Serological testing remains important for detecting antibody responses and documenting previous exposure, as demonstrated by the Philippine seroepidemiological investigation of Quelapio et al. [15]. However, reliance exclusively on antibody detection may be insufficient during the earliest phase of infection. Molecular testing may complement serology by enabling viral RNA detection during acute infection and potentially facilitating earlier laboratory confirmation.

Importantly, diagnostic preparedness should not be equated simply with possession of PCR instrumentation. Operational molecular testing requires validated assays, appropriate primers and controls, reliable reagent supply, trained personnel, quality-assurance procedures, safe specimen processing, appropriate interpretation, and mechanisms for confirmatory testing or referral. Consequently, the presence of general molecular laboratory infrastructure in the Philippines cannot by itself be interpreted as evidence of hantavirus-specific diagnostic readiness.

Biosafety as an Essential Component of Preparedness

The evidence further demonstrates that expansion of hantavirus diagnostic capacity must occur alongside appropriate biosafety measures. This is particularly important because personnel may encounter potentially infectious clinical specimens, animal tissues, or infected animals during diagnostic, research, or surveillance activities. Historical occupational evidence provides important lessons. Lee and Johnson [34] documented nine clinically apparent laboratory-acquired Hantaan virus infections among personnel working with wild or infected laboratory rodents, with aerosol exposure considered the probable mechanism of transmission. Wong et al. [35] similarly identified substantial hantavirus infection among laboratory rats and serological evidence of exposure among laboratory personnel. These studies demonstrate that occupational risk is not merely theoretical when infected animals or potentially infectious material are handled without adequate controls.

Nolte et al. [36] further emphasized respiratory protection, biological safety cabinets, and biocontained centrifugation during the handling of potentially infectious specimens. Together, these findings indicate that hantavirus preparedness requires a risk-based biosafety approach incorporating appropriate engineering controls, personal protective equipment, safe centrifugation and specimen-processing procedures, spill and waste management, exposure reporting, and occupational risk assessment. Accordingly, expanding diagnostic testing without strengthening the corresponding biosafety infrastructure could create avoidable occupational risks. Laboratory preparedness should therefore develop diagnostic capability and biosafety competency simultaneously rather than treating them as separate objectives.

Philippine Biosafety Capacity and Remaining Preparedness Gaps

The Philippines has an existing foundation upon which hantavirus preparedness could potentially be strengthened. Medina et al. [37] demonstrated implementation of a structured three-tier biosafety training program at the Research Institute for Tropical Medicine, comprising foundational biosafety education, applied training for laboratory personnel, and advanced training for biosafety officers and outbreak responders. The reported improvement in biosafety awareness illustrates the potential effectiveness of structured workforce-development initiatives.

However, the existence of general biosafety systems should not be interpreted as evidence of pathogen-specific readiness. Destura et al. [38] identified limitations within the broader Philippine biorisk-management environment, including challenges involving implementation of existing protocols, emergency-response coordination, facility capacity, training, and professionalization of biosafety officers. These observations suggest a potential gap between general laboratory and biosafety capacity and the operational requirements necessary for hantavirus-specific diagnosis and response. This distinction is important because preparedness requires more than infrastructure. Laboratories must know when hantavirus testing is indicated, how potentially infectious specimens should be handled, where confirmatory testing can be performed, how specimens should be transported, and how results should be communicated to surveillance and clinical teams. Therefore, future preparedness assessments should examine these operational components rather than relying solely on the presence of general laboratory facilities or biosafety policies.

Reservoir Surveillance and the One Health Perspective

Another important finding is that human diagnostic preparedness should be connected to animal and environmental surveillance. Arai et al. [30] identified Quezon virus in a Philippine fruit bat, demonstrating that hantavirus diversity within the country cannot be assessed solely through recognized human cases. This finding is particularly relevant because surveillance restricted to clinically apparent human disease may overlook viral circulation occurring within wildlife populations. Smith et al. [31] subsequently identified the closely related Robina virus in Australian flying foxes, reinforcing the value of phylogenetic and genomic surveillance for understanding hantavirus diversity and evolutionary relationships. Xu et al. [32] likewise demonstrated hantavirus diversity among bats in China, while Blasdel et al. [33] documented hantavirus circulation among rodent populations across several Southeast Asian countries. Together, these studies support broader ecological surveillance as a component of preparedness.

These findings favor a One Health approach integrating clinical laboratories with epidemiological, veterinary, wildlife, and environmental surveillance.

Such collaboration could facilitate identification of circulating viruses, characterization of reservoir species, recognition of geographical areas of potential exposure, and investigation of unusual human infections. Nevertheless, wildlife detection must be interpreted cautiously. Detection of hantavirus RNA in an animal reservoir does not establish that the identified virus causes human disease or represents an immediate public health threat. Reservoir identification, molecular characterization, evidence of human exposure, and demonstration of human pathogenicity represent distinct levels of evidence. This distinction is particularly important when interpreting Quezon virus and other newly characterized hantaviruses.

Clinical Recognition and Differential Diagnosis

Laboratory capacity will have limited public health value if hantavirus infection is not considered when clinically and epidemiologically appropriate. The investigations by de Oliveira et al. [26] and Matheus et al. [27] illustrate the potential consequences of delayed recognition, particularly when patients initially present with nonspecific manifestations or rapidly progress to severe cardiopulmonary disease. For the Philippine setting, the evidence supports heightened awareness rather than indiscriminate testing. Hantavirus may warrant consideration in appropriately selected patients presenting with otherwise unexplained acute febrile illness accompanied by compatible epidemiological exposure, thrombocytopenia, renal involvement, hemorrhagic manifestations, or rapidly progressive respiratory disease. Decisions to test should therefore integrate clinical presentation, epidemiological history, and laboratory findings. Improved communication between clinicians, medical laboratory scientists, epidemiological surveillance units, and reference laboratories would be important in this context. Clear case-recognition and specimen-referral pathways could help ensure that suspected cases are investigated appropriately without placing unnecessary demands on frontline laboratories.

Implications for Philippine Laboratory Preparedness

The collective evidence suggests that a tiered laboratory strategy may be appropriate for the Philippines. It may neither be necessary nor practical for every frontline laboratory to maintain specialized hantavirus molecular testing. Instead, frontline facilities should be capable of recognizing potentially relevant cases and specimens, implementing appropriate biosafety precautions, collecting and packaging specimens correctly, and referring samples through established laboratory networks. Higher-level or reference laboratories could maintain validated serological and molecular testing capacity, confirmatory procedures, quality-control systems, and, where appropriate, sequencing capability. Such an approach could make use of existing laboratory networks while avoiding unnecessary duplication of highly specialized testing.

Priority areas emerging from the evidence include strengthening clinical and laboratory awareness of hantavirus; establishing validated diagnostic algorithms integrating molecular and serological testing; developing clearly defined specimen-referral pathways; strengthening competency-based biosafety training; maintaining laboratory quality-assurance systems; improving occupational protection for personnel handling potentially infectious specimens or animals; integrating human and wildlife surveillance through a One Health framework; and conducting contemporary Philippine seroepidemiological and laboratory-capacity studies. Of these priorities, contemporary local evidence is particularly important. Much of the direct evidence of human hantavirus exposure in the Philippines is relatively old. New investigations using contemporary and well-validated serological and molecular methods would help determine whether historical evidence of exposure persists and whether clinically relevant infections are currently being recognized.

Strengths and Limitations of the Evidence

A major strength of this review is the integration of evidence from human seroepidemiology, clinical diagnosis, molecular diagnostics, reservoir surveillance, occupational exposure, and laboratory biosafety. This broad approach reflects the multidimensional nature of laboratory preparedness and permits consideration of both diagnostic capacity and the systems required to support safe and effective testing. However, the evidence base has important limitations. The included studies varied substantially in design, population, geographical setting, viral species, diagnostic methods, and reported outcomes, limiting direct comparison and precluding meaningful quantitative synthesis across several domains. Some of the most directly relevant Philippine evidence, particularly the population seroepidemiological study, is relatively old and may not accurately reflect contemporary patterns of exposure.

Furthermore, wildlife surveillance studies establish viral detection and ecological diversity but cannot independently determine human pathogenicity or disease burden. Evidence specifically evaluating current hantavirus diagnostic capacity within Philippine laboratories was also limited. General biosafety programs and laboratory infrastructure provide important contextual information but cannot establish whether individual facilities currently possess validated hantavirus assays, appropriate reagents, trained personnel, quality-control systems, and functional referral pathways. These limitations identify a major research gap: contemporary empirical assessment is needed to determine both the current epidemiology of hantavirus exposure and the level of hantavirus-specific diagnostic and biosafety preparedness within the Philippine laboratory system.

Overall Interpretation

The available evidence indicates that hantavirus exposure and viral circulation are relevant considerations for the Philippines despite the limited

recognition of clinically confirmed disease. Historical serological evidence of human exposure and molecular identification of Quezon virus in Philippine wildlife provide a rationale for maintaining diagnostic awareness and strengthening surveillance. However, these findings should not be interpreted as evidence of a substantial or currently increasing national burden of hantavirus disease. International evidence demonstrates that effective preparedness depends on complementary serological and molecular diagnostics, timely clinical recognition, appropriate biosafety controls, and surveillance of relevant animal reservoirs. Existing Philippine biosafety experience and laboratory infrastructure provide a useful foundation, but the available evidence is insufficient to establish comprehensive hantavirus-specific operational readiness. Overall, the findings support a risk-based, tiered, and One Health-oriented preparedness strategy integrating clinical recognition, laboratory diagnosis, biosafety, specimen-referral networks, quality assurance, workforce competency, occupational protection, and human-animal surveillance. Contemporary Philippine studies are needed to determine the present extent of human exposure, characterize circulating hantaviruses, and assess whether existing laboratory systems can safely and rapidly identify and respond to suspected cases.

CONCLUSION

This systematic review demonstrates that hantavirus infection remains an important but potentially underrecognized zoonotic disease, particularly in settings where clinical suspicion, diagnostic capacity, and surveillance are limited. The included evidence highlights considerable variation in the epidemiology and clinical expression of hantavirus infections, ranging from hemorrhagic fever with renal syndrome (HFRS) to hantavirus pulmonary syndrome (HPS), with laboratory testing playing a central role in distinguishing hantavirus infection from other febrile, respiratory, and hemorrhagic illnesses with overlapping clinical presentations. The findings further emphasize the importance of serological and molecular methods for accurate diagnosis and surveillance, together with appropriate specimen handling, biosafety practices, and laboratory quality systems. Evidence of hantavirus exposure in the Philippines indicates that the infection should not be regarded solely as a concern of traditionally recognized endemic regions. However, the limited Philippine-specific evidence and scarcity of recent local epidemiological and molecular studies make it difficult to determine the current burden, circulating strains, reservoir distribution, and clinical significance of hantavirus infection in the country. Strengthening laboratory preparedness, clinician awareness, integrated human-animal surveillance, biosafety capacity, and access to confirmatory diagnostic testing is therefore essential. Future research in the Philippines should prioritize contemporary seroepidemiological studies, molecular characterization of circulating hantaviruses, systematic investigation of rodent reservoirs, and evaluation of suspected human cases.

Such efforts would provide a stronger evidence base for determining the true public health significance of hantavirus infection and for developing context-appropriate strategies for surveillance, diagnosis, prevention, and outbreak preparedness.

LIMITATIONS

This systematic review has several limitations that should be considered when interpreting its findings. First, the available evidence was heterogeneous in terms of study design, geographical setting, population characteristics, sample size, diagnostic methods, and reported outcomes. Such variability limited direct comparison across studies and made quantitative pooling inappropriate for several outcomes; consequently, much of the evidence was synthesized narratively.

Second, the evidence specifically addressing hantavirus infection in the Philippines was limited. Although available Philippine studies provide evidence of human exposure and demonstrate the relevance of hantavirus to the local setting, the scarcity of recent epidemiological, clinical, molecular, and reservoir studies prevents a reliable estimation of the current national disease burden. Older studies may also not adequately reflect contemporary patterns of viral circulation, environmental exposure, diagnostic capacity, or population risk.

Third, differences in laboratory methods, including serological and molecular diagnostic approaches, may have contributed to variability in case identification and prevalence estimates. Some studies relied primarily on antibody detection, while others incorporated molecular confirmation or sequencing. These methodological differences should be considered when comparing findings across studies. Finally, despite systematic efforts to identify relevant literature, publication bias and incomplete retrieval of unpublished or locally reported data cannot be excluded. The relatively small number of eligible studies also limits the generalizability of some conclusions. Therefore, the findings should be interpreted as a synthesis of the currently available evidence rather than a definitive estimate of hantavirus prevalence or disease burden, particularly in the Philippines. Future well-designed, contemporary studies using standardized diagnostic methods and integrated human, animal, and environmental surveillance are needed to address these evidence gaps.

RECOMMENDATIONS

Based on the findings of this systematic review, coordinated action among public health, laboratory, healthcare, and research authorities is recommended to strengthen preparedness for hantavirus infection, particularly in the Philippines.

Department of Health (DOH). The DOH should consider strengthening surveillance for suspected hantavirus infections, particularly among patients presenting with unexplained acute febrile illness, thrombocytopenia, renal impairment, hemorrhagic manifestations, or severe respiratory distress when more common differential diagnoses have been excluded.

Hantavirus should also be considered within appropriate differential diagnostic algorithms for clinically compatible cases.

Research Institute for Tropical Medicine (RITM) and reference laboratories. National and regional laboratory capacity for hantavirus detection should be strengthened through access to validated serological and molecular methods, appropriate confirmatory testing, quality-assurance systems, and standardized procedures for specimen collection, storage, transport, and testing. Laboratory personnel handling potentially infectious specimens should receive appropriate biosafety training and follow risk-based biosafety practices.

Local Government Units and public health offices. Local authorities should strengthen community-based prevention efforts in areas where human–rodent contact is likely. Environmental sanitation, safe food storage, appropriate waste management, rodent-control measures, and public education regarding safe cleaning of rodent-contaminated environments should form part of preventive health programs.

Hospitals and healthcare institutions. Healthcare facilities should improve awareness among physicians, medical laboratory scientists, nurses, and other healthcare professionals regarding the clinical and laboratory features of hantavirus infection. Clear pathways should be established for recognizing suspected cases, requesting appropriate diagnostic testing, safely handling specimens, and referring samples to reference laboratories when confirmatory testing is unavailable locally.

Department of Agriculture, veterinary authorities, and environmental agencies. Because hantaviruses are zoonotic and closely associated with rodent reservoirs, a One Health approach should be encouraged. Collaboration between human health, animal health, environmental, and wildlife authorities would facilitate rodent surveillance, identification of potential reservoir species, monitoring of environmental risk factors, and investigation of areas where evidence of human infection is detected.

Academic and research institutions. Further Philippine-based research should be prioritized. Contemporary seroepidemiological studies are needed to establish the current extent of human exposure, while molecular and genomic studies are necessary to characterize circulating hantaviruses. Research should also investigate rodent reservoirs, geographical distribution, occupational and environmental risk factors, and the clinical characteristics of suspected and confirmed human infections.

The relevant authorities should prioritize surveillance, laboratory preparedness, biosafety, professional awareness, rodent-risk reduction, and One Health collaboration rather than assuming that the limited number of documented cases reflects absence of disease.

Strengthening these areas would improve early recognition and provide the evidence necessary to determine the true public health significance of hantavirus infection in the Philippines.

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