



Monaldi Archives for Chest Disease

elSSN 2532-5264

https://www.monaldi-archives.org/

Publisher's Disclaimer. E-publishing ahead of print is increasingly important for the rapid dissemination of science. The *Early Access* service lets users access peer-reviewed articles well before print / regular issue publication, significantly reducing the time it takes for critical findings to reach the research community.

These articles are searchable and citable by their DOI (Digital Object Identifier).

The **Monaldi Archives for Chest Disease** is, therefore, e-publishing PDF files of an early version of manuscripts that have undergone a regular peer review and have been accepted for publication, but have not been through the typesetting, pagination and proofreading processes, which may lead to differences between this version and the final one.

The final version of the manuscript will then appear in a regular issue of the journal.

E-publishing of this PDF file has been approved by the authors.

All legal disclaimers applicable to the journal apply to this production process as well.

Monaldi Arch Chest Dis 2025 [Online ahead of print]

To cite this Article:

Debnath A, Halder P, Achary T, et al. **Prevalence of human metapneumovirus infection among children suffering from acute respiratory illness in India: a systematic review and meta-analysis.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2025.3383

©The Author(s), 2025 Licensee PAGEPress, Italy

Note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries should be directed to the corresponding author for the article.

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.



Prevalence of human metapneumovirus infection among children suffering from acute respiratory illness in India: a systematic review and meta-analysis

Aninda Debnath,¹ Pritam Halder,² Thejas Achary,³ Raunak Bir,⁴ Anubhav Mondal,³ Pranav Ish⁵

¹Department of Community Medicine, Maulana Azad Medical College, New Delhi; ²Department of Community Medicine, School of Public Health, Postgraduate Institute of Medical Education and Research, Chandigarh; ³Department of Community Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi; ⁴Department of Microbiology, ESIC Medical College and Hospital, Faridabad, Haryana; ⁵Department of Pulmonary Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

Correspondence: Pranav Ish, Department of Pulmonary Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India. Tel.: 9958356000. E-mail: <u>pranavish2512@gmail.com</u>

Contributions: all authors were involved in conceptualization, literature search, writing the original manuscript draft, literature search, planning, conduct, and editing. All the authors have read and agreed with the submitted manuscript.

Conflict of interest: the authors declare no potential conflict of interest.

Ethics approval and consent to participate: an ethics committee certificate is only required for original patient research. For systematic review and meta-analysis of previously published studies, PROSPERO registration is needed. This study was registered in PROSPERO (Registration ID: CRD42025635684).

Informed consent: not applicable.

Patient consent for publication: not applicable.

Availability of data and materials: data are available from the corresponding author upon request.

Funding: none.

Abstract

Acute respiratory infections (ARI) are a leading cause of pediatric morbidity and mortality worldwide, with India bearing a significant burden. Human metapneumovirus (HMPV), an under-recognized respiratory pathogen, has been implicated in ARI, yet its prevalence in India remains inadequately characterized. The objective of this study was to estimate the prevalence of HMPV among children with ARI in India and assess regional, temporal, and demographic trends to guide public health interventions. This systematic review and meta-analysis was conducted following PRISMA guidelines. Data were extracted from 30 studies encompassing 12,534 children with ARI across India from 2004 to 2024. A random-effects model was used to calculate pooled prevalence, with subgroup and sensitivity analyses to explore heterogeneity. Publication bias was assessed using Egger's test and funnel plots. The pooled prevalence of HMPV was 5% (95% confidence interval: 4-6%), with significant heterogeneity (I²=95%). Subgroup analyses revealed higher prevalence in the northeast region (7%) and among children under 5 years (6%), compared to older age groups (2%). No significant differences were observed in prevalence pre- and post-COVID-19. Sensitivity analyses confirmed the robustness of findings, with minimal impact of publication bias. HMPV is a significant contributor to pediatric ARI in India, particularly among children under 5 years, highlighting its public health importance. The lack of a post-COVID-19 surge in prevalence suggests sustained circulation and widespread immunity. These findings underscore the need for enhanced diagnostic capacities, routine surveillance, and targeted interventions to mitigate the burden of HMPV-related ARI in vulnerable populations.

Key words: human metapneumovirus, acute respiratory infections, severe acute respiratory illness, acute lower respiratory tract infection, prevalence.

Introduction

Acute respiratory tract infections (ARIs) are a leading cause of morbidity and mortality worldwide, with a particularly severe impact in low- and middle-income countries like India [1]. Specially, acute lower respiratory tract infections (ALRTIs) account for an estimated 2.3 million deaths annually, making them the sixth leading cause of mortality globally and the primary cause of death among children under five years of age [2]. In India, ALRTIs contribute to approximately 14.3% of infant deaths and 15.9% of deaths in children under five [3]. Despite advancements in diagnostic techniques, a significant proportion of respiratory infections remain unidentified, necessitating the discovery of new pathogens [4]. Among these, Human Metapneumovirus (HMPV) has been identified as a significant contributor to paediatric ARI since its discovery in 2001 [5]. HMPV, a single-stranded RNA virus from the Pneumoviridae family, was first isolated through genetic analysis of nasopharyngeal samples from 28 hospitalized children [6]. It is associated with a wide range of respiratory symptoms, including cough, fever, wheezing, and dyspnoea, with severe cases predominantly affecting infants and immunocompromised individuals [7].

Globally, HMPV accounts for 6.1–6.4% of ALRI-related hospital admissions in individuals under 20 years of age [8,9]. In India, where ALRIs are a leading cause of mortality in children under five, HMPV poses a significant yet underexplored public health challenge. Although most children are infected by HMPV by the age of five, severe infections disproportionately impact younger age groups, especially infants [10]. Studies suggest that India has observed sporadic cases of HMPV since its first detection in Pune in 2004 [11]. While sporadic cases have been reported in India since its first detection in Pune in 2004, comprehensive data on the prevalence and impact of HMPV remain scarce.

Recently, HMPV has gained renewed attention due to a sharp increase in cases reported in China in late 2024, indicating potential shifts in its epidemiology [12]. These developments raise concerns about similar trends occurring in India, especially given the altered circulation of respiratory viruses post-COVID-19, attributed to reduced natural immunity due to masking and lockdown measures. The objective of this study was to estimate the prevalence of HMPV among children with ARI in India, examining regional, age-specific, and temporal trends, to provide evidence for public health interventions and policy planning.

Methods

Study protocol and design

This systematic review and meta-analysis aimed to examine the prevalence of HPMV among children who were suffering from ARI in India. The study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [13]. The study protocol

was registered with the International Registration of Systems Reviews (PROSPERO) under the registration number CRD42025635684.

Inclusion and exclusion criteria

This systematic review and meta-analysis included studies based on predefined criteria to ensure relevance and quality. Observational studies, including cross-sectional, case-control, and cohort studies, were eligible for inclusion. The population considered comprised children aged 18 years or below diagnosed with ARI, including influenza-like illness (ILI, defined as fever >38°C and cough with onset within 10 days), severe acute respiratory infection (SARI, defined as ILI cases requiring hospitalization), ALRTI, and non-specific ARI cases with upper respiratory tract infection (URTI) symptoms. The review was geographically restricted to primary studies conducted in India, ensuring regional applicability of the findings. Only articles published in English were included, facilitating consistent interpretation, and the analysis encompassed studies published up to January 3, 2025, with no specific start date. This comprehensive inclusion framework provided a robust basis for analysing the prevalence and characteristics of ARI among children in India. Non-observational studies, such as interventional trials, qualitative research, case reports, were excluded. Studies not focused on ARI or conducted outside India were deemed ineligible. Only full-text articles published in English were included, while those with insufficient outcome data were excluded (Supplementary Table 1).

Information sources and search strategy

We conducted electronic searches across four databases, namely Excerpta Medica database (EMBASE), PubMed, Scopus and Web of Science, with the search period limited up to January 3rd , 2025. A thorough search was performed using keywords and Medical Subject Headings (MeSH) related to HMPV, including terms such as HMPV, Metapneumovirus, ARI, Severe SARI, ILI, Prevalence, Seroprevalence, Epidemiology. Articles were identified by combining terms and utilizing Boolean operators like "(Metapneumovirus OR Metapneumoviruses OR Human Metapneumovirus) AND (Prevalence OR Epidemiology OR Seroepidemiology) AND India" (*Supplementary Table 2*). Subsequently, we refined the results to include only the most pertinent ones. The search process was double-blinded and carried out collaboratively by authors (AD and RB). To ensure comprehensive coverage, we conducted reference checking, hand searches of citations, and scrutinized the reference lists of included studies identified during the search. Additionally, when necessary, we searched the authors' files to confirm the inclusion of all relevant materials.

Study selection

All citations obtained from the electronic searches were uploaded to the Rayyan software in 2025, and duplicate entries were systematically eliminated. Subsequently, two independent researchers (TA and PH) conducted a comprehensive screening of titles and abstracts from the retrieved studies to identify articles eligible for potential inclusion and any disagreement were resolved by discussion and agreement. Any remaining disagreements were consulted with the other co-authors (AD & RB) to assess the inclusion of studies for the next step. The identified articles underwent a thorough review of the full text by the same independent authors (TA and PH), adhering to a pre-defined eligibility criterion to determine relevance for inclusion in the review. In instances where additional information was needed to address queries about eligibility, collaboration with the remaining authors was sought. Any disagreements were resolved through discussion. Furthermore, the reasons for excluding articles were meticulously documented at each stage, and any remaining uncertainties or disagreements were addressed by a third reviewer (AD).

Data extraction

Key details for our data extraction template included the first author's name, year of publication, year of study, sample size, study regions, study design, study population, type of admission, mode of diagnosis, HMPV prevalence and most common symptoms. A standardized Microsoft Excel spreadsheet was used as the data extraction form, ensuring consistency in collecting pertinent information from eligible articles. The authors (TA, PH) independently performed the data extraction from the included articles, and any discrepancies were resolved through discussion and mutual agreement among the authors.

Statistical analysis

The pooled prevalence of HMPV among children with ARI was calculated using a randomeffects model to account for between-study variability. Heterogeneity was assessed using Cochran's Q statistic and the I² statistic. Subgroup analyses were performed to explore sources of heterogeneity based on temporal, regional, clinical, and age-based categories used to assess prevalence of HMPV. Sensitivity analysis was conducted using Baujat plots, leave-one-out analyses, and influence diagnostics to identify studies contributing disproportionately to heterogeneity and to examine the robustness of the pooled estimates. To assess publication bias, funnel plots were visually inspected, and Egger's regression test was performed to detect small-study effects. Trim-and-fill analysis was applied to adjust for potential publication bias by imputing missing studies and recalculating the pooled prevalence. Meta-regression analyses were conducted to identify potential covariates influencing the prevalence of HMPV, including sample size, proportion of female participants, and mean age, on the observed prevalence of HMPV among children. The proportion of heterogeneity explained by these covariates was assessed using R^2 , and the relationships were visually represented using bubble plots. Statistical analyses were performed using STATA-18 software, with significance set at p < 0.05.

Assessment quality and the risk of bias

Two independent researchers (TA and PH) evaluated the methodological quality and risk of bias in the included studies using the 9 item Joanna Briggs Institute (JBI) Critical Appraisal tools specifically tailored for prevalence studies [14]. Studies that scored 1 to 3 were categorised as poor, 4 to 6 as fair and 7 to 9 as good quality. A higher score indicates a lower risk of bias, while a lower score indicates a higher risk of bias.

Results

A systematic and comprehensive literature search was conducted across four major electronic databases, including PubMed (64 records), Scopus (45 records), Web of Science (49 records), and Embase (133 records), yielding a total of 291 records. After the removal of 111 duplicate entries, 180 unique studies were identified and screened for eligibility based on their titles and abstracts. During this screening phase, 137 studies were excluded as they did not meet the predefined criteria. Subsequently, 43 studies were selected for full-text review. Of these, one study could not be retrieved despite exhaustive efforts. The full-text review of the remaining 42 studies led to the exclusion of 12 articles, with 6 studies excluded due to differences in the study population and an additional 6 studies excluded because the required outcome variable was not reported. Following this rigorous selection process, 30 studies satisfied the inclusion criteria and were included in the final review and meta-analysis (Figure 1).

This meta-analysis included 30 studies conducted across India, spanning a data collection period from 2004 to 2021, with the earliest study undertaken by Banerjee et al. during 2004–2005 [15]. The studies were geographically diverse, encompassing states such as Delhi, Tamil Nadu, West Bengal, Assam, Haryana, Rajasthan, Odisha, Karnataka, Maharashtra, and Puducherry (Figure 2). Collectively, the studies analyzed data from 12,534 children diagnosed with ARI. The settings were predominantly hospital-based, with participants recruited from outpatient departments (OPD), inpatient departments (IPD), or specialized pediatric units. The sample sizes varied widely, ranging from 45 participants in the study by Viswanathan et al. to 1,863 participants in the study by Agarwal et al. [16,17]. All included studies employed RT-PCR as the diagnostic method, with multiplex RT-PCR being the most commonly used technique, ensuring robust detection of HMPV. The prevalence of HMPV varied significantly across studies, with the highest prevalence observed in the study by Malhotra et al. (2016),

which reported HMPV in 22.6% (35 out of 155) of children with ARI, while the lowest prevalence was recorded in the study by Jambagi et al. (2018), with a rate of 0.2% [18,19] (Table 1 and Figure 2) [3,15-42]. In quality assessment of the studies, we found 27 studies to be of good quality, where has three studies were of moderate quality. We did not find any study of poor quality in this meta-analysis (Table 2).

Pooled prevalence of HMPV

A comprehensive meta-analysis was conducted to evaluate the prevalence of HMPV among children with ARI across India. The analysis included 12,534 participants, among whom HMPV was identified in 558 of cases. The pooled prevalence was estimated at 5%, with a 95% confidence interval (CI) of 4% to 6%. Substantial variability in findings was observed, as indicated by a high I² value of 95.09% (P < 0.01), suggesting real differences in HMPV prevalence rather than random chance. Consequently, the analysis was conducted using a random-effects model to account for this heterogeneity (Figure 3).

Subgroup analysis

Subgroup analyses were conducted to explore variability in HMPV prevalence across temporal, regional, clinical, and age-based categories, revealing important insights into the distribution of HMPV among children. Stratification by publication year showed a pooled prevalence of 5.0% (95% CI: 3.0%-7.0%) for studies published between 2007-2019, with high heterogeneity ($I^2 = 97.94\%$), compared to a slightly lower prevalence of 4.0% (95% CI: 3.0%-5.0%) for 2020–2024, with moderate heterogeneity ($I^2 = 49.84\%$), though differences were not statistically significant (Qb = 0.95, p = 0.33) (Supplementary Figure 1). Geographic analysis revealed pooled prevalence estimates of 3.0% (95% CI: 2.0%–5.0%) in the East, 6.0% (95% CI: 3.0%–9.0%) in the North, 7.0% (95% CI: 4.0%–10.0%) in the North-East, 5.0% (95% CI: 2.0%–7.0%) in the South, and 6.0% (95% CI: 3.0%–10.0%) in the West, with no significant differences across regions (Qb = 6.59, p = 0.16) (Supplementary Figure 2). Stratification by clinical presentation showed similar prevalence for ALRTI (5.0%; 95% CI: 2.0%-7.0%, I² = 82.21%), ILI (4.0%; 95% CI: 1.0%-7.0%, I² = 73.92%), and ILI/SARI (4.0%; 95% CI: 1.0%-7.0%, $I^2 = 94.81\%$), with higher prevalence in SARI (12.0%; 95% CI: -8.0%-32.0%, $I^2 =$ 97.16%), though group differences were not significant (Qb = 0.70, p = 0.87) (Supplementary *Figure 3*). Six studies evaluated children over 5 years of age, reporting a pooled prevalence of 2.0% (95% CI: 1.0%–3.0%). Heterogeneity within this subgroup was low (I² = 17.02%, τ^2 = 0.00, $H^2 = 1.21$), suggesting consistency in findings across studies for this age group and Sixteen studies analyzed children under 5 years, with a pooled prevalence of 6.0% (95% CI:

4.0%–8.0%). Substantial heterogeneity was observed ($I^2 = 94.55\%$, $\tau^2 = 0.00$, $H^2 = 18.36$). There was significant difference between these two age groups (*Supplementary Figure 4*).

Publication bias

Publication bias was assessed using a combination of visual and statistical methods, including a funnel plot, Egger's test, and the trim-and-fill method, to evaluate the potential influence of small-study effects on the pooled prevalence estimate of HMPV. The funnel plot displayed slight asymmetry, with smaller studies (those with higher standard error) tending to report higher prevalence rates, suggesting potential small-study effects or reporting bias. Egger's regression test confirmed the presence of small-study effects, with a highly significant result ($\beta 1 = 3.34$, SE = 0.491, p < 0.0001), indicating that smaller studies with higher prevalence were disproportionately represented. However, the trim-and-fill method, which accounts for potential missing studies, identified no additional imputed studies, and the pooled prevalence remained stable at 4.9% (95% CI: 3.5%–6.2%), suggesting that the overall estimate was robust despite evidence of publication bias (Figure 4).

Meta-regression analysis was conducted to explore the influence of study-level covariates, including sample size, proportion of female participants, and mean age, on the observed prevalence of HMPV among children. The analysis revealed that none of these factors significantly explained the variability in prevalence across studies. Sample size showed a weak inverse association with prevalence (coefficient: -0.0000151, p = 0.306), suggesting that smaller studies tended to report slightly higher prevalence rates, although this trend was not statistically significant. Similarly, the proportion of females in the study populations had a minimal, non-significant effect on prevalence (coefficient: -0.0010086, p = 0.649), indicating that gender distribution did not substantially influence the findings. Mean age also exhibited a weak, non-significant negative association with prevalence (coefficient: -0.0064917, p = 0.679), with studies involving older participants reporting marginally lower prevalence rates, potentially reflecting reduced susceptibility due to prior exposure or immunity (*Supplementary Figure 5*).

Sensitivity analysis was performed to evaluate the robustness of the pooled prevalence estimate and the impact of individual studies on overall heterogeneity. Sequentially omitting individual studies showed that the pooled prevalence consistently ranged between 4.0% and 5.0%, demonstrating the stability of the overall estimate despite substantial heterogeneity. Studies such as Malhotra et al. (2016), Narayanan et al. (2013), and Mazumdar et al. (2013) were identified as major contributors to heterogeneity, primarily due to their high prevalence rates (e.g., 23% and 13%) or small sample sizes. Exclusion of these studies led to a reduction in heterogeneity, though the pooled prevalence remained largely unaffected. Influence plots further highlighted the disproportionate contributions of these outliers, with most studies clustering near the pooled estimate, indicating limited individual influence on the overall result. These findings emphasize that while heterogeneity is driven by a few influential studies, the overall pooled prevalence estimate is robust (Figure 5).

Discussion

This meta-analysis is the first to estimate the prevalence of HMPV infection among children under five years of age presenting with symptoms of ARI in the Indian context. The pooled prevalence of HMPV was 5% (95% CI: 4%–6%), based on studies spanning two decades (2004–2024). Globally, HMPV has been in circulation since its identification in 2001, and it continues to contribute to respiratory infections worldwide, including India. Among children under five years of age, the global prevalence of HMPV varies significantly, ranging from 1.1% to 86%, as reported in diverse regions Notably, the highest prevalence (86%) was recorded in a Sri Lankan study with a small sample size of only 21 participants, which may be considered an outlier [43]. Excluding this study, global prevalence ranges from 1.1% to 22.2%, with Algeria reporting the next highest prevalence [44].

Subgroup analysis of regional prevalence in India revealed a higher prevalence in the North Eastern region (7%; 95% CI: 4%-10%). However, HMPV cases were documented across all regions of the country, suggesting widespread circulation of the virus. Interestingly, this metaanalysis found no significant increase in the prevalence of HMPV in India post-COVID-19. Studies published before and after 2020 showed no substantial differences in prevalence. This contrasts with findings from China, where Ji et al. and Kunag et al. reported a surge in HMPV infections after the pandemic, particularly in Henan and Southern China [45,46]. The observed increase in these regions has been attributed to reduced natural immunity due to limited exposure to respiratory viruses during the pandemic because of pharmaceutical interventions such as lockdowns and masking [47]. The meta-analysis underscores that HMPV is a notable cause of respiratory infections in children, with a higher prevalence observed in SARI cases (12%) compared to general outpatient visits (4%–5%). While the cross-sectional nature of the included studies prevents a longitudinal assessment of HMPV's role in hospitalization rates compared to other viruses, the findings suggest a correlation between HMPV presence and respiratory illness severity. The prevalence of HMPV was higher among children under five years of age compared to older age groups. Within this age group, children under two years were particularly vulnerable, consistent with global findings [10,48]. This increased susceptibility is likely due to underdeveloped immune systems in younger children, influenced by intrinsic cellular immaturity, active immune suppression, and environmental or genetic factors [49-51].

Unlike novel viruses such as SARS-CoV-2, HMPV is not new and has been circulating in humans for decades [52]. Since its identification in 2001, serological studies have shown widespread immunity, with antibodies present in almost all individuals aged five and older. This suggests that the population is generally well-protected against severe outcomes due to prior exposure [6]. Furthermore, HMPV infections are typically mild and self-limiting, with most cases resolving without complications [53]. Severe disease, such as bronchiolitis or pneumonia, occurs primarily in high-risk groups, including infants, elderly individuals, and those who are immunocompromised [54]. The virus's transmission patterns are more akin to those of RSV and seasonal influenza, which cause localized outbreaks rather than global pandemics. Experts agree that HMPV has limited epidemic potential due to its stable pathology, lack of significant mutations, and absence of widespread asymptomatic transmission [52]. Although concerns about interactions with other respiratory viruses or potential zoonotic events remain theoretical, there is currently no evidence of such interactions contributing to increased transmissibility or virulence.

In the winter season, there is an increased trend in ILI and ARI activity in the northern hemisphere of the globe. Many countries have routine surveillance systems to measure these trends. In China, there is an established surveillance system for ILI and ARI. The recent surveillance data from China shows a seasonal rise in ILI and ARI activity, with HMPV contributing to 6.2% of ILI and 5.0% of SARI cases as of January 2025 [12]. These trends align with expected seasonal patterns, as noted by the WHO, and indicate no abnormal outbreaks. Similarly, India has not observed any unusual rise in cases of ILI or SARI attributable to HMPV, as confirmed by data from the Integrated Disease Surveillance Programme (IDSP) and ICMR sentinel surveillance. Moreover, the virus's presence in India for over two decades suggests widespread immunity in the population, further reducing its potential to cause severe outbreaks. Preventive measures such as frequent handwashing, avoiding contact with symptomatic individuals, and practicing respiratory hygiene should be promoted to mitigate transmission.

This is the first meta-analysis of HMPV prevalence among children in India, showcasing notable strengths such as adherence to PRISMA guidelines, a comprehensive dataset of 30 studies encompassing 12,534 children across diverse regions (2004–2024), and robust subgroup analyses. Rigorous sensitivity and bias testing further validated the findings, while the predominance of high-quality studies enhances their reliability and generalizability. However, some limitations warrant attention. The high heterogeneity in pooled estimates (I² = 95%) reflects variability across studies, likely due to differences in design, population demographics, and diagnostic methods, despite thorough subgroup and sensitivity analyses. Additionally, the exclusion of gray literature and unpublished studies may have omitted

relevant data, potentially affecting prevalence estimates. While these limitations do not detract from the study's validity, they may impact the broader applicability of the findings.

Conclusions

This systematic review and meta-analysis provide the first comprehensive estimate of HMPV prevalence among children with ARI in India, reporting a pooled prevalence of 5% over two decades. The findings underscore the significant public health burden of HMPV, particularly among children under five years of age. Despite substantial heterogeneity, this study confirms the widespread circulation of HMPV in India and its stable prevalence post-COVID-19, contrary to trends observed in other regions. These insights offer critical evidence to guide resource allocation, public health interventions, and policy planning aimed at mitigating the impact of ARIs in vulnerable paediatric populations.

References

1. UNICEF. Levels & trends in child mortality. Rreport 2023. Available from: https://childmortality.org/wp-content/uploads/2024/03/UNIGME-2023-Child-Mortality-Report.pdf. Accessed on: 22/01/2025.

2. Naghavi M, Abajobir AA, Abbafati C, et al. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390:1151-210.

3. Chandy S, Manoharan A, Hameed A, et al. A study on pediatric respiratory tract infections in hospitalised children from Chennai. Clin Epidemiol Glob Health 2022;15:101067.

4. Kahn JS. Newly discovered respiratory viruses: significance and implications. Curr Opin Pharmacol 2007;7:478-83.

5. Amarasinghe GK, Ayllón MA, Bào Y, et al. Taxonomy of the order mononegavirales: update 2019. Arch Virol 2019;164:1967-80.

6. Van den Hoogen BG, de Jong JC, Groen J, et al. A newly discovered human pneumovirus isolated from young children with respiratory tract disease. Nat Med 2001;7:719-24.

7. Panda S, Mohakud NK, Pena L, et al. Human metapneumovirus: review of an important respiratory pathogen. Int J Infect Dis 2014;25:45-52.

8. Lefebvre A, Manoha C, Bour J-B, et al. Human metapneumovirus in patients hospitalized with acute respiratory infections: a meta-analysis. J Clin Virol 2016;81:68-77.

Wang M, Cai F, Wu X, et al. Incidence of viral infection detected by PCR and real-time PCR in childhood community-acquired pneumonia: a meta-analysis. Respirology 2015;20:405-12.
Heikkinen T, Österback R, Peltola V, et al. Human metapneumovirus infections in children. Emerg Infect Dis 2008;14:101-6.

11. Rao BL, Gandhe SS, Pawar SD, et al. First detection of human metapneumovirus in children with acute respiratory infection in India: a preliminary report. J Clin Microbiol 2004;42:5961-2.

12. WHO. Trends of acute respiratory infection, including human metapneumovirus, in the Northern Hemisphere. 2025. Available from: <u>https://www.who.int/emergencies/disease-outbreak-news/item/2025-DON550</u>. Accessed on: 22/01/2025.

13. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71.

14. Barker TH, Stone JC, Sears K, et al. The revised JBI critical appraisal tool for the assessment of risk of bias for randomized controlled trials. JBI Evid Synth 2023;21:494-506.

15. Banerjee S, Bharaj P, Sullender W, et al. Human metapneumovirus infections among children with acute respiratory infections seen in a large referral hospital in India. J Clin Virol 2007;38:70-2.

16. Viswanathan R, Bafna S, Choudhary ML, et al. Looking beyond pertussis in prolonged cough illness of young children. Vaccines 2022;10:1191.

17. Agrawal AS, Roy T, Ghosh S, et al. Genetic variability of attachment (G) and Fusion (F) protein genes of human metapneumovirus strains circulating during 2006-2009 in Kolkata, Eastern India. Virol J 2011;8:67.

18. Malhotra B, Swamy MA, Janardhan Reddy PV, et al. Viruses causing severe acute respiratory infections (SARI) in children 5 years of age at a tertiary care hospital in Rajasthan, India. Indian J Med Res 2016;144:877-85.

19. Jambagi M, Jadhav A, Atmanathan S, et al. Abstract P-194: burden of viral etiology in acute respiratory infections in children - a single centre study in India. Pediatr Crit Care Med 2018;19:107.

20. Bharaj P, Sullender WM, Kabra SK, et al. Respiratory viral infections detected by multiplex PCR among pediatric patients with lower respiratory tract infections seen at an urban hospital in Delhi from 2005 to 2007. Virol J 2009;6:89.

21. Banerjee S, Sullender W, Ahuja R, et al. Seroepidemiological study of human metapneumovirus in New Delhi, India. Indian J Med Microbiol 2011;29:363-7.

22. Narayanan H, Sankar S, Simoes EA, et al. Molecular detection of human metapneumovirus and human bocavirus on oropharyngeal swabs collected from young children with acute respiratory tract infections from rural and peri-urban communities in South India. Mol Diagn Ther 2013;17:107-15.

23. Roy Mukherjee T, Chanda S, Mullick S, et al. Spectrum of respiratory viruses circulating in eastern India: prospective surveillance among patients with influenza-like illness during 2010–2011. J Med Virol 2013;85:145-65.

24. Mazumdar J, Chawla-Sarkar M, Rajendran K, et al. Burden of respiratory tract infections among paediatric in and out-patient units during 2010-11. Eur Rev Med Pharmacol Sci 2013;17:802-8.

25. Biswas D, Yadav K, Borkakoty B, Mahanta J. Human metapneumovirus infection among outpatient children in Dibrugarh. Indian Pediatr. 2014;51:931-2.

26. Broor S, Dawood F, Pandey B, et al. Rates of respiratory virus-associated hospitalization in children aged <5 years in rural northern India. J Infect 2013;68:281-9.

27. Singh A, Jain A, Jain B, et al. Viral aetiology of acute lower respiratory tract illness in hospitalised paediatric patients of a tertiary hospital: one year prospective study. Indian J Med Microbiol 2014;32:13-8.

28. Sarkar S, Ratho RK, Singh M, et al. Role of viral load and host cytokines in determining the disease severity of respiratory syncytial virus-associated acute lower respiratory tract infections in children. Jpn J Infect Dis 2023;76:233-9.

29. Nandhini G, Sujatha S, Jain N, et al. Prevalence of human metapneumovirus infection among patients with influenza-like illness: report from a tertiary care centre, southern India. Indian J Med Microbiol 2016;34:27-32.

30. Panda S, Mohakud N, Suar M. Etiology, seasonality, and clinical characteristics of respiratory viruses in children with respiratory tract infections in Eastern India (Bhubaneswar, Odisha): epidemiology of respiratory viruses in eastern India. J Med Virol 2016;89:553-8.

31. Swamy MA, Malhotra B, Janardhan Reddy P, et al. Profile of respiratory pathogens causing acute respiratory infections in hospitalised children at Rajasthan a 4 year's study. Indian J Med Microbiol 2018;36:163-71.

32. Biswal B, Dwibedi B, Hansa J, et al. Bacterial and viral pathogen spectra of ari among the children below 5 years age group in tribal and coastal regions of Odisha. Indian J Public Health Res Dev 2018;9ù:366-72.

33. Sonawane AA, Shastri J, Bavdekar SB. Respiratory pathogens in infants diagnosed with acute lower respiratory tract infection in a tertiary care hospital of western India using multiplex real time PCR. Indian J Pediatr 2019;86:433-8.

34. Anand M, Nimmala P. Seasonal incidence of respiratory viral infections in Telangana, India: utility of a multiplex PCR assay to bridge the knowledge gap. Trop Med Int Health 2020;25:1503-9.

35. Palani N, Sistla S. Epidemiology and phylogenetic analysis of respiratory viruses from 2012 to 2015 - a sentinel surveillance report from union territory of Puducherry, India. Clin Epidemiol Glob Health 2020:8:1225-35. Erratum in: Clin Epidemiol Glob Health 2002;13:100991.

36. Kumar A, Bahal A, Singh L, et al. Utility of multiplex real-time PCR for diagnosing paediatric acute respiratory tract infection in a tertiary care hospital. Med J Armed Forces India 2023;79:286-91.

37. Muruganandam N, Roy A, Sivanandan N, et al. Respiratory viruses among ethnic Nicobarese during COVID-19 pandemic. BMC Infect Dis 2022;22:463.

38. Sarkar S, Ratho R, Singh M, et al. Comparative analysis of epidemiology, clinical features, and cytokine response of respiratory syncytial and human metapneumovirus infected children with acute lower respiratory infections. Jpn J Infect Dis 2021;75:56-62.

39. Hindupur A, Menon T, Dhandapani P. Molecular investigation of human metapneumovirus in children with acute respiratory infections in Chennai, South India, from 2016–2018. Braz J Microbiol 2022;53:655-61.

40. Koul P, Saha S, Ahmed K, et al. Respiratory syncytial virus among children hospitalized with severe acute respiratory infection in Kashmir, a temperate region in northern India. J Glob Health 2022;12:04050.

41. Kang M, Sarkar S, Kumar S, et al. Paradigm shift of respiratory viruses causing lower respiratory tract infection in children during COVID-19 pandemic in India. J Infect Dev Ctries 2023;17:961-70.

42. Taduri DA, Reddy S, Srikrishna D. A hospital based study on clinico – epidemiological profile and outcome in infants with bronchiolitis. Eur J Cardiovasc Med 2023;13:220-7.

43. Noordeen F, Pitchai FNN, Kudagammana ST, et al. A mini outbreak of human metapneumovirus infection with severe acute respiratory symptoms in a selected group of children presented to a teaching hospital in Sri Lanka. Virusdisease 2019;30:307-10.

44. Derrar F, Izri K, Kaddache C, et al. Virologic study of acute lower respiratory tract infections in children admitted to the paediatric department of Blida University Hospital, Algeria. New Microbes New Infect 2019;30:100536.

45. Kuang L, Xu T, Wang C, et al. Changes in the epidemiological patterns of respiratory syncytial virus and human metapneumovirus infection among pediatric patients and their correlation with severe cases: a long-term retrospective study. Front Cell Infect Microbiol 2024;14:1435294.

46. Ji W, Chen Y, Han S, et al. Clinical and epidemiological characteristics of 96 pediatric human metapneumovirus infections in Henan, China after COVID-19 pandemic: a retrospective analysis. Virol J 2024;21:100.

47. Nagasawa M, Udagawa T, Okada M, et al. COVID-19 pandemic-altered epidemiology of respiratory syncytial virus and human metapneumovirus infections in young children. GHM Open 2024;4:47-9.

48. Edwards KM, Zhu Y, Griffin MR, et al. Burden of human metapneumovirus infection in young children. N Engl J Med 2013;368:633-43.

49. PrabhuDas M, Adkins B, Gans H, et al. Challenges in infant immunity: implications for responses to infection and vaccines. Nat Immunol 2011;12:189-94.

50. Gervassi AL, Horton H. Is infant immunity actively suppressed or immature? Virology 2014;2014:1-9.

51. Maródi L. Innate cellular immune responses in newborns. Clin Immunol 2006;118:137-44.

52. Schildgen V, van den Hoogen B, Fouchier R, et al. Human metapneumovirus: lessons learned over the first decade. Clin Microbiol Rev 2011;24:734-54.

53. Haas LEM, Thijsen SFT, van Elden L, et al. Human Metapneumovirus in adults. Viruses 2013;5:87-110.

54. Uddin S, Thomas M. Human metapneumovirus. Treasure Island, FL, USA: StatPearls; 2025.

Online supplementary material:

Supplementary Figure 1. Forest plot of pooled prevalence of human metapneumovirus among children with acute respiratory infections, stratified by study publication year (2007–2019 *vs.* 2020–2024).

Supplementary Figure 2. Forest plot of pooled prevalence of human metapneumovirus among children with acute respiratory infections, stratified by geographic region in India. Supplementary Figure 3. Forest plot of pooled prevalence of human metapneumovirus among children with acute respiratory infections, stratified by clinical presentation. Supplementary Figure 4. Forest plot of pooled prevalence of human metapneumovirus among children with acute respiratory infections, stratified by age groups (more than 5 years *vs.* under 5 years).

Supplementary Figure 5. a) Bubble plot representing the relationship between human metapneumovirus (HMPV) proportion and total sample size of studies; b) bubble plot showing the relationship between HMPV proportion and percentage of females across studies; c) bubble plot depicting the association between HMPV proportion and mean age of participants in years.

Supplementary Table 1. Inclusion and exclusion criteria.

Supplementary Table 2. Search strategy.

Table 1. Characteristics of the all included studies

Author	Year of	Study state	Study population	Total	HMPV	Prevalence
	study			sample size	cases	of HMPV
Banerjee et al. (2007)	2004-2005 Delhi 2005-2007 Delhi		children < 5years of age with ARI in OPD or IPD	97	12	12.4
Bharaj et al. (2009)			Children attending OPD or Addmited in Ward	301	11	3.7
Agrawal et al. (2011)	2006-2009	West Bengal	Patients with all age group attending OPD with ARTI	1863	107	5.7
Banerjee et al. (2011)	2005-2007	Delhi	Children less than 6 years with ARI	662	21	3.2
Narayanan et al. (2013)	2010-2011	Tamil Nadu	Children less than or equal to 5 years with ARI	300	38	12.7
Mukherjee et al. (2013)	2010-2011	West Bengal	Patients with ARI (adults and children)	1741	78	4.5
Mazumdar et al. (2013)	2010-2011	West Bengal			8	0.9
Biswas et al. (2014)	2009-2012			276	20	7.2
Broor et al. (2014)	2009-2011	Haryana	Acute medical conditions	245	3	1.2
Singh et al. (2014)	2011-12	Uttar Pradesh	Children aged upto 14 years presenting with ALRI and hospitalised in paediatric wards		2	1.1
Malhotra et al. (2016)	2012-2013	Rajasthan			35	22.6
Sarkar et al. (2016)	2014-2015	Chandigarh	Patients (children and adults) attending OPD with ILI or hospitalised patients with SARI	142	14	9.9
Nandhini et al. (2016)	2011-2013 Puducherry		Acute lower respiratory tract infection	209	8	3.8
Panda et al. (2016)	2012-2014 Odisha		SARI	332	7	2.1
Swamy et al. (2018)	2012-16	Rajasthan	Children with ARI	997	44	4.4
Biswal et al. (2018)	2014-2016	Odisha	Children with ARI	1063	30	2.8
Jambagi et al. (2018)[19]	2017-2018	Karnataka	Children with clinical manifestations of respiratory infections were included in the study	407	1	0.2
Sonawane et al. (2019)	ne et al. (2019) 2014-2015 Maharasht		Infants admitted with ALRI	100	7	7.0
Anand et al. (2020)			patients with ARTI (all age groups)	50	3	6.0
Palani et al. (2020)			Patients with Symptoms of ARI (292 children)	292	8	2.7
Kumar et al. (2021)	et al. (2021) 2019 De		All respiratory samples of children <5 years from OPD ward and ICU	94	7	7.4
Viswanathan et al. (2022)	2019-2021 Maharashtra		Children below 2 years with prolonged cough>2 weeks attending OPD or admitted	45	6	13.3
Muruganandam et al. (2022)	2019-2021	Andaman and Nicobar Islands	Patients with ARI or ILI (all age groups)	105	11	10.5
Sarkar et al. (2022)	2013-2016	Chandigarh	Children below 18 years of age with ARI	349	23	6.6
Chandy et al. (2022)	2019-2020	Tamil Nadu	Children between > 2 months and < 5years with ALRI	256	13	5.1
Hindupur et al. (2022)	2016-2018	Tamil Nadu	Children with WHO pneumonia criteria, with tachypnoea or wheeze with or without hypoxia <5 years	350	14	4.0
Koul et al. (2022)	2013-2014 Jammu Kashmir		Admitted patients with SARI	412	9	2.2
Kang et al. (2023)	2019-2022 Chandigarh		children aged 0- 5years with URI	355	11	3.1
Agarwal et al. (2023)	2021-2022 Delhi		Children aged 1 month to 12 years with ARTI/ Pneumonia/ ARDS	180	5	2.8
Taduri et al. (2023)	2021-2022	Telangana	children 2 months to 2 years presenting with bronchiolitis and respiratory distress	88	2	2.3

<u> </u>					,					
Authors	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Score
Banerjee et al. (2007)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Bharaj et al. (2009)	Yes	Yes	No	8/9						
Agrawal et al. (2011)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Banerjee et al. (2011)	Yes	Yes	No	8/9						
Mukherjee et al. (2013)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/9
Narayanan et al. (2013)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8/9
Mazumdar et al. (2013)	Yes	Yes	No	8/9						
Biswas et al. (2014)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Broor et al. (2014)	Yes	Yes	Yes	9/9						
Singh et al. (2014)	Yes	No	Yes	No	Yes	Yes	Yes	No	Yes	6/9
Panda et al. (2016)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Nandhini et al. (2016)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Sarkar et al. (2016)	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	7/9
Malhotra et al. (2016)	Yes	Yes	Yes	9/9						
Jambagi et al. (2018)	Yes	No	Yes	No	No	No	Yes	Yes	No	4/9
Biswal et al. (2018)	Yes	Yes	No	8/9						
Swamy et al. (2018)	Yes	N	No	No	Yes	Yes	Yes	No	Yes	5/9
Sonawane et al. (2019)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	7/9
Anand et al. (2020)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Palani et al. (2020)	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	7/9
Kumar et al. (2021)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Viswanathan et al. (2022)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Muruganandam et al. (2022)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Hindupur et al. (2022)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Sarkar et al. (2022)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Chandy et al. (2022)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Koul et al. (2022)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	7/9
Agarwal et al. (2023)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Kang et al. (2023)	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	7/9
Taduri et al. (2023)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8/9
		11					1 1 1		00.11/	

Table 2. Quality assessment of the included studies using the JBI critical appraisal tool for prevalence studies.

Q1: Was the sample frame appropriate to address the target population?; Q2: Were study participants sampled in an appropriate way?; Q3: Was the sample size adequate?; Q4: Were the study subjects and the setting described in detail?; Q5: Was the data analysis conducted with sufficient coverage of the identified sample?; Q6: Were valid methods used for the identification of the condition?; Q7: Was the condition measured in a standard, reliable way for all participants?; Q8: Was there appropriate statistical analysis?; Q9: Was the response rate adequate, and if not, was the low response rate managed appropriately?



Figure 1. PRISMA flow chart



Figure 2. Prevalence of HMPV in various studies conducted in india. (2004-2022)

Author (Year of publication)	Number of patients suffering from hMPV	Total patients	3	Proportion with 95% Cl	Weight (%)
Banerjee et al. (2007)	12	97		0.12 [0.06, 0.19]	2.05
Bharaj et al. (2009)	11	301	-	0.04 [0.02, 0.06]	3.71
Agrawal et al. (2011)	107	1,863		0.06 [0.05, 0.07]	3.99
Banerjee et al. (2011)	21	662		0.03 [0.02, 0.05]	3.93
Mukherjee et al. (2013)	78	1,741		0.04 [0.04, 0.05]	4.01
Narayanan et al. (2013)	38	300		0.13 [0.09, 0.16]	3.08
Mazumdar et al. (2013)	8	880		0.01 [0.00, 0.02]	4.06
Biswas et al. (2014)	20	276		0.07 [0.04, 0.10]	3.36
Broor et al. (2014)	3	245		0.01 [0.00, 0.03]	3.92
Singh et al. (2014)	2	188		0.01 [0.00, 0.03]	3.90
Panda et al. (2016)	7	332	-	0.02 [0.01, 0.04]	3.88
Nandhini et al. (2016)	8	209		0.04 [0.01, 0.06]	3.54
Sarkar et al. (2016)	14	142		0.10 [0.05, 0.15]	2.63
Malhotra et al. (2016)	35	155		0.23 [0.16, 0.29]	2.04
Jambagi et al. (2018)	1	407		0.00 [0.00, 0.01]	4.08
Biswal et al. (2018)	30	1,063		0.03 [0.02, 0.04]	4.01
Swamy et al. (2018)	44	997		0.04 [0.03, 0.06]	3.95
Sonawane et al. (2019)	7	100		0.07 [0.02, 0.12]	2.59
Anand et al. (2020)	3	50		0.06 [0.00, 0.13]	2.04
Palani et al. (2020)	8	292	-	0.03 [0.01, 0.05]	3.79
Kumar et al. (2021)	7	94		0.07 [0.02, 0.13]	2.47
Viswanathan et al. (2022)	6	45		0.13 [0.03, 0.23]	1.24
Muruganandam et al. (2022)	11	105		0.10 [0.05, 0.16]	2.28
Hindupur et al. (2022)	14	350	-	0.04 [0.02, 0.06]	3.73
Sarkar et al. (2022)	23	349		0.07 [0.04, 0.09]	3.54
Chandy et al. (2022)	13	256		0.05 [0.02, 0.08]	3.51
Koul et al. (2022)	9	412	-	0.02 [0.01, 0.04]	3.92
Agarwal et al. (2023)	5	180		0.03 [0.00, 0.05]	3.61
Kang et al. (2023)	11	355	-	0.03 [0.01, 0.05]	3.81
Taduri et al. (2023)	2	88	-	0.02 [0.00, 0.05]	3.34
Overall			•	0.05 [0.04, 0.06]	
Heterogeneity: $\tau^2 = 0.00$, $I^2 = 95$	5.09%, H ² = 20.36				
Test of $\theta_i = \theta_j$: Q(29) = 302.95,	p = 0.00				
Test of $\theta = 0$: $z = 7.17$, $p = 0.00$)				
			0.1.2	.3	

Figure 3. Forest plot showing the pooled prevalence of HMPV among children with acute respiratory illness in India.



Figure 4. Funnel plot assessing publication bias for studies reporting the prevalence of HMPV among children with acute respiratory illness



Figure 5. a) Baujat plot indicating the influence of individual studies on overall results and contribution to heterogeneity; b) leave-one-out sensitivity analysis of studies included in the meta-analysis; c) influence analysis for individual studies across multiple metrics.