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

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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 from 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.

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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]. Specifically, 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 5 years of age [2]. In India, ALRTIs contribute to approximately 14.3% of infant deaths and 15.9% of deaths in children under 5 [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 dyspnea, 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 5, HMPV poses a significant yet underexplored public health challenge. Although most children are infected with HMPV by the age of 5, 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 ARIs (SARI) (defined as ILI cases requiring hospitalization), ALRTI, and non-specific ARI cases with upper respiratory tract infection 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 analyzing the prevalence and characteristics of ARI among children in India. Non-observational studies, such as interventional trials, qualitative research, and 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 to January 3, 2025. A thorough search was performed using keywords and Medical Subject Headings (MeSH) related to HMPV, including terms such as HMPV, metapneumovirus, ARI, 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 disagreements 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 random-effects model to account for between-study variability. Heterogeneity was assessed using Cochran's Q statistic and the I^2 statistic. Subgroup analyses were performed to explore sources of heterogeneity based on temporal, regional, clinical, and age-based categories used to assess the 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 Critical Appraisal tools specifically tailored for prevalence studies [14]. Studies that scored 1 to 3 were categorized 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, inpatient departments, or specialized pediatric units. The sample sizes varied widely, ranging from 45 participants in the study by Viswanathan *et al.* to 1863 participants in the study by Agarwal *et al*. [16,17]. All included studies employed reverse transcription polymerase chain reaction (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, with three studies being of moderate quality. We did not find any study of poor quality in this meta-analysis (Table 2).

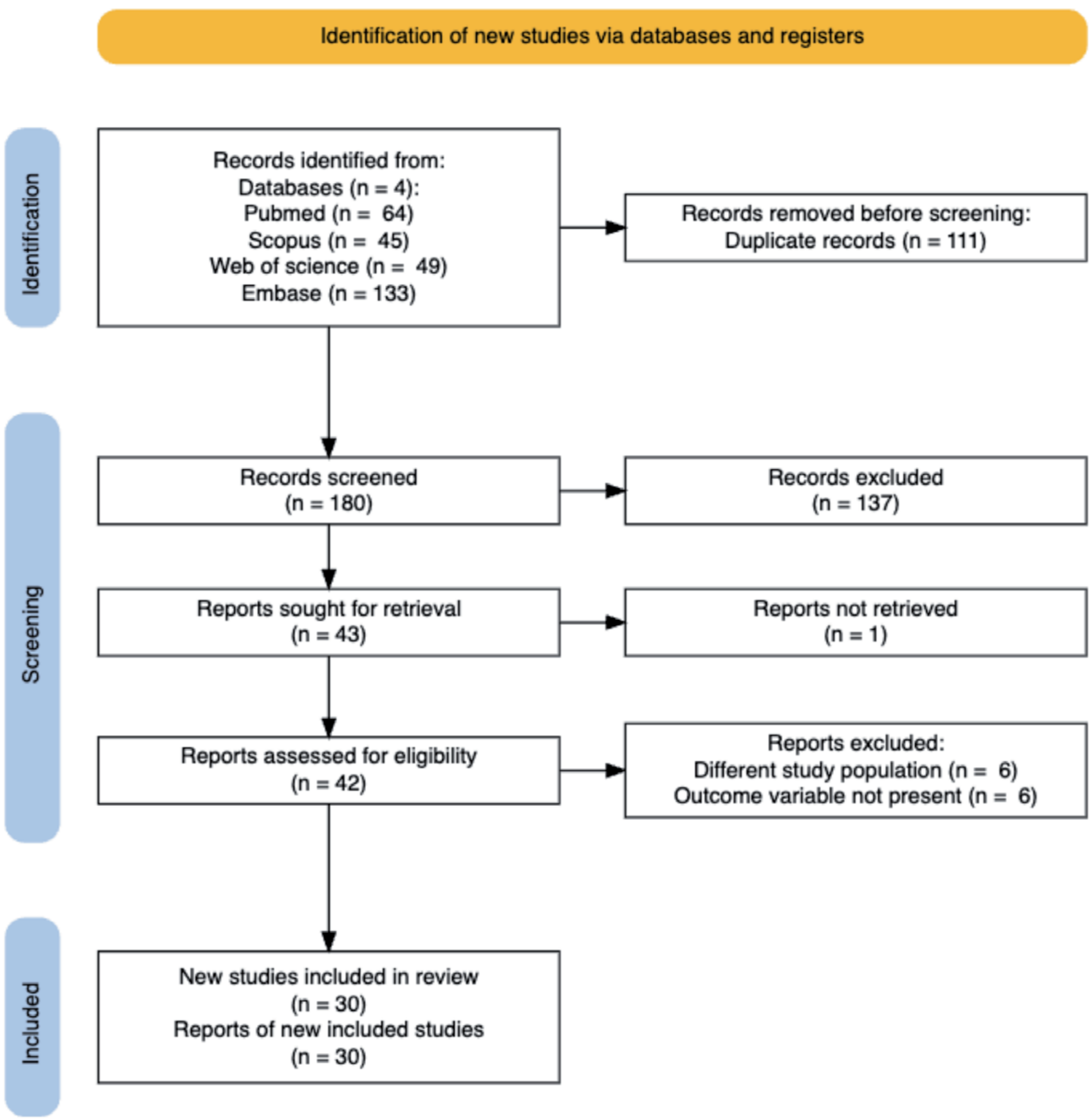

Figure 1. PRISMA flow chart.

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Pooled prevalence of human metapneumovirus

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 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 I^2 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 and 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

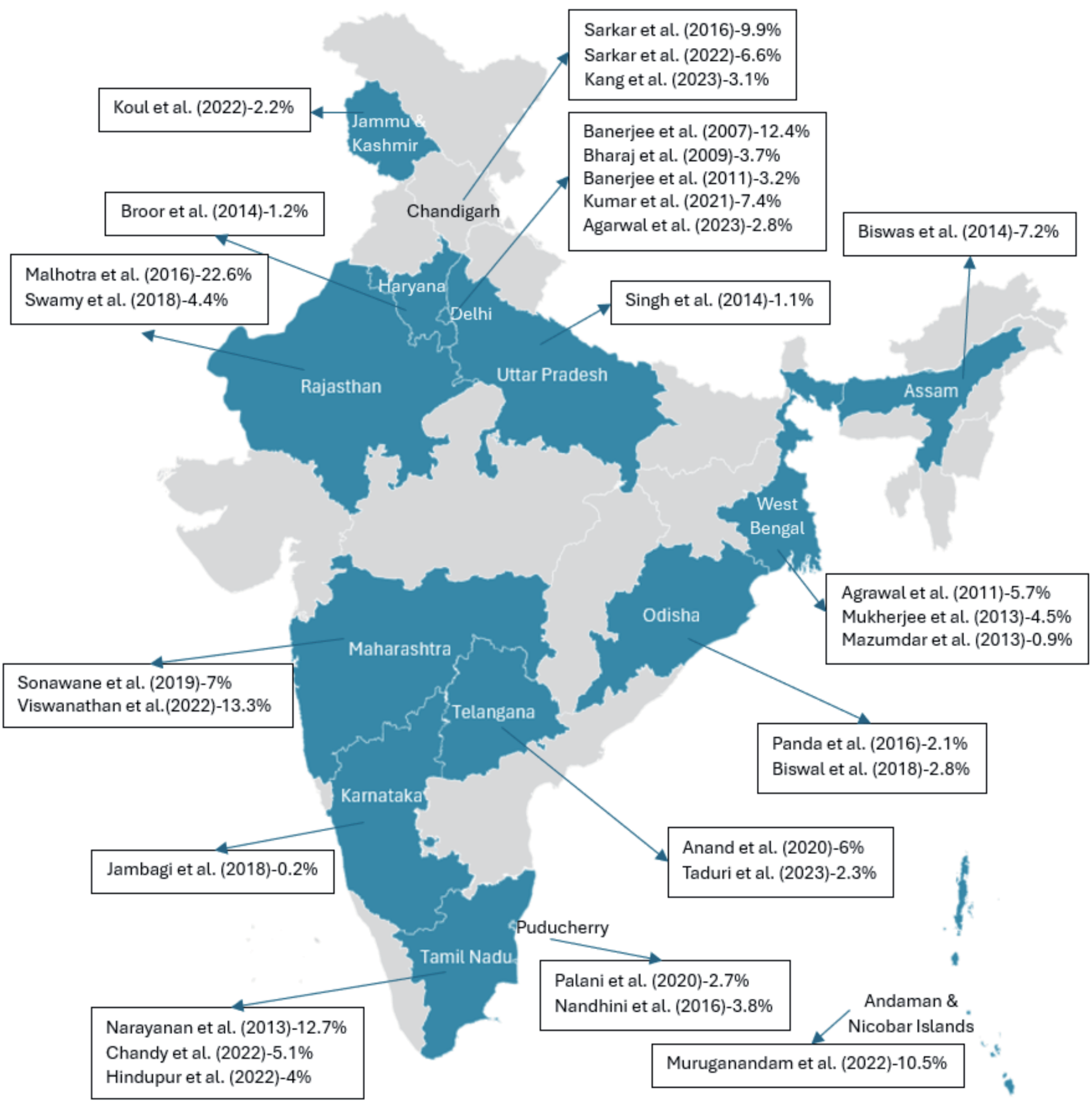

Figure 2. Prevalence of human metapneumovirus in various studies conducted in India (2004-2022).

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%, I^2=82.21%), ILI (4.0%; 95% CI: 1.0-7.0%, I^2=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 (I^2=17.02%, τ^2=0.00, H^2=1.21), suggesting consistency in findings across studies for this age group. A total of 16 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%, τ^2=0.00, H^2=18.36). There was a significant difference between these two age groups (*Supplementary Figure 4*).

Table 1. Characteristics of all included studies.

Author	Year of study	Study state	Study population	Total sample size	HMPV cases	Prevalence of HMPV
Banerjee *et al.* (2007)	2004-2005	Delhi	Children <5years of age with ARI in OPD or IPD	97	12	12.4
Bharaj *et al.* (2009)	2005-2007	Delhi	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	Children below 12 years with ILI	880	8	0.9
Biswas *et al.* (2014)	2009-2012	Assam	Children aged less than or equal to 5 years with ARTI	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	188	2	1.1
Malhotra *et al.* (2016)	2012-2013	Rajasthan	All children under 13 years of age with ARTI	155	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)	2017-2018	Karnataka	Children with clinical manifestations of respiratory infections were included in the study	407	1	0.2
Sonawane *et al.* (2019)	2014-2015	Maharashtra	Infants admitted with ALRI	100	7	7.0
Anand *et al.* (2020)	2017-2019	Telangana	Patients with ARTI (all age groups)	50	3	6.0
Palani *et al.* (2020)	2012-15	Pondicherry	Patients with Symptoms of ARI (292 children)	292	8	2.7
Kumar *et al.* (2021)	2019	Delhi	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

ARI, acute respiratory infection; OPD, outpatient departments; IPD, inpatient departments; ARTI, acute respiratory tract infection; ILI, influenza-like illness; SARI, severe acute respiratory infection; ICU, intensive care unit; ALRI, acute lower respiratory tract infection; ARDS, acute respiratory distress syndrome.

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

Table 2. Quality assessment of the included studies using the Joanna Briggs Institute critical appraisal tool for prevalence studies.

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	Yes	Yes	Yes	Yes	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	Yes	Yes	Yes	Yes	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	Yes	Yes	Yes	Yes	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	Yes	Yes	Yes	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	Yes	Yes	Yes	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	Yes	Yes	Yes	Yes	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

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?

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 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 in India. Among children under 5 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%

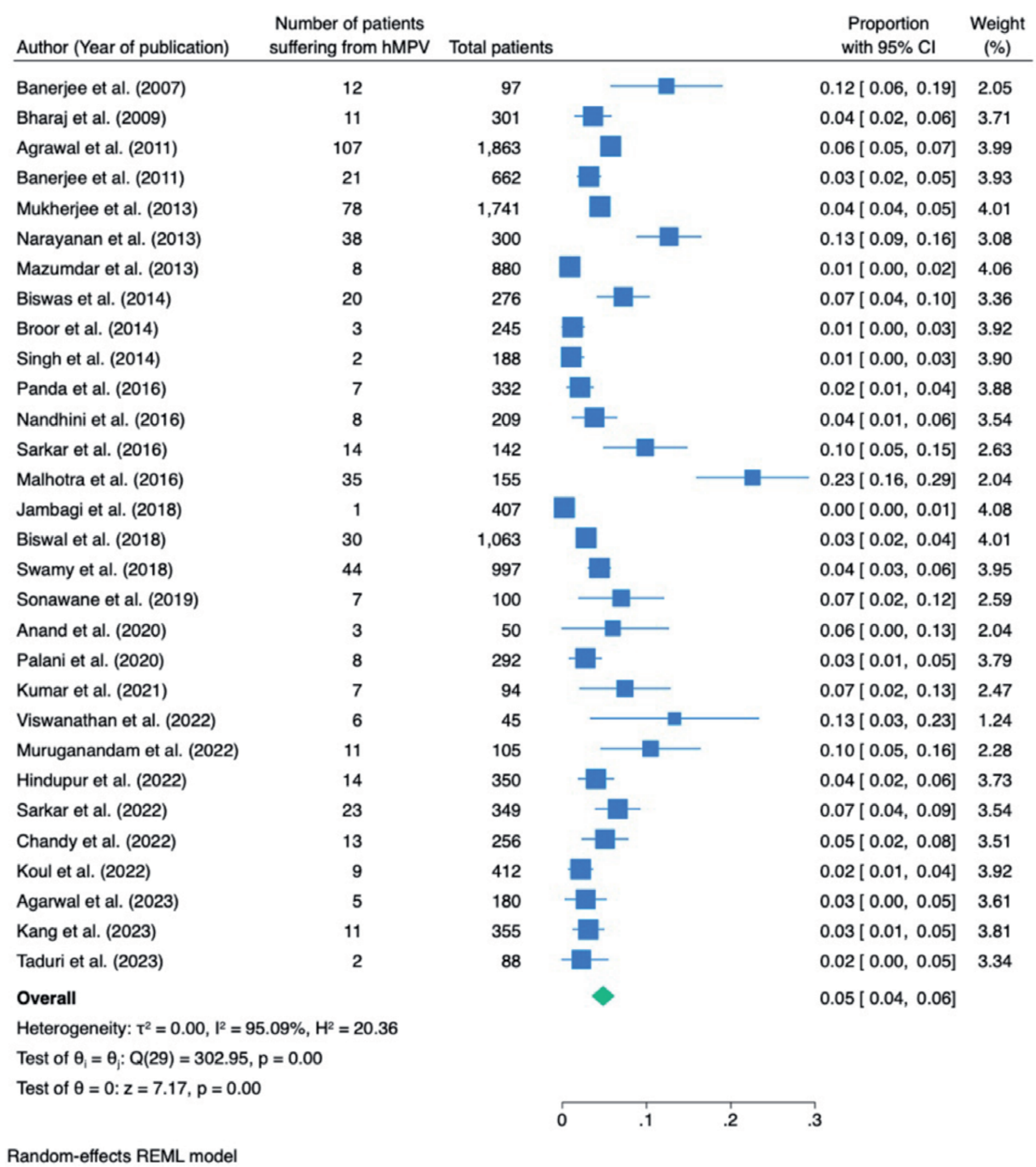

Figure 3. Forest plot showing the pooled prevalence of human metapneumovirus (hMVP) among children with acute respiratory illness in India. CI, confidence interval.

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 meta-analysis 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 5 years of age compared to older age groups. Within this age group, children under 2 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 5 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 respiratory syncytial virus 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 World Health Organization, 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 Program and Indian Council of Medical Research 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 (I^2=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.

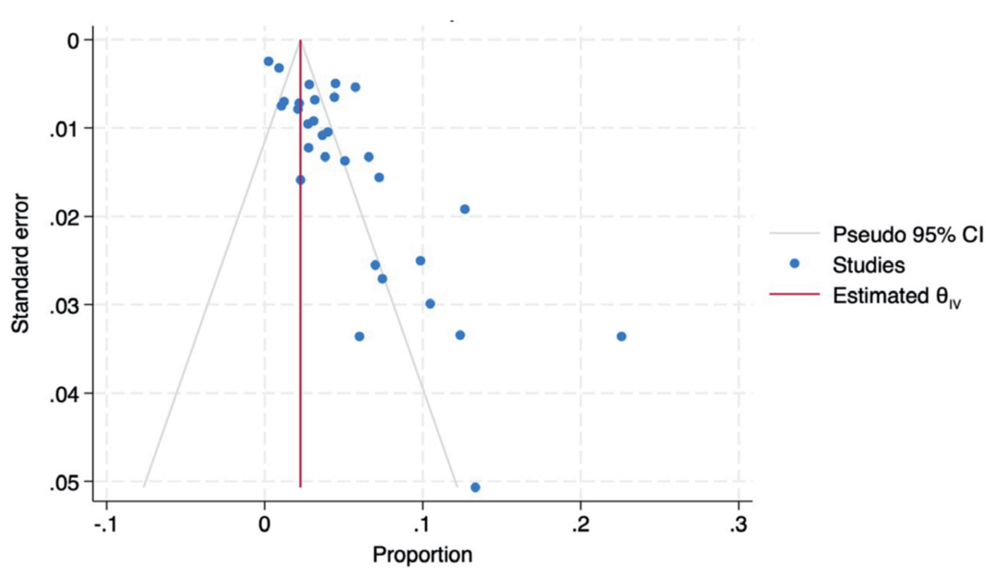

Figure 4. Funnel plot assessing publication bias for studies reporting the prevalence of human metapneumovirus among children with acute respiratory illness. CI, confidence interval.

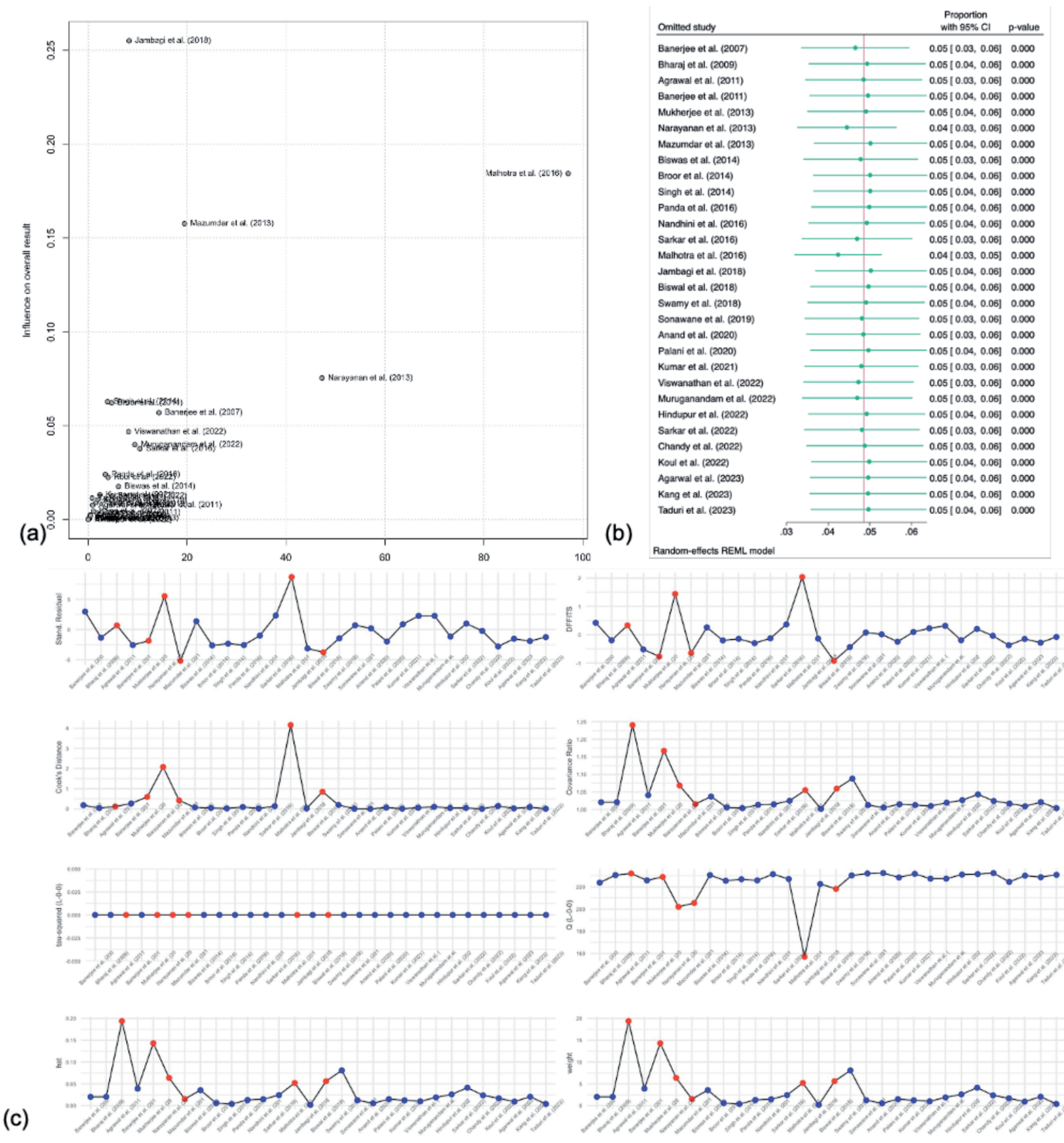

Figure 5. a) Baujat plot indicating the influence of individual studies on overall results and contribution to heterogeneity; b) leave-one-out sensitivity analysis of studies included in the meta-analysis; c) influence analysis for individual studies across multiple metrics. CI, confidence interval.

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 5 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 pediatric populations.

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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.

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Informed consent: not applicable.

Patient consent for publication: not applicable.

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