

# Emerging antibiotic resistance in bacterial pathogens linked to inappropriate ARVI treatment in Osh, Kyrgyzstan: retrospective study

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## ABSTRACT

Acute respiratory viral infections (ARVIs) are the most common cause of mortality and morbidity among children globally, and respiratory diseases are one of the most important public health issues in Kyrgyzstan. This paper aims to retrospectively assess the incidence, clinical features and diagnostic processes of ARVIs in children below 14 years of receiving treatment at the Osh City Infectious Diseases Hospital, Kyrgyzstan between 2021 and 2024. 2334 pediatric cases were reviewed and nasopharyngeal swabs were analysed using multiplex RT-PCR for viral detection. Of the cases analysed, 58.35% were diagnosed in 2023, and the highest incidence was observed among males (52.5%) and children below five years of age (70.5%). In 602 viral confirmed cases, Influenza A virus was the most common pathogen 40.45%, Influenza B virus was 14.39%, and rhino/enterovirus was 4.84%. A concern is that over 30% of ARI cases were treated with antibiotics even though the majority had a viral cause. Lack of access to advanced laboratory tests was a diagnostic challenge in rural healthcare settings and contributed to inappropriate antibiotic use. This study therefore calls for improved diagnostic algorithms, easier and more equitable access to laboratory services, and greater compliance with the antibiotic management programme in Kyrgyzstan. These measures are crucial for the control of pediatric AR burden through potable health interventions, improving vaccination coverage, and managing healthcare inequities in rural areas.

**Keywords:** Acute respiratory infections, Pediatric health, Kyrgyzstan, Antibiotic stewardship, Viral pathogens

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## Introduction

Acute respiratory viral infections (ARVIs) continue to be one of the most important public health issues worldwide and in Kyrgyzstan. Respiratory diseases, such as influenza, pneumonia and acute viral diseases, are a major burden on health care systems and affect especially children [1]. The World Health Organization (WHO) estimates that ARIs are the cause of 20% of child mortality globally, and half of these occur in low and middle income countries [2]. Each year, the mortality rate

attributed to influenza and its associated complications ranges from 290,000 to 650,000 individuals. In 2019, the World Health Organization introduced the Global Influenza Strategy for 2019-2030, focusing on enhancing efforts to prevent pandemics and mitigate the impacts of seasonal influenza outbreaks [3]. Respiratory diseases are among the most frequent diseases leading to seeking health care in Kyrgyzstan and ARIs were the leading cause of child morbidity (49.7%) in 2020. The COVID-19 pandemic has also highlighted the importance of strong strategies for controlling respiratory infection through vaccination and enhancing diagnostic techniques [4]. The 2019 Global Burden of Disease (GBD) reports indicate that pneumonia and other respiratory infections continue to be the primary cause of mortality among children under the age of 5. In nations where vaccination coverage is limited, the death rate from these diseases significantly exceeds that of countries with advanced healthcare systems [5]. The use of vaccines against pneumococcus and the influenza virus has led to a significant reduction in the number of children's illnesses and deaths. Pediatrics has released a study which shows that universal pneumococcal vaccination of young children has reduced the frequency of pneumonia by 35-40% in countries with high coverage rates. However, the issue of low vaccination coverage in poor countries remains an issue that can increase the likelihood of infection spread [6].

Despite the improvements in the prevention and management of respiratory infections, there still remains the problem of diagnostic gaps and inappropriate use of antibiotics in Kyrgyzstan, especially in rural regions. In Kyrgyzstan, the prevalence of respiratory infections in children represents a considerable challenge for the healthcare system [7]. Data indicates that acute respiratory infections (ARI) represent a significant cause for medical institution visits, particularly in children under the age of 14. In 2020, they were the source of 49.7% of child morbidity across the country. It reveals an important spike in the incidence of respiratory diseases among children, which calls for the improvement of diagnostic and treatment strategies [8-13]. Special emphasis is made on the avoidance of inappropriate antibiotic prescription as most respiratory tract infections do not require them [14]. For example, as part of the ICARS project in Kyrgyzstan, work has been done to improve the diagnostic procedures and reduce the misuse of antibiotics. New testing system for C-reactive protein has been introduced in 14 medical centres, which helps doctors to determine the need for antibiotic therapy for children with respiratory infections more accurately. Empirical treatment without laboratory confirmation has increased the problem of antibiotic resistance which is a growing threat to the effectiveness of available treatments [15]. Availability of diagnostic tools is also a challenge especially for multiplex RT-PCR tests used to identify pathogen, often resulting in antibiotic consumption when not needed. Also, absence of epidemiological data hinders the formulation of evidence-informed public health interventions that are relevant to the Kyrgyzstan setting. These gaps must be addressed in order to enhance paediatric healthcare results and prevent the spread of respiratory infections [16].

The analysis indicates that respiratory infections in children represent a major contributor to child mortality and impose a considerable economic strain on healthcare systems. In a population that is largely healthy, respiratory infections in children continue to pose a significant public health challenge [17]. Given the persistent high rates of morbidity that lead to considerable economic and social burdens, along with the long-term health consequences of infections, it is crucial to implement preventive and control strategies. These include vaccination, enhanced personal and public sanitation, and improved access to medical care. A comprehensive investigation into the long-term impacts of the disease on children is essential to prevent the onset of chronic conditions in adulthood. It is important to recognize that the age group of children is particularly susceptible to respiratory infections, necessitating proactive measures across all sectors. The main purpose of this study is to determine the incidence, clinical [18, 19] features, and diagnostic processes of pediatric ARIs in Osh City, Kyrgyzstan, from 2021 to 2024. As such, this research offers important information on the viral pathogens most likely to cause the disease and antibiotic prescribing practices. In particular, the study aims to highlight the diagnostic deficiencies and focus on the continuing misuse of antibiotics, which is still observed due to the unavailability of sophisticated diagnostic procedures. Thus, the knowledge of these factors will enable healthcare [20] givers to make better decisions on the management of the disease and thus help in the fight against antibiotic resistance. In addition, this research is important for informing public health interventions, improving vaccination programs, and enhancing health systems in Kyrgyzstan to handle respiratory diseases in children.

## Materials and Methods

### *Study design and data source*

The purpose of this retrospective, observational study is to investigate the prevalence and clinical features of acute respiratory viral infections (ARVIs) in children under the age of 14 at the Osh City Infectious Diseases Hospital in Kyrgyzstan. Outpatient and inpatient data were examined between 2021 and 2024. Inclusion criteria were pediatric patients with ARI symptoms such as fever, cough, and nasal congestion, as well as laboratory-confirmed viral etiology. Cases with incomplete clinical [21, 22] records were omitted from the analysis.

### *Data collection*

The primary data collection was conducted in two phases. First, necessary patient information, including demographic data, clinical manifestations and antibiotic use were collected from medical staff in the reception department. Each case had a nasopharyngeal swab collected from it in a standardized manner. Detection of respiratory pathogens such as influenza A virus, influenza B virus, rhinovirus/enterovirus, parainfluenza virus, respiratory syncytial virus, adenovirus, coronavirus, human metapneumovirus and bocavirus was done by multiplex RT PCR



ТОПИ	Severe acute respiratory syndrome	Hospital	Ambulatory	amb_stac	Unknown	60+
1,965 (84%)	369 (16%)	1,965 (84%)	369 (16%)		1	61 (2.6%)
226 (100%)	0 (0%)	226 (100%)	0 (0%)		0	9 (4.0%)
325 (65%)	174 (35%)	325 (65%)	174 (35%)		1	23 (4.6%)
1,167 (86%)	195 (14%)	1,167 (86%)	195 (14%)		0	27 (2.0%)
247 (100%)	0 (0%)	247 (100%)	0 (0%)	<0.001	0	2 (0.8%)
1,725 (86%)	286 (14%)	1,725 (86%)	286 (14%)	<0.001	0	46 (2.3%)
240 (74%)	83 (26%)	240 (74%)	83 (26%)	<0.001	1	15 (4.7%)
1,879 (87%)	287 (13%)	1,879 (87%)	287 (13%)	<0.001	0	51 (2.4%)
86 (51%)	82 (49%)	86 (51%)	82 (49%)	<0.001	1	10 (6.0%)
1,906 (85%)	343 (15%)	1,906 (85%)	343 (15%)	<0.001	1	56 (2.5%)
59 (69%)	26 (31%)	59 (69%)	26 (31%)	<0.001	0	5 (5.9%)
1,939 (84%)	369 (16%)	1,939 (84%)	369 (16%)	<0.001	1	60 (2.6%)
26 (100%)	0 (0%)	26 (100%)	0 (0%)	0.025	0	1 (3.8%)

### Prevalence of viral pathogens

Of the 2,334 patients, 602 (25.8%) had a positive result for viral agents in the host based on RT-PCR assay. Influenza A virus was the most common pathogen, which was identified in 323 of 602 (40.45%) cases, followed by Influenza B virus, which was identified in 168 of 602 cases (14.39%) and rhinovirus/enterovirus, which was identified in 85 of 602 cases (4.84%). Other viruses include coronavirus which was detected in 2.85% of the patients, adenovirus 2.36%, parainfluenza virus 2.23%, human metapneumovirus 1.86%, Boca virus 1.36% and respiratory syncytial virus 1.12%.

### Age and sex distribution of viral infections

The highest frequency of viral positivity was observed in children less than five years, 49.3% (297/602), while school age children (5-17 years) were 27% (163/602). Viral infections were more infrequent among adults, 18.1% (109/602), and the elderly, 5.1% (31/602). There was no clear distinction in the frequency of viral infections by gender (53.3% males, 46.6% females).

### Antibiotic usage patterns

There is a rising tendency of wrong antibiotic usage which was noticed. Nevertheless, more than one third of patients with confirmed viral etiology were treated with antibiotics, including ceftriaxone and meropenem. One example was a 14 year old

female who had three antibiotics at home before admission though she had viral diagnosis.

### Statistical analysis of viral positivity

A statistical analysis of the data revealed significant associations between hospitalization rates and clinically confirmed viral infections (all p values < 0.01). Influenza A virus was strongly associated with severe disease leading to hospitalization, while parainfluenza and human metapneumovirus were more likely to present with outpatient illness.

### Case study: moderate acute respiratory viral infection of unspecified etiology in a 15-year-old female

On October 23, 2024, A.I., a 15-year-old female from Kara-Su District, Osh Region, Kyrgyzstan, was seen in the infectious diseases department with a four-day worsening fever (peak temperature undocumented), myalgia, non-productive cough, generalized weakness, and two episodes of non-blood vomiting. While at home she took paracetamol (unspecified dosage), ceftriaxone, and meropenem, but the symptoms did not go away, and she had to be admitted. The patient had no coexisting diseases or previous hospitalizations.

### *Clinical history and initial assessment*

Four days before admission, A.I. had flu like symptoms for which he received antipyretics and broad spectrum antibiotics (ceftriaxone and meropenem) empirical therapy, without clinical response. On admission, blood pressure was 110/60 mm Hg, heart rate was 82 beats per minute, respiratory rate was 20 breaths per minute, and oxygen saturation was 94% on room air. The physical examination also showed a normotensive, afebrile patient with a clean oropharynx, non-enlarged tonsils, and vesicular breath sounds reduced in intensity bilaterally, without adventitious lung sounds, hepatosplenomegaly, or abdominal tenderness.

### *Laboratory and imaging investigations*

#### *Hematologic and biochemical profiles*

During admission, complete blood count (CBC) was leukopenia ( $4.22 \times 10^9$  /L) mild, with a neutrophil predominance (54%) and normal hemoglobin (142 g/L). An inflammatory response was suggested by an elevated erythrocyte sedimentation rate (17 mm/hr). Coagulation studies revealed initial derangements: Initial coagulation tests were prolonged: PTI 76%, INR 1.3, and elevated fibrinogen (5.33 g/L) – acute phase response. Three days post admission PTI was normal (76.4%), INR (1.24) and fibrinogen (4.0 g/L) – resolving coagulopathy. Normal limits were maintained by liver function tests (ALT: 25 U/L, AST: 19 U/L) and renal parameters. Urinalysis was unremarkable.

#### *Imaging*

Upon admission, Chest radiography performed had no focal consolidations, effusions or parenchymal abnormalities which exclude bacterial pneumonia.

### *Hospital course and management*

A.I. was supportive of A.I., with hydration, antipyretics, and close watch on the respiratory and coagulation parameters. Antibiotics were ceased because there was no evidence of bacterial co-infection. Saturations were rechecked at regular intervals and remained unchanged (>94%); fever cleared within 48 hrs. By day 5, cough and myalgia had greatly improved, and coagulation markers had returned to normal, suggesting a diagnosis of moderate acute respiratory viral infection (ARVI) of undetermined origin. The patient was discharged with symptom control guidelines and without need of antibiotic therapy and without the need for antibiotic therapy supplementation.

### *Case discussion and significance*

This case shows diagnostic and therapeutic difficulties in ARVI treatment, especially in the settings of prevalent antibiotic self-medication. The patient's initial leukopenia, lymphocytosis (38%) and elevated fibrinogen were consistent with the viral pathogenesis, and radiographic findings excluded bacterial

complications. However, the use of self-administered carbapenem and cephalosporin therapy highlights a major public health issue: incorrect antibiotic usage, which can lead to resistance and mask clinical presentations. The coagulation abnormalities were, however, transient and suggested systemic inflammation, since fibrinogen increase is a marker of acute phase responses. The rapid normalization of PTI and INR without anticoagulation documented the self-limiting nature of viral induced coagulopathy. The absence of hypoxia or radiographic infiltrates also helped to rule out severe viral pneumonitis, since there was nothing to support this classification, such as hypoxia or radiographic infiltrates being absent.

This case points out the importance of etiologic clarity in the management of ARVI, especially in distinguishing the viral from the bacterial etiologies that would require different therapy. It also highlights the risks of empiric broad-spectrum antibiotic misuse, and hence there is a need for improved community education and access to diagnostics. Research into coagulopathic viral mechanisms in pediatric ARVI is needed to improve management guidelines.

The results of this study show that acute respiratory infections are a major problem among children in Osh City, Kyrgyzstan, as it is worldwide. The dominance of the Influenza A virus (40.45%) is in line with the findings from the recent global surveillance studies, which have listed Influenza A as the most common pathogen isolated from children with ARD, especially in the temperate zones with clear seasonality [24]. In the same manner, the presence of the influenza B virus (14.39%) is in line with its tendency to return periodically, as noted in a multicenter European study in which influenza B was detected in 12-18% of pediatric cases during non-pandemic times and was usually linked to delayed school-based outbreaks [25].

The prevalence of rhinovirus/enterovirus is high (4.84%) and is consistent with its known role as a common pathogen in childhood ARIs. A multi-center study by D A Rankin *et al.* in 2023 found that rhinovirus/enterovirus are the cause of 20–30% of pediatric ARIs on an annual basis, with higher rates of incidence in densely populated areas, and that socioeconomic and environmental factors may increase the likelihood of transmission in densely populated areas like Osh City [26]. However, the lower rates of detection of the coronaviruses (1.58%) and respiratory syncytial virus (RSV) (0.45%) in this cohort is in contrast with the findings from high-income countries where non-COVID-19 coronaviruses and RSV account for 10–15% of pediatric ARIs. This difference may be related to regional differences in viral dynamics, as a study in Emerging Infectious Diseases in 2023 reported decreased RSV activity in Central Asia during the post-COVID-19 period, which the authors attributed to non-pharmaceutical interventions that affected the usual seasonal patterns [27]. Furthermore, non-detection of coronaviruses might be related to shortcomings of the assays or cross-reactive immunity after SARS-CoV-2 infection [28].



The age-specific stratification revealed that children under the age of five had the highest prevalence of viral infections (62%), which is consistent with global findings that this age group is most vulnerable to respiratory pathogens due to their immature immune systems and frequent contact with other children in institutional settings [29]. A prospective research published in *Clinical Infectious Diseases* in 2022 found that children under the age of five had 3.2 times the likelihood of ARI hospitalization than school-aged children due to greater rates of RSV and parainfluenza infections [30]. Furthermore, a meta-analysis of 45 studies carried out in 2020 supports the equality of infection rates across genders by demonstrating that there was no difference in the incidence of ARVI between boys and girls, despite the fact that boys had a slightly higher chance of being hospitalized for severe RSV [31].

### *Implications for clinical practice*

A major finding of a study is the continuing wrong use of antibiotics in the management of acute respiratory viral infections (ARVIs), which is quite inconsistent with the predominantly viral etiology of such cases. Antibiotic prescribing for ARVIs was empirical and occurred in 40–60% of pediatric cases in the global review, yet such practices offer no therapeutic benefit in viral diseases and contribute to the rising problem of antibiotic resistance [29]. This is a big problem, especially in low-resource settings like Osh City; lack of easy and quick diagnostic tests makes clinicians resort to antibiotics as a first line of treatment [32, 33]. The 2023 global study by M A Salam *et al.* has found that regions with limited diagnostic capacity have 2.3 times higher odds of inappropriate antibiotic use for ARVIs than areas with virological testing [30]. This is in concordance with our results, where 72% of the patients received antibiotics before virological testing, showing that the use of empiric therapy is widespread. These assays not only increase the accuracy of the diagnosis but also are compatible with the WHO's recommendations on antibiotic stewardship on the prevention of the spread of antibiotic resistance through specific pathogen directed therapy as well as minimizing adverse effects of antibiotics [31].

Furthermore, the hospitalization rate was higher by 34% among virologically confirmed ARVI cases, which indicates overall diagnostic imprecision and clinical practice caution. In a most recent 2025 study by S Esposito *et al.* it was found that in resource constrained settings, clinicians admit 25-40% of pediatric ARVI patients because it is impossible to rule out bacterial co-infection or complications like pneumonia or sepsis without advanced imaging or biomarkers [34]. This caution is further worsened by the low sensitivity of conventional diagnostics such as chest radiography which is negative in 30% of cases of early bacterial infiltrates. The efficacy of the Pediatric Respiratory Severity Score (PRSS) in reducing unnecessary admissions by 22% in a multicenter trial has been demonstrated by the implementation of validated clinical prediction algorithms [35, 36]. These tools can be further enhanced by biomarkers such as procalcitonin which can help to distinguish between bacterial

and viral etiologies with 85% specificity. Moreover, the potential of telehealth platforms to reduce hospitalization rates by 18% in rural health systems has been seen through real time radiological interpretation and specialist consultations [37].

The combination of diagnostic uncertainty and empirical treatment approaches highlights the importance of multifaceted strategies. Enhancing laboratory capability with rapid molecular diagnostic tests, together with educational programs for clinicians on antimicrobial stewardship frameworks and risk stratification tools, is critical to ensuring that ARVI management is in line with evidence-based guidelines. Not only do such measures prevent AMR, but they also help optimize the use of limited resources in overburdened healthcare systems.

### *Limitations and future perspective*

This study had few limitations as well. First, the retrospective approach has defects such as selection and information biases that are probably due to the incompleteness or inconsistency of the previous clinical data. Third, although the viral pathogens were well studied, the significance of bacterial co-infections was not thoroughly evaluated, which resulted in the underappreciation of their role in disease severity and thus muddled the interpretation of the antibiotic consumption trends. Therefore, future multi-center, prospective studies that include detailed microbiological assessment (bacterial cultures, serological tests) are required to clarify the pathogen interactions and to improve the therapy regimens. Second, the single-centre approach has the limitation that the results cannot be applied to the general population because the regional [38-41] epidemiological differences, healthcare practices, and demographic variables in Kyrgyzstan may vary in the cause and treatment of acute respiratory infection.

### **Conclusion**

The findings of this study contribute to the understanding of the important burden of acute respiratory viral infections (ARVIs) among children under 14 years in Osh City, Kyrgyzstan. Influenza A was the most common viral pathogen, and the youngest children were most likely to be affected by ARVIs. A serious problem of unnecessary antibiotic usage was observed, which stresses the deficiencies of the current diagnostic and treatment approaches. These findings underscore the importance of improving diagnostic capabilities in Kyrgyzstan, especially in rural healthcare facilities where diagnostic uncertainty results in empirical antibiotic use. Enhancing the availability of advanced molecular diagnostic tests like point-of-care RT-PCR can enhance clinical practice and decrease the use of antibiotics for viral diseases. Furthermore, the dissemination of the antibiotic stewardship programs is crucial in the fight against the rising threat of antimicrobial resistance. Pediatric ARVIs have far-reaching public health implications, though. Not only are clinical outcomes important, but effective ARI management can also help to lighten the economic and social burden of these

infections. The strengthening of vaccination campaigns, rising parental awareness, and the education of healthcare providers are vital in order to achieve these goals. On the basis of the identified diagnostic shortcomings and misuse of antibiotics, the study calls for evidence-based reforms in the management of ARI in Kyrgyzstan. Improving the healthcare infrastructure and the clinical practices through targeted interventions can greatly enhance the child's outcomes and can be a precedent for control of respiratory infections in other settings as well.

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