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Characterisation of nasopharyngeal colonisation by *Staphylococcus aureus* and the factors associated with colonisation in comorbid adults in a low- and middle-income country

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ABSTRACT

Introduction *Staphylococcus aureus* is a major cause of pneumonia globally, with a particularly high burden in low- and middle-income countries (LMICs). Nasopharyngeal colonisation (NPC) by *S. aureus* plays a critical role in the pathogenesis of respiratory infections. However, existing research has predominantly focused on paediatric and immunocompromised populations. Data on general adult populations, especially in LMICs, are limited. This study aimed to determine the prevalence of *S. aureus* NPC in adults with chronic comorbidities and identify associated risk factors.

Methods Participants with chronic comorbidities were recruited from community-based settings. Samples were processed using conventional culture techniques to isolate *S. aureus*. Bacterial identification was confirmed by matrix-assisted laser desorption ionisation-time of flight mass spectrometry. To characterise antimicrobial resistance profiles, cefoxitin disc diffusion and D-zone tests were performed in accordance with standardised clinical microbiology protocols. Participants were longitudinally followed and resampled at 6, 12 and 18 months postenrolment to evaluate colonisation dynamics over time.

Results A total of 810 adults were enrolled. Baseline *S. aureus* NPC prevalence was 15.3% (124/810), with 11.2% (14/124) of isolates being methicillin-resistant *S. aureus* (MRSA) and 6.4% (8/124) showing clindamycin resistance. At 6-month follow-up, the cumulative incidence of *S. aureus* colonisation was 14.2%. In multivariable logistic regression, active smoking (OR 1.73, 95% CI 1.06 to 2.85, p=0.02) and rheumatoid arthritis (OR 3.03, 95% CI 1.38 to 6.67, p<0.01) were independently associated with colonisation. Influenza vaccination was associated with reduced risk (OR 0.60, 95% CI 0.38 to 0.94, p=0.02).

Conclusion *S. aureus* NPC, including MRSA, was common among adults with chronic comorbidities. Active smoking and autoimmune diseases, particularly rheumatoid arthritis, were independently associated with increased colonisation risk. These findings have direct implications for community-acquired pneumonia management, supporting consideration of empiric anti-MRSA therapy in high-risk patients. Preventive strategies, including smoking cessation and targeted vaccination, should be prioritised in this population.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ *Staphylococcus aureus* colonisation increases the risk of pneumonia, but data in adults with comorbidities from low- and middle-income countries (LMICs) are scarce.

WHAT DOES THIS STUDY ADD

⇒ In 810 Colombian adults with chronic diseases, the prevalence of colonisation was 15.3% (11.2% methicillin-resistant *Staphylococcus aureus* (MRSA)).

⇒ Colonisation was dynamic over the 18 months, with both new and persistent cases.

⇒ Smoking and rheumatoid arthritis may increase the risk, while influenza vaccination appears to be protective.

HOW MIGHT THIS STUDY AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ Findings support LMIC-specific MRSA risk stratification, smoking cessation, vaccination strategies and informed empiric therapy decisions.

INTRODUCTION

Staphylococcus aureus is a leading cause of community-acquired pneumonia (CAP)[1] and hospital-acquired pneumonia (HAP).[2 3] Methicillin-resistant *S. aureus* (MRSA) is particularly concerning due to its resistance to first-line beta-lactam antibiotics, which limits treatment options and leads to delayed therapy, higher rates of treatment failure and increased mortality. It is also

associated with longer hospital stays and significantly greater healthcare costs compared with non-resistant strains.[4–7] In 2019, over one million deaths from *S. aureus* lower respiratory tract infections were reported globally, with low- and middle-income countries (LMICs) bearing the highest burden. MRSA-CAP prevalence varies widely by patient risk factors and local epidemiology.[8 9] Nasopharyngeal colonisation (NPC) with *S. aureus* is a risk factor for infection,[5 10 11] yet it remains under-recognised in adult populations with chronic comorbidities.

Despite its potential severity, MRSA is not routinely covered in current CAP treatment guidelines.[12] This is largely due to its uncertain and highly variable prevalence, which ranged from 0% to 18.5% globally in 2015, even between countries within the same region.[5] Consequently, treatment decisions rely on local epidemiology and individual risk factors such as prior MRSA infection or colonisation, severe pneumonia requiring intensive care and recurrent skin or soft tissue infections.[5] Although many studies have examined the prevalence of *S. aureus* NPC, including both methicillin-susceptible (MSSA) and MRSA, most have focused on vulnerable subgroups such as individuals with HIV, chronic lung disease, immunosuppression or diabetes.[13–17] In contrast, data on *S. aureus* NPC in the general adult population, particularly those with chronic comorbidities, remain extremely limited and are almost exclusively derived from high-income settings.[18 19] Critically, there is a striking lack of evidence from LMICs, where the burden of *S. aureus*-related pneumonia is highest and where colonisation patterns may differ substantially. This gap hinders the development of effective, risk-based prevention and treatment strategies.

While NPC is recognised as a key risk factor for the development of these infections, the prevalence and dynamics of colonisation remain poorly understood in adults with chronic comorbidities, an increasingly vulnerable population in LMICs. Moreover, the lack of longitudinal data limits our ability to identify individuals at risk of persistent colonisation and to implement effective prevention strategies.[20–22] This study was designed to address this critical gap. The primary objective of this study is to estimate the prevalence of *S. aureus* NPC, including MRSA, in adults with chronic diseases living in LMICs. Additionally, we aim to assess the cumulative incidence of colonisation at 6, 12 and 18 months. Secondary objectives include identifying demographic, clinical and behavioural factors associated with colonisation, particularly concerning modifiable risks such as smoking. We also seek to characterise the temporal patterns of colonisation (whether persistent, intermittent or absent) throughout the follow-up period and to explore potential protective factors, such as influenza vaccination, which may influence colonisation dynamics. By clarifying the epidemiology and determinants of *S. aureus* NPC in this high-risk population, this study aims to inform targeted prevention strategies and guide antimicrobial stewardship efforts in LMIC settings.

METHODS

This multicentre cohort study was conducted in Bogotá and Chía, Colombia, between December 2020 and March 2022. Adult patients with chronic comorbid conditions who provided consent had nasopharyngeal aspirates (NPA) taken and were followed every 6 months for up to 18 months. Patient data were collected using the Research Electronic Data Capture,[23] hosted on a secure server at Universidad de La Sabana. The protocol and informed consent were developed by the Translational Science in Infectious Diseases and Critical Care Medicine (TSID-CCM) research group at the Universidad de La Sabana and reviewed by the Institutional Review Board/Independent Ethics Committee of each participating institution (CUS 01-20, February 2020; Shaio 301, 26 August 2020; IPS-Clínicos 01-02, February 2020 and Baxter 05-01, September 2021); additionally, a grant by Universidad de la Sabana (MED-285—2020) was given to LFR/JL.

Settings and study population

This study was conducted in four reference hospitals in Chia and Bogotá, Colombia. Patients aged 18 and older with chronic diseases (specified in the online supplemental file 1) were prospectively included. Exclusion criteria included a diagnosis of CAP within 90 days prior to enrolment, hospitalisation within the previous 7 days, the presence of respiratory symptoms (eg, cough and fever) or an inability to provide informed consent. These exclusion criteria were applied to avoid transient alterations in colonisation from recent infection, healthcare exposure or active respiratory symptoms and to ensure ethical participation.

Definitions

S. aureus NPC was defined as the presence of *S. aureus* in the NPA sample, identified by yellow beta-haemolytic colonies and confirmed by matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) mass spectrometry. Chronic diseases were grouped to support analysis. Cardiovascular disease included arrhythmia, coronary artery disease, heart failure and hypertension. Immunocompromised status included rheumatoid arthritis (RA), lupus, autoimmune disease, HIV or recurrent leucopenia/neutropenia (<500 cells/dL). Pulmonary diseases included chronic obstructive pulmonary disease and bronchiectasis. Neurological disease included dementia, mental illness or neurological disorders.

Sample collection

Following informed consent, trained staff obtained NPA samples using an 8 mm Nelaton catheter (Medex, INVIMA 2008DM—0001689 R2, Colombia) and 8–10 mL of sterile physiological saline (0.9% sodium chloride; Baxter, Viaflex; mmol/L: sodium ion 154, chloride ion 154; pH 4.5–7). The catheter was gently inserted

10–15 cm into the posterior nasal cavity to collect secretions. Procedures followed WHO guidelines for nasopharyngeal sampling.[24 25]

Microorganism identification and resistance testing

A 100 µL aliquot of NPA was plated on lamb blood agar. Additional aliquots were stored in 2 mL cryovials, refrigerated (2–8°C) and transported within 8 hours to the TSID-CCM laboratory, following expert guidelines.[25] Agar plates were incubated at 37°C±2°C for 24–48 hours. Bacterial growth was assessed semiquantitatively. Colonies with a beta-haemolytic appearance and ≥10 colony-forming units (CFU) per 100 µL were subcultured. Microorganisms exhibiting yellow beta-haemolytic characteristics and exceeding a concentration of 10 CFU/100 µL were subsequently subcultured on lamb's blood agar. Isolates were confirmed as catalase- and coagulase-positive, cryopreserved at −80°C in glycerol broth and identified by MALDI-TOF (score >1.8=confirmed).

The strains identified as *S. aureus* were further assessed using the cefoxitin and disc diffusion tests (D-tests). The cefoxitin test determined oxacillin resistance, while the D-test assessed clindamycin inducible resistance based on the Clinical and Laboratory Standards Institute (CLSI) cut-off points. A D-test following CLSI guidelines was performed on the identified *S. aureus*.[26] A suspension of each strain was prepared at a concentration of 0.5 McFarland; then, they were inoculated with a swab in Mueller-Hinton Agar. The cefoxitin disc (30 µg) was placed for the Fox test. The erythromycin (15 µg) and clindamycin (2 µg) discs were placed at 15 mm and incubated for 24 hours at 37°C for the D-test, then the diameter of the inhibition halos around each disc was measured.

Antimicrobial resistance was defined as inhibition zones <21 mm (cefoxitin), <14 mm (clindamycin) and <13 mm (erythromycin). Flattening of the clindamycin halo indicated inducible resistance.[26]

Statistical analysis

Continuous variables were summarised using minimum and maximum values, mean and SD, or median and IQR based on their distribution. Dichotomous variables were presented as frequencies and percentages. Categorical variables were reported as frequencies and percentages. Between-group comparisons used the χ^2 or Fisher's exact test for categorical data and the t-test or Mann-Whitney U test for continuous data. To evaluate changes in *S. aureus* colonisation over the follow-up period, we used Cochran's Q test to assess variability in colonisation incidence across time points. McNemar's test was applied to compare paired colonisation status between baseline and follow-up visits at 6, 12 and 18 months, including only participants with matched data for each time point. To address potential bias from non-random loss to follow-up, we conducted a sensitivity analysis that restricted the data to participants with complete data at all three follow-up intervals. Baseline characteristics of participants with and without complete follow-up were compared using Student's t-test for continuous variables and the χ^2 test for categorical variables. Additionally, we applied a generalised estimating equation (GEE) model with an exchangeable correlation structure to estimate the probability of *S. aureus* detection over time, adjusting for relevant baseline covariates. This longitudinal approach accounted for intrasubject correlation and minimised potential bias due to differential follow-up.[27]

To identify predictors of colonisation, Random Forest (RF) analysis was applied. A multivariable logistic regression model was then constructed, adjusting for demographic, clinical and vaccination variables identified in univariate analysis ($p<0.20$).[28 29] Model fit was evaluated using the Hosmer-Lemeshow test. ORs with a 95% CI were calculated based on the exponential values of the coefficients obtained from the final model. The area under the curve was used to assess the performance of the logistic regression model. A 10-fold cross-validation method was employed, dividing the dataset into 10 subsets. The validation process was repeated 10 times, with one subset used as the test cohort and the remaining nine subsets as training cohorts. Analyses were performed using SPSS V.29.0.2 and RStudio V.2024.12.1+563.

Patient and public involvement statement

Patients or members of the public were not involved in the design, conduct, reporting or dissemination plans of our research. The study population comprised adults with chronic comorbidities recruited from participating healthcare institutions. All participants provided informed consent before enrolment, and findings will be shared with participating institutions to inform local prevention strategies.

RESULTS

A total of 810 participants were enrolled, with a mean age of 62 years (SD=15). 48.6% (394/810) were female. Cardiovascular disease was present in 63% (510/810) of participants, chronic kidney disease in 17.4% (141/810) and immunosuppression in 12.5% (101/810). Overcrowded housing was reported in 4.4% (36/810) of cases, and 14.4% (117/810) were active smokers. Influenza and pneumococcal vaccination rates were 31.6% (256/810) and 10.7% (87/810), respectively. Detailed cohort characteristics and group comparisons appear in table 1 and figure 1. Online supplemental table 1 provides ungrouped comorbidity variables.

Baseline colonisation was 15.3% (124/810). Among isolates, 11.2% (14/124) were MRSA strains (online supplemental figure 2). 6.4% (8/124) showed clindamycin-inducible resistance, and 110 (88.7%) were MSSA.

During the 6-month follow-up, samples from 494 participants (60.9%) were collected, 18% (89/494) were colonised, including 78.7% (70/89) incident cases (cumulative incidence 14.2% (70/494)) (table 2). At

Table 1 Baseline characteristics of the patients included in the study

	Total patients sampled n=(810)	No *S. aureus* colonised n=(686)	*S. aureus* colonised n=(124)	P value
Demography				
Age mean±SD	62±15	62±15	63±13	0.39
Gender female, n (%)	394 (48.6%)	334 (48.7%)	60 (48.4%)	0.95
Healthcare worker, n (%)	62 (7.7%)	55 (8%)	7 (5.6%)	0.36
Lives in the following condition				
Overcrowded, n (%)	36 (4.4%)	32(4.7%)	4 (3.2%)	0.47
Geriatric home, n (%)	16 (2%)	11 (1.6%)	5 (4%)	0.74
Habits				
People who smoke, n (%)	117 (14.4%)	91 (13.3%)	26 (21%)	**0.02**
Alcoholic, n (%)	1 (0.1%)	1 (0.1%)	0 (0%)	0.67
Drug abuse, n (%)	1, (0.1%)	1 (0.1%)	0 (0%)	0.67
Vaccination against				
Influenza, n (%)	256 (31.6%)	226 (32.9%)	30 (24.2%)	**0.05**
Pneumococcus, n (%)	87 (10.7%)	75 (10.9%)	12 (9.7%)	0.67
Comorbidities				
Cardiovascular diseases, n (%)	510, (63%)	438, (63.8%)	72 (58.1%)	0.22
Chronic kidney disease, n (%)	141 (17.4%)	114 (16.6%)	27 (21.8%)	0.16
Diabetes, n (%)	125 (15.4%)	104 (15.2%)	21 (16.9%)	0.61
Immunocompromised status n (%)	101 (12.5%)	84 (12.2%)	17 (13.7%)	0.65
Pulmonary diseases, n (%)	69 (8.5%)	54 (7.9%)	15 (12.1%)	0.12
Neurological diseases, n (%)	45 (5.6%)	38 (5.5%)	7 (5.6%)	0.96
Haematological compromise, n (%)	24 (3%)	20 (2.9%)	4 (3.2%)	0.85
Chronic hepatic disease, n (%)	11 (1.4%)	8 (1.2%)	3 (2.4%)	0.27

12 months, follow-up samples were available for 35.5% (288/810) of patients, with a colonisation rate of 23.6% (68/288). Of these, 16.7% (48/288) were newly colonised (incident cases), while 6.9% (20/288) had persistent colonisation (prevalent cases). By 18 months, 23.6% (191/810) of patients remained in follow-up, with *S. aureus* colonisation identified in 23.6% (45/191). Within this group, 12.6% (24/191) were incident cases, whereas 11% (21/191) were considered prevalent, resulting in an overall incidence of 12.6% (table 2 and figure 2).

RF analyses identified smoking, cardiovascular disease, influenza and pneumococcal vaccination, and chronic respiratory disease as the most important variables predicting the studied outcome (online supplemental figure 2). A bivariate analysis was conducted to explore the association between colonisation and sociodemographic and clinical variables, as presented in table 3. In the logistic regression, smoking emerged as a statistically significant risk factor for colonisation (OR 1.83, 95% CI 1.11 to 3.02, p=0.02), while influenza vaccination emerged as an important protective factor against *S. aureus* colonisation after adjusting for comorbid conditions and socioeconomic factors (OR 0.58, 95% CI 0.37 to 0.92, p=0.02). Detailed outcomes for both univariate and multivariate analyses can be found in table 3. The Hosmer-Lemeshow test indicated goodness of fit (p value of 0.48). Additionally, the RF analysis identified smoking, residence in a nursing home and RA as the most relevant predictors, reinforcing the findings from the regression model.

Comparisons between baseline and follow-up colonisation using the McNemar test showed no significant difference at 6 months (p=0.287), but significant increases at 12 (p=0.0177) and 18 months (p=0.0499), suggesting a progressive shift in colonisation patterns over time. Cochran's Q test confirmed variation over the three follow-up periods (Q=295.19, p<0.001). These results confirm that *S. aureus* colonisation does not remain constant over time. We fitted the GEE model for sensitivity analysis, only including participants with complete follow-up data, to control for potential non-random loss to follow-up (online supplemental table 2). Current smoking status, after controlling for potential confounders, was significantly associated with an increased odds of *S. aureus* infection (OR 1.83, 95% CI 1.09 to 3.09, p=0.021). Conversely, vaccination against seasonal influenza was associated with lower odds of *S. aureus* infection (OR 0.55, 95% CI 0.32 to 0.94, p=0.028) (online supplemental table 3).

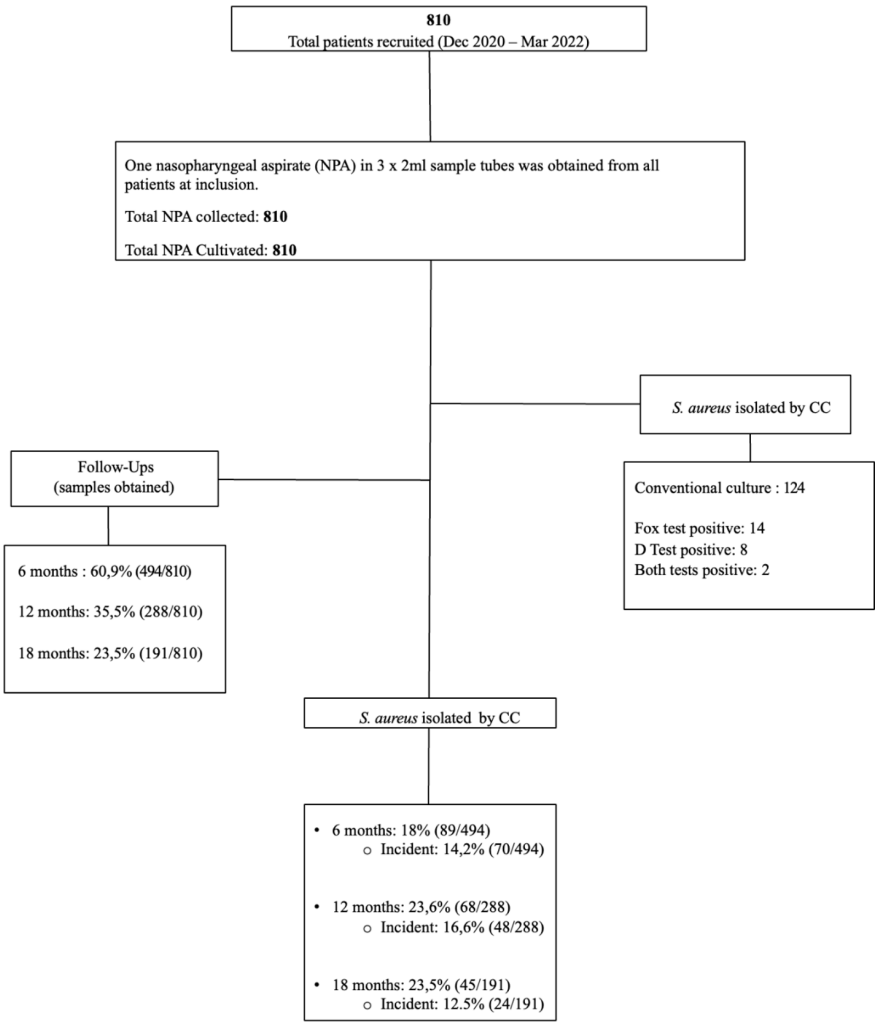

Figure 1 Study flowchart and *Staphylococcus aureus* colonisation. This flowchart illustrates the recruitment and follow-up of 810 participants from December 2020 to March 2022. NPA samples were collected, with follow-up at 6 months (494/810), 12 months (288/810) and 18 months (191/810). *Staphylococcus aureus* colonisation was detected in 124 samples, with 14 positive for the Fox test, eight for the diffusion disc test and two for both. Colonisation rates at 6, 12 and 18 months were 18%, 23.6% and 23.5%, respectively, with incident cases reported at each time point. CC, conventional culture; NPC, nasopharyngeal aspirate.

DISCUSSION

In this prospective cohort study of adults with chronic comorbidities in an LMIC, *S. aureus* NPC was found to be common, including a notable proportion of methicillin-resistant strains. Colonisation patterns varied over time, with evidence of both new acquisitions and persistent carriage throughout the follow-up period. Smoking and RA emerged as significant risk factors for colonisation, while influenza vaccination appeared to have a protective effect. These findings underscore the dynamic nature of *S. aureus* colonisation in vulnerable populations, highlighting the importance of addressing modifiable risk factors and strengthening preventive strategies, particularly in resource-limited settings where the disease burden is highest.

S. aureus NPC is a well-established risk factor for invasive infections, particularly CAP and HAP, whose empiric treatment remains challenging due to rising antimicrobial

Table 2 Longitudinal assessment of *Staphylococcus aureus* colonisation and incidence over 18 months

Follow-up period	Patients with samples (n/N, %)	Colonised patients (n, %)	Incident cases (n, %)	Prevalent cases (n, %)	Cumulative incidence (%)
6 months	494/810 (60.9%)	89 (18.0%)	70 (14.2%)	19 (3.8%)	8.6% (70/810)
12 months	288/810 (35.5%)	68 (23.6%)	48 (16.7%)	20 (6.9%)	5.9% (48/810)
18 months	191/810 (23.6%)	45 (23.6%)	24 (12.6%)	21 (11.0%)	2.9% (24/810)

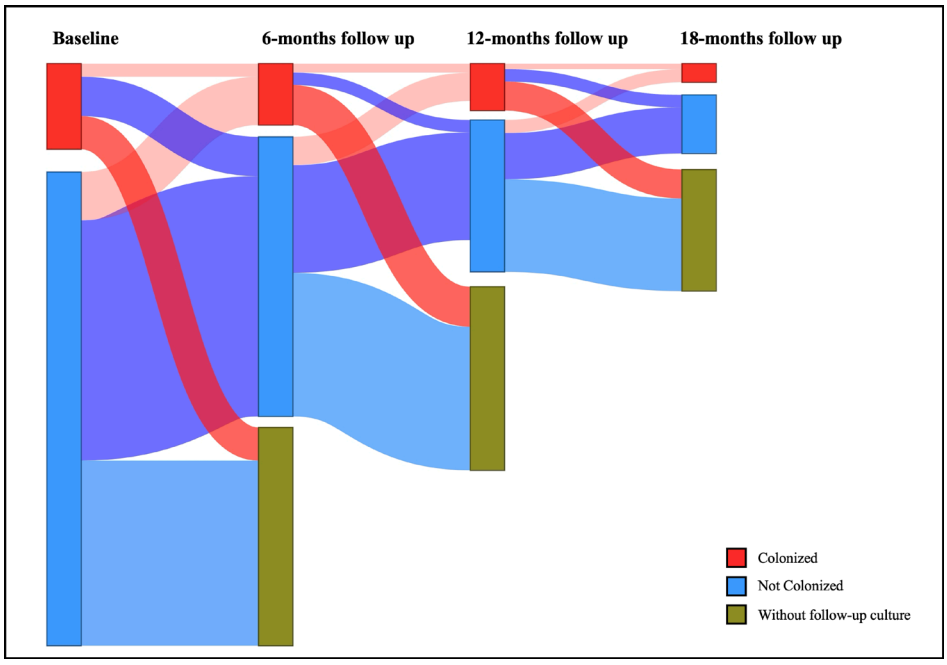

Figure 2 Sankey diagram depicting *Staphylococcus aureus* colonisation dynamics across follow-up periods.

resistance.[2 3] The global initiative for MRSA pneumonia reported an overall low global prevalence of MRSA pneumonia. Still, it revealed marked geographic disparities—for instance, significantly higher point prevalences were observed in North and South America. Previous MRSA colonisation was identified as an independent risk factor for MRSA pneumonia across all regions.[5] Separately, multiple point prevalence studies have shown that *S. aureus* colonisation itself exhibits substantial geographic variability,[30–32] which may contribute to differences in disease burden. These findings underscore the importance of understanding colonisation patterns to anticipate clinical risk better. Contributing to this global understanding, our study describes a higher prevalence of *S. aureus* colonisation in community-dwelling adults with comorbidities in an LMIC, providing valuable data from a setting where epidemiological evidence remains scarce. Unlike most existing studies, our prospective design allowed for longitudinal follow-up, offering a more comprehensive view of colonisation dynamics over time.

Regarding longitudinal changes in colonisation, carriers are typically classified as either persistent or intermittent.[33] However, the mechanisms underlying persistent colonisation remain poorly understood, as do the host or environmental factors that drive temporal variability.[34] Mathematical models suggest that individuals with abnormal mucus characteristics (eg, increased viscosity) or intrinsic differences in nasal mucosa, such as those with pre-existing illnesses, may be particularly susceptible to persistent colonisation.[35] In our cohort, persistent colonisation was observed in a minority of participants. Most exhibited intermittent or oscillatory colonisation patterns, with notable shifts over time. These findings support the notion that colonisation is a dynamic and host-dependent process. Further research is needed to identify the mechanisms that impair clearance and promote sustained colonisation.

Understanding local colonisation prevalence and its determinants is particularly important in guiding empiric antibiotic strategies. Current CAP guidelines do not routinely recommend empiric MRSA coverage, making identifying patients at increased risk of MRSA infection critical to inform appropriate antibiotic use and avoid overuse of anti-MRSA agents.[5] In our cohort, active smoking was independently associated with *S. aureus* NPC. This finding supports previous studies reporting a strong correlation between smoking and persistent colonisation, with up to a threefold increase in carriage.[21 36 37] These effects are thought to be mediated by impaired mucociliary clearance and altered immune responses,[36 37] reinforcing tobacco exposure as a modifiable risk factor for *S. aureus* colonisation and highlighting the potential value of smoking cessation programmes in reducing colonisation and its downstream clinical consequences.

Likewise, RA was found as an independent risk factor for colonisation, which aligns with previous literature describing higher rates of persistent *S. aureus* NPC in this subset of patients, particularly among those with moderate to high disease activity or undergoing biologic therapy.[38 39] The underlying mechanisms are likely multifactorial, including impaired mucosal immunity, reduced neutrophil function and alterations in local microbial ecology secondary to chronic inflammation and immunosuppressive treatment. The clinical relevance of this finding lies in the opportunity to prioritise this subgroup for enhanced preventive strategies, such as targeted

Table 3 Univariate and multivariate analysis for factors associated with colonisation

	Univariate analysis		Multivariate analysis	
Variables	OR (95% CI)	P value	OR (95% CI)	P value
Demography				
Age	1.00 (0.99 to 1.02)	0.63		
Gender	1.01 (0.69 to 1.48)	0.95		
Healthcare worker	0.68 (0.31 to 1.54)	0.36		
Lives in the following condition				
Geriatric home	2.57 (0.88 to 7.55)	0.08	2.98 (1.00 to 8.88)	0.05
Overcrowded	0.68 (0.23 to 1.96)	0.47		
Pneumococcal nasopharyngeal aspirate colonisation by				
Conventional culture	1.19 (0.33 to 4.20)	0.78		
Quantitative PCR	1.16 (0.62 to 2.19)	0.62		
Vaccination status				
Pneumococcal vaccine	0.87 (0.46.1.66)	0.68		
Influenza vaccine	0.65 (0.42 to 1.00)	0.05	0.58 (0.37 to 0.92)	0.02
Habits				
People who smoke	1.73 (1.06 to 2.81)	0.02	1.83 (1.11 to 3.02)	0.02
Alcoholic	0.70 (0.99 to 1.01)	1.00		
Psicoactive substances	0.99 (0.99 to 1.01)	1.00		
Comorbidities				
Haematologic compromise	1.11 (0.37 to 3.30)	0.85		
Immunocompromised status	1.14 (0.65 to 1.99)	0.65		
Rheumatoid arthritis	2.52 (1.17 to 5.45)	0.02	3.03 (1.38 to 6.67)	<0.01
Pulmonary diseases	1.61 (0.87 to 2.96)	0.12	1.63 (0.87 to 3.05)	0.12
Neurological diseases	1.02 (0.44 to 2.34)	0.96		
Chronic kidney disease	1.40 (0.87 to 2.24)	0.16	1.49 (0.92 to 2.43)	0.10
Chronic hepatic disease	2.10 (0.55 to 8.03)	0.23		
Diabetes	1.14 (0.68 to 1.91)	0.61		
Cardiovascular diseases	0.78 (0.53 to 1.15)	0.22		

vaccination campaigns, and to consider RA at the time of CAP diagnosis to guide anti-MRSA empiric coverage.

Live attenuated influenza vaccine may transiently increase upper respiratory tract colonisation by bacterial pathogens such as *S. aureus* and *Streptococcus pneumoniae*, potentially increasing the risk of viral-bacterial co-infection.[40–42] This effect has been linked to type I interferon responses induced by influenza antigens, which may impair bacterial clearance by modulating innate immunity.[43] However, evidence remains conflicting. While some trials report increased bacterial density post-vaccination, other observational studies have found no association or a protective effect against bacterial coinfection.[44 45] In our cohort, influenza vaccination was associated with a reduced risk of *S. aureus* NPC. One potential explanation is that transient increases in bacterial density following vaccination may stimulate antibody production, enhancing mucosal immunity and preventing sustained colonisation. Further investigation is warranted to clarify how vaccine-induced immune responses influence bacterial carriage.

This study presents several notable strengths and limitations. One of the main strengths is the inclusion of a large and well-characterised cohort, comprising over 800 participants at baseline, representing, to our knowledge, the most extensive study to date investigating *S. aureus* NPC in Latin America. Despite this, a significant limitation was the high attrition rate over the 18-month follow-up period, which exceeded 60%, potentially introducing bias due to attrition. Although key variables, such as comorbidity status, smoking history and vaccination records, were cross-validated with medical records when possible, some degree of recall and information bias may still have affected the self-reported data. Additionally, while nasopharyngeal aspirates were collected per WHO protocols to ensure proper technique, we could not assess sample quality before processing. It is worth noting, however, that even

in rigorously conducted studies, an aetiologic agent is identified in only a minority of respiratory infections. In our study, microbial identification was performed using culture-based methods followed by MALDI-TOF mass spectrometry. This validated approach enhances diagnostic accuracy and reduces the risk of misclassification or detection bias. Finally, unassessed aspects included the occurrence of hospitalisations during follow-up, a detailed characterisation of skin diseases among comorbidities and a comparison of risk factors between patients colonised with MSSA and those colonised with MRSA.

Our findings indicate a high prevalence of *S. aureus* nasopharyngeal colonisation among community-dwelling adults with chronic comorbidities in an LMIC, including a notable proportion of methicillin-resistant strains. Colonisation status showed substantial temporal variability, with patterns of both new acquisition and persistent carriage observed over time, highlighting the dynamic nature of colonisation in this population. Active smoking and RA emerged as independent risk factors, while prior influenza vaccination appeared to have a protective effect. These results underscore the need to address modifiable host factors and implement targeted prevention strategies, particularly in resource-limited settings where the burden of disease is disproportionately high. Additionally, our findings support the clinical relevance of incorporating colonisation data into treatment decisions for community-acquired pneumonia, particularly when evaluating the need for empiric MRSA coverage. Further research is warranted to explore the long-term clinical consequences of colonisation and its impact on patient outcomes.

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Patient consent for publication Consent obtained directly from patient(s).

Ethics approval This study involves human participants. This study was reviewed and approved by the Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs) of all participating institutions before recruitment and data collection. The following ethics approvals were granted: Clínica Universidad de La Sabana IRB, approval ID: 01-20, approved February 2020; Fundación Clínica Shaio IRB, approval ID: 301, approved 26 August 2020; Baxter Renal Care Services Chía IRB, approval ID: 05-01, approved September 2021; IPS-Clínicos IRB, approval ID: 01-02, approved 2 January 2021. All participants provided written informed consent prior to participation. The study was conducted in accordance with the ethical standards of each institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments. Participants gave informed consent to participate in the study before taking part.

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