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Determinants of antibiotic use in hospitalized children with confirmed adenoviral upper respiratory tract infection: a retrospective single-center study

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ABSTRACT

Introduction: The aim of this study was to identify clinical, demographic, and laboratory factors associated with the initiation of antibiotic therapy in children hospitalized with confirmed adenoviral upper respiratory tract infection, as well as to assess determinants of potentially avoidable antibiotic use.

Material and methods: A retrospective, single-center observational study was conducted based on medical records of children aged 0–18 years hospitalized between 2019 and 2025 in a pediatric infectious diseases department. Inclusion required a diagnosis of adenoviral infection confirmed by antigen testing. Patients with concomitant bacterial infections requiring antibiotics were excluded. Collected data included age, sex, day of illness at admission, and C-reactive protein (CRP) levels. Antibiotic use before and during hospitalization was analyzed. Statistical analysis included the Mann-Whitney *U* test and χ^2 test, with $p < 0.05$ considered significant.

Results: Eighty children were included in the analysis. Overall, 60% of patients received antibiotics, most frequently prior to hospital admission. No statistically significant difference in CRP levels was observed between children treated and not treated with antibiotics ($p = 0.24$). In contrast, age was significantly associated with antibiotic administration; antibiotics were used in 84% of children older than 2 years compared with 40% of younger patients. A decreasing trend in antibiotic use was observed over the study period, from 89% in 2019–2022 to 50% in 2025.

Conclusions: Antibiotic use in adenoviral infections was primarily driven by clinical presentation rather than objective inflammatory markers. C-reactive protein was not a reliable predictor of antibiotic initiation. The observed temporal decline in antibiotic use suggests improving stewardship practices. Early and wider implementation of rapid adenoviral diagnostics may further reduce unnecessary antibiotic therapy.

KEY WORDS:

C-reactive protein, adenovirus, antibiotic therapy, upper respiratory tract infection.

INTRODUCTION

Infections caused by human adenoviruses (HAdV) constitute an important epidemiological, clinical, but also therapeutic problem for contemporary medicine. The in-

cidence of HAdV infection peaks in infants and children between 6 months and 5 years of age [1]. Adenoviruses usually are transmitted by respiratory tract secretions through person-to-person contact, airborne droplets and

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fomites. The incubation period for respiratory tract infection is 2–14 days [2].

More than 100 genotypes and 52 serotypes of HAdV have been identified and classified into seven species designated HAdV-A through G. Different types display different tissue tropisms that correlate with clinical manifestations of infection [3]. Replication and release of adenovirus in the respiratory system may persist for many months, even in the absence of symptoms [4].

In clinical practice, adenoviral infections may imitate bacterial infections both in terms of physical findings and the intensity of the inflammatory response, which is reflected in a significant increase in C-reactive protein (CRP). A high frequency of fever, pharyngeal and palatine tonsil hyperemia, cough and auscultatory changes in the form of crackles have been described as the most common symptoms of those infections. Consequently, therapeutic decisions taken under conditions of diagnostic uncertainty may lead to the implementation of antibiotic therapy despite the absence of bacterial etiology of infection [4, 5].

Importantly, not all patients with HAdV infections or viremia require treatment at all. Treatment remains exclusively symptomatic [6, 7].

In the era of increasing microbial resistance to antibiotics, the rationalization of antibiotic therapy constitutes one of the key challenges of medicine. In this context, adenoviral infections of the upper respiratory tract require particular attention, as they combine a high frequency of occurrence in the pediatric population with a marked inflammatory response and significant clinical similarity to bacterial infections. Understanding the mechanisms leading to decisions to start antibiotic therapy is of great importance for optimizing therapeutic management and limiting unjustified antibiotic therapy [8].

The aim of this study was to identify clinical, demographic, and laboratory determinants influencing the initiation of antibiotic therapy, as well as to characterize factors that may support the avoidance of inappropriate or unwarranted antibiotic use.

MATERIAL AND METHODS

STUDY DESIGN

A retrospective, single-center observational study was conducted, based on the analysis of the medical records of all consecutive patients meeting the inclusion criteria.

IDENTIFICATION AND SELECTION OF PATIENTS

The study included patients aged 0–18 years hospitalized in the Department of Infectious Diseases and Pediatrics of the Żeromski Specialist Hospital – in the years 2019–2025, in whom the diagnosis of adenoviral upper respiratory tract infection was coded according to ICD-10 as B34.0 (adenoviral infection, unspecified) or B97.0 (ade-

noviruses as the cause of diseases classified in other chapters). In the analyzed center, the assignment of the above codes was preceded by a positive adenovirus antigen test result. After 2020, a rapid combo-type immunochromatographic test was introduced into routine diagnostics, detecting antigens of influenza virus types A and B, adenovirus, *Mycoplasma pneumoniae*, and SARS-CoV-2 (Assure Tech, Hangzhou, China; distribution: Hydrex Diagnostics, Poland). The test was performed on admission in all patients with symptoms of respiratory tract infection, and the results were interpreted as point-of-care tests.

For each patient, demographic and clinical data were obtained, including age, sex, year of hospitalization, CRP concentration on admission and day of illness at the time of admission.

Among them, the frequency of antibiotic use before hospital admission and during hospitalization in the department was recorded, while also registering the specific antibiotic administered in each case.

Patients with concomitant bacterial infection, which justifiably required the use of antibiotic therapy, were excluded from the analysis ($n = 5$): two patients with acute sinusitis, two with otitis media, and one with pneumonia.

The reference range for CRP is 0–5 mg/l.

Informed consent for hospitalization and for the use of anonymized medical data for scientific purposes was routinely obtained from all patients' legal guardians at the time of hospital admission. This study was based on a retrospective analysis of anonymized electronic medical records of hospitalized patients.

STATISTICAL ANALYSIS

Quantitative data, such as patients' age, CRP concentration, and day of illness at admission, were presented as means with standard deviation, medians, and minimum and maximum values. Qualitative data, including sex, year of hospitalization, and administration of an antibiotic, were presented as numbers and percentages.

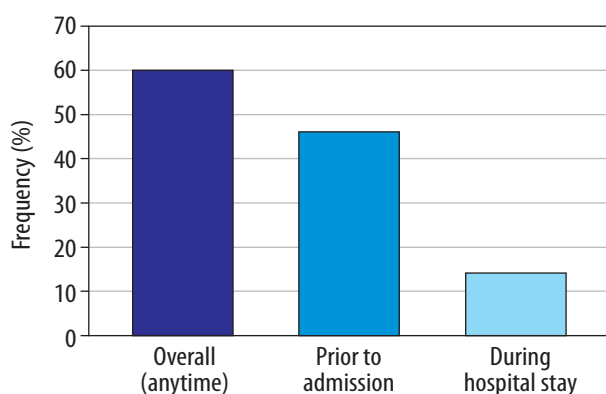
Relationships between antibiotic administration and selected demographic and clinical variables were analyzed. C-reactive protein concentration between children treated and not treated with antibiotics was compared using the Mann-Whitney U test, while the association between CRP categories (≥ 50 mg/l; < 50 mg/l) and antibiotic use was analyzed using the χ^2 test. The relationship between antibiotic administration and age group (≤ 2 years; > 2 years) was assessed using the χ^2 test. A p -value < 0.05 was considered significant. The results of statistical tests and descriptive analyses were presented in tabular form and with the help of charts.

RESULTS

A total of 80 patients hospitalized due to adenoviral respiratory tract infection were included in the analysis,

TABLE 1. Characteristics of the study population ($N = 80$)

Characteristics	Number (%) / median (IQR)
Sex	
Male/female	48 (60)/32 (40)
Age	
Median of years (IQR)	2 (1–5)
< 12 months	6 (7.5)
1–2 years	37 (46.25)
3–4 years	15 (18.75)
5–6 years	14 (17.5)
≥ 7 years	8 (10)

**FIGURE 2.** Frequency of antibiotic initiation: overall; before admission; during hospitalization

after excluding 5 children with concomitant bacterial infection.

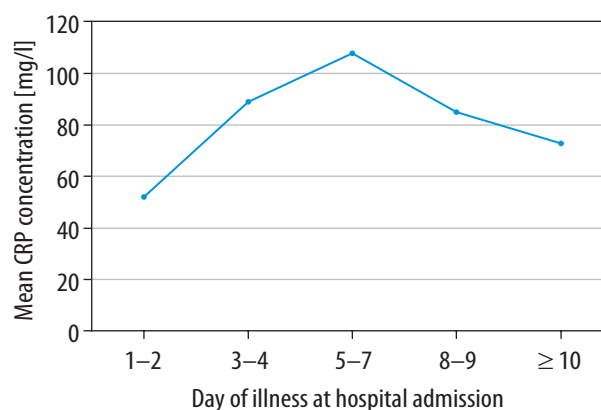
In the study population, boys constituted 60% ($n = 48$), and girls 40% ($n = 32$), with the youngest patient aged 5 months and the oldest aged 15 years. When analyzing the distribution by age groups, the largest group consisted of children aged 1–2 years ($n = 37$). Detailed data are presented in Table 1.

The highest number of patients were hospitalized in 2023 ($n = 34$), 2025 ($n = 24$), and 2024 ($n = 16$). In the remaining years, the number of admissions was significantly lower: 2022 – 7 patients, 2020 – 2 patients, and 2019 – 1 patient. This reflects the fact that widespread virus testing was only introduced after the COVID-19 pandemic, and cases were rarely identified before that.

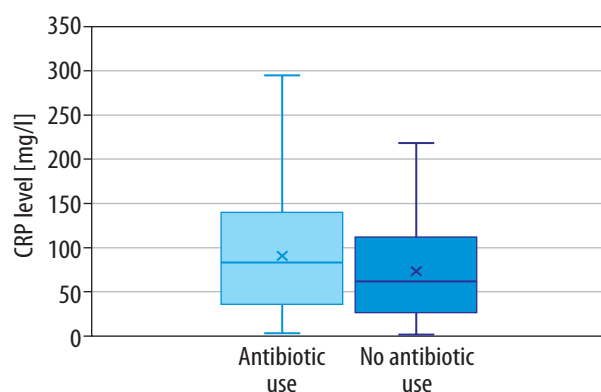
The day of illness at the time of admission to hospital averaged 4.85 ± 3.24 days, with a median of 4 days.

The C-reactive protein on admission averaged 86 ± 64 mg/l, and the median was 76 mg/l. The maximum recorded concentration was 295 mg/l. Mean CRP changed depending on the day of illness at admission. Initially (days 1–2), the mean values were relatively low (52 mg/l), then increased, reaching a peak on days 5–7 (108 mg/l), after which they gradually decreased on subsequent days, reaching a mean of 73 mg/l on day ≥ 10 (Figure 1).

In total, at any point during the illness, an antibiotic was used in 48 patients, which constituted 60% of the study

**FIGURE 1.** Mean C-reactive protein concentration depending on the day of illness at admission

CRP – C-reactive protein concentration

**FIGURE 3.** C-reactive protein levels according to antibiotic administration

CRP – C-reactive protein concentration

population. Of these, 46% ($n = 37$) received an antibiotic before hospital admission, and 11 patients (14%) during hospitalization. These data are visualized in Figure 2. The most commonly used antibiotics were, in order amoxicillin, cephalosporins (cefuroxime, ceftriaxone), phenoxymethylpenicillin and crystalline penicillin.

Analysis of the relationship between children's age and the decision to administer an antibiotic showed a clear and statistically significant difference between age groups. Among children older than 2 years, an antibiotic was used in 84% of patients (31 of 37 patients), whereas in the group of children ≤ 2 years it was used in 17 of 43 patients which accounted for 40% (χ^2 test, $p = 0.000056$).

C-reactive protein concentration was analyzed both as a continuous and categorical variable. When treated as a continuous variable, no statistically significant difference was found between children treated and not treated with antibiotics (Mann-Whitney U test, $p = 0.24$) (Figure 3). Similarly, when analyzed categorically, no significant association between CRP categories and antibiotic use was observed (χ^2 test, $p = 0.25$) (Table 2).

The percentage of hospitalized children who received an antibiotic decreased in successive years: in 2019–2022 an antibiotic was used in 8 of 9 children (89%), in 2023 in 20 of 32 children (63%), in 2024 in 8 of 15 children (53%),

TABLE 2. Frequency of antibiotic use depending on C-reactive protein concentration ranges

CRP group [mg/l]	Total number of children	Number of children receiving antibiotics	Percentage
≥ 50	51	33	65
< 50	29	15	52

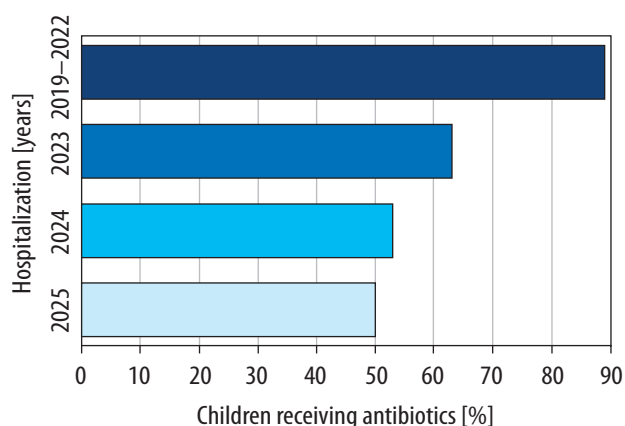


FIGURE 4. Trend of changes in the percentage of children receiving an antibiotic in the years 2019–2025

and in 2025 in 12 of 24 children (50%). This relationship is presented in Figure 4.

DISCUSSION

The present study demonstrates that antibiotic therapy is used in a significant proportion of children with adenoviral respiratory tract infection despite its viral etiology.

An important observation was that in the majority of cases antibiotic therapy was implemented in outpatient settings, whereas during hospitalization the proportion of children receiving an antibiotic was clearly lower. In outpatient care, the therapeutic decision is based mainly on the clinical picture, which may imitate a bacterial infection, especially streptococcal tonsillitis, which increases the risk of inadequate administration of antibiotics in this group of patients. Also in primary care settings, CRP levels are not routinely assessed; inflammatory markers are often assessed only after hospital admission. Secondly, in hospital conditions, rapid viral diagnostics, including antigen tests, are routinely performed, which enables early confirmation of the etiology and more frequent withdrawal from antibiotic therapy. This difference emphasizes the importance of the availability of diagnostic tests in the rationalization of treatment.

In available clinical studies [9, 10] it has been shown that adenoviral infections in children often develop with symptoms significantly resembling bacterial infections. A high frequency of fever (91.9%), cough (83.9%), pharyngeal hyperemia (62.3%), as well as auscultatory changes in the form of crackles (32.6%) has been described. In the vast majority of patients, significantly elevated CRP concentration (93.9%) was also found. These symptoms may clinically suggest bacterial etiology, which in practice may lead to diagnostic difficulties and increased fre-

quency of initiation of antibiotic therapy despite the viral background of the infection and the lack of signs and symptoms of the bacterial superinfection. Rapid antigen detection tests for *Streptococcus pyogenes* were performed selectively in patients with clinical features that require differential diagnosis of streptococcal pharyngitis. In hospital practice, StrepTests were performed infrequently, mainly in children presenting with tonsillar exudates, lymphadenopathy, and elevated inflammatory markers, while many tests were performed in primary care prior to hospitalization. At the same time, caution is required due to the possibility of bacterial carriage, as patients may present with a concomitant viral infection and pharyngeal streptococcal colonization. Therefore, the test result should not be interpreted in isolation from the clinical picture. We do not aim to treat the test result itself, but the patient as a whole, taking into account primarily the clinical presentation.

The results of the present study are consistent with the observations of other authors that adenoviral infection is particularly often associated with the initiation of antibiotic therapy. In a study published in 2024 in Italy [10] it was shown that among 98 children with confirmed adenoviral infection, as many as 78% of patients received an antibiotic, whereas in the case of other viral respiratory tract infections this percentage was 27%. These data confirm that adenovirus constitutes a particular diagnostic and therapeutic challenge and requires special caution in making treatment decisions.

In another Italian cohort study, Buonsenso *et al.* [11] retrospectively analyzed 258 children with confirmed adenoviral lower respiratory tract infection. Antibiotics were used in 61% of patients, although bacterial co-infection was found in only about 7% of children. The authors, similarly to the present analysis, in this way emphasize the scale of the problem of unjustified antibiotic therapy in patients with adenoviral infection. Similarly, a decreasing percentage of children receiving an antibiotic in subsequent years was observed. The authors from Italy linked this decline with the introduction of rapid viral diagnostics and the period after the COVID-19 pandemic, which is consistent with the trend visible in our cohort. During the pandemic period (2020–2021), due to sanitary restrictions, all respiratory droplet-transmitted infections were reported with significantly lower incidence. Conversely, the year 2019 was still a pre-pandemic period, and routine viral testing had not yet been introduced at that time. Routine viral testing in patients with respiratory symptoms was introduced only after the COVID-19 pandemic, which increased the number of diagnoses from 2022 onward. These aspects further support the multifactorial nature of the observed differences.

In the same study, a statistically significant relationship was demonstrated between higher CRP values and more frequent initiation of antibiotic therapy. In contrast to these observations, in our cohort this relationship was not considered statistically significant. Although it has been scientifically confirmed that CRP in the course of adenoviral infections is often significantly elevated [12], making therapeutic decisions more difficult, the results from our center suggest that CRP concentration alone is not an unambiguous factor determining the initiation of an antibiotic. It may, however, coexist with other clinical and demographic factors that together influence therapeutic management.

In our analysis, the patient's age was a significant factor influencing the decision to initiate antibiotic therapy. Interestingly, antibiotics were administered more frequently in children older than 2 years, whereas younger children received them less often. This finding is somewhat unexpected, as one might intuitively anticipate broader antibiotic coverage in younger children. A possible explanation is that in older children the clinical presentation more closely resembles bacterial infections, which may increase the likelihood of initiating antibiotic therapy. This may also reflect a more cautious approach by clinicians in the management of very young children, who may have a less predictable clinical course and a higher perceived risk of complications. Importantly, these observations are consistent with previously published data [13] indicating that older age is a key determinant of expert antibiotic recommendations, with inappropriate antibiotic prescriptions highlighting the need for strengthened antibiotic stewardship in pediatric emergency departments. This further supports the notion that decision-making in adenoviral infections is multifactorial in nature and is not based exclusively on CRP values.

Given that elevated CRP levels are frequently observed in children with adenoviral infection, we reviewed available studies to guide the selection of a clinically relevant threshold. In one study [12], the median CRP concentration was 49 mg/l, while in another pediatric cohort with confirmed adenoviral infection [10], the mean CRP level was 50.8 ± 54.2 mg/l. Therefore, the cut-off value of 50 mg/l used in the present study was derived from these observations and applied to distinguish between lower and higher inflammatory response. For comparison, in other viral respiratory infections, CRP levels are considerably lower. In RSV infection, median CRP concentrations were 10.4 mg/l in children with acute bronchiolitis [14] and 1.94 mg/l in another cohort [15], indicating a relatively mild systemic inflammatory response. Also, in a comparative study [16], mean CRP levels were 18.21 ± 34.79 mg/l in COVID-19 and 18.37 ± 28.82 mg/l in influenza A, suggesting comparable and overall moderate inflammatory responses in these viral infections. These values are markedly lower than those observed in adenoviral infections which further emphasizes that those infections represent a distinct clinical entity among viral respiratory infections, warrant-

ing particular attention in the context of inflammatory markers and therapeutic decision-making.

Despite the observed significant frequency of antibiotic use in children with adenoviral respiratory tract infection, in our cohort more than 70% of patients hospitalized in the department were treated without an antibiotic (individual symptomatic treatment together with observation). This result emphasizes that responsible management and refraining from unjustified antibiotic therapy are possible and constitutes an essential element of the rationalization of treatment, contributing to limiting the risk of increasing microbial resistance to antibiotics.

To our best knowledge, this is one of the few studies emphasizing that the clinical picture rather than elevated CRP levels may play a more important role in decisions regarding antibiotic therapy in children with adenoviral infections.

This study has limitations related to its retrospective design and the lack of detailed information regarding the reasons for initiating antibiotic therapy before hospital admission.

CONCLUSIONS

The main factor influencing the use of antibiotics in adenoviral infections was a clinical presentation mimicking bacterial infection. Elevated CRP levels were associated with increased antibiotic use; however, this relationship was not statistically significant. Early laboratory confirmation of adenoviral infection is crucial for reducing unnecessary antibiotic therapy. Within the framework of rational antibiotic stewardship, emphasis should be placed on implementing diagnostic assays for the detection of adenoviral antigens and DNA in respiratory tract specimens, particularly when obtained at an early stage of infection and in primary care settings.

DISCLOSURES

1. Institutional review board statement: This study was approved by the Ethics Committee of the Regional Medical Chamber in Cracow (approval decision no. OIL/KBL/19/2026, dated: 26.02.2026).
2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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