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Characteristics of pediatric patients claimed with acute upper respiratory infection during otorhinolaryngology consultations: A descriptive study of a large Japanese medical claims database

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ABSTRACT

This study aimed to clarify other diseases claimed simultaneously with acute upper respiratory infection (URI), antibiotic prescriptions, and examinations associated with infectious diseases in pediatric patients with acute URI insurance claims at otorhinolaryngology outpatient visits. Pediatric patients who visited an otolaryngology department between 2019 and 2021 and were definitively diagnosed with URI were selected using a large Japanese medical claims database. Patient backgrounds, antibiotic use, and examinations were descriptively evaluated. In total, 8010 patients were included in the analysis. The median number (interquartile range) of diseases claimed in the same month as acute URI was 4 (3–6). Only 519 (6.5 %) patients were claimed as acute URI alone. Regardless of the prescription of antibiotics, the most commonly redundantly claimed disease in these patients was allergic rhinitis, followed by acute bronchitis, acute sinusitis, and earwax impaction. The frequently prescribed antibiotics were third-generation cephalosporins, macrolides, and penicillins with extended-spectrum, including amoxicillin which was recommended by the Japanese manual; the proportion of patients with examinations was low (2.9–21.7 %). Among patients with acute URI, diagnoses requiring antibiotics were also claimed; therefore, when evaluating acute URI using the Japanese medical claims database, care must be taken in patient selection. Moreover, the implementation rate of examinations necessary for diagnosis was low, so there is an urgent need to develop an environment where examinations can be conducted in outpatient settings.

Antimicrobial resistance (AMR) has become a global problem in recent years. In Japan, a national action plan on AMR, which requires the promotion of antimicrobial stewardship, was published in 2016 and revised in 2023 [1,2]. Inappropriate antibiotic use includes antibiotics administration for treating viral infections, including acute upper respiratory infection (URI) [3]. The Manual of Antimicrobial Stewardship, published in Japan in 2017 and revised in 2019, recommends that antibiotics should not be used for viral acute URI [4].

WHO categorized antibiotics as "Access," "Watch," "Reserve," and "Not recommended" according to the AWaRe classification to prioritize the use of antibiotics [5]. In Japan, amoxicillin hydrate, classified as "Access" in the AWaRe classification, is recommended for bacterial URI [4]. Furthermore, implementing diagnostic stewardship is essential to promote the appropriate use of antibiotics [6]. In the Manual of Antimicrobial Stewardship, a rapid diagnostic test for Group A β-hemolytic *Streptococcus* is recommended for the diagnosis of acute pharyngitis [4]. Although antibiotic use has been evaluated worldwide, the use of antibiotics based on diagnosis and the implementation status of examinations have not been sufficiently clarified.

In Japan, the medical reimbursement system was revised to introduce a fee for implementing an antimicrobial stewardship fee for pediatric patients in 2018. The medical fees can be obtained if unnecessary

Abbreviations: AMR, antimicrobial resistance; AWaRe, Access Watch Reserve; URI, upper respiratory infection; WHO, World Health Organization.

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antibiotics are not prescribed to pediatric patients and sufficient explanation is given. Furthermore, this medical reimbursement system was expanded to include otorhinolaryngology in 2022. The frequency of antibiotic use in Japanese otorhinolaryngology outpatient clinics is higher than in other departments [7] and needs to be evaluated in the future, but little basic information is available.

In Japan, registering the name of the disease for each prescription and examination at the time of insurance claim is necessary [8]. A study showed that 64.0 % of outpatients in Japan received insurance claims for multiple diseases within the same month [8]. Therefore, patients diagnosed with URI may have registered disease names related to other infectious diseases. However, diseases claimed simultaneously with acute URI have not been previously reported.

In this study, we aimed to clarify other diseases claimed simultaneously with acute URI, antibiotic prescriptions, and examinations associated with infectious diseases in pediatric patients with acute URI insurance claims at otorhinolaryngology outpatient visits.

We used a large Japanese medical claims database provided by IQVIA Solutions Japan K.K. The database is based on information collected from health insurance in Japan, including data on approximately 3.3 % of the whole Japanese population as of fiscal year 2021. Because this study focused on diseases presumed to be claimed simultaneously with acute URI, only diagnosis data related to URI were used (Table S1). The data items included in the tables of drug and medical practice are shown in Tables S2 and S3.

Patients who visited an otolaryngology department between 2019 and 2021 and were definitively diagnosed with URI were selected. Among them, pediatric patients aged <15 years who had received some prescriptions were targeted in this study. (Fig. 1). Patients who visited multiple hospitals and clinics in the same month as acute URI were excluded.

The number of antibiotic prescriptions was calculated per 1000 patients according to the AWaRe classification [5]. Test related to acute pharyngitis, such as rapid diagnostic tests for Group A β-hemolytic *Streptococcus* (Japanese medical practice code: 160044110), throat culture testing (160058210, 160144410, 160144510), and collection of nasal and pharyngeal swabs (160208510) were considered to have been performed if the claims were verified for these reimbursements was confirmed in the same month as acute URI, the examination was considered to have been implemented.

Patient backgrounds, antibiotic use, and examinations were descriptively evaluated. Moreover, diseases claimed in the same month as acute URI were investigated, and the five most frequent diseases were identified in patients with and without antibiotic prescriptions. Stata version 17.0 (Stata Corp LLC, College Station, TX, USA), Excel (Microsoft, Redmond, WA, USA) were used for the analysis. The study was approved by the Ethics Committee of Kyoto Pharmaceutical University (approval number: E-00031). The requirement for obtaining informed consent was waived because this was a retrospective analysis of routinely collected anonymized data.

In total, 8010 patients were included in the analysis, of whom 4429 (55.3 %) were men, and 5813 (72.6 %) visited the clinic (Table 1). The median number (interquartile range) of diseases claimed in the same month as acute URI was 4 (3–6). Only 519 (6.5 %) of the patients were claimed as acute URI alone. The most commonly redundantly claimed disease in these patients, regardless of the prescription of antibiotics, was allergic rhinitis, followed by acute bronchitis, acute sinusitis, and earwax impaction. Among patients prescribed antibiotics, acute pharyngitis ranked 8th in frequency of claims, while among those not prescribed antibiotics, it ranked 9th.

Among all patients, the proportion of patients with examinations ranged from 2.9 to 21.7 %. Especially, 870 patients claimed acute pharyngitis, the implementation rates of rapid diagnostic tests for Group A β-hemolytic *Streptococcus*, throat culture testing, collection of nasal and pharyngeal swabs were 117 (13.4 %), 41 (4.7 %), 266 (30.6 %), respectively.

Antibiotics classified as “Watch” were prescribed most frequently (Table 2). Among “Watch”, third-generation cephalosporins, macrolides, and fluoroquinolones were in order. The most frequently prescribed antibiotics in “Access” was J01CA, which contains amoxicillin.

This study revealed that patients claimed with acute URI were simultaneously claimed with some diagnosis requiring antibiotics and were prescribed antibiotics. Care must be taken in patient selection when evaluating URI using the Japanese medical claims database. Moreover, the implementation rate of recommended tests to determine the need for antibiotics was low, suggesting the need to further promote testing.

Only 6.5 % of patients were claimed to have acute URI alone. The median number of diseases claimed in the same month as acute URI was 4 per patient. A previous study using an insurance claims database

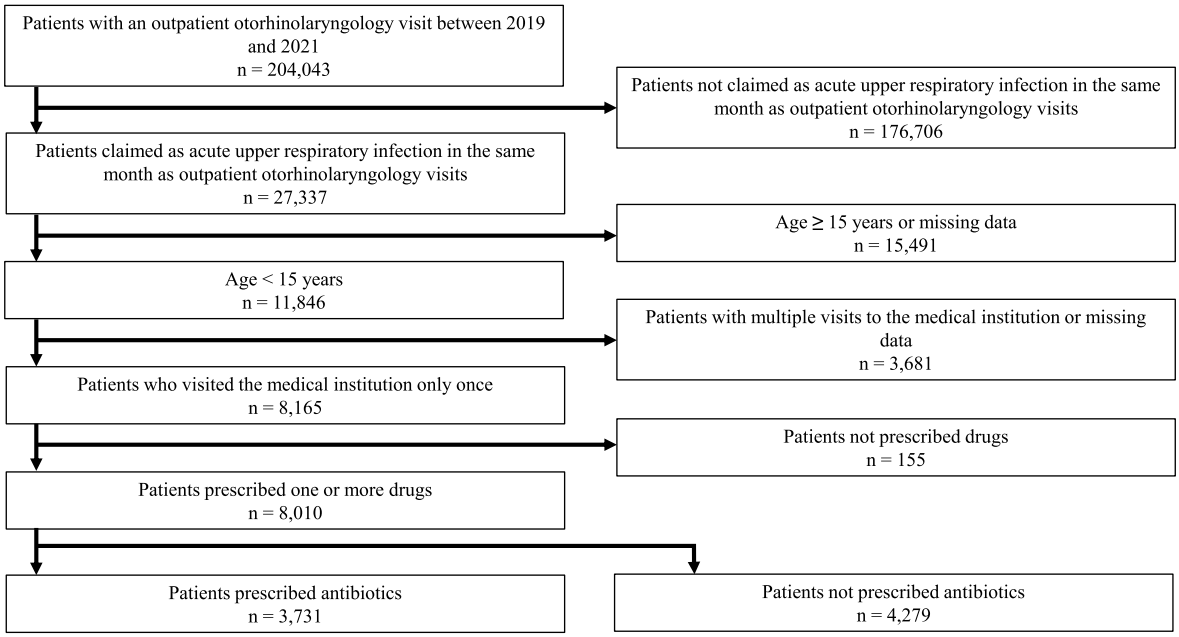

Fig. 1. Flowchart of patient selection.

Table 1
Characteristics of patients with acute upper respiratory infection insurance claims between 2019 and 2021.

			n (%)
Sex			
Man			4429 (55.3 %)
Woman			3581 (44.7 %)
Medical institution			
Clinic			5813 (72.6 %)
Hospital			2197 (27.4 %)
Number of diseases claimed/month			4.0 (3.0–6.0)
The five most frequent disease names claimed in the same month	Rank	Disease name	
Patient with antibiotic prescription (n = 3731)	1	Allergic rhinitis	1768 (47.4 %)
	2	Acute bronchitis	1289 (34.5 %)
	3	Acute sinusitis	1253 (33.6 %)
	4	Cerumen impaction	982 (26.3 %)
	5	Acute pharyngolaryngitis	836 (22.4 %)
Patients without antibiotic prescription (n = 4279)	1	Allergic rhinitis	1733 (40.5 %)
	2	Cerumen impaction	1196 (28.0 %)
	3	Acute bronchitis	1137 (26.6 %)
	4	Acute sinusitis	537 (12.5 %)
	5	Bronchial asthma	495 (11.6 %)
Examination			
Rapid diagnostic test for Group A β hemolytic *Streptococcus*			519 (6.5 %)
Throat culture testing			233 (2.9 %)
Collection of nasal and pharyngeal swabs			1736 (21.7 %)

Data are expressed as number (%) or median (interquartile range).

reported that 64.0 % of outpatients in Japan received insurance claims for multiple diseases in the same month [8]. A study conducted in the United States reported that sinusitis, suppurative otitis media, and pharyngitis were frequently associated with antibiotic prescriptions [9]. In our study, diseases such as acute bronchitis, sinusitis, and pharyngolaryngitis, for which antibiotic treatment may be indicated [4], were often claimed simultaneously with acute URI. Therefore, when assessing the appropriateness of antibiotic prescriptions in patients with acute URI, other disease claims also need to be considered.

The frequently prescribed antibiotics were third-generation cephalosporins, macrolides as classified "Watch," and extended-spectrum penicillins as classified "Access." Third-generation cephalosporins

Table 2
Prescribed antibiotics according to the World Health Organization Access, Watch, Reserve (AWaRe) classification.

AWaRe	ATC4 or 5		Patients prescribed antibiotics (n = 3731)
Watch			903.5
	J01DD	Third-generation cephalosporins [a]	410.3
	J01FA	Macrolides	342.3
	J01MA	Fluoroquinolones	67.3
	J01GB	Aminoglycosides [b]	37.0
	J01DC	Second-generation cephalosporins	9.6
	J01DH	Carbapenems	19.3
	J01AA	Minocycline (oral)	2.7
	J01XX01	Fosfomycin (oral)	10.2
	J01FF	Lincomycin (iv)	4.3
	J01CA	Piperacillin (iv)	0.5
Access			374.4
	J01CA	Penicillins with extended-spectrum [c]	292.1
	J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors [d]	55.5
	J01FF	Clindamycin	3.5
	J01DB	First-generation cephalosporins	10.7
	J01GB	Aminoglycosides [e]	7.5
	J01AA	Tetracyclines [f]	2.4
	J01EE	Combinations of sulfonamides and trimethoprim, incl. derivatives	1.3
	J01CE	Beta-lactamase sensitive penicillins	1.3
Reserve			8.6
	J01XX01	Fosfomycin (iv)	4.3
	J01DI03	Faropenem (oral)	4.3
Not recommended			0.5
	J01CR	Combinations of penicillins, incl. beta-lactamase inhibitors	0.3
	J01DD	Cefoperazone/sulbactam	0.3

Data are expressed as number of prescriptions/1000 patients. AWaRe, Access, Watch, Reserve; iv, intravenous; ATC, Anatomical Therapeutic Chemical. ATC4 indicates chemical subgroup and ATC5 indicates chemical substance.

[a] Cefditoren-pivoxil, cefcapene-pivoxil, ceftriaxone, cefdinir, cefpodoxime-proxetil, cefteram-pivoxil, cefotaxime, cefixime, ceftazidime, cefmenoxime.

[b] Dibekacin, isepamicin, tobramycin.

[c] Amoxicillin, ampicillin, bacampicillin.

[d] Amoxicillin/clavulanic acid, ampicillin/sulbactam, sultamicillin.

[e] Amikacin, gentamicin.

[f] Tetracycline, doxycycline.

were prescribed frequently, which may be influenced by the high prevalence of ampicillin-resistant *Haemophilus influenzae* in Japan [10]. Macrolides may be frequently used because they also have anti-inflammatory effects [11]. Conversely, the Manual of Antimicrobial Stewardship recommends the use of amoxicillin, or a combination of amoxicillin and clavulanic acid, classified as "Access," when prescribing antibiotics for bacterial acute URI [4]. In this study, the antibiotic use classified as "Watch" decreased over time, but the antibiotic use classified as "Access" stopped decreasing (Table S4). Therefore, it was speculated that AMR measures in Japan and the decrease in respiratory diseases due to infection control measures against COVID-19 [12] may have had an influence. Additionally, the pharmaceutical supply was a problem in Japan at the time and may have affected the prescribing of antibiotics [13].

Rapid diagnostic test for Group A β-hemolytic *Streptococcus* is recommended in the diagnostic and treatment protocol for acute pharyngitis in URI [6]. However, the proportion of patients with examinations associated with infectious diseases was extremely low. It has been shown that the implementation rate of the Rapid diagnostic test for Group A β hemolytic *Streptococcus* was as low as 5.6 % in a report using insurance claims database [14], and was comparable to the results in the present study. On the other hand, the Japanese insurance claim system has a limitation that only one of the two tests can be calculated even if both examinations are performed at the same time. Therefore, it may not reflect the implementation of examinations correctly, and further development of the claim system is necessary in the future. In addition, the implementation rate of each examination decreased over time (Table S5). Because the incidence of respiratory diseases, such as influenza, has decreased since 2020 owing to infection control measures, such as masks and behavioral changes related to COVID-19 [12], it is speculated that the implementation rate of each examination has decreased. Antibiotic prescriptions have been reported to be 25 % lower when rapid diagnostic tests for Group A β-hemolytic *Streptococcus* and throat culture testing are performed [15]. There is a need to develop a system to further promote diagnostic stewardship in outpatient settings.

This study had some limitations. First, the commercial data source used in this study is based on information collected from the health insurance of company employees and their families. Thus, this study did not cover all patients in Japan. Therefore, the results obtained in this study may not completely reflect the general population. Second, this study was conducted based on the medical claims database, and it does not include procedures that are not claimed by insurance. Therefore, the actual situation may be underestimated. Even with these limitations, this finding provides one of the fundamental pieces of information for future AMR measures and reimbursement evaluations.

This study revealed that among patients with acute URI, diagnoses requiring antibiotics were also claimed, and the implementation rate of examinations necessary for diagnosis was low. When evaluating URI using the Japanese medical claims database, care must be taken in patient selection. In addition, there is an urgent need to develop environment in which examinations can be conducted in outpatient settings.

Authorship statement

All authors meet the ICMJE authorship criteria.

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Institutional review board statement

The study was approved by the Ethics Committee of Kyoto Pharmaceutical University (approval number: E-00031).

Informed consent statement

The requirement for obtaining informed consent was waived because the study was based on a retrospective analysis of routinely collected data.

Data availability statement

The data that support the findings of this study are available from IQVIA Solutions Japan K.K; however, restrictions apply to the availability of these data, which were used under license for the current study and are not publicly available. However, data are available from the authors upon reasonable request and with permission from IQVIA Solutions Japan K.K.

CRediT authorship contribution statement

Saki Ito: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing, Visualization. **Yuichi Muraki:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing, Project administration, Funding acquisition. **Ryo Inose:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing. **Kanako Mizuno:** Methodology, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing. **Ryota Goto:** Methodology, Validation, Formal analysis, Investigation, Resources, Writing – original draft, Writing – review & editing. **Makiko Kiyosuke:** Writing – review & editing. **Yoshitsugu Iinuma:** Writing – review & editing. **Tetsuya Yagi:** Writing – review & editing. **Hiroki Ohge:** Writing – review & editing.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jiac.2024.01.015.

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