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Seroprevalence of hantavirus infection in non-epidemic settings over four decades: a systematic review and meta-analysis

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Abstract

Introduction Hantavirus infection is a zoonotic disease from rodents to humans, necessitating seroprevalence assessment for disease burden clarification and control measure implementation. This study aimed to estimate global hantaviruses seroprevalence, examining variations by regions, populations or settings.

Methods A comprehensive database search identified studies on human hantaviruses seroprevalence using IgG detection until january 2024. A random-effects meta-analysis estimated pooled seroprevalence, with subgroup analyses for geographical region, population, setting or occupation.

Results Out of 3,382 abstracts reviewed, 110 studies were selected, comprising 81,815 observations and 3207 events. The global seroprevalence was calculated at 2.93% (2.34%-3.67%). In terms of geographical distribution, our analysis encompassed 61 studies from the Americas, where the seroprevalence was estimated at 2.43% (95% CI: 1.71%—3.46%), 33 studies from Europe indicating a seroprevalence of 2.98% (95% CI: 2.19%—4.06%), 10 studies from Asia revealing a seroprevalence of 6.84% (95% CI: 3.64%—12.50%), and 6 studies from Africa demonstrating a seroprevalence of 2.21% (95% CI: 1.82%—2.71%). Subgroup analysis underscored varying seroprevalence rates across different populations, settings, and occupations, highlighting the necessity for targeted interventions and preventive measures.

Conclusion The analysis reveals a moderate global hantaviruses seroprevalence, emphasizing the viral family's complex transmission dynamics influenced by exposure and geographical factors. This highlights the need for targeted prevention and control strategies.

Keywords Hantavirus, Seroprevalence, Zoonotic disease, Meta-analysis, Geographic variation, Population groups, Exposure risk

Introduction

Hantaviruses are negative stranded, tripartite RNA viruses belonging to a genus within the Bunyaviridae family. The natural reservoirs of pathogenic hantaviruses are certain rodents, in which chronic and asymptomatic infection occurs [1–3]. Hantaviruses are commonly transmitted from rodents to humans, mainly through inhalation of aerosols contaminated with feces, urine, or saliva of infected mice. The distribution of hantaviruses is solely dependent on the ecology of its reservoir.

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Therefore, if the distribution of virus-carrying rodents is known, the occurrence of human cases can be predicted [4–8]. A systematic review by Toledo et al. [9] has explored the evidence for human-to-human transmission of hantaviruses, particularly focusing on the Andes virus (ANDV). This review examines 22 studies and concludes that, while there is limited evidence supporting human-to-human transmission, it remains a possibility under certain conditions [9].

Human hantavirus infection can manifest in various clinical syndromes. In the Old World, severe hantavirus infections commonly manifest as hemorrhagic fever with renal syndrome with mortality rates ranging from 0.1% to 15%, whereas the New World species, such as ANDV, cause cardiopulmonary syndrome with a mortality rate of 40%. Furthermore, it was demonstrated that ANDV, a New World species, can be transmitted person to person. While assessments of occupational and environmental risks for hantavirus exposure have been carried out in certain regions, a critical gap remains in conducting a broader and more comprehensive evaluation of seroprevalence across diverse populations, occupational sectors, and environmental contexts [10–15].

Research on the overall seroprevalence of hantavirus infection in humans and the assessment of associated risk factors are pivotal in advancing our understanding of disease transmission dynamics. In this study, we conducted a comprehensive systematic review and meta-analysis to assess the global prevalence of hantaviruses antibodies in the human population. Understanding the dynamics of this disease is crucial for implementing effective measures against it. Seroprevalence data offer valuable insights into transmission patterns and prevalence rates, thereby guiding preventive strategies. By elucidating the extent of hantavirus exposure across diverse populations, our aim is to contribute to a deeper understanding of this infectious disease and facilitate the development of targeted preventive measures. Furthermore, we have explored the prevalence of these antibodies across various geographic regions, and in individuals with distinct population, occupation or setting [16, 17].

Methods

Systematic review and meta-analysis

We conducted this systematic review in accordance with the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines for systematic reviews of observational studies [18] and reported following PRISMA guidelines (Appendix 1). We registered the protocol in PROSPERO (CRD42022339202). Furthermore, we used an adaptation of the classic research PICO question framework for prevalence studies proposed by Munn et al [19].

Eligibility criteria and study selection

We included studies that tested hantaviruses specific IgG antibodies and reported seroprevalence in a sample of individuals. To comprehensively evaluate seroprevalence among asymptomatic individuals under typical circumstances, we deliberately omitted studies conducted during epidemic outbreaks and excluded symptomatic patients from our analysis. We did not impose restrictions on language or study design.

At least two of the authors (FT, GC, FP, and LL) independently and in pairs assessed articles during each screening stage, first by title and abstract and subsequently by full text. We resolved disagreements through discussion.

Search strategies

We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, Virtual Health Library, Epistemonikos, Scielo up to January 2, 2024. In addition, we screened the references of all included studies and contacted authors for information when necessary. A description of the search strategy is reported in Appendix 1.

Data extraction and management

Four reviewers (FT, GC, FP, and LL) independently and in duplicate, extracted study characteristics and information from the included studies using a standardized data extraction template. We resolved discrepancies through consensus.

Outcomes

The primary outcome of interest was the seroprevalence of hantavirus IgG-specific antibodies for specific hantavirus types across different regions and subpopulations. We selected studies employing ELISA for detecting hantaviruses IgG antibodies. Additionally, any diagnostic method assessing the presence of IgG against hantaviruses was recorded, including confirmatory methods such as IFA (Indirect Immunofluorescence Assay) or Western Blot.

Statistical analysis

We obtained the seropositivity prevalence estimate and variance (e.g., standard deviation) from each study. We then combined the results from all studies using meta-analysis to obtain a weighted mean. To pool and compare prevalence data, we used the inverse variance method (Dersimonian-Laird) [20–22]. Additionally, we performed a common effects model analysis in parallel, and both models were presented in the forest plots.

We carried out subgroup analysis based on geographical region (Europe, America, Asia and Africa), and different population, occupation or setting categories. We presented the results in tables and graphically in forest plots [23–25]. We conducted all analyses using R programming language version 4.1.0 (R Core Team, 2021) and the RStudio integrated development environment version 2023.03.0 + 386 "Cherry Blossom" Release for Windows RStudio.

Risk of bias

Four reviewers (FT, GC, FP, and LL) independently and in pairs assessed the quality of the studies using the Risk of Bias in Prevalence Studies tool according to the RoB-SPEO guidelines. The assessment included a thorough review of study selection, measurement, comparability, and exposure-related aspects. Any differences in evaluation were resolved through consensus [26].

Certainty of the evidence

The evaluation of the certainty of evidence concerning prevalence across various populations, settings, and occupations in numerous studies was performed using the GRADE approach. This was augmented by the QoE-SPEO tool, specifically adapted for studies that assess exposure. This method evaluates various domains, including risk of bias, indirectness, inconsistency, imprecision, and publication bias. Summary of findings tables were generated, and the certainty of evidence was categorized as high, moderate, low, or very low based on the evaluation of each domain. Further details on the assessment of certainty of evidence are provided in Appendix 1 [27–29].

Results

Characteristics of included studies

The selection process for the studies is detailed in Fig. 1. We included a total of 110 studies [30–140], collectively reporting 81,815 observations, of which 3,207 events were recorded (positive IgG determinations). The global seroprevalence estimated across these studies was 3.88% (95% CI: 3.75% to 4.01%). The characteristics of the included can be observed in Table 1. Excluded studies with reasons can be observed in Appendix 1, Table of excluded studies.

Risk of bias of included studies

Despite the absence of confirmatory tests in many cases due to potential antibody cross-reactivity, we evaluated the body of evidence for seroprevalence as having a low risk of bias. Our assessment is based on the uniform application of testing methods across the majority of studies, which supports the reliability of the seroprevalence rates reported. Although most of the studies included likely had a high risk of misclassification and incomplete exposure data bias, we did not evaluate exposure risk nor assess it as an infection risk in the rest of the manuscript. Therefore, for the purposes of evaluating seroprevalence, this was not considered a high risk of bias. (See further details in Appendix 1: Table of Risk of Bias).

Regional seroprevalence stratified by population, setting and occupation

The seroprevalence results for each population or scenario, as well as the corresponding certainty in the estimated seroprevalence values, are presented in Table 2.

For the Americas, exploration into subgroups revealed varying seroprevalence rates across 61 studies and 33,156 observations. The overall prevalence was estimated at 2.43% (95% CI: 1.70%—3.46%) with high certainty (⨁⨁⨁⨁). Forestry workers exhibited a prevalence of 3.14% (95% CI: 1.15%—8.32%) with moderate certainty (⨁⨁⨁◯) across 8 studies, the general population showed 2.39% (95% CI: 1.56%—3.65%) with high certainty (⨁⨁⨁⨁) across 29 studies, while Indigenous peoples and the rural population had rates of 3.77% (95% CI: 0.97%—13.59%) with very low certainty (⨁◯ ◯◯) and 2.93% (2.34%-3.67) with moderate certainty (⨁⨁⨁◯) respectively. Healthcare workers exhibited a lower prevalence of 0.54% (95% CI: 0.11%—2.57%) with low certainty (⨁⨁◯◯) based on data from 4 studies, and people exposed to rodents at work exhibited a prevalence of 0.86% (95% CI: 0.13%—5.33%) with low certainty (⨁⨁◯◯) across 5 studies (Fig. 2).

In Europe, 33 studies were reviewed, with data from 40820 individuals, revealing a seroprevalence proportion of 2.98% (95% CI: 2.19%—4.06%) with high certainty (⨁⨁⨁⨁). Forestry workers exhibited a prevalence of 4.22% (95% CI: 3.35%—5.30%) with high certainty (⨁⨁⨁⨁) across 4 studies, while the rural population showed a prevalence of 7.00% (95% CI: 2.40%—18.76%) with low certainty (⨁⨁◯◯) across 2 studies. The general population demonstrated a prevalence of 2.70% (95% CI: 1.70%—4.28%) with high certainty (⨁⨁⨁⨁) across 14 studies. Individuals exposed to rodents at work exhibited a prevalence of 3.35% (95% CI: 1.64%—6.73%) with moderate certainty (⨁⨁⨁◯) across 8 studies (Fig. 3).

For Asia, 10 studies were analyzed, involving a total of 3219 patients, showing a seroprevalence proportion of 6.84% (95% CI: 3.64%—12.50%) with moderate certainty (⨁⨁◯◯). Subgroup analysis indicated diverse seroprevalence rates: among people exposed to rodents at work, the prevalence was 5.17% (95% CI: 1.99%—12.79%) with low certainty (⨁◯ ◯◯) across 6 studies, while

Table 1 Characteristics of included studies

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
Abbas A 2019 [66]	Sudan	Chronic kidney disease patients on replacement therapy (dialysis)	9	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	cross-sectional study	91	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Adesiyun 2011 [30]	Trinidad and Tobago	Rural area workers	27	hantavirus immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA)	Seroprevalence survey	236	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Ahlm 1998 [110]	Sweden	Forestry workers	74	ELISA IgG confirmed with IFA	Seroprevalence survey	1573	Puumala (PUUV)
Ahlm C1994 [111]	Sweden	Forestry workers	83	ELISA IgG confirmed with IFA	Seroprevalence survey	1538	Puumala (PUUV)
Akar 2019 [112]	Turkey	Rural population	6	ELISA IgG confirmed with WB	Seroprevalence survey	193	Puumala (PUUV), Dobrava (DBV)
Alves Morais 2016 [31]	Brazil	General population	82	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	1310	Araraquara virus (ARAV)
Amaral 2018 [113]	Brazil	Forestry workers	17	ELISA IgG	Seroprevalence survey	240	Araraquara (ARAV), Juquitiba viruses (JUQV),
Armien 2004 [32]	Panama	General population	228	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	1346	Choclo virus (CHOV)
Badra S2012 [33]	Brazil	General population	27	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	198	Araraquara virus (ARAV)
Barrera 2015 [107]	Colombia	Indigenous people	7	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	cross-sectional study	87	Hantaan (HTNV)
Bolaños 2020 [34]	Colombia	Indigenous people	7	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Cross-sectional study	506	Maciel virus (MACV)
Botros B 2004 [67]	Egypt	Chronic renal disease	7	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	695	Hantaan (HTNV)
Brummer-Korvenkontio 1999 [114]	Finland	General population	160	IFA	Seroprevalence survey	5347	Puumala (PUUV)
Campos G2003 [35]	Brazil	Rural population	117	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	818	Andes virus (ANDV)

Table 1 (continued)

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
Castillo 2002 [36]	Chile	Rural population	5	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	cross-sectional epidemiologic and serologic survey	200	Andes virus (ANDV)
Castillo 2004 [37]	Chile	Close contacts and healthcare workers	3	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Cohort study	215	Andes virus (ANDV)
Castillo 2012 [39]	Peru	General population	36	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Cross-sectional study retrospective and serological survey	2063	Andes virus (ANDV)
Castillo H. 1997 [38]	Chile	Healthcare workers with high exposure	0	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	67	Sin Nombre virus (SNV)
Chandy 2008 [68]	India	General population and high exposure	47	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	661	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Chen H 1998 [69]	Taiwan	Occupational risk population	4	indirect immunofluorescent antibody technique	Seroprevalence survey	222	Seoul (SEOV)
Christova 2017 [70]	Bulgaria	General population	55	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Country-wide seroepidemiological studies	1500	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Cordova C2014 [115]	Brazil	General population	14	ELISA IgG	Seroprevalence survey	314	Araraquara virus (ARAV)
Dargevicius 2007 [71]	Lithuania	Chronic kidney disease patients on replacement therapy (dialysis)	16	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	218	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
de Araujo 2015 [116]	Brazil	General population	27	ELISA IgG—PCR-RT	Seroprevalence survey	688	Juquitiba (JUQV), Araraquara (ARAV)
de Courten M 1995 [72]	United States	Indigenous peoples	0	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	174	Seoul (SEOV) and Sin Nombre virus (SNV)
Diglisic 1999 [41]	USA	General population	9	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	1212	Hantaan (HTN), Seoul (SEO), and Convict Creek (HN017)
Diwan A1985 extracted from Yanahihara et al. [117]	USA	General population	15	IFA	Seroprevalence survey	252	Hantaan (HTVN)

Table 1 (continued)

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
Duggan J 2017 [73]	United Kingdom	People exposed to rodents at work and pet rat owners	55	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	844	Hantaan, Puumala, Seoul, Saareema, Dobrava, Sin Nombre
Elbers 1999 [118]	Netherlands	People who work with farm animals	3	ELISA IgG	Seroprevalence survey	293	Puumala (PUUV)
Engler 2013 [119]	Switzerland	Military personnel and blood donors	59	ELISA IgG confirmed by IFA	Seroprevalence survey	6363	Puumala (PUUV)
Fernandes 2018 [120]	Brazil	Rural population	12	ELISA IgG	Seroprevalence survey	465	Maciel virus (MCV)
Fernandes 2019 [121]	Brazil	Forestry workers	12		Seroprevalence survey	319	Maciel virus (MACV)
Ferrer J 1998 [42]	Paraguay/Argentina	Indigenous people	116	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	415	Sin Nombre virus (SNV)
Forthal D1987 [122]	USA	Forestry workers	13	IFA	Seroprevalence survey	2514	Hantaan (HTVN)
Fritz C2002 [123]	USA	General population	0	ELISA IgG	Seroprevalence survey	81	Sin Nombre virus (SNV)
Gamage C 2017 [75]	Sri Lanka	General population and exposure to rodents in occupational settings	99	immunofluorescence antibody assay (IFA)	Cross-sectional Study	332	Seoul (SEOV)
Gardner 2005 [124]	USA	Forestry workers	0	SIA	Seroprevalence survey	101	Sin Nombre virus (SNV)
Gegúndez M 1996 [76]	Spain	General population	12	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	537	Hantaan (HTNV) and Puumala (PUUV)
George 1998 [77]	Israel	General population and high exposure	17	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	186	Hantaan (HTNV) and Puumala (PUUV)
Gibbs CJ J1982 [125]	USA	Health personnel	3	IFA	Seroprevalence survey	183	Hantaan (HTVN)
Gimaque JB 2012 [43]	Brazil	General population	27	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	106	Araraquara virus (ARAV)
Gnanasekaran 2013 [126]	India	General population	5		Seroprevalence survey	72	Hantaan (HTVN), Puumala (PUUV), Dobrava (DBV), Sin Nombre virus (SNV), Seoul (SEOV)
Gonzalez L.2001 [127]	USA	Forestry workers	3	ELISA igG, SIA, WB	Seroprevalence survey	436	Sin Nombre virus (SNV)
Groen 1995 [128]	Netherlands	People exposed to rodents in work	34	ELISA IgG confirmed with IFA	Seroprevalence survey	2425	Puumala (PUUV)
Gut 2007 [78]	Poland	Occupational risk population	15	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	78	Hantaan (HTNV) and Puumala (PUUV)

Table 1 (continued)

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
Holmes 2000 [44]	Brazil	General population	7	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	567	Sin Nombre virus (SNV)
Hukic 2010 [79]	Bosnia	Occupational risk population	69	IgG ELISA, and Western blot (Bunyavirus IgG)	Seroprevalence survey	1331	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Jameson L2014 [129]	United Kingdom	General population	9	ELISA IgG	Seroprevalence survey	119	Puumala (PUUV), Dobrava (DBV), Seoul (SEOV)
Khabbaz R 1994 [80]	United States	Intravenous drug users	1	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	635	Seoul (SEOV)
Klempa 2010 [130]	Guinea	General population	8	ELISA IgG confirmed by IFA	Seroprevalence survey	649	Sangassou virus (SANGV)
Krug 2019	France	Forestry workers	50	ELISA IgG	Seroprevalence survey	1714	Puumala (PUUV)
Latronico 2018 [82]	Finland	General population	254	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	nationwide health survey	2000	Puumala virus (PUUV)
Limongi J2009 [131]	Brazil	General population	12	ELISA IgG	Seroprevalence survey	400	Araraquara virus (ARAV)
Lledó 2002 [83]	Spain	General population	12	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	3852	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Lledó 2003 [84]	Spain	General population	5	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	165	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Lledó 2007 [85]	Spain	General population	14	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	278	Puumala virus (PUUV)
Londoño 2010 [45]	Colombia	History of fever	2	indirect IgG enzyme linkedimmunosorbent assay(ELISA) and RT-PCR	Serologic survey	220	Calabazo
Lozynskyi 2020 [132]	Ukraine	General population	15	ELISA IgG	Seroprevalence survey	966	Puumala (PUUV), Dobrava (DBV)
Lundkvist 2002 [86]	Latvia	General population	14	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	333	Saaremaa and Dobrava and Puumala

Table 1 (continued)

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
[100, 101]	Germany	Healthcare workers	7	Recombinant enzyme immunoassay Positive samples were reanalyzed for confirmation with an indirect immunofluorescence assay and a recombinant immunoblotting	Seroprevalence survey	694	Hantaan (HTNV) and Puumala (PUUV)
Mascarenhas-Batista A 1998 [87]	Brazil	School-aged population	50	indirect Immunofluorescent Antibody (IFA) IgG for Hantaan Virus (HTN) and Immunoenzymatic test (ELISA)	Cross-sectional Study	379	Hantaan (HTNV)
Máttar 2004 [46]	Colombia	Rural area workers	12	indirect IgG enzyme linkedimmunosorbent assay(ELISA) and RT-PCR	Serologic survey	88	Sin Nombre virus (SNV)
Medeiros D 2010 [133]	Brazil	Rural population	84	ELISA IgG	Seroprevalence survey	2737	Andes (ANDV)
Meheretu 2021 [106]	Ethiopia	General population	6	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	114	Puumala virus (PUUV)
Mendes W 2010 [47]	Brazil	Rural population	65	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Cross-sectional study	1389	Sin Nombre virus (SNV)
Meng 1997 [88]	China	Individuals with non-infectious acute hepatitis	13	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	83	Hantaan (HTNV)
Mertens 2009 [134]	Germany	General population	13	ELISA IgG	Seroprevalence survey	386	Puumala (PUUV)
Montgomery J 2012 [48]	Bolivia	Rural area workers	48	NR	Cross-sectional antibody-prevalence studies	494	Sin Nombre virus (SNV) and Laguna Negra virus (LANV)
Moreli M 2017 [49]	Brazil	General population	17	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	429	Araraquara virus (ARAV)
Muñoz-Zanzi 2015 [50]	Chile	General population	10	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	934	Andes virus (ANDV)
Nelson 2010 [51]	Panama	General population	10	enzyme immuno assays (EIAs) and strip immunoblot	Cross-sectional antibody-prevalence studies	588	Choclo virus (CHOV)

Table 1 (continued)

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
Nuti 1991 [89]	Equatorial Guinea, Tanzania, Somalia, Cameroon, Seychelles, Indonesia, Nepal	General population	22	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	1154	Hantaan (HTNV)
Oldal 2014 [135]	Hungary	Forestry workers	35	ELISA IgG confirmed by Western Blot	Seroprevalence survey	835	Puumala (PUUV), Dobrava (DBV)
Oscarsson 2016	Sweden	Rural population	214	ELISA IgG	Seroprevalence survey	1600	Puumala (PUUV)
Pejcoch 2010 [90]	Czech Repubic	Hemodialisis	5	ELISA IgG	Seroprevalence survey	301	Puumala (PUUV), Hantaan (HTVN)
Pereira G 2012 [52]	Brazil	General population	8	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	257	Araraquara virus (ARAV)
Poeppl 2012 [91]	Austria	Military personnel	7	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	cross-sectional study	526	Puumala virus (PUUV)
Polat 2020 [105]	Turkey	Volunteers residing in high-risk areas (rural areas, farmers, veterinarians, soldiers)	2	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	346	Dobrava (DBV) and Puumala (PUUV)
Prince H 2013 [53]	USA	General population	13	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	266	Sin Nombre virus (SNV)
Quelapio I 2000 [92]	Philippines	General population	23	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	cross-sectional study	461	Hantaan (HTNV)
Rabemananjara H 2020 [103]	Madagascar	General population	46	Indirect immunofluorescence assay (IFA), PUUV orthohantavirus culture in Vero cells, detection of antibodies against PUUV nucleocapsid protein and glycoproteins, cross-reactivity testing with other orthohantaviruses	Cross-sectional study	1680	Dobrava (DBV) and Hantaan (HTNV)
Restrepo 2016 [54]	Colombia	General population	5	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	324	Maciel and Junin viruses
Rivas Y 2003 [55]	Venezuela	General population	23	ELISA confirmed by indirect immunofluorescence and Western-blot assays	Seroprevalence survey	1380	New York hantavirus (NY-1)

Table 1 (continued)

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
Romaní Romaní 2020 [56]	Peru	Rural workers	1	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Cross-sectional study	250	Maciel virus (MACV)
Rozental 2018 [136]	Brazil	General population	12	ELISA IgG	Seroprevalence survey	300	Araraquara virus (ARAV)
Sanfeliu 2011 [57]	Spain	General population	4	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	217	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Santos I 2013 [58]	Brazil	General population	7	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	54	Cuiabá-Santarém virus
Schultze 2007 [93]	Switzerland	Occupational risk population	64	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	cross-sectional study	1693	Hantaan (HTNV) and Puumala (PUUV)
Serra 2006 [59]	Brazil	Indigenous people	5	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	259	Araraquara virus (ARAV)
Sevencan 2015 [94]	Turkey	Individuals with history of fever and thrombocytopenia	7	Hantavirus IgG and IgM ELISA and immunoblotting assays	cross-sectional study	442	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
[59, 60]	Brazil	Intravenous drug users	12	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	300	Not specified
Souza 2011 [61]	Brazil	General population	16	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	340	Rio Mamore virus (RMV)
Sunil-Chandra N 2020 [102]	Sri Lanka	General population	52	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	case–control study	291	Hantaan (HTNV) and Puumala (PUUV)
Täger Frey 622,003 [62]	Chile	Rural population	6	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	829	Andes virus (ANDV)
Terças-Trettel AC 2021 [63]	Brazil	Indigenous people	35	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	301	Araraquara virus (ARAV)
Truong T 2009 [95]	Vietnam	Occupational risk population	12	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	837	Seoul (SEOV)

Table 1 (continued)

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
Tsai T 1982 extracted from Yanahihara et al. 117	USA	Rodent control personel	0	IFA	Seroprevalence survey	57	Hantaan (HTVN)
Tsai T1985 [137]	USA	Persons exposed to rodents	42	IFA	Seroprevalence survey	1133	Hantaan (HTVN)
Vacková 2002 [96]	Czech Republic	Military personnel	9	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	542	Hantaan (HTNV) and Puumala (PUUV), Dobrava (DBV), Sin Nombre (SNV), Seoul (SEOV)
Vieira C2016 [138]	Brazil	Rural population	27	ELISA IgG	Seroprevalence survey	198	Araraquara virus (ARAV)
Vitek 1996 [109]	USA	Health Care Workers	0	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	396	Sin Nombre virus (SNV)
Wells R 1998 [64]	Argentina	General population and exposure to rodents in occupational settings	6	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	764	Andes virus (ANDV)
Wilken 2015 [139]	USA	General population	1	ELISA IgG	Seroprevalence survey	526	Sin Nombre virus (SNV)
Wilson M 1995 [97]	United States	General population	11	Indirect fluorescent antibody technique (IFAT)	Seroprevalence survey	619	Seoul (SEOV)
Witkowski P 2015 [98]	Ivory Coast	General population	27	ELISA with recombinant nucleocapsid antigens, Western Blot (WB) with Sangassou virus antigen, recomLine HantaPlus strip blot, immunofluorescence assay (IFA) with VERO-E6 cells infected with Hantaan virus	Cross-sectional Study	687	Puumala virus and Sangassou virus
Wong T 1988 [99]	Singapore	Occupational risk population	2	Indirect fluorescent antibody technique (IFAT)	Seroprevalence survey	74	Hantaan (HTNV)
Wood 2014 [140]	Antigua-Barbuda, Belize, Bermuda, Dominica, Grenada, Jamaica, Montserrat, St. Kitts-Nevis, St. Lucia, and St. Vincent-Grenadines	General population	0	HantaPlus IgG kit (Phoenix AirMid Biomedical, Ontario, Canada)	Seroprevalence survey	50	Sin Nombre virus (SNV)
Yanagihara 1984 extracted from Yanahihara et al. [117]	USA	Persons exposed to rodents	2	IFA	Seroprevalence survey	203	Hantaan (HTVN)
Zeitz P 1997 [65]	United States	Occupational risk population	0	indirect IgG enzyme linkedimmunosorbent assay(ELISA)	Seroprevalence survey	494	Sin Nombre virus (SNV)

Table 1 (continued)

Author	Country/Region	Population, setting or occupation (predominant)	IgG Positive	Method	Study design	N Total	Virus Type
Zöller 1995 [100]	Germany	General population and exposure to rodents in occupational settings	70	solid phase enzyme immunoassay based on the recombinant nucleocapsid proteins of a Hantaan and a Puumala serotype strain	Seroprevalence survey	1571	Hantaan (HTNV) and Puumala (PUUV)

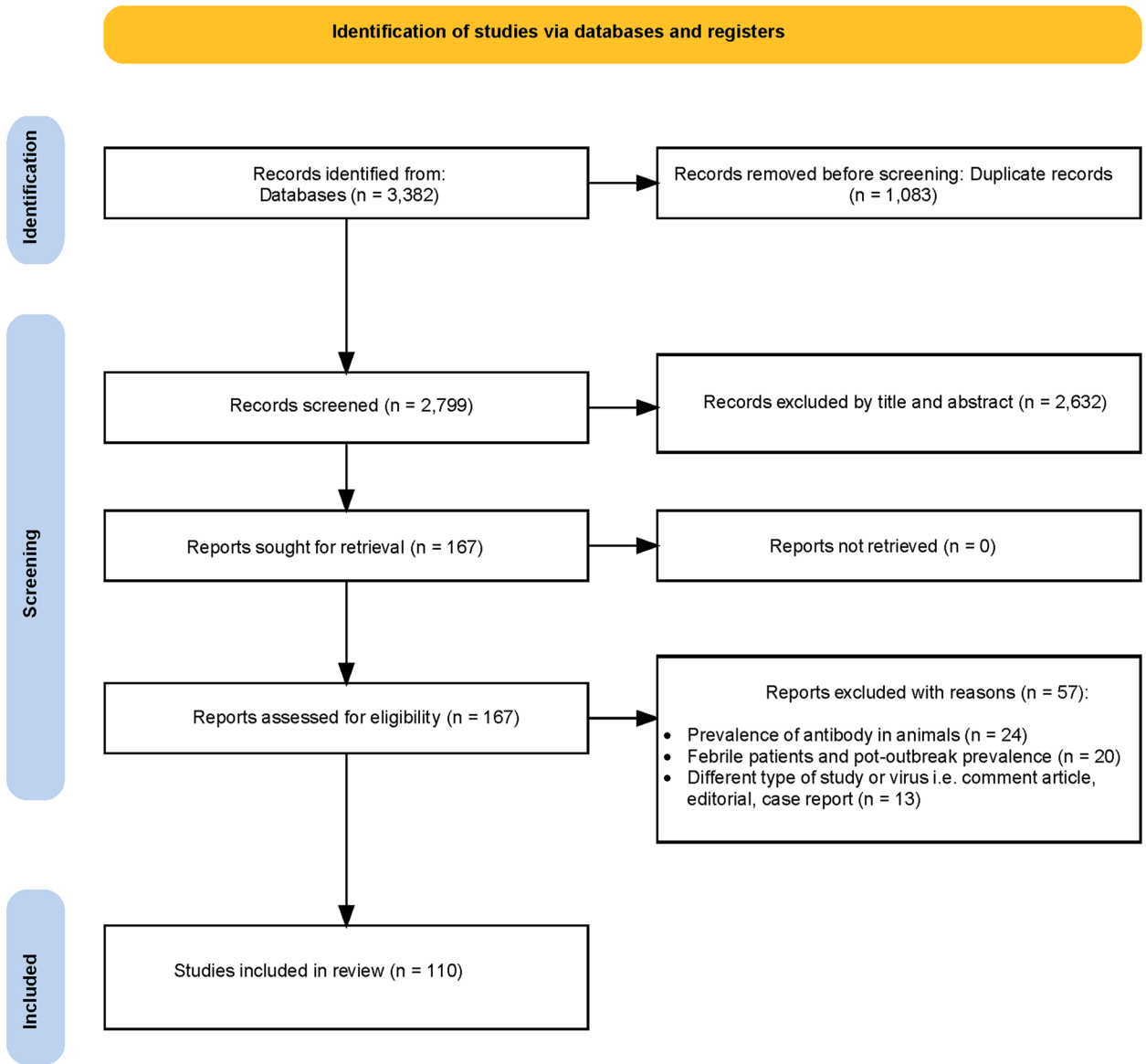

Fig. 1 PRISMA Flow Diagram

the general population exhibited a higher prevalence of 10.12% (95% CI: 5.66%—17.44%) with low certainty (⊕⊖ ⊖⊖) across 4 studies (Fig. 4).

Lastly, for Africa, 6 studies were identified, comprising data from a total of 5253 patients, with a seroprevalence proportion of 2.21% (95% CI: 1.82%—2.71%) with high certainty (⊕⊕⊕⊕). Subgroup analysis revealed varying seroprevalence rates: among individuals with chronic kidney disease, the prevalence was notably higher at 9.89% (95% CI: 5.23%—17.93%) with low certainty (⊕⊖ ⊖⊖) based on data from one study. In contrast, the general population exhibited a lower prevalence of 1.83% (95% CI: 1.32%—2.53%) with high certainty (⊕⊕⊕⊕) across six studies (Fig. 5).

Other analysis

Although we performed a subgroup analysis by viral species, these results, presented in Appendix 1 were evaluated using the ICEMAN tool [141] and were found not to be credible in terms of the subgroup effect.

Discussion

This systematic review offers valuable insights into the seroprevalence of hantavirus infections worldwide. The range of observed seroprevalence in multiple and varied

Table 2 Summary of findings table

Population	Overall			Americas			Europe			Asia			Africa		
	studies (patients)	seroprevalence	Certainty	studies (patients)	seroprevalence	Certainty	studies (patients)	seroprevalence	Certainty	studies (patients)	seroprevalence	Certainty	studies (patients)	seroprevalence	Certainty
Global	111 (82,701)	2.93% [2.34%; 3.67%]	⊕⊕⊕⊕	61 (33,156)	2.43% [1.70%; 3.46%]	⊕⊕⊕⊕	33 (40,820)	2.98% [2.19%; 4.06%]	⊕⊕⊕⊕	10 (3219)[b, d]	6.84% [3.64%; 12.5%]	⊕⊕⊖ ⊖	6 (5253)	2.21% [1.72%; 2.81%]	⊕⊕⊕⊕
General population	53 (39,684)	2.66% [2.00%; 3.54%]	⊕⊕⊕⊕	29 (16,919)	2.39% [1.56%; 3.65%]	⊕⊕⊕⊕	14 (16,443)	2.70% [1.70%; 4.28%]	⊕⊕⊕⊕	4 (907)[b, d]	10.12%% [5.66%-17.44%]	⊕⊖ ⊖ ⊖	5 (5162)[d]	1.83% [1.32%; 2..53%]	⊕⊕⊕⊖
Forestry workers	12 (10,088)	3.63% [1.97%; 6.61%]	⊕⊕⊕⊕	8 (4428)[d]	3.14% [1.15%; 8.32%]	⊕⊕⊕⊖	4 (5660)[d]	4.22% [3.35%; 5.30%]	⊕⊕⊕⊖	-	-	-	-	-	
Rural population	10 (7344)[d]	4.08% [1.95%; 8.33%]	⊕⊕⊕⊖	8 (5551)[d]	3.56% [1.49%; 8.27%]	⊕⊕⊕⊖	2 (1793)[a,d]	7.00% [2.40%; 18.76%]	⊕⊕⊖ ⊖	-	-	-	-	-	-
People exposed to rodents at work	19 (14,169)[d]	2.94% [1.62%; 5.30%]	⊕⊕⊕⊖	5 (3276)[d]	0.86% [0.11%; 2.57%]	⊕⊕⊕⊖	8 (8581)[d]	3.35% [1.64%; 6.73%]	⊕⊕⊕⊖	6 (2312)[b, d]	5.17% [1.99%; 12.79%]	⊕⊖ ⊖ ⊖	-	-	-
Indigenous people	6 (1742)[a,d]	3.77% [0.97%; 13.59%]	⊕⊖ ⊖ ⊖	6 (1742)[a,d]	3.77% [0.9%; 13.59%]	⊕⊖ ⊖ ⊖	-	-	-	-	-	-	-	-	-
Healthcare workers	5 (1555)[d]	0.78% [0.36%; 1.70%]	⊕⊕⊕⊖	4 (861)[b,d]	0.54% [0.31%; 1.54%]	⊕⊕⊖ ⊖	1 (694)[b]	1.01% [0.48%; 2.10%]	⊕⊕⊖ ⊖	-	-	-	-	-	-
School-age population	1 (379)[c]	13.19% [10.14%; 16.99%]	⊕⊖ ⊖ ⊖	1 (379)[c]	13.19% [10.14%; 16.99%]	⊕⊖ ⊖ ⊖	-	-	-	-	-	-	-	-	-
Chronic kidney disease with replacement therapy (dialysis)	2 (309)[c,d]	8.09% [5.53%; 11.70%]	⊕⊖ ⊖ ⊖	-	-	-	1 (218)[c]	7.34% [4.54%; 11.64%]	⊕⊖ ⊖ ⊖	-	-	-	1 (91)[c]	9.89% [5.23%; 17.93%]	⊕⊖ ⊖ ⊖
Military personnel	3 (7431)[a,d]	1.01% [0.81%; 1.26%]	⊕⊕⊖ ⊖	-	-	-	3 (7431)[a,d]	1.01% [0.81%; 1.26%]	⊕⊕⊖ ⊖	-	-	-	-	-	-

Certainty		Explanation
High	⊕⊕⊕⊕	We are very confident about this seroprevalence value
Moderate	⊕⊕⊕⊖	We are somewhat confident about this seroprevalence value
Low	⊕⊕⊖⊖	We are not very confident about this seroprevalence value
Very Low	⊕⊖⊖⊖	We are uncertain about this seroprevalence value

Notes:

a. We downgraded one level due to imprecision.
b. We downgraded two levels due to imprecision.
c. We downgraded three levels due to severe imprecision
d. We downgraded one level due to unexpected heterogeneity (inconsistency)
e. We downgraded one level due to risk of bias.
f. We downgraded one level due to publication bias.

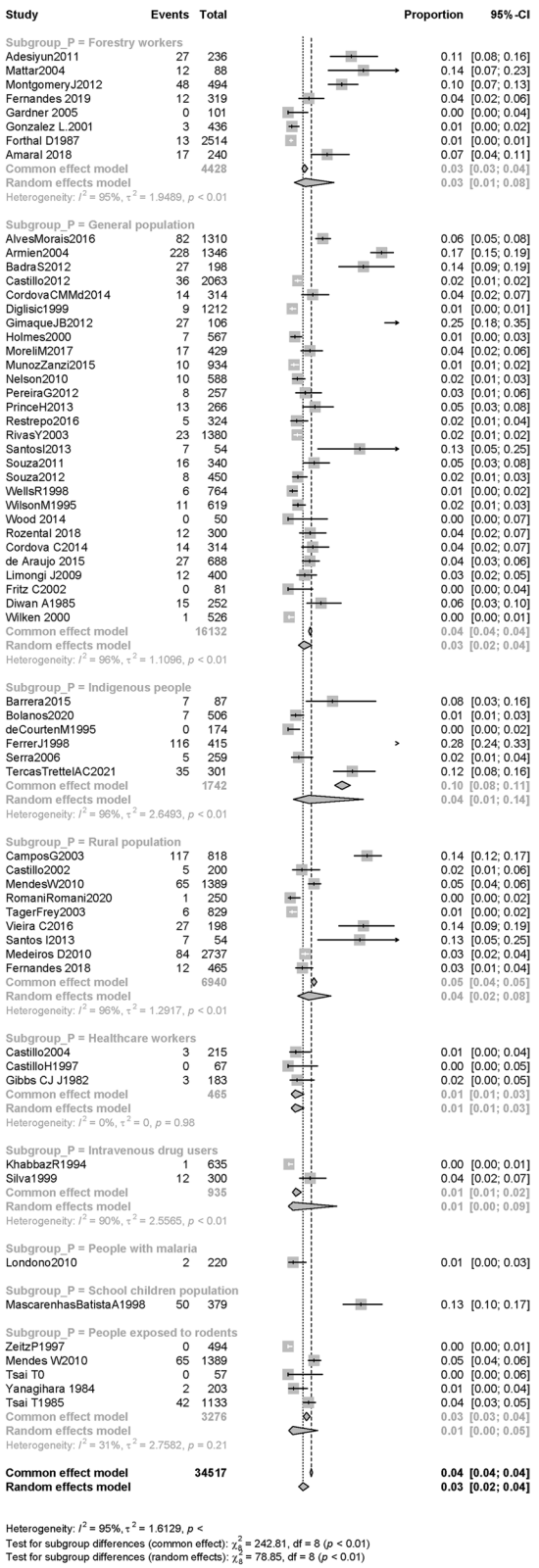

Fig. 2 Forest plot, Subgroups by Geographical Region and population, setting or occupation: Americas

regions around the globe was from 2.43% to 6.84%. The presence of these viruses across the world, even in areas where clinical cases are rare, suggests that widespread exposure has occurred globally, with many individuals likely coming into contact with the virus without developing severe illness [142, 143]. While occasional reports mention oligo symptomatic or asymptomatic illness among patients, the certainty regarding the existence of asymptomatic infections, particularly concerning hantaviruses species that induce hantavirus pulmonary syndrome, remains insufficiently established [108]. Furthermore, it is possible that unidentified hantaviruses species or groups circulating in rodent, shrew, bat, and other zoonotic reservoir populations may result in clinically insignificant asymptomatic infections, explaining some of the background seropositivity [144, 145].

Our results support the notion that rural populations, especially indigenous communities, are at a greater risk of coming into contact with these viruses. Clear examples include the Americas, where rural settings have a higher exposure risk compared to the general population, and Europe, where non-healthcare-related occupational risk surpasses that observed for the general population. Additionally, in Asia, distinct occupational categories reveal varying levels of seroprevalence, with some groups, like tribal members involved in rodent trapping, showing higher seroprevalence rates [3, 13, 15, 16].

On the other hand, healthcare workers, who are generally less exposed to rodents, consistently showed lower seroprevalence rates, further reinforcing the hypothesis that rodent contact remains the primary transmission route [9–17].

Our study also reinforces the understanding that hantavirus transmission primarily occurs through contact with rodents in interface areas between urban and rural environments, rather than through direct human-to-human transmission. This conclusion is based on the observation that occupations and residential areas with greater exposure to rodents, such as rural and indigenous communities, showed higher seroprevalence compared to other groups. Although less common, evidence of human to human transmission also exist, particularly in areas where Andes virus (ANDV) is endemic [146, 147]. For example, studies conducted in Chile and Argentina have documented probable cases of human-to-human transmission of ANDV, especially in close household contacts, such as sexual partners [146, 147]. These studies, though limited in number and with some methodological constraints, highlight that while most human contacts did not result in infections, there were instances where human-to-human transmission was likely.

The limitations of the present study highlight the geographic constraints of the available data. In particular,

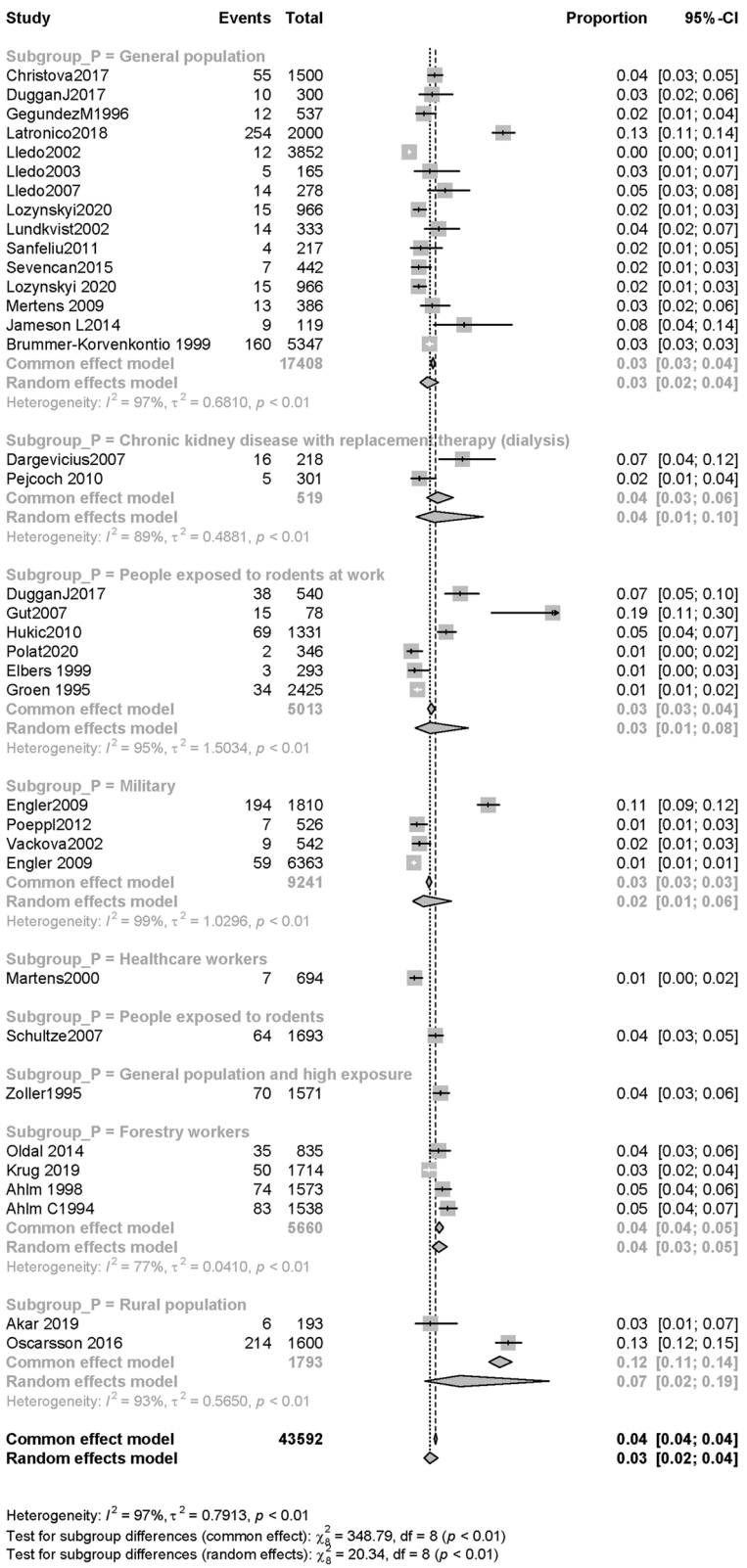

Fig. 3 Forest plot, Subgroups by Geographical Region and population, setting or occupation: Europe

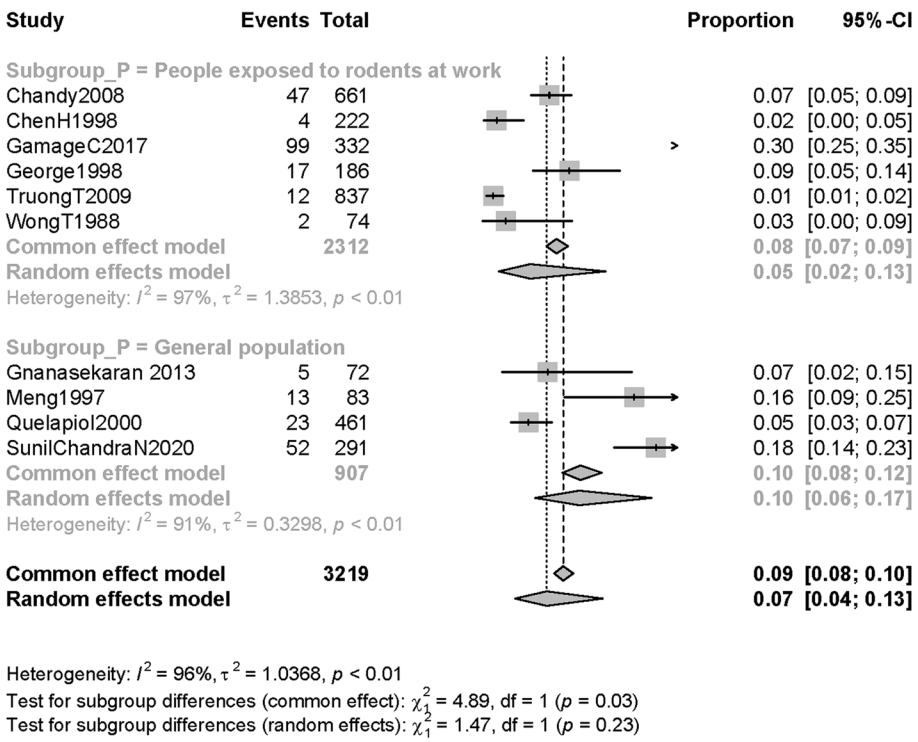

Fig. 4 Forest plot, Subgroups by Geographical Region and population, setting or occupation: Asia

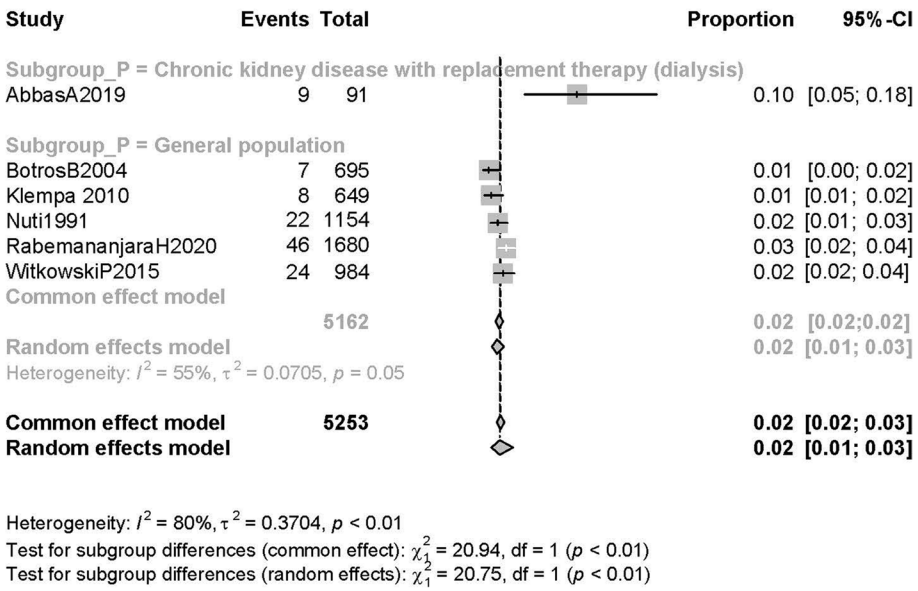

Fig. 5 Forest plot, Subgroups by Geographical Region and population, setting or occupation: Africa

data from Africa and Asia are notably sparse, and even within the Americas and Europe, certain regions—such as the Caribbean—are underrepresented, with only two studies included. Additionally, the small number of studies and the high degree of variability significantly limit the interpretability of the subgroup analyses.

To our knowledge, this is the first systematic review to assess the global seroprevalence of hantaviruses. We conducted a comprehensive search and employed

state-of-the-art methods for evidence synthesis and analysis. Our findings reveal a moderate global hantavirus seroprevalence, underscoring the complex transmission dynamics influenced by exposure and geographical factors. These results highlight the need for targeted prevention and control strategies.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-024-20014-w.

Supplementary Material 1.

Authors' contributions

F.T.: Conceived the study, led the research design and coordination, and substantively revised the manuscript. Also responsible for final approval of the version to be published. F.P.: Contributed to data acquisition and analysis, and assisted in drafting the manuscript. C.T.: Played a key role in the interpretation of data and critically revised the manuscript for important intellectual content. L.L.: Assisted with data collection and analysis and contributed to the drafting of the manuscript. G.C.: Involved in the data analysis and interpretation, provided critical revisions to the manuscript. G.G.: Contributed to the conception and design of the work, helped in the drafting and revision of the manuscript. A.I. and Y.E.: Both contributed equally to the acquisition and analysis of data and to drafting parts of the manuscript related to their expertise. A.I.: Oversaw the methodology, was involved in the critical revision of the manuscript for key intellectual content, and approved the final version to be published.
All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors have read and agreed to the published version of the manuscript.
Author Consent Declaration:All listed authors have actively participated in the conception and design of this study, or analysis and interpretation of data, and/or have been involved in the drafting or revising of the manuscript critically for important intellectual content. Each author has provided explicit consent to submit the manuscript in its current form and has approved the final version to be published.

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Availability of data and materials

All data generated or analyzed during this study are publicly available in the Figshare repository under DOI: https://doi.org/10.6084/m9.figshare.26946898. This includes the datasets that underlie Figs. 1, 2, 3, 4, 5, Tables 1 and 2, and supplementary figures. The repository ensures long-term access and citation, allowing for further research and verification of the study's claims. Data are shared in compliance with relevant ethical standards and in line with repository best practices for transparency and accessibility.

Declarations

Ethics approval and consent to participate

As this study involves secondary data and does not include direct involvement of human participants, the requirement for ethics approval is not applicable. Given that this study is a systematic review using secondary data, there were no direct human participants involved. Human Ethics and Consent to Participate declarations: not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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