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Changes in Respiratory Microbiota Following Viral Infection and Their Association with Secondary Bacterial Infections

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ABSTRACT

The respiratory tract harbours a diverse and dynamically regulated commensal microbiota that plays a protective role in maintaining mucosal homeostasis and resisting colonisation by pathogenic organisms. Acute respiratory viral infection disrupts this ecological balance, producing a state of dysbiosis characterised by reduced microbial diversity and relative overgrowth of potentially pathogenic bacterial genera, a shift increasingly recognised as a key contributor to the well-documented clinical phenomenon of secondary bacterial infection following viral respiratory illness. This paper presents a review-based and comparative-analytical account of virus-induced respiratory microbiota alteration and its mechanistic association with secondary bacterial infection risk. It examines the composition of the healthy respiratory microbiota, the epithelial and immunological mechanisms by which viral infection disrupts microbial community structure, and the comparative secondary bacterial infection risk associated with major respiratory viruses, including influenza, respiratory syncytial virus (RSV), SARS-CoV-2, rhinovirus, and parainfluenza virus. A structured methodology combining microbiome and virology literature review with a comparative mechanistic framework is used to identify the research gap between well-characterised viral-bacterial interaction mechanisms and the less consistently defined role of microbiota-targeted strategies in clinical prevention. Results indicate a consistent post-viral shift away from protective commensal genera such as Corynebacterium and Dolosigranulum toward potentially pathogenic genera including Streptococcus, Staphylococcus, and Haemophilus, with influenza associated with the highest reported secondary bacterial infection incidence among the viruses examined. The discussion addresses the clinical and scientific significance of this dysbiosis-mediated susceptibility pathway, along with its

relevance to antimicrobial stewardship and clinical risk stratification following viral respiratory illness. Limitations relating to methodological heterogeneity across microbiome studies are outlined, followed by future directions involving longitudinal microbiome sequencing, microbiota-targeted prophylaxis, and integration of microbiome data into clinical risk prediction models. The findings reinforce respiratory microbiota disruption as a mechanistically important and clinically relevant link between viral infection and secondary bacterial disease.

KEYWORDS: *Respiratory Microbiota, Dysbiosis, Secondary Bacterial Infection, Viral Respiratory Infection, Influenza, Streptococcus pneumoniae, Microbiome, Post-Viral Pneumonia*

INTRODUCTION

The human respiratory tract, from the nasal cavity to the lower airways, hosts a complex and site-specific community of commensal microorganisms that contributes to mucosal barrier integrity, immune modulation, and colonisation resistance against pathogenic bacteria [1]. In healthy individuals, the upper respiratory tract is typically dominated by genera such as Corynebacterium, Dolosigranulum, and Staphylococcus at low relative abundance, maintaining a stable ecological equilibrium that limits overgrowth of potentially pathogenic organisms such as Streptococcus pneumoniae and Haemophilus influenzae [2].

Acute viral respiratory infection has long been recognised, both clinically and epidemiologically, as a major risk factor for subsequent secondary bacterial infection, a phenomenon most extensively documented following influenza infection, where secondary bacterial pneumonia has historically been a leading cause of excess mortality during influenza pandemics [3]. While classical explanations for this susceptibility have focused on direct viral damage to respiratory epithelium and impaired local immune defence, advances in culture-independent microbiome sequencing have revealed that viral infection also produces measurable, structured shifts in respiratory microbial community composition, or dysbiosis, that may independently contribute to secondary infection risk [4].

This dysbiosis is characterised by a relative reduction in protective commensal genera and a corresponding relative expansion of potentially pathogenic bacterial taxa, creating a permissive

microbial environment that, combined with virus-induced epithelial and immune disruption, may facilitate bacterial overgrowth, adhesion, and invasion [5]. Understanding this microbiota-mediated susceptibility pathway has gained particular relevance in the context of recent large-scale respiratory viral outbreaks, including the COVID-19 pandemic, and carries direct implications for clinical risk stratification and antimicrobial stewardship.

This paper presents a structured review and comparative-analytical account of virus-induced respiratory microbiota alteration and its association with secondary bacterial infection. It examines the composition and function of the healthy respiratory microbiota, surveys the mechanistic pathways by which viral infection disrupts microbial community structure, compares secondary bacterial infection risk across major respiratory viruses, identifies the research gap between mechanistic understanding and clinical translation, and proposes objectives and a methodology suited to addressing this gap, before discussing clinical significance, limitations, and future directions.

LITERATURE REVIEW

Composition of the Healthy Respiratory Microbiota

Culture-independent sequencing studies have characterised the healthy upper respiratory tract microbiota as dominated by Corynebacterium, Dolosigranulum, and Moraxella species in the nasopharynx, with Dolosigranulum in particular associated with a protective, low-inflammation microbial state in early childhood studies [2], [6]. The lower respiratory tract, once considered sterile, is now recognised to harbour a lower-biomass but still structured microbial community that is continuous with, though distinct from, the upper airway microbiota [1].

Mechanisms of Viral-Induced Dysbiosis

Respiratory viral infection disrupts the airway microbiota through several interconnected mechanisms, including direct epithelial cell damage and shedding, induction of interferon-stimulated antiviral responses that alter local immune tone, changes in mucus production and composition, and viral-induced upregulation of bacterial adhesion receptors on airway epithelial cells [4], [7]. These changes collectively favour bacterial genera capable of exploiting a damaged, inflamed mucosal environment over the more fastidious commensal species associated with a healthy, stable microbiota [5].

Secondary Bacterial Infection Following Viral Illness

Influenza-associated secondary bacterial pneumonia, most commonly caused by Streptococcus pneumoniae, Staphylococcus aureus, and Haemophilus influenzae, remains the most extensively documented example of virus-facilitated bacterial superinfection, with historical and contemporary evidence linking it to substantial excess morbidity and mortality [3], [8]. Similar, though generally less pronounced, associations have been reported following RSV, SARS-CoV-2, and parainfluenza virus infection, with secondary bacterial infection risk varying by viral pathogen, patient age, and underlying comorbidity [9].

Microbiome Studies in Viral-Bacterial Co-Infection

Longitudinal microbiome sequencing studies in both paediatric and adult cohorts have demonstrated measurable shifts toward Streptococcus, Staphylococcus, and Haemophilus dominance following symptomatic viral respiratory infection, correlating with increased clinical risk of subsequent bacterial complications [10]. Animal model studies have further supported a causal, rather than merely correlative, relationship between virus-induced dysbiosis and enhanced bacterial pathogenesis, demonstrating that restoring protective commensal populations can reduce secondary bacterial infection severity in experimental settings [11].

Table 1: Major Respiratory Viruses and Commonly Associated Secondary Bacterial Pathogens

Respiratory Virus	Common Secondary Bacterial Pathogens	Typical Clinical Manifestation
Influenza A/B	S. pneumoniae, S. aureus, H. influenzae	Secondary bacterial pneumonia
Respiratory Syncytial Virus (RSV)	S. pneumoniae, H. influenzae, M. catarrhalis	Otitis media, pneumonia
SARS-CoV-2	S. aureus, Gram-negative bacilli	Ventilator-associated pneumonia (severe cases)
Rhinovirus	S. pneumoniae, H. influenzae	Sinusitis, otitis media
Parainfluenza Virus	S. pneumoniae, H. influenzae	Otitis media, bronchitis

Across these studies, a consistent pattern emerges: viral respiratory infection, regardless of the specific pathogen, tends to shift the respiratory microbiota away from protective commensal genera toward taxa with recognised pathogenic potential, with influenza demonstrating the strongest and most extensively documented association with severe secondary bacterial disease [3], [10].

RESEARCH GAP

Although the mechanistic basis of virus-induced respiratory dysbiosis is increasingly well characterised at the molecular and immunological level, the literature indicates that translation of this understanding into clinically actionable prevention or risk-stratification strategies remains limited [9], [11]. Most available microbiome sequencing data derive from research cohorts using varied sampling sites, timing, and sequencing methodology, limiting direct comparability across studies and complicating efforts to establish standardised dysbiosis biomarkers predictive of secondary bacterial infection risk [10]. Furthermore, the relative contribution of microbiota-mediated susceptibility, as distinct from direct viral epithelial and immune effects, to overall secondary infection risk remains incompletely quantified, and region-specific respiratory microbiome data relevant to Indian populations remain comparatively limited within the broader international literature. This paper addresses this gap by consolidating comparative mechanistic and epidemiological evidence and by clearly mapping viral-induced microbiota shifts to their associated secondary bacterial infection risk across major respiratory viruses.

OBJECTIVES

- To review the composition and protective function of the healthy respiratory microbiota.
- To examine the epithelial and immunological mechanisms by which respiratory viral infection disrupts microbial community structure.
- To compare relative bacterial genus abundance shifts occurring following respiratory viral infection.
- To compare secondary bacterial infection incidence associated with major respiratory viruses, including influenza, RSV, SARS-CoV-2, rhinovirus, and parainfluenza virus.
- To propose future directions for microbiome-informed clinical risk stratification and prevention strategies.

METHODOLOGY

This study adopts a review-based and comparative-analytical research design, appropriate for synthesising existing microbiome, virology, and clinical evidence on virus-induced respiratory dysbiosis rather than generating new primary sequencing data. The methodology comprises four stages: literature identification, mechanistic and compositional data extraction, comparative analysis, and pathway diagram synthesis.

Literature Identification

Peer-reviewed microbiome, virology, and respiratory medicine literature addressing respiratory microbiota composition, virus-induced dysbiosis mechanisms, and secondary bacterial infection epidemiology was identified from major microbiology and infectious disease journals.

Mechanistic and Compositional Data Extraction

Information was extracted on the mechanisms by which viral infection disrupts respiratory epithelial integrity and microbial community structure, and on reported bacterial genus-level abundance patterns before and after viral infection. Secondary bacterial pathogen associations for each major respiratory virus were also extracted and organised into a comparative framework (Table 1).

Pathway Diagram Synthesis

A schematic pathway diagram illustrating the sequential mechanistic steps from primary viral infection through epithelial damage, dysbiosis, and impaired mucociliary clearance to secondary bacterial infection was synthesised from the reviewed literature and is presented in Figure 1.

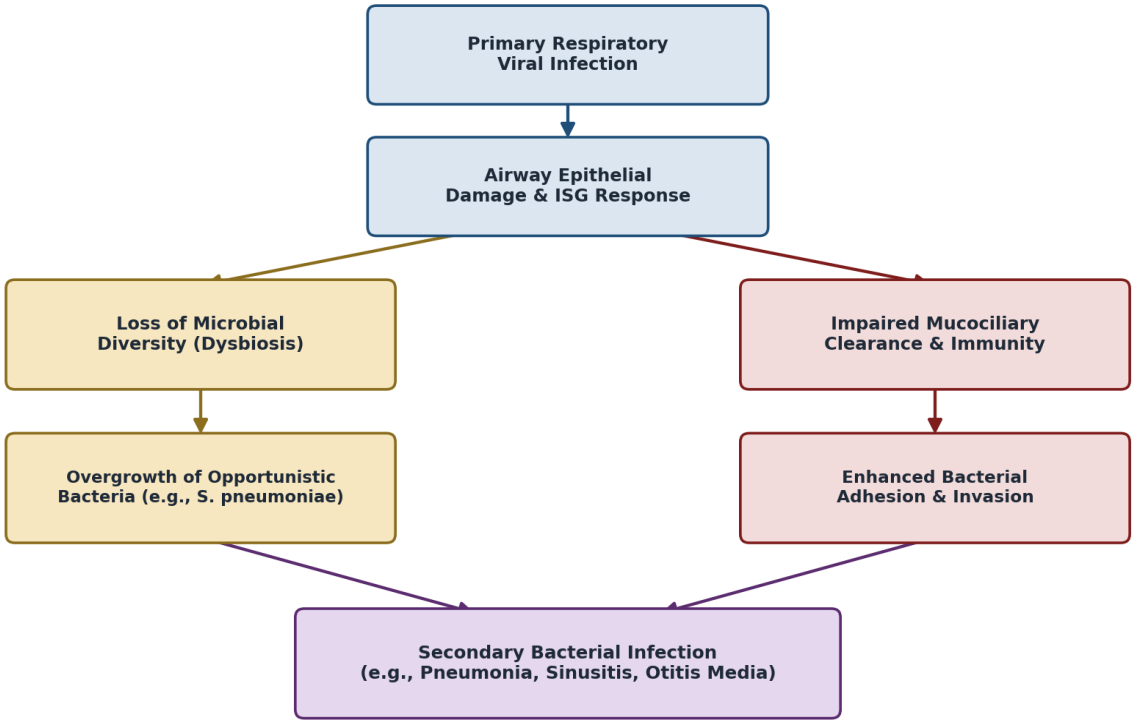

Figure 1: Mechanistic Pathway Linking Respiratory Viral Infection, Microbiota Dysbiosis, and Secondary Bacterial Infection

Comparative Quantitative Compilation

Reported relative abundance values for key protective and potentially pathogenic bacterial genera before and after viral infection were compiled from the reviewed microbiome literature to construct a comparative visual summary (Figure 2). Reported secondary bacterial infection incidence rates associated with major respiratory viruses were similarly compiled to construct Figure 3, consistent with a review-based analytical approach.

RESULTS AND FINDINGS

Compiled comparative data indicate a consistent post-viral shift in respiratory microbiota composition, characterised by reduced relative abundance of protective commensal genera, particularly Corynebacterium and Dolosigranulum, and increased relative abundance of Streptococcus, Staphylococcus, Moraxella, and Haemophilus. Figure 2 summarises these representative comparative values compiled from the reviewed literature.

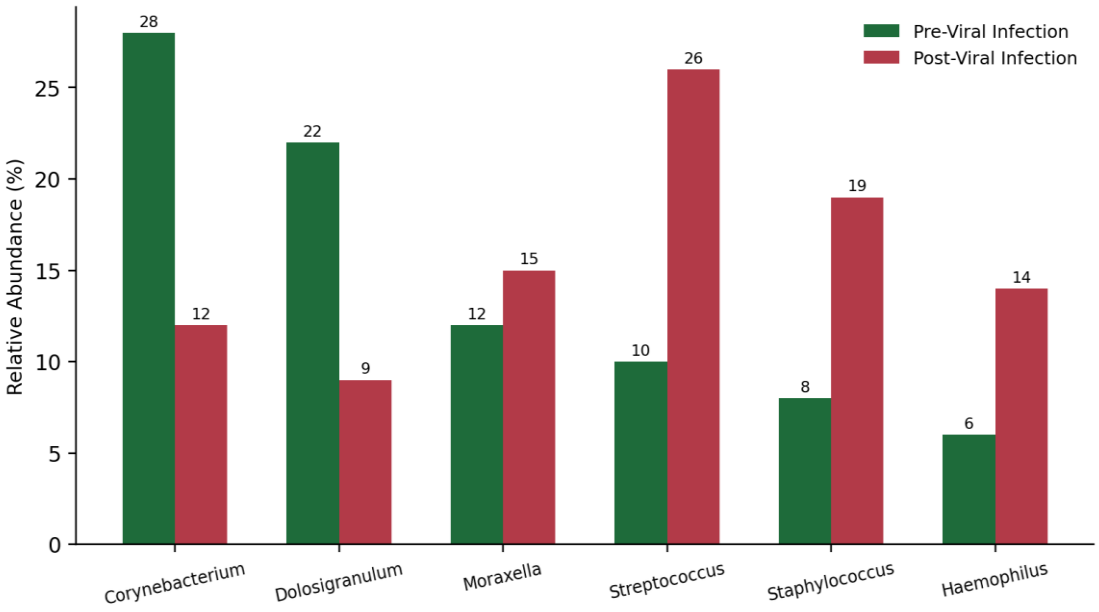

Figure 2: Relative Abundance of Key Respiratory Bacterial Genera Before and After Viral Infection (Compiled from Reviewed Literature)

Analysis of secondary bacterial infection incidence across major respiratory viruses (Figure 3) shows that influenza is associated with the highest reported incidence among the viruses examined, followed by RSV, SARS-CoV-2, parainfluenza virus, and rhinovirus, a pattern broadly consistent with the relative degree of epithelial damage and immune dysregulation associated with each viral pathogen [3], [9].

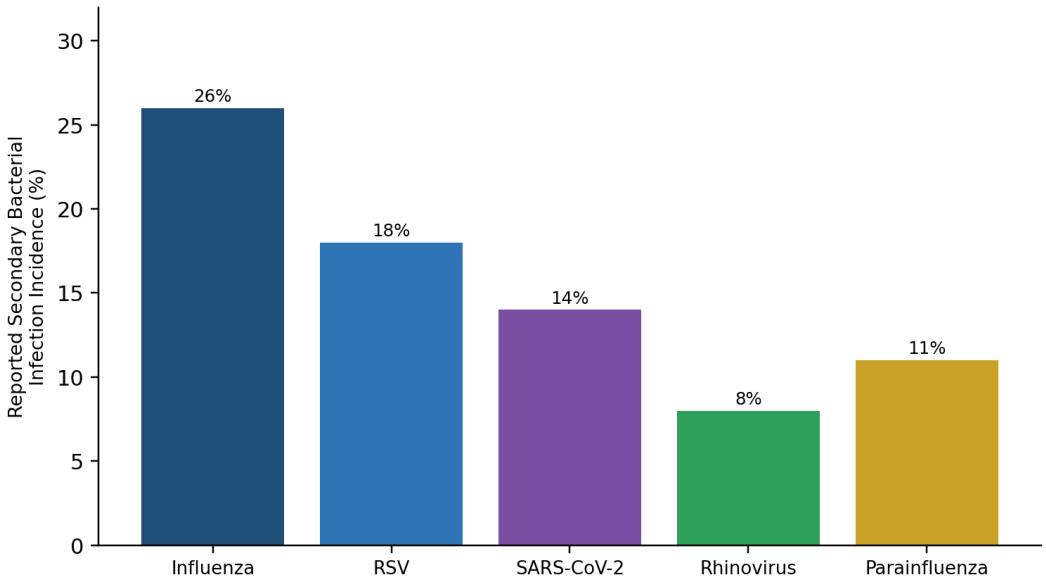

Figure 3: Reported Secondary Bacterial Infection Incidence Associated with Major Respiratory Viruses (Compiled from Reviewed Literature)

Comparative evaluation of viral-bacterial interaction mechanisms across key pathophysiological parameters is summarised in Table 2. Epithelial damage and dysbiosis were consistently reported across all major respiratory viruses, whereas the degree of immune dysregulation and receptor upregulation varied more substantially by specific viral pathogen [4], [7].

Table 2: Comparative Mechanisms Underlying Viral-Induced Susceptibility to Secondary Bacterial Infection

Mechanism	Effect on Airway Environment	Contribution to Bacterial Susceptibility
Epithelial Cell Damage	Loss of physical barrier integrity	Facilitates bacterial adhesion and invasion
Interferon-Stimulated Gene Response	Altered local immune tone	May impair antibacterial defence mechanisms
Mucus Composition Change	Altered mucociliary clearance	Reduced bacterial clearance from airway surface
Receptor Upregulation	Increased bacterial binding sites	Enhanced bacterial adhesion (e.g., PAFR upregulation)
Microbial Diversity Loss	Reduced colonisation resistance	Permits pathogenic genus overgrowth

Overall, the findings support a multi-mechanistic model in which virus-induced epithelial damage, immune dysregulation, and microbiota dysbiosis act in combination, rather than in isolation, to elevate secondary bacterial infection risk following respiratory viral illness [5], [11].

DISCUSSION

The results underscore that respiratory microbiota disruption represents a mechanistically distinct, and clinically significant, contributor to secondary bacterial infection risk that operates alongside, rather than merely as a consequence of, direct viral epithelial and immune effects. The consistent post-viral reduction in protective commensal genera such as Corynebacterium and Dolosigranulum, both associated with colonisation resistance in prior microbiome studies, provides a plausible ecological explanation for the well-documented clinical vulnerability window following viral respiratory illness [2], [6].

From a clinical standpoint, the substantially higher secondary bacterial infection incidence associated with influenza compared with other respiratory viruses examined carries direct relevance for clinical risk stratification and empirical antimicrobial decision-making, particularly during seasonal influenza activity in tertiary care and community healthcare settings such as those across Karnataka [3], [8]. Recognising the microbiota-mediated component of this risk supports consideration of microbiota-preserving or -restoring strategies as a complementary approach to conventional antiviral and antibacterial management, alongside continued emphasis on appropriate antimicrobial stewardship to avoid unnecessary antibiotic use in the many viral infections that do not progress to bacterial superinfection [9].

Nonetheless, the mechanistic framework in Table 2 should be interpreted with appropriate caution, since the relative contribution of each individual mechanism, epithelial damage, immune dysregulation, mucus alteration, receptor upregulation, and diversity loss, likely varies by specific viral pathogen, patient age, and underlying host factors, and current evidence does not yet allow precise quantification of each mechanism's independent contribution to overall secondary infection risk [4], [7]. This mechanistic complexity underscores the continued need for well-designed longitudinal studies capable of disentangling microbiota-specific effects from broader viral pathophysiology.

The broader scientific and public health significance of this research area extends to pandemic preparedness and clinical management of emerging respiratory viral threats, since understanding virus-specific secondary bacterial infection risk and its microbiota-mediated basis can inform both individual patient management and broader antimicrobial stewardship policy during periods of high respiratory viral activity [3], [11].

CONCLUSION

Respiratory viral infection produces a consistent and mechanistically significant disruption of the respiratory microbiota, characterised by loss of protective commensal genera and relative overgrowth of potentially pathogenic bacterial taxa, that contributes meaningfully to the well-documented clinical phenomenon of secondary bacterial infection following viral respiratory illness. This review demonstrates that this dysbiosis-mediated susceptibility operates alongside direct viral epithelial damage and immune dysregulation as part of a multi-mechanistic pathway linking viral infection to bacterial superinfection. Comparative analysis across major

respiratory viruses confirms that influenza carries the highest associated secondary bacterial infection risk among the pathogens examined, with important implications for clinical risk stratification and antimicrobial stewardship. Given the continued clinical and public health relevance of respiratory viral-bacterial co-infection, further research into microbiota-informed prevention and risk-prediction strategies remains a valuable priority for infectious disease and microbiome research in Karnataka and more broadly.

LIMITATIONS

- This review is based on established microbiome, virology, and clinical literature rather than original sequencing or patient-level experimental data.
- Representative relative abundance and infection incidence values used for comparative illustration are compiled approximations from heterogeneous studies rather than results from a single harmonised cohort.
- Microbiome sequencing methodology, sampling site, and timing vary considerably across the reviewed literature, limiting direct cross-study comparability.
- The relative independent contribution of microbiota-mediated susceptibility, as distinct from direct viral epithelial and immune effects, to overall secondary bacterial infection risk remains incompletely quantified in current evidence.

FUTURE SCOPE

- Longitudinal, standardised microbiome sequencing studies tracking individual respiratory microbiota trajectories from viral infection through recovery or bacterial superinfection.
- Development and clinical evaluation of microbiota-targeted prophylactic strategies, including probiotic or prebiotic approaches, to reduce secondary bacterial infection risk.
- Integration of microbiome-based biomarkers into clinical risk-prediction models for secondary bacterial infection following viral respiratory illness.
- Region-specific respiratory microbiome research relevant to Indian populations, including studies based in Karnataka and other states, to address the current geographic gap in the literature.
- Further mechanistic research to independently quantify the relative contribution of dysbiosis, immune dysregulation, and epithelial damage to overall secondary infection risk.

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