Expanded PCR panel testing for Identification of coinfecting Pathogens in viral respiratory tract infections

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INTRODUCTION

Bacterial and viral coinfected Respiratory Tract Infections (RTI) including community-acquired pneumonia (CAP) is poorly characterized in adults. Patients with CAP often require hospitalization with an increased risk of mortality. RTIs are one of the largest causes of mortality in the world, particularly in the elderly. The clinical manifestations of viral and bacterial illnesses are often similar, and testing may be required to identify and differentiate the cause of infection. However, sputum cultures carry specificities of 70% and sensitivities of 64% overall. This poor performance can lead to over or under treatment. Furthermore, it is not uncommon to have coinfections with multiple pathogens in individuals with RTIs or CAPs which can be associated with complicated diseases. Expanded panels based on multiplex PCR tests can enable rapid identification of pathogens and coinfections within 24 hours. The goal of this study was to identify and evaluate bacterial and viral coinfecting organisms among samples positive for four main viral respiratory pathogens.

METHODS

Nasopharyngeal swabs were collected from 11,309 subjects aged >49 years old presenting with RTI symptoms, between August 2022 and January 2023. All samples were tested on an expanded PCR platform: Respira-ID™ that uses TaqMan® OpenArray® plates containing 36 viral and bacterial targets. PCR was performed using the Applied Biosystems™ QuantStudio™ 12K Flex Real-time PCR system. Results were first sorted based on the identification of four main viral organisms (designated as study viral test targets (SVTT)): SARS-CoV-2, Influenza A/B, human metapneumovirus (hMPV) and respiratory syncytial virus (RSV). Further analyses were performed to identify potential bacterial and viral coinfections among SVTT positive samples.

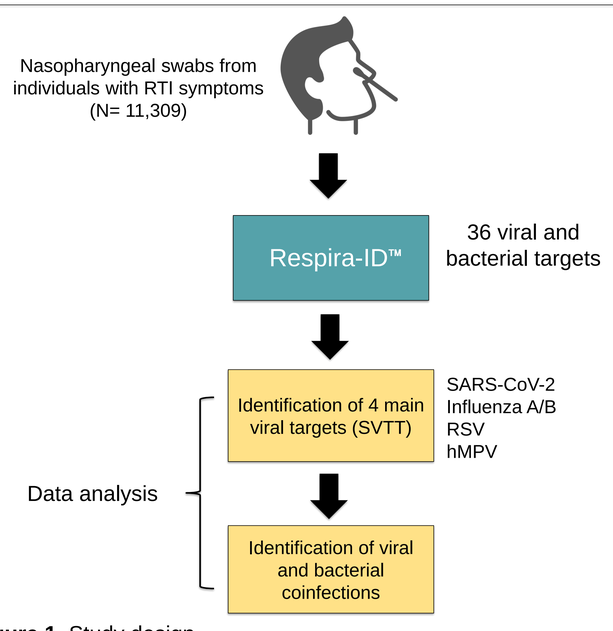

Figure 1. Study design

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RESULTS

The demographics of the study population are presented in Table 1. Of the 11,309 tested samples, 1,852 samples tested positive for at least one SVTT: SARS-CoV-2 (N=585), Influenza A/B (N=603), RSV (N=501), and hMPV (N=197) (Table 1). Among the 1,852 SVTT positive samples, 59% (N=1,090) tested positive for at least one coinfecting organism (Figure 2A). Of all coinfections, bacterial-viral were the most common (80%, N=867) while viral-viral accounted for only 20% (N=223) (Figure 2B).

Table 1: Demographics of the study population

Characteristic		Total	COVID-19	Influenza	hMPV	RSV
Samples N, (%)		11,309	585, (4.4)	603, (4.53)	197, (1.48)	501, (3.76)
Gender N, (%)	Male	3,372, (29.8)	185, (31.6)	206 (34.2)	60, (30.5)	152, (30.3)
	Female	6,777, (50.9)	338, (57.8)	351, (58.2)	124, (62.9)	300, (59.9)
	Undisclosed	1,160, (8.7)	62, (10.6)	46, (7.6)	<20	49, (9.8)
Race N, (%)	Undisclosed / Other	8,507, (63.9)	434, (74.2)	442, (73.3)	157, (79.7)	387, (77.2)
	White	2,802, (21.1)	151, (25.8)	161, (26.7)	40, (20.3)	114, (22.8)
Age Mean in Years (SD)		68.5 (11.7)	69.5 (12.1)	68.2 (12.0)	69.3 (11.7)	70.6 (12.1)

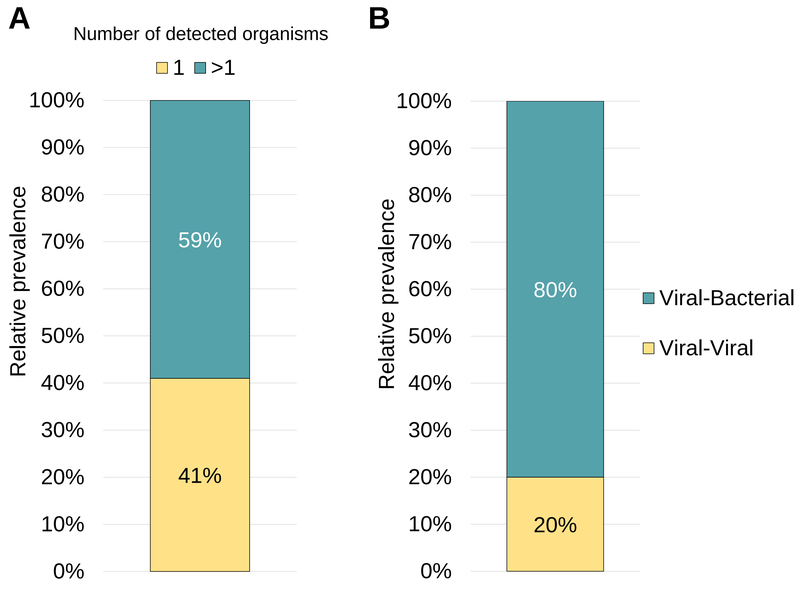

Figure 2: Relative prevalence of A/ mono- or poly- microbial infections; and B/ co-infecting types of pathogens among SVTT positive samples.

RESULTS (Contd.)

Among all coinfecting bacteria, *Staphylococcus aureus* was the most common (51%) followed by *Haemophilus influenzae* (22%), *Streptococcus pneumoniae* (13%) and *Klebsiella pneumoniae* (13%) (Figure 3A). Epstein-Barr virus (EBV) (35%), human Rhinovirus (hRV) (32%) and human herpesvirus 6 (HHV6) (14%) were among the most detected viral coinfections (Figure 3B). Between August 2022 and January 2023, positivity rate curves of SVTT, bacterial and viral infections were very similar in terms of epidemic trends over time (Figure 4).

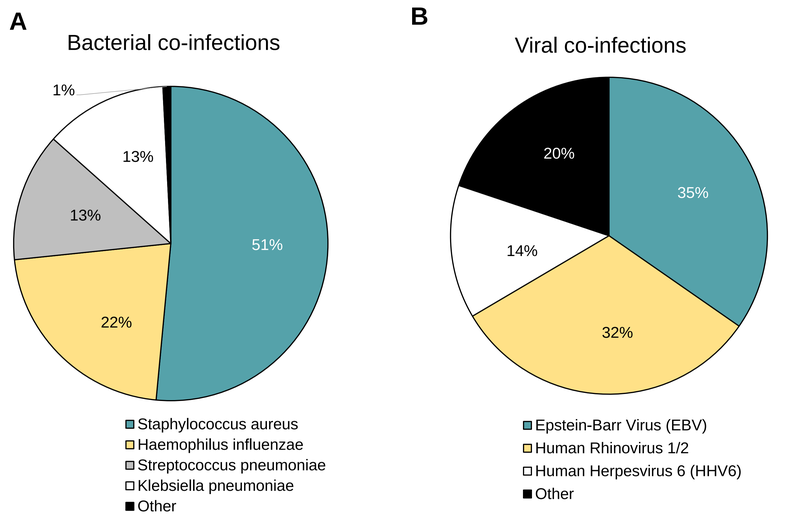

Figure 3: Relative prevalence of the different organisms identified among A/ bacterial and B/ viral co-infections for the SVTT positive samples

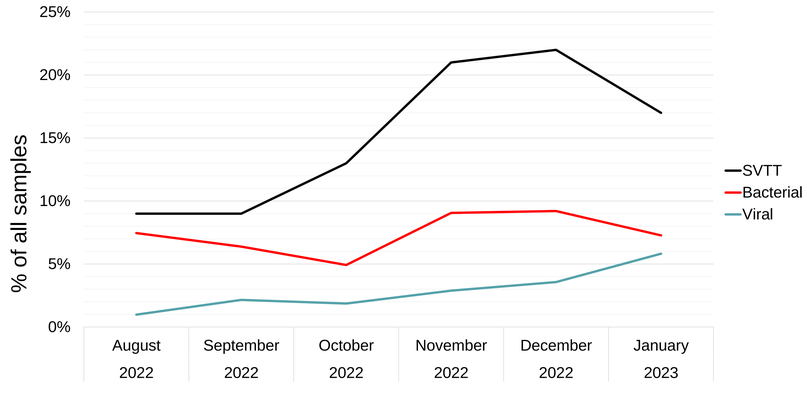

Figure 4: Positivity rates over time among all tested samples for SVTT, bacterial and viral infections.

CONCLUSIONS

We found that coinfections are common in RTIs caused by SARS-CoV-2, Influenza A/B, RSV and hMPV confirming that syndromic panel based multiplex PCR tests enable the identification of pathogens contributing to coinfections