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Is it in their eyes? Correlation between microorganisms isolated from bronchial aspirates and conjunctival swabs in a Pediatric Intensive Care Unit

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ABSTRACT

Objectives. Our observational, retrospective study aimed to determine the correlation between bacteria isolated from bronchial aspirates of pediatric ICU patients (PICU) with respiratory infections and those obtained from conjunctival swabs of the same patients exhibiting clinical conjunctivitis.

Material and methods. Throughout the period from 2015 to 2022, we reviewed all clinically significant bronchial aspirates (≥10^5 CFU/mL) and positive conjunctival swabs obtained from PICU patients. These records were retrieved from the microbiology database, cross-referencing the data to identify patients who tested positive for both during the same clinical episode.

Results. The median age of the patients was 5 months (interquartile range: 1-7). Among the cohort, twenty-one patients exhibited positivity in both bronchial aspirate and conjunctival swab samples, showcasing a microbial match in 85.71% of cases (18 out of 21). The most frequently isolated microorganisms were *Haemophilus influenzae* (55.6%), followed by *Pseudomonas aeruginosa* (14.3%), *Klebsiella aerogenes* (9.5%), and *Escherichia coli*, *Stenotrophomonas maltophilia*, and *Enterobacter cloacae*, each accounting for 4.8% of the isolates.

Conclusions. Our study demonstrates a strong concordance between the isolated microorganisms from both samples in patients presenting clear symptoms of clinical conjunctivitis. These findings provide a basis for future prospective studies that may leverage conjunctival swabs as a predictive tool for identifying microorganisms involved in respiratory infections.

Keywords: bronchial aspirate, conjunctival swab, respiratory bacterial superinfection.

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¿Está en sus ojos? Correlación entre microorganismos aislados de aspirados bronquiales e hisopos conjuntivales en una Unidad de Cuidados Intensivos Pediátricos

RESUMEN

Objetivos. Nuestro estudio observacional y retrospectivo tuvo como objetivo determinar la correlación entre las bacterias aisladas de aspirados bronquiales de pacientes de UCI pediátrica (UCIP) con infecciones respiratorias y las obtenidas de hisopos conjuntivales de los mismos pacientes que presentaban conjuntivitis clínica.

Material y métodos. A lo largo del periodo comprendido entre 2015 y 2022, se revisaron todos los aspirados bronquiales clínicamente significativos (≥10^5 UFC/mL) y los hisopos conjuntivales positivos obtenidos de pacientes de UCIP. Estos registros se recuperaron de la base de datos de microbiología, cruzando los datos para identificar a los pacientes que dieron positivo en ambos durante el mismo episodio **clínico.**

Resultados. La mediana de edad de los pacientes fue de 5 meses (rango intercuartílico: 1-7). Entre la cohorte, veintiún pacientes presentaron positividad tanto en las muestras de aspirado bronquial como en las de hisopo conjuntival, mostrando una coincidencia microbiana en el 85,71% de los casos (18 de 21). Los microorganismos más frecuentemente aislados fueron *Haemophilus influenzae* (55,6%), seguido de *Pseudomonas aeruginosa* (14,3%), *Klebsiella aerogenes* (9,5%) y *Escherichia coli, Stenotrophomonas maltophilia* y *Enterobacter cloacae*, cada uno de los cuales representó el 4,8% de los aislamientos.

Conclusiones. Nuestro estudio demuestra una fuerte concordancia entre los microorganismos aislados de ambas muestras en pacientes que presentan síntomas claros de conjuntivitis clínica. Estos hallazgos proporcionan una base para futuros estudios prospectivos que podrían aprovechar los hisopos conjuntivales como herramienta predictiva para identificar microorganismos implicados en infecciones respiratorias.

Palabras clave: aspirado bronquial; hisopo conjuntival; sobreinfección bac-

teriana respiratoria.

INTRODUCTION

Purulent conjunctivitis is a common infectious disease during childhood. The predominant pathogens of bacterial conjunctivitis in children are *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis* [1]. Bacterial conjunctivitis is more common than the viral form in children. These microorganisms are normal inhabitants of the nasopharynx, especially in children, and can spread to other sites, including the eye, ear, and lower respiratory tract [2].

Respiratory syncytial virus (RSV) is a common cause of childhood pneumonia, and bacterial coinfections can affect clinical severity in those requiring Pediatric Intensive Care Unit (PICU). The prevalence of bacterial coinfections has been established in RSV-positive pneumonia [3]. Some studies have shown that co-detections are associated with longer need for mechanical ventilation and hospital stays. Almost one-third of the patients harbored bacterial pathogens [4], although other studies have detected a bacterial coinfection rate of 43.6% in hospitalized children using washed sputum culture [5].

Hospital-acquired respiratory infections are common in the intensive care unit (ICU). Hospital-acquired pneumonia (HAP), defined as occurring in patients with at least 48 hours of hospital admission, is highly prevalent in the ICU. The common pathogens associated with HAP include Enterobacterales, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. In 30% of cases, the infection is polymicrobial. Microbiological confirmation is a crucial step in the diagnosis of hospital respiratory infections. Routinely, diagnosis is based on qualitative or quantitative cultures of respiratory samples, and a pathogen is isolated from these samples and identified in about 70% of suspected cases [6].

The objective of this study is to ascertain whether a correlation exists between bacteria isolated from bronchial aspirates of patients infected in the respiratory tract and those isolated from conjunctival samples of these patients exhibiting clinically relevant conjunctivitis.

MATERIAL AND METHODS

Throughout the study period, there were 7459 admissions to the PICU, with 1472 bronchial aspirates and 259 conjunctival swabs sent for microbiological culture. For this investigation, only positive and clinically significant (≥ 10^5CFU/mL) bronchial aspirates and conjunctival swabs were selected from the Microbiology department database, focusing on Pediatric Intensive Care Unit (PICU) patients between 2015 and 2022. Conjunctival swabs were exclusively obtained when clinical conjunctivitis was present and were not acquired as part of colonization studies. Respiratory isolates from patients were cross-referenced in the database to identify cases where a positive conjunctival swab was also present. The isolated microorganisms and their sensitivity patterns were subsequently compared. Patient medical records were scrutinized, with age and underlying infections documented. To be included in this retrospective study, patients had to have both samples collected during the same clinical episode.

The study complies with the postulates of Helsinki´s Declaration. No human biological material or identifiable human data were used, therefore ethical approval was exempted.

RESULTS

The median age of the patients was 5 months (range 0.5-22). Twenty-one patients had both positive bronchial aspirate and conjunctival swab results. However, in three out of these 21 cases, the microorganisms isolated from the bronchial aspirate and conjunctival swab did not match. The details of the isolated microorganisms and sampling dates for both types of samples are presented in Table 1. In the remaining 18 cases, the microorganisms isolated from the bronchial aspirate matched with those isolated in the conjunctival swab, and vice versa. The susceptibility profiles of the isolated microorganisms were also the same in these cases. The coincidence in the isolated microorganisms from both samples in this cohort was 85.71% (18 out of 21). In only three patients, the isolated microorganisms differed in both samples (14.29%). It is worth noting that in two out of these three cases, the samples were collected more than three weeks apart. The most frequently isolated microorganisms were *H. influenzae* (55.6%, 10 out of 21 isolates), followed by *P. aeruginosa* (14.3%, 3 out of 21 isolates), *K. aerogenes* (9.5%, 2 out of 21 isolates) and *E.cloacae*, *S.maltophilia* and *E.coli* with 4.8% of the isolates (1 out of 21 isolates). Notably, *Pseudomonas aeruginosa* and Enterobacterales isolates are associated with nosocomial respiratory infections, including ventilator-associated pneumonia or tracheobronchitis, and aspirative pneumonia. *H. influenzae* isolates are commonly associated with bacterial superinfections in patients with active viral infections.

DISCUSSION

H. influenzae, M. catarrhalis, and *S. pneumoniae* are common colonizers of the oropharynx and can also cause bacterial conjunctivitis and otitis by spreading from the respiratory tract to the ear and conjunctiva [2]. Additionally, Enterobacterales, *S. aureus*, *P. aeruginosa*, and *A. baumannii* are pathogens causing HAP, the most common infection in the intensive care unit (ICU) [6]. These microorganisms can also cause hospital-acquired conjunctivitis. Although in our study we did not analyze viral conjunctival infections, viruses such as RSV and SARS-CoV-2 can cause conjunctivitis, albeit less frequently. For instance, in the study conducted by Wrotek *et al.* [7], focusing on the prevalence of complications in hospitalized children due to RSV, among 111 children examined, 12 also presented with conjunctivitis. Regarding COVID-19, a meta-analysis published by Nasiri *et al.* [8] revealed that among 7300 patients with COVID-19, the pooled prevalence of ocular manifestations was 11.03%, with conjunctivitis being the most prevalent ocular condition (88.8%).

Table 1 Age, samples and microorganisms isolated in each patient

Patient*	Age	BAS microorganism isolated	Conjunctival microorganism isolated	Difference in days between the two samples	Antimicrobial resistance features	Respiratory infection
1	1 month	*H. influenzae*	*H. influenzae*	17	Positive betalactamase. Same susceptibility pattern	RSV + bacterial superinfection
2	3 months	*P. aeruginosa*	*P. aeruginosa*	Same day	Same susceptibility pattern	Hospital acquired respiratory infection
3	6 months	*K. pneumoniae*	*H. influenzae*	50	Not the same microorganisms	Hospital acquired respiratory infection
4	12 months	*H. influenzae*	*H. influenzae*	1	Negative betalactamase. Same susceptibility pattern	RSV + bacterial superinfection
5	7 months	*H. influenzae*	*H. influenzae*	Same day	Negative betalactamase	Ventilator associated pneumonia (VAP)
6	22 months	*P. aeruginosa*	*H. influenzae*	28	Not the same microorganisms	Aspirative pneumonia
7	1 month	*H. influenzae*	*H. influenzae*	Same day	Negative betalactamase. Same susceptibility pattern	RSV + bacterial superinfection
8	15 days	*H. influenzae*	*H. influenzae*	Same day	Negative betalactamase. Same susceptibility pattern	RSV + bacterial superinfection
9	16 days	*H. influenzae*	*H. influenzae*	Same day	Negative betalactamase. Same susceptibility pattern	RSV+ bacterial superinfection
10	2 months	*H. influenzae*	*H. influenzae*	1	Negative betalactamase. Same susceptibility pattern	Pertussis and bacterial superinfection
11	15 days	*H. influenzae*	*H. influenzae*	1	Negative betalactamase. Same susceptibility pattern	Rhinovirus + bacterial superinfection
12	5 months	*E. coli*	*E. coli*	3	Same susceptibility pattern	Tracheobronchitis associated to mechanical ventilation
13	1 month	*P. aeruginosa* + *S. marcescens*	*S. aureus*	Same day	Not the same microorganisms	RSV + bacterial superinfection
14	6 months	*K. aerogenes*	*K. aerogenes*	2	Same susceptibility pattern	Ventilator associated pneumonia
15	1 month	*H. influenzae*	*H. influenzae.*	Same day	Negative betalactamase. Same susceptibility pattern	Metapneumovirus + bacterial superinfection
16	17 months	*P. aeruginosa VIM*	*P. aeruginosa*	39	Rectal colonization with *P. aeruginosa* VIM	Nosocomial respiratory infection
17	13 months	*K. aerogenes*	*K. aerogenes*	2	Same susceptibility pattern	Hospital acquired respiratory infection
18	8 months	*P. aeruginosa*	*P. aeruginosa*	10	Same susceptibility pattern	Hospital acquired respiratory infection
19	6 months	*E. cloacae*	*E. cloacae*	7	Same susceptibility pattern	Aspirative pneumonia
20	6 months	*S. maltophilia*	*S. maltophilia*	1	Same susceptibility pattern	Hospital acquired respiratory infection
21	3 months	*H. influenzae*	*H. influenzae*	Same day	Negative betalactamase. Same susceptibility pattern	RSV + bacterial superinfection

*The years have been avoided to ensure the anonymity of the samples and the patients.
BAS: Bronchial aspirates, RSV: Respiratory syncitial virus.

In our observational study, we searched for patients admitted to the PICU who underwent sampling of bronchial aspirate and conjunctival swabs. We collected patients with positive cultures for significant microorganisms, as described above. We observed an 85.7% agreement between the microorganisms isolated in both types of samples.

Given the high degree of concordance between microorganisms in both types of samples, we question whether the conjunctival swab could be useful in predicting which microorganism is causing the respiratory infection. There is currently no scientific evidence on the usefulness of the conjunctival swab for this purpose. However, there are manuscripts describing the usefulness of the methicillin-resistant *S. aureus* (MRSA) nares screening (MNS) to help limit empiric anti-MRSA antibiotic therapy in both children and adults [9,10]. The specificity and the negative predictive value of the MNS to predict a clinical MRSA infection were both 95.5% and it has proven to be useful for limiting unnecessary anti-MRSA therapy, making it a useful antimicrobial stewardship tool for hospitalized children [9]. Additionally, rectal colonization studies for the detection of carbapenemase-producing microorganisms appear to be useful in predicting sepsis caused by these microorganisms. Colonized patients are more likely to develop bacteremia due to these microorganisms than those who are not colonized [11]. Therefore, a prospective study to corroborate our observation is mandatory. The conjunctival swab could be useful in predicting the microorganism that is causing the respiratory infection if similar results are obtained. This prospective study should be designed without the limitations of our retrospective study, including a small number of patients and patients with a conjunctival swab who had clinical conjunctivitis rather than being included as part of colonization studies. Therefore, conjunctival swabs should be taken as part of colonization studies without clinical symptoms to determine whether there is a coincidence with the microorganisms isolated in respiratory specimens.

In conclusion, we observed a high coincidence between the microorganisms isolated in both types of samples. These results provide the basis for future prospective studies to evaluate the conjunctival swab as a tool for predicting the microorganisms that are causing respiratory infection. The usefulness of the conjunctival swab in the identification of microorganisms causing respiratory pathology in children should be tested. The conjunctival swab could have potential use as a tool for antimicrobial stewardship programs in patients with respiratory bacterial infection or superinfection for adjustment of antibiotic therapy in cases where bronchial aspirate or respiratory samples cannot be obtained.

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None to declare

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Hu YL, Lee PI, Hsueh PR, *et al.* Predominant role of *Haemophilus influenzae* in the association of conjunctivitis, acute otitis media and acute bacterial paranasal sinusitis in children. Sci Rep 2021; 11. 2021 Jan 8;11(1):11. doi: 10.1038/s41598-020-79680-6.
2. Teweldemedhin M, Gebreyesus H, Atsbaha AH, Asgedom SW, Saravanan M. Bacterial profile of ocular infections: a systematic review. BMC Ophthalmol 2017; 17(1):212. doi: 10.1186/s12886-017-0612-2.
3. Hedberg P, Johansson N, Ternhag A, Abdel-Halim L, Hedlund J, Nauclér P. Bacterial co-infections in community-acquired pneumonia caused by SARS-CoV-2, influenza virus and respiratory syncytial virus. BMC Infect Dis 2022; 22(1):108. doi: 10.1186/s12879-022-07089-9.
4. Lin HC, Liu YC, Hsing TY, *et al.* RSV pneumonia with or without bacterial co-infection among healthy children. J Formos Med Assoc 2022; 121(3):687-693. doi: 10.1016/j.jfma.2021.08.012..
5. Hishiki H, Ishiwada N, Fukasawa C, *et al.* Incidence of bacterial coinfection with respiratory syncytial virus bronchopulmonary infection in pediatric inpatients. J Infect Chemother 2011; 17(1):87-90. doi: 10.1007/s10156-010-0097-x.
6. Leone M, Bouadma L, Bouhemad B, *et al.* Hospital-acquired pneumonia in ICU. Anaesth Crit Care Pain Med 2018; 37(1):83-98. doi: 10.1016/j.accpm.2017.11.006.
7. Wrotek A, Kobiałka M, Grochowski B, Kamińska I, Pędziwiatr K, Skoczek-Wojciechowska A, Godek M, Jackowska T. Respiratory Complications in Children Hospitalized with Respiratory Syncytial Virus Infection. Adv Exp Med Biol. 2020;1279:113-120. doi: 10.1007/5584_2020_530
8. Nasiri N, Sharifi H, Bazrafshan A, Noori A, Karamouzian M, Sharifi A. Ocular Manifestations of COVID-19: A Systematic Review and Meta-analysis. J Ophthalmic Vis Res. 2021 Jan 20;16(1):103-112. doi: 10.18502/jovr.v16i1.8256.
9. Sands A, Mulvey N, Iacono D, Cerise J, Hagmann SHF. Utility of Methicillin-Resistant Staphylococcus aureus Nares Screening in Hospitalized Children with Acute Infectious Disease Syndromes. Antibiotics (Basel) 2021; 10(12):1434. doi: 10.3390/antibiotics10121434.
10. Parente DM, Cunha CB, Mylonakis E, Timbrook TT. The Clinical Utility of Methicillin-Resistant *Staphylococcus aureus (*MRSA) Nasal Screening to Rule Out MRSA Pneumonia: A Diagnostic Meta-analysis With Antimicrobial Stewardship Implications. Clin Infect Dis 2018; 67(1):1-7. doi: 10.1093/cid/ciy024.
11. Ara-Montojo MF, Escosa-García L, Alguacil-Guillén M, *et al.* Predictors of mortality and clinical characteristics among carbapenem-resistant or carbapenemase-producing Enterobacteriaceae bloodstream infections in Spanish children. J Antimicrob Chemother 2021; 76(1):220-225. doi: 10.1093/jac/dkaa397.