ANALYSIS OF INFLAMMATORY DISEASES OF THE UPPER RESPIRATORY TRACT AND ANTIBIOTIC DRUGS USED IN THEM

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Annotation. The purpose of the study*: to identify cases of infection with inflammation of the upper respiratory tract and their sensitivity to antibiotics of the population of the Republic of Uzbekistan for the period 2023-2024 in administrative regions (by cross section of Regions).* ***Materials and methods:*** *in the bacteriological Lobaratorium of the Tashkent Medical Academy of the Republic of Uzbekistan, infections detected in patients with nasal infections from the second half of 2023 to the beginning of 2024, as well as microorganisms detected in them, their sensitivity to antibiotics were analyzed. Bacteriological, statistical methods were used.* ***Results analysis and discussion.*** *During this 6-month period, 148 patients (30 men, 118 women) had complaints of inflammatory diseases in the nasal cavity. Samples from them were collected in 145 of the total patients when the laboratory was diagnosed with 160 different bacteria (Streptococcus ssp.-25%, Staphylacocus aureus-30%, Candida ssp.-20%, Proteus mirabilis -10%, Pseudomonas auriginosa-10% and Klebsiella ssp.-5%). Microorganisms were not detected in 3 patients.* ***Conclusion:*** *as a result of the analyzes, we can see more (80%) women with inflammation of the nose get sick (the average age was 30-35). The bacterium that causes the most inflammation is Staphylacococcus aureus (30%), as well as the bacteria from the most effective antibiotics: sulfamethoxazole, Levofloxocin, amoxicillin and ampicillin, gave a good result.*

Keywords: *inflammation of the upper respiratory tract, bacteria, antibiotics, microorganisms*

Relevance. Acute upper respiratory tract infections are a global health problem according to the World Health Organization (15). RS is an inflammation of the nasal and paranasal sinuses (2). Allergic rhinitis (AR) is a common disorder that afflicts 400 million people worldwide and it represents a global concern as its prevalence has increased over the years (8). Respiratory tract infections are defined as inflammation and damage to the upper respiratory tract caused by viruses and bacteria (6). Respiratory tract infections are a leading cause of morbidity and mortality worldwide (3). They can also be inhaled into the lungs during travel (13). The health consequences of these conditions are related to the activity of infectious agents, and the intensity of their occurrence is directly related to social (level of urban development and sanitary culture of the population) and natural and climatic conditions (15). They are caused by mucosal inflammation, which inhibits mucociliary function of the nose and paranasal sinuses (9). Several gram-positive and gram-negative bacteria are the main causative agents of upper respiratory tract infections, with Pseudomonas aeruginosa, Staphylococcus aureus, and Streptococcus pneumoniae species being the main causative agents (10). Resistance to antibiotics is currently a global threat to the establishment of a safe and effective treatment. If no action is taken, the estimated annual death toll of 700,000 is expected to rise to 10 million by 2050 (4). In the Republic of Uzbekistan, many efforts have been made to combat the disease, with some epidemics being eradicated. The diversity of infectious agents has led to the development of new drugs. The most important thing in doing so is to make the right diagnosis and provide the right treatment. Incorrect prescriptions remain a major problem, especially for primary health care providers and for the population as a whole (12).

Research objective: Incidence of upper respiratory tract infections and their sensitivity to antibiotics in the population of Tashkent city during 2023-2024.

Inspection material and methods: In the Bacteriological Laboratory of the Tashkent Medical Academy of Tashkent city, infections detected in patients with nasal infections from the second half

of 2023 to the beginning of 2024, as well as microorganisms identified in them, and their antibiotic sensitivity were analyzed. Samples of patients were cultured on Endo, Blood agar, Saburo, VSA, JSA, Muller Hilton nutrient media and we observed daily microbial colonies on agar media, and we evaluated the grown colonies according to their cultural, tinctorial, and morphological characteristics to determine the pure culture of bacteria. The isolated colonies were cultured on neutral agar and the disk diffusion method was used to determine antibiotic sensitivity. Bacteriological and statistical methods were also used. **Analysis and discussion of results.** During this 6-month period, 148 patients (30 men, 118 women) complained of inflammatory diseases of the nasal cavity. When samples taken from them were subjected to laboratory diagnosis, 160 different bacteria were detected in 145 of the patients (Streptococcus ssp.-25%, Staphylococcus aureus-30%, Proteus mirabilis-10%, Candida ssp.-20%, Pseudomonas auriginosa-10% and Klebsiella ssp.-5%). No microorganisms were detected in 3 patients. The following antibiotics were found to be highly sensitive to the above-identified bacteria: Streptococcus - amoxicillin, ampicillin, ceftriaxone, azithromycin, levofloxacin and clindamycin, Staphylococcus aureus - sulfamethoxazole, ampicillin, vancomycin, Candida ssp. - nystatin, amphotericin-b, fluconazole, Pseudomonas auriginosa - gentamicin, meropenem, cefepime, levofloxacin, Klebsiella ssp. - ceftriaxone, meropenem, gentamicin, sulfamethoxazole. The type and dose of these drugs are selected depending on the type of infectious agent and its amount in the body.

In this diagram, we have determined the level of infection by gender: in men and women.

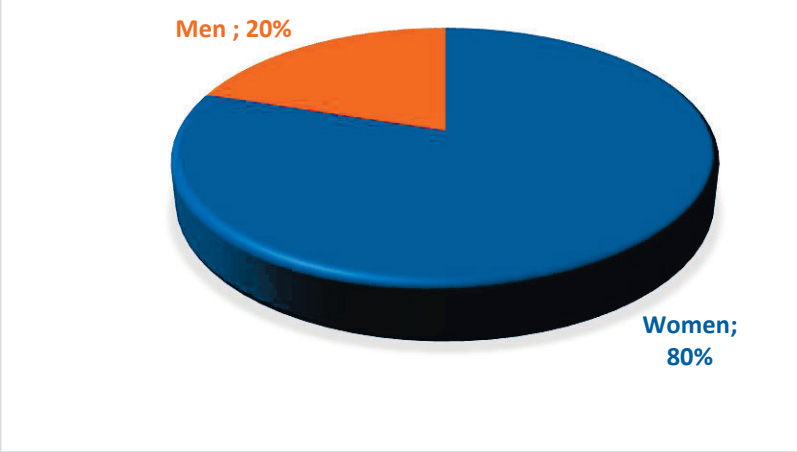

Fig 1. Distribution of patients by gender.

As you can see from the table, we can see that women are 4 times more likely to suffer from nasal infections than men.

Table 1.

Bacteria isolated from patients with throat infections, comparative analysis CFU/ml 1g (M±m)

Isolated microorganisms	KHQB/ml 1g
Staphylococcus aureus	4,11±0,3
Klebsiella spp.	4,5±0,3
Klebsiella pneumoniae	4,5±0,1
Escherichia coli	3±0,2
Pseudomonas aeruginosa	4,5±0,1
Streptokokk ssp.	4,25±0,2
Candida ssp.	4,44± 0,6
Proteus mirabilis	3,83±0,2

***Note:** *-; **- significant difference compared to group 1 (P<0.05, P<0.01).*

As a result of our investigation (Table 1), it was found that not only one bacteria, but also different bacteria, develop the disease in patients with nasal infections. We distributed the quantitative indicators of the bacteria according to the results of the analysis of each patient. We also calculated the percentage of their disease-causing bacteria in the patients and presented them in the form of a diagram (Fig 2).

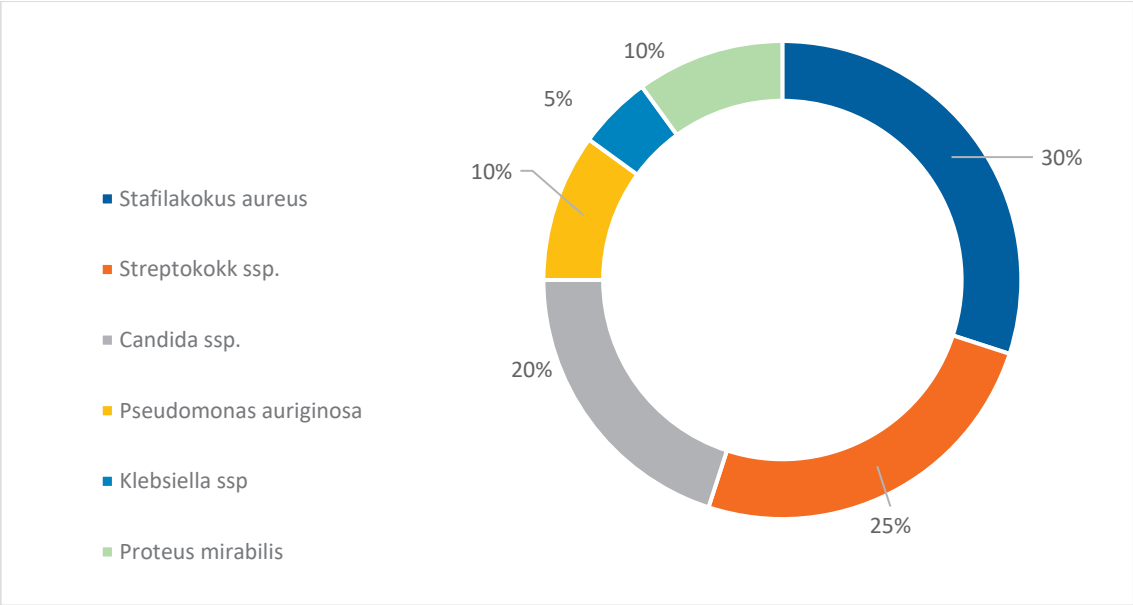

Fig 2. Percentage of bacteria causing disease

Our study also revealed that (diag.2), in patients (Streptococcus ssp.-25%, Staphylococcus aureus-30%, Candida ssp.-20%) caused 3 times more diseases than other bacteria. Also, cases of monoinfection and diinfection were observed among patients. We calculated the results of the conducted studies and presented these cases in the form of a diagram.

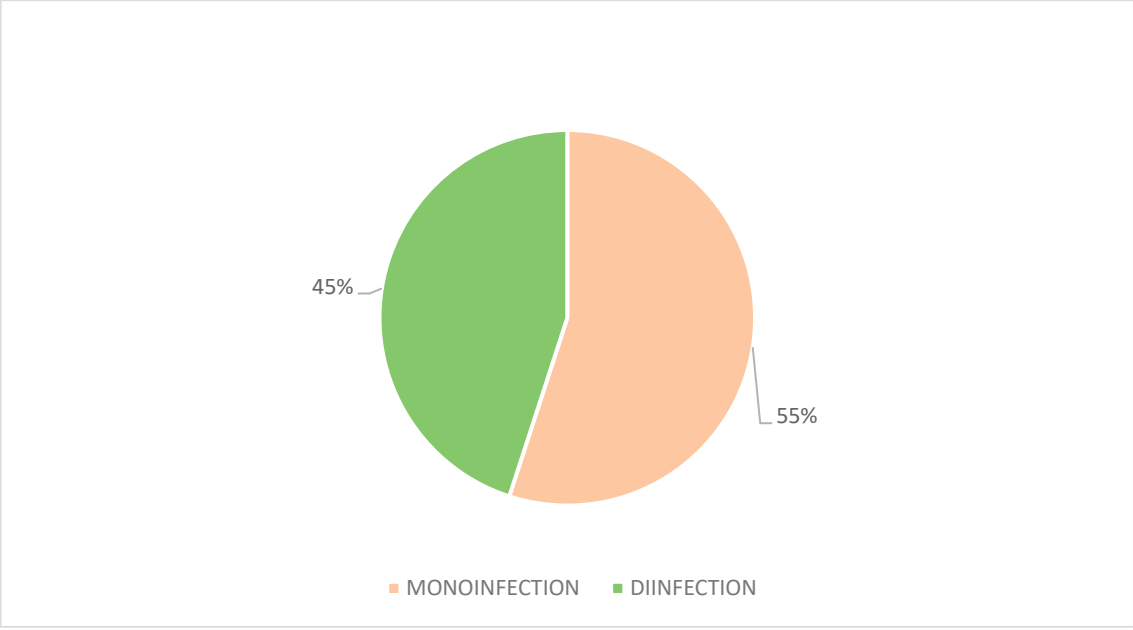

Fig 3. Occurrence of mono and di infections in patients.

This diagram shows that patients with dual infection are 1.22 times more likely to be infected than patients with mono infection. In the treatment of diseases caused by these bacteria, antibiotics sensitive to each bacterium were used, and patients were cured within 1-2 weeks, and in some cases up to 1 month.

During our research, we used and studied many foreign literatures, below we present the results of some of these articles for comparison:

The oral microbiota acts as the primary barrier against the invasion of respiratory viruses into the human body. Disruptions in the local airway microbiota caused by respiratory viral infections might initially occur in the oral cavity and subsequently affect distant microbial com munities at sites connected through the oral-lung or oral-gut axes. The dual interaction between the oral microbiome, inflammation, and the immune system during the disease suggests that changes in the oral microbiota could potentially serve as non-invasive biomarkers for ecological disturbances in the lung microbiome or the invasion of po tential pathogens into the lungs, thus giving early warning of disease severity. Microbiome ecological imbalances can facilitate the invasion of respiratory viruses and the inflammatory environment necessary for virus replication. Therefore, we believe that patients with oral micro biome imbalances might face significantly increased risks of disease complications and mortality during seasonal outbreaks of respiratory viruses and sporadic epidemics. Consequently, during periods of epidemic outbreaks, conducting oral microbiome testing for patients with compromised oral environments and promptly implementing oral microbiome interventions is of paramount importance to prevent the occurrence of uncontrolled inflammation or to mitigate its severity(15).

Baseline characteristics.

There were 280 patients diagnosed as URTI with fever for screening from March 2016 to December 2019. A total of 278 patients meeting the inclusion criteria were enrolled finally. The eligible patients were randomly assigned to the CQQNC group and the QKLC group. During this trial, 5 subjects in the CQQNC group and 4 subjects in the QKLC group dropped out. Finally, 134 subjects in the CQQNC group and 135 subjects in the QKLC group were analyzed summarizes the demographic and baseline characteristics. There were no significant differences in demographic characteristics and vital signs between the two groups, except for the diastolic blood pressure. Fig. 4. Flow diagram.

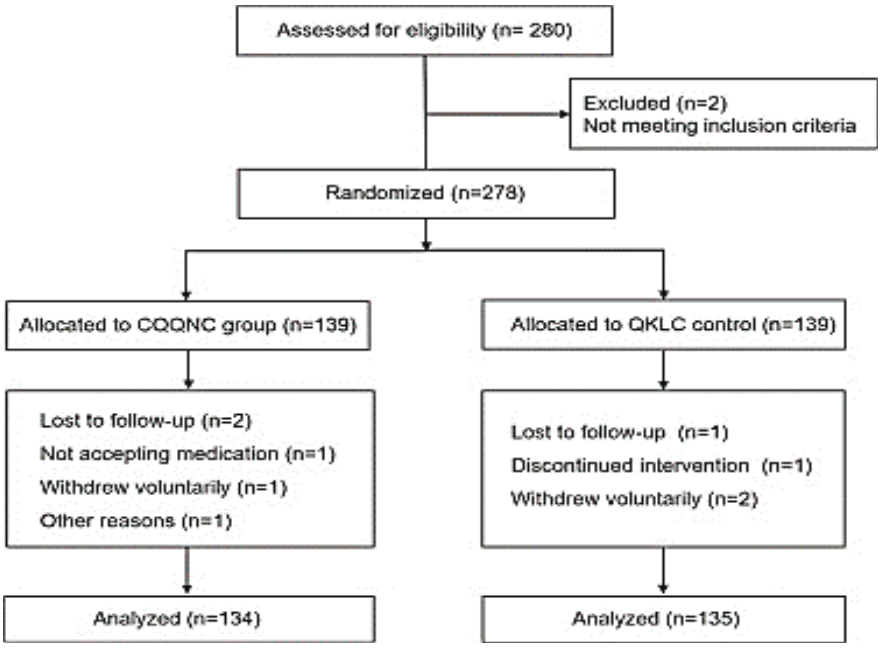

Fig. 4. Flow diagram.

Table 2.

Demographic and baseline characteristics.

Empty Cell	Total (N = 269)	QKLC group (N = 135)	CQQNC group (N = 134)	*P value*
Age, Mean ± Sd, y	43.14 ± 12.66	43.08 ± 12.76	43.19 ± 12.60	0.939
Sex, No.%				0.303
Male	108 (38.71)	50 (35.71)	58 (41.73)	
Female	171 (61.29)	90 (64.29)	81 (58.27)	
BMI, Mean ± Sd, kg/m^2	23.00 ± 2.71	23.01 ± 2.64	23.00 ± 2.78	0.993
Course, Mean ± Sd, h	17.39 ± 7.78	17.55 ± 7.92	17.23 ± 7.67	0.772
Vital signs				
Temperature, Mean ± Sd, ℃	38.37 ± 0.31	38.34 ± 0.32	38.41 ± 0.30	0.061
Respiratory rate, Mean ± Sd, bpm	19.28 ± 1.88	19.21 ± 1.90	19.34 ± 1.87	0.583
Heart rate, Mean ± Sd, bpm	80.76 ± 12.97	80.51 ± 13.06	81.01 ± 12.93	0.752
Systolic blood pressure, Mean ± Sd, mmHg	121.46 ± 9.89	122.48 ± 10.34	120.44 ± 9.33	0.085
Diastolic blood pressure, Mean ± Sd, mmHg	76.81 ± 7.93	77.79 ± 8.44	75.83 ± 7.28	0.038

Abbreviations: *BMI, body mass index; bpm, beats per minute; SD, standard deviation; CQQNC, Chaiqin Qingning Capsules; QKLC, Qingkailing Capsules (14).*

Primary outcome

The body temperature of patients in both treatment groups decreased after 3 days of medication. The median antipyretic onset time was 5 h (IQR: 5, 6) in the CQQNC group and 10 h (IQR: 10, 12) in the QKLC group. The between-group differences [0.19 (95%CI: 0.14–0.26); $P < 0.0001$] in the proportion of antipyretic onset during the observation period were given in. The median temperature recovery time was 19 h (IQR: 15, 20) in the CQQNC group and 27 h (IQR: 23, 28) in the QKLC group. illustrated the between-group difference in the proportion of temperature recovery [0.57 (95%CI: 0.45–0.7); $P < 0.0001$] (14).

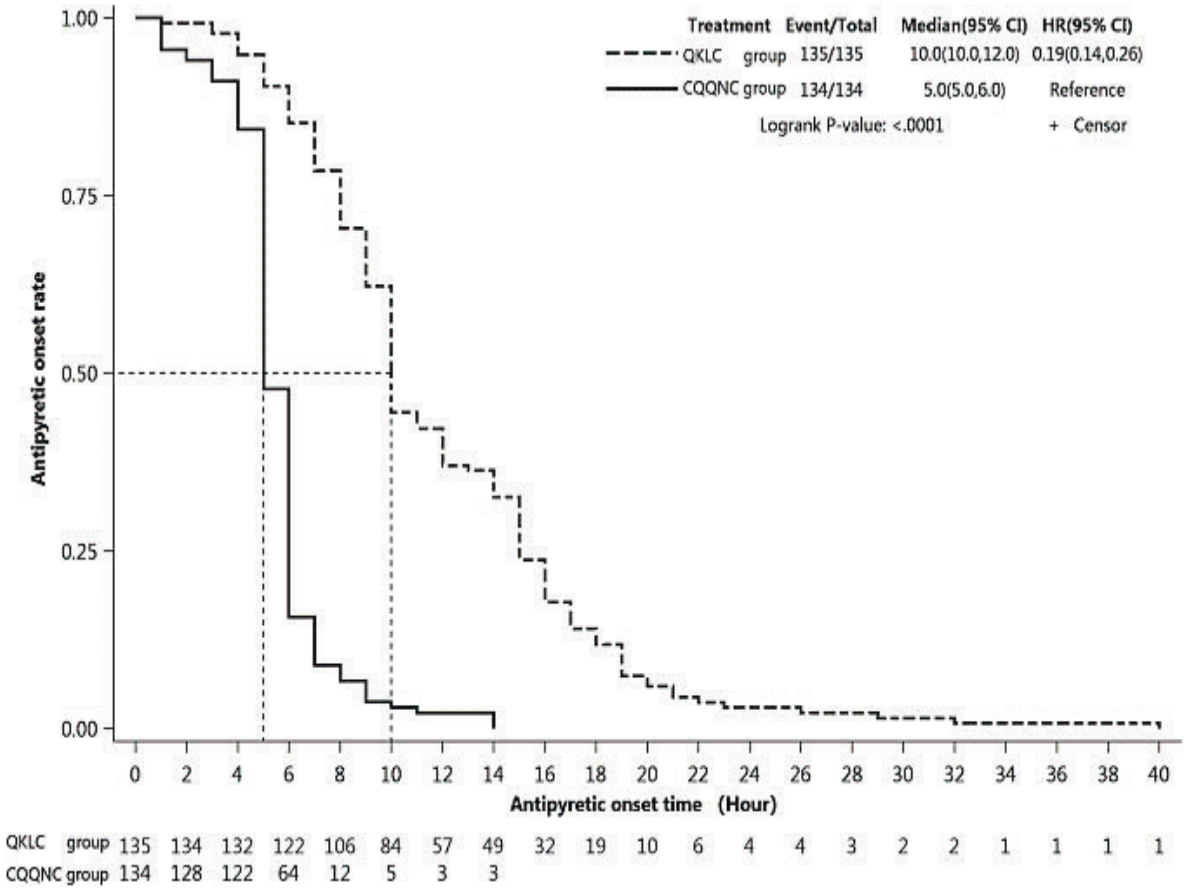

Fig. 5. Kaplan-Meier curves of antipyretic onset rate after medication.

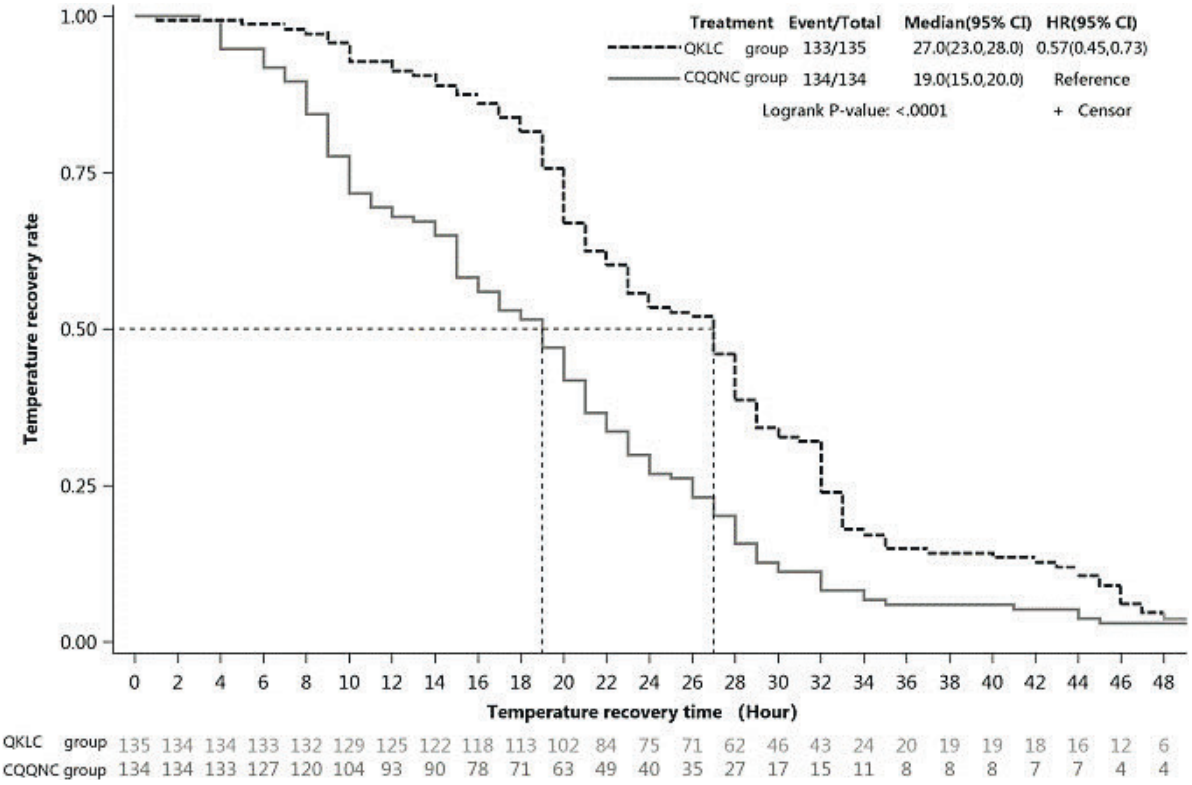

Fig. 6. Kaplan-Meier curves of temperature recovery rate after medication.

Local administration of antibiotics can combat pre-systemic meta bolism, alleviate systemic adverse effects, mitigate deactivation by metabolic enzymes, improve drug bioavailability, and enable the commencement of remedial activity. However, regarding antibiotics applied to manage bacterial CF, administering the medication directly to the lungs via the respiratory tract encounters various challenges as well. Along with complications revealed by cells, organelles, and bacterial biofilms, delivering drugs locally to the lungs needs to circumvent the biological obstacles posed by the unique configurations and actions of the respiratory tract [71,85]. The lungs possess robust natural defences and physical hurdles that create challenges for inhalable medications to effectively target their intended site of action. Even when inhaled medications successfully penetrate deep into the lungs, they are swiftly eliminated or rendered ineffective by body's defence mechanisms. As a result, achieving drug delivery to specific pulmonary targets is a com plex undertaking.

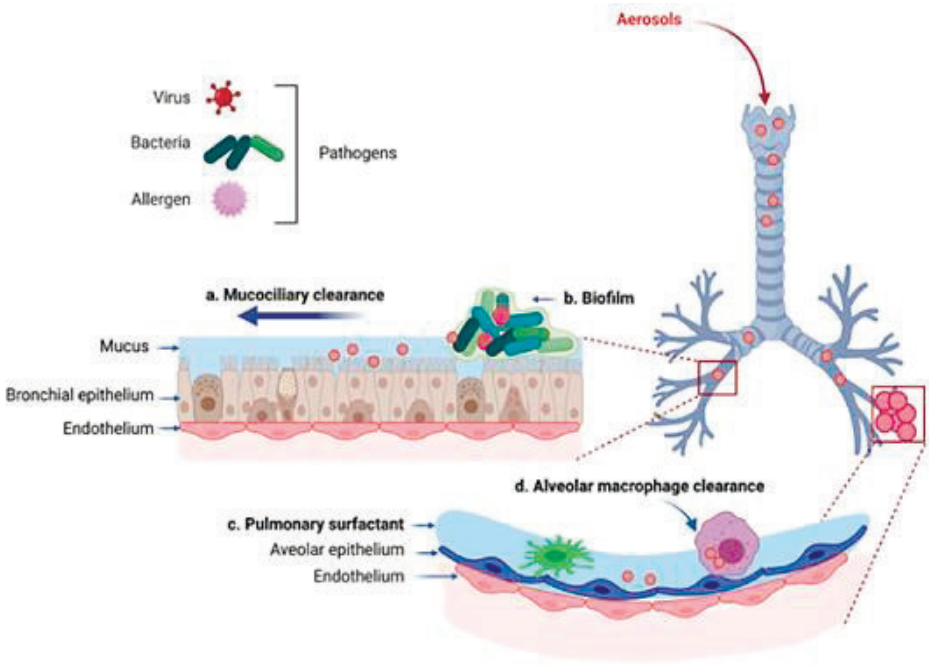

Fig. 7. Barriers in the pulmonary delivery of antibiotics. Reproduced with permission and without modification from Ref.

To achieve precise drug delivery to the lungs, there are three vital hurdles to overcome. The first barrier is anatomical in nature. The lungs comprise an intricate bronchial network with ciliary cells, responsible for pulmonary mucociliary clearance to eliminate particles that accu mulate in the airways. These activities represent a mechanical obstacle that hinders drug delivery to the lungs. The second hurdle entails the mucous layer. The respiratory mucus that lines the airways, from the nose to the smaller bronchial tubes, aids in capturing and expelling external substances, encompassing xenobiotic compounds like antibi otics. Moreover, this mucous barrier operates synergistically with anatomical obstacles, enhancing the efficacy of lung mechanical barriers through airway narrowing due to inflammation and excessive mucus production (13).

Nasal and oral microbiomes of infants with fewer early-life respiratory tract infections are enriched with *Prevotella* spp

We performed differential abundance analysis to examine niche-specific taxa across health states. At the genus level, we did not identify significant differences in abundance of nasal taxa between those with or without early-life LRTI or >4/y URIs, including *Dolosigranulum,* which has been implicated in respiratory health. Examination at the species level identified 6 nasal species and 7 oral species that were differentially abundant between those with or without a history of LRTI.

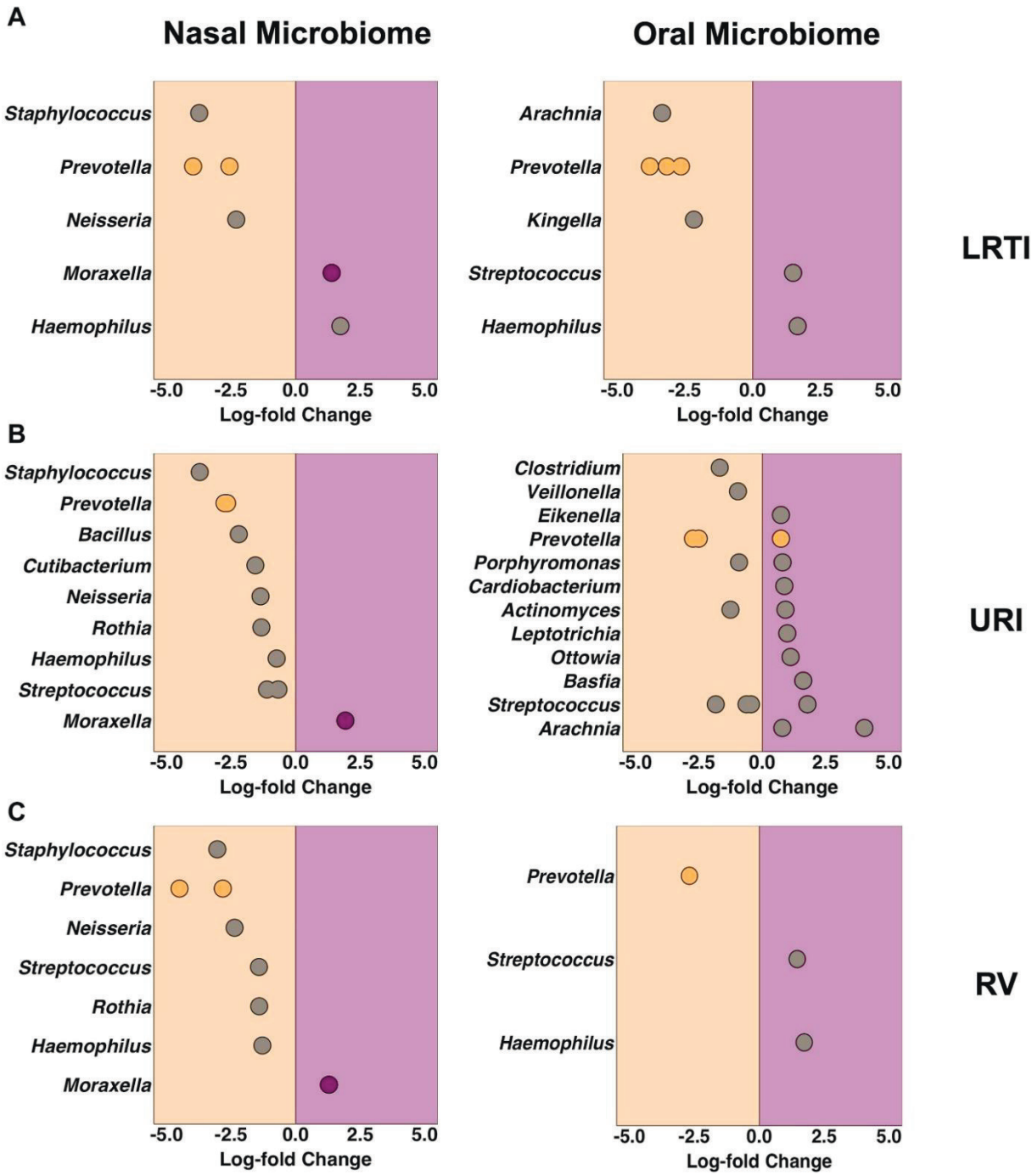

Fig 8. Nasal and oral microbiomes of infants with early-life respiratory tract infections are depleted of *Prevotella* spp. Differential abundance analyses via edge R of nasal *(left)* and oral *(right)* bacteria demonstrate lower abundance of several *Prevotella* spp *(yellow points),* as well as higher nasal abundance of *M catarrhalis (purple points)* among participants with (A) ≥1 episode of LRTI, (B) >4/y URIs, and (C) >4/y symptomatic RV infections from birth to age 24 months *(purple shading)* relative to healthy participants *(yellow shading).* Individual points represent species grouped by genus, with taxa of interest colored. Taxa with false discovery rate (FDR)-corrected $P < .05$ is shown (12).

A total of 2,858 records were identified through database searching and an additional 14 were identified through other sources. After duplicates were removed, 1,990 records remained. These records were screened and 1,926 were excluded. The remaining 64 full-text studies were assessed for eligibility with 35 records excluded for not reporting barriers (n=14), respiratory POCT (n=12),

primary care (n=3), other reasons (n=3), abstract-only (n=2) and a review (n=1). Of the 29 remaining studies, one was removed as it related to nursing homes only. The key barriers and facilitators were then identified from the 28 included studies (10).

After exclusion of 298,775 RTI episodes (24.8%) with codes of low specificity (i.e., not specific enough to differentiate between lower and upper RTI), a total of 905,964 lower or upper RTI episodes with at least one antibiotic prescription were identified. Almost half of all RTI episodes concerned adults consulting their GP for upper RTI (48.6%) and – in general – the main class of initial antibiotic prescription was an oral penicillin (66–90%). Among adults, individuals with lower RTI were older (median age 62 years) and more likely to have a history of comorbidities such as COPD, asthma and pneumonia, compared to those with upper RTI (median age 37 years). In children, 89.9% of episodes were related to upper RTI.

Within-episode antibiotic repeat prescription rates, stratified by age and RTI type, as well as rates per GP are illustrated in. The overall proportion of within-episode repeat prescriptions was 12.7% (95% CI 12.5–12.9%), but with considerable variability between individual GPs. Among adults, within-episode repeat rates were higher for lower RTI (19.9%, 95% CI 19.3–20.5%) than for upper RTI (10.5%, 95% CI 10.3–10.8%). In children, rates were similar for lower RTI (10.5%, 95% CI 9.4–11.5%) and upper RTI (10.0%, 95% CI 9.7–10.4%). Pre- and intra-pandemic within-episode prescription proportions did not change in most groups, except for upper RTIs in adults, which increased during the pandemic (4).

Meta-analysis: effect of vitamin D supplementation on immune markers.

We undertook a statistical pooling of estimates across 13 studies, to quantify the difference in the levels of various immunological markers (CRP, IL-6, IL-10, INF gamma) and vitamin D levels after vitamin D supplementation in the intervention group as compared to the control group, through a meta-analysis. At least three studies with common immune markers were subjected to meta-analysis.

Five studies (n = 788) were included to assess the difference in CRP levels after vitamin D supplementation. The standard mean difference of −0.25 with low heterogeneity among studies (I^2 = 0.0 %). There was a significant decrease in CRP levels after intervention with an overall effect of Z = 3.47 (P < 0.00) (fig.9).

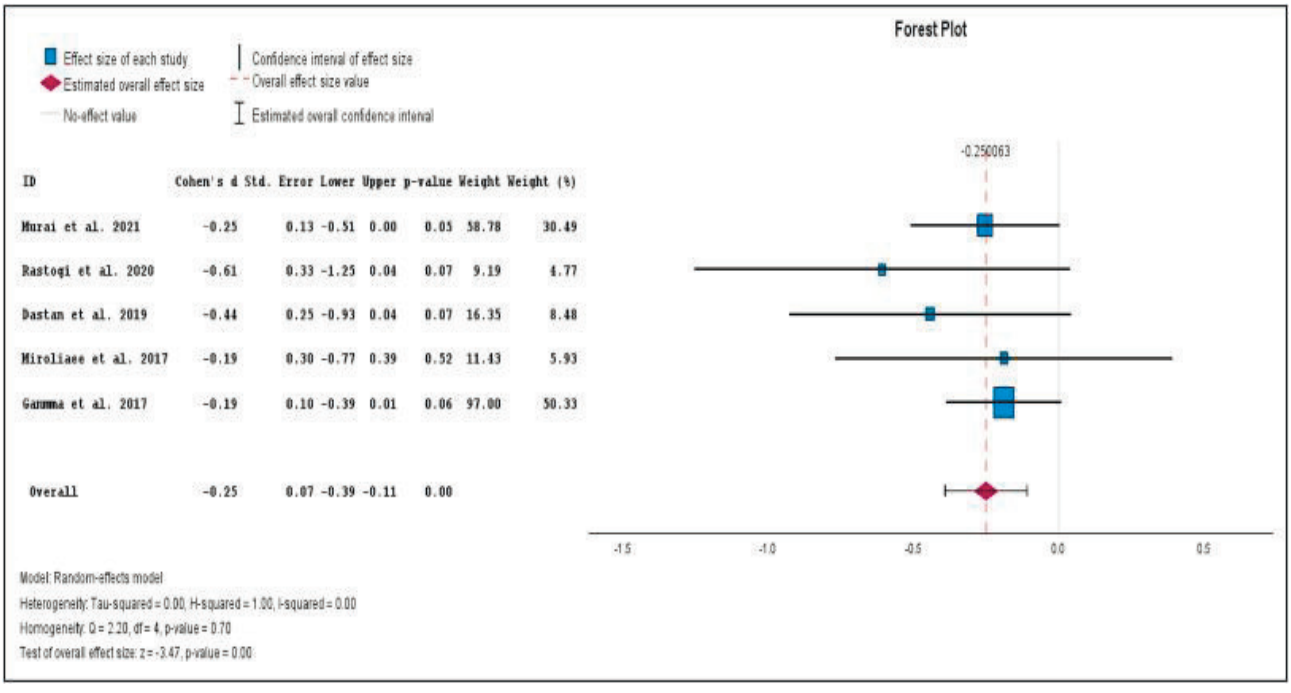

Fig. 9. Forest plot for the difference in CRP levels after the intervention (3).

Conclusion. The results of the analysis showed that nasal diseases are mainly manifested as an additional symptom in seasonal infectious diseases. In addition, in a smaller percentage, the infectious agent itself causes the disease independently. As a result of the analysis, we can see that women (80%) are more likely to suffer from nasal inflammation (average age 30-35). The most common cause of inflammation is Staphylococcus aureus (30%), and the most effective antibiotics for the bacteria: Sulfamethoxazole, Levofloxacin, Amoxicillin and Ampicillin gave good results. The use of correct treatment methods for patients with this infection helps to cure the disease faster.

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