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All-cause hospital admissions and incidence of asthma in children in Kazakhstan: a population-based retrospective cohort study

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This study describes the incidence of asthma and all-cause hospital admissions among children in Kazakhstan diagnosed between 2014 and 2021. In this retrospective cohort study, we included children aged 0–17 years diagnosed with asthma (ICD-10 codes J45.x) and registered in the Unified National Electronic Health System (UNEHS) during 2014–2021. In the outpatient asthma subgroup, we analyzed asthma incidence rates per 100,000 population and all-cause hospitalization rates per 1,000 person-years. Cox regression was used to assess hospitalization risks. The cohort included 53,463 children, 63.7% male, 47.9% aged 5–11 years, and 74.1% urban residents. The incidence rate ranged from 67.5 to 185.9 among boys and 38.2 to 115.7 among girls per 100,000 population, highest in the 5–11 age group (308–351 cases). Among 31,525 outpatients, 915 (2.8%) were hospitalized, with an incidence rate of 6.91 per 1,000 person-years. The 5–11 age group had a 2.59 times higher hospitalization risk than the 0–4 age group. Respiratory infections, allergic rhinitis, and acute rhinosinusitis were the factors associated with the highest risks of hospitalization (HRs: 14.48, 12.95, and 7.28, respectively). The insights from this study enhance our understanding of asthma in Kazakhstan and offer valuable lessons applicable to similar contexts globally.

Keywords Asthma, Children, Epidemiology, Hospitalization, Incidence, Pediatric

Background

Asthma is a non-communicable chronic inflammatory airway condition that is 3.3 times more common in children under the age of 18 years than in adults[1]. It was estimated to affect 9.9–14.0 children per 1,000 population in the USA, where the age group with the highest annual incidence of asthma was 0–4 years (23/1,000), followed by 5–11 years (11.1/1,000), and 12–17 years (4.4/1,000)[1].

Globally, the incidence of asthma is highest in children under the age of 5, reaching 36% of all cases. The ages of 5–19 years follow, cumulatively accounting for ~28% of all asthma cases[2]. The highest point prevalence of asthma was observed in the age category of 5–9 years, reaching 57.2 and 45.1 cases per 1,000 population among males and females, respectively[3].

Asthma is a complex multifactorial condition associated with various intercurrent conditions and complications that impact its severity and clinical intensity[4]. Commonly associated conditions of asthma include allergic rhinitis, gastroesophageal reflux disease, obesity, diabetes mellitus, cardiovascular disease, chronic and recurrent respiratory infections, and chronic obstructive pulmonary disease (COPD)[4,5].

Nearly 50% of children with asthma experience acute episodes yearly, often resulting in hospital admissions[6]. Pediatric hospitalizations constitute around 59% of all asthma-related hospitalizations[7]. The risk of subsequent hospitalization is 33–50% higher in children with asthma than in pediatric patients with other diagnoses[6]. Subsequent hospitalizations occur in approximately 15.6% of children with asthma within 1 year and are most commonly due to asthma (73.9%), pneumonia (7.9%), acute respiratory infections (3.8%), and other lung diseases (0.9%)[6].

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In Kazakhstan, epidemiological research on asthma is limited and primarily focuses on a selected population[8–10]. These studies present several limitations, including small sample sizes, restricted generalizability of the findings, and loss to follow-up. What can be inferred from these studies is that the continental climate in Kazakhstan, characterized by severe temperature fluctuations, extended winter periods, dust storms, and high levels of ambient particulate matter, contributes to an increased risk of asthma exacerbations. Additionally, there are inefficiencies in the proper and timely diagnosis of asthma and the effective management of the condition. These factors contribute to increased asthma-related hospital admissions. Beyond this, there is insufficient research into asthma epidemiology in Kazakhstan, especially national-scale, population-based epidemiological research on pediatric populations.

Beginning in 2014, the Unified National Electronic Health System (UNEHS) in Kazakhstan aggregated nationwide administrative health data. The availability of patients' medical records under inpatient and outpatient care on a national scale creates an excellent opportunity to conduct retrospective population-based research into the epidemiology of various conditions, including asthma, in pediatric populations. Using these data, we aim to describe the incidence of asthma and all-cause hospital admissions among children with asthma in Kazakhstan diagnosed between 2014 and 2021.

Methods

Study population

This retrospective cohort study included 0–17-year-old patients diagnosed with asthma and registered in the inpatient or outpatient registry of the Unified National Electronic Health System (UNEHS) between January 1st, 2014, and December 31st, 2021. Individual patient records containing socio-demographic and clinical data were extracted from the UNEHS database. Asthma diagnosis was defined using the International Classification of Diseases 10 (ICD-10) as code J45.x.

Exposures and covariates

Patient records extracted from the UNEHS database contained the following information: age, sex, ethnicity, residence, ICD-10 codes of the diagnoses, anonymized population registry number (RPN), dates of birth, diagnosis, date of death, date of admission, and date of discharge.

Outcome assessment

For each year of follow-up between 2014 and 2021, incidence rates per 100,000 population were estimated for pediatric asthma patients by dividing the number of incident cases in a year by Kazakhstan's total population of ages 0–17 years in that year. The population parameters of Kazakhstan were obtained from the Statistics Committee[11]. The risk of all-cause hospital admissions was investigated in the outpatient subgroup of the cohort. Incidence rates of all-cause hospital admissions were estimated per 1,000 person-years. The follow-up period was defined from the date of asthma diagnosis to December 31st, 2021, or the date of the earliest hospitalization due to all causes.

Statistical methods

Data were summarized as patient numbers and percentages for categorical variables. The median and interquartile range (IQR) were used to summarize continuous variables. One-way ANOVA, Chi-Square, and Fisher's exact tests were used for bivariate analysis. Cox regression modeling produced crude and adjusted hazard ratios (HR) with 95% confidence intervals (CI) corresponding to the associations between risk factors and the risk of all-cause hospital admissions.

All statistical analyses were performed using STATA 15 MP2 Version (STATA Corporation, College Station, TX). P values are two-sided and reported as statistically significant at $<=0.05$ for all analyses. Nazarbayev University Institutional Research Ethics Committee (NU-IREC) approved this project to be exempt from further NU IREC oversight (NU-IREC 505/06122021). The study was performed according to international and local ethics guidelines and regulations, as well as the Declaration of Helsinki.

Results

Figure 1 depicts a flowchart of cohort selection. From the inpatient and outpatient registries of the UNEHS for 2014–2021, records of 132,410 and 62,746 patients were identified, respectively. After merging the patient records into a single dataset and removing the records of patients 18 years of age and older, the final pediatric cohort of 53,463 asthma patients was derived. Out of this, there were 21,322 inpatient and 32,141 outpatient records.

Table 1 presents the baseline characteristics of the cohort in terms of sex, residence, hospitalizations, associated conditions, and mortality stratified by age at diagnosis. Among the total cohort, 34,047 (63.7%) were male, 25,593 (47.9%) were of age 5–11 years at asthma diagnosis, 32,222 (74.1%) were urban residents, 21,322 (39.9%) were hospitalized due to asthma at least once, and 73 (0.1%) died. The most common associated conditions were respiratory infections, affecting 10,815 (20.2%) patients; allergic rhinitis, affecting 3,137 (5.9%) patients; acute rhinosinusitis, affecting 638 (1.2%) patients; and atopic dermatitis, affecting 346 (0.7%) patients. A complication of asthma considered in this study was respiratory failure, affecting 3,557 (6.7%) patients. Respiratory infections were more common in younger patients, affecting 5,700 (31.4%) patients of age 0–4 years, 4,335 (16.9%) patients of age 5–11 years, and 780 (8.0%) patients of age 12–17 years. Median follow-up was 334 days (122–826).

The incidence of asthma in the cohort was relatively consistent between 2014 and 2019, fluctuating between 149.7 and 185.9 cases per 100,000 population among boys and between 91.1 and 115.7 cases per 100,000 population among girls (Fig. 2). In 2020–2021, the estimates decreased to 94.0-67.5 cases and 55.0-38.2 cases per

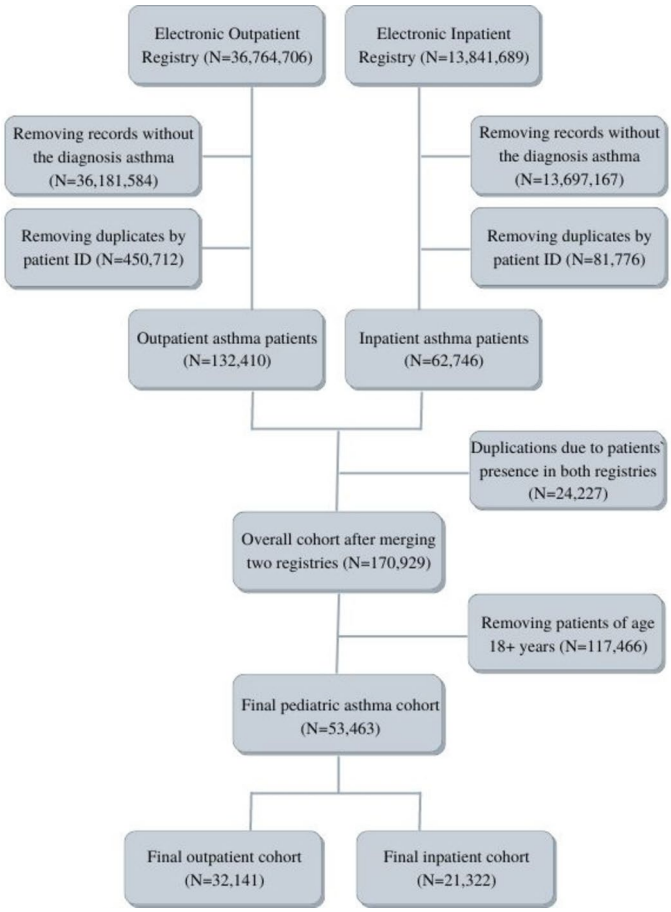

Fig. 1. Flowchart of cohort selection of pediatric patients with asthma registered in UNEHS in 2014–2021.

100,000 population among boys and girls, respectively. The incidence of asthma was consistently higher among boys by approximately 60–80%, compared to girls.

Figure 3 illustrates asthma incidence rates with stratification by year of diagnosis and age category. The highest incidence was found in the age groups of 5–11 years, fluctuating between 308 and 351 cases per 100,000 population between 2014 and 2019, dropping to 170 and 111 cases per 100,000 population in 2020 and 2019, respectively. The incidence estimates were the lowest in the age groups of 12–17 years, ranging between 191 and 235 cases per 100,000 population between 2014 and 2019 and 84 – 58 cases in 2020–2021.

The incidence rates of all-cause hospital admissions per 1,000 person-years in the outpatient cohort for each year are depicted in Figs. 4 and 5, with stratification by sex and age category, respectively. The estimates did not differ substantially between boys and girls, ranging from 5.6 to 17.2 cases per 1,000 person-years with an upward trend. Between 2014 and 2019, 5-11-year-old patients had the highest incidence of all-cause hospitalization, ranging from 9.4 to 10.2 cases per 1,000 person-years. In 2020–2021, the hospitalization rates were higher in the age groups of 0–4 and 12–17 years, reaching 15.8–18.5 and 11.3–20.1 cases 1,000 person-years, respectively.

As presented in Table 2, the risk factors significantly associated with the risk of all-cause hospital admissions were age and related conditions. The age category of 5–11 years had a 2.59 times higher risk of hospital admissions due to all causes than the age category of 0–4 years (95% CI: 2.10–3.19, $p < 0.001$). The presence of respiratory infections was associated with a 14.48 times higher risk of hospitalization (95% CI: 12.34–16.11, $p < 0.001$), allergic rhinitis – with a 12.95 times higher risk (95% CI: 10.41–16.11, $p < 0.001$), and acute rhinosinusitis – with a 7.28 times higher risk (95% CI: 4.65–11.39, $p < 0.001$).

Discussion

This study provided an overview of asthma incidence in children in Kazakhstan based on the aggregated patient data from the Unified National Electronic Healthcare System (UNEHS) for 2014–2021. The results showed that the incidence of asthma was higher among boys and the age group of 5–11 years. The incidence rates remained relatively consistent in 2014–2019 but decreased considerably in 2020–2021 for all patient subgroups in the cohort. Respiratory infections, allergic rhinitis, acute rhinosinusitis, and atopic dermatitis were the most common associated conditions in the cohort. In the outpatient asthma subgroup, 915 (2.8%) patients had all-cause hospitalizations over the follow-up period after the diagnosis of asthma. The analysis of all-cause hospitalizations in the outpatient asthma subgroup yielded estimates of incidence, common causes, and risk

	Total	0–4 years	5–11 years	12–17 years	*p*-value
Total	53,463	18,131 (33.9)	25,593 (47.9)	9739 (18.2)	
Sex, N (column %)					
Female	19,416 (36.3)	6369 (35.1)	9259 (36.2)	3788 (38.9)	< 0.001
Male	34,047 (63.7)	11,762 (64.9)	16,334 (63.8)	5951 (61.1)	
Residence, N (column %)					
Urban	32,222 (74.1)	10,218 (75.4)	15,817 (73.5)	6187 (73.8)	< 0.001
Rural	11,250 (25.9)	3334 (24.6)	5716 (26.6)	2200 (26.2)	
Registry, N (column %)					
Outpatient	32,141 (60.1)	11,457 (63.2)	14,748 (57.6)	5936 (61.0)	< 0.001
Inpatient	21,322 (39.9)	6674 (36.8)	10,845 (42.4)	3803 (39.1)	
Associated conditions, N (column %)					
Respiratory infections (J09-J21)	10,815 (20.2)	5700 (31.4)	4335 (16.9)	780 (8.0)	< 0.001
Allergic rhinitis (J30)	3137 (5.9)	360 (2.0)	1989 (7.8)	788 (8.1)	< 0.001
Acute rhinosinusitis (J01)	638 (1.2)	137 (0.8)	371 (1.5)	130 (1.3)	< 0.001
Atopic dermatitis (L20)	346 (0.7)	128 (0.7)	182 (0.7)	36 (0.4)	0.001
Complications, N (column %)					
Respiratory failure (J96)	3557 (6.7)	1344 (7.4)	1627 (6.4)	586 (6.0)	< 0.001
Death, N (column %)					
No	53,390 (99.9)	18,100 (99.8)	25,569 (99.9)	9721 (99.8)	0.036
Yes	73 (0.1)	31 (0.2)	24 (0.1)	18 (0.2)	
All-cause hospitalizations in the outpatient cohort, N (%)					
No	31,610 (97.2)	8529 (98.1)	17,193 (96.2)	5888 (98.8)	< 0.001
Yes	915 (2.8)	164 (1.9)	678 (3.8)	73 (1.2)	
Median time to all-cause hospitalization in the outpatient cohort, days (IQR)	334 (122–826)	210 (79–552)	372 (133–899)	381 (119–1135)	0.011
Causes for hospitalization in the outpatient cohort, N (%)					
Allergic asthma (J45.0)	326 (35.6)	36 (22.0)	269 (39.7)	21 (28.8)	< 0.001
Mixed asthma (J45.8)	121 (13.2)	11 (6.7)	98 (14.5)	12 (16.4)	0.022
Bacterial pneumonia (J15.8)	65 (7.1)	19 (11.6)	45 (6.6)	1 (1.4)	0.012
Acute bronchitis due to other specified organisms (J20.8)	37 (4.0)	14 (8.5)	21 (3.1)	2 (2.7)	0.010

Table 1. Baseline characteristics of pediatric patients with asthma registered in UNEHS in 2014–2021.

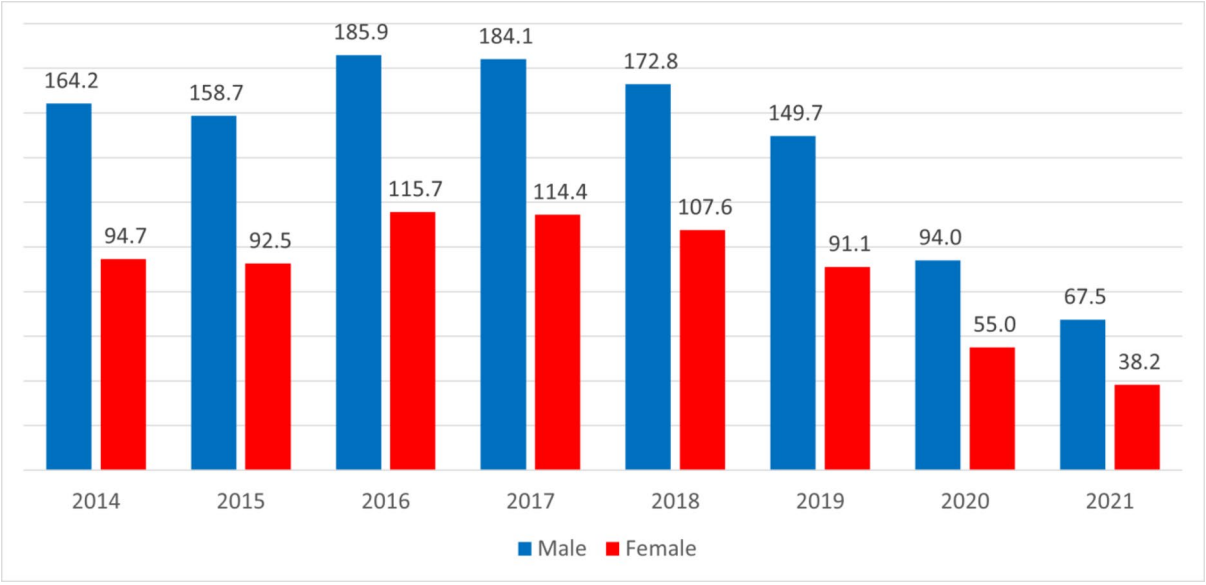

Fig. 2. Incidence rates per 100,000 population stratified by sex & year of diagnosis.

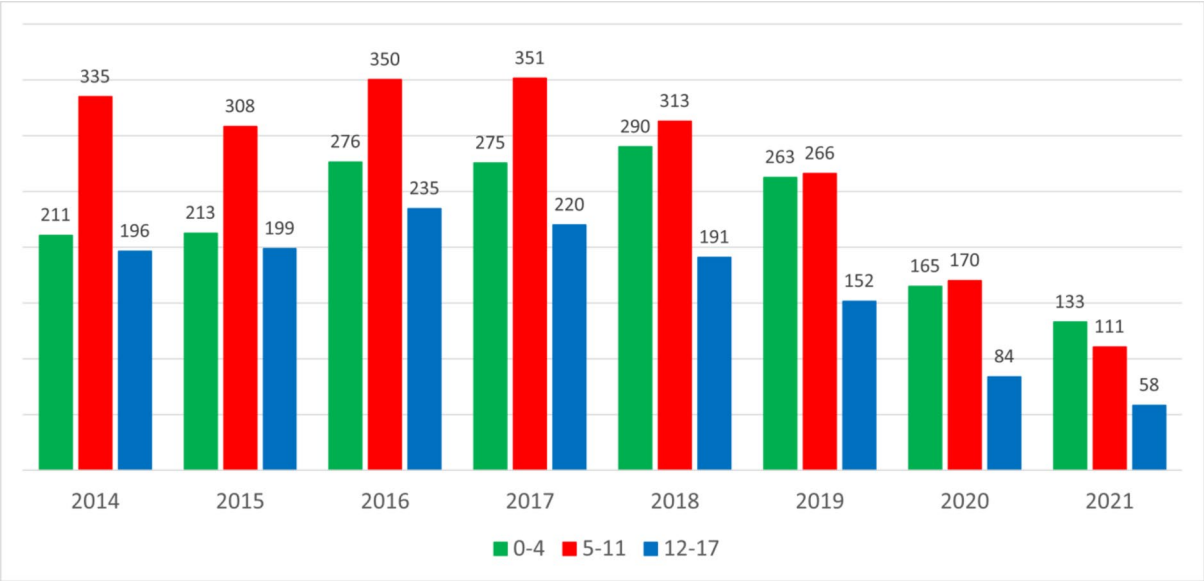

Fig. 3. Incidence rates per 100,000 population stratified by age category & year of diagnosis.

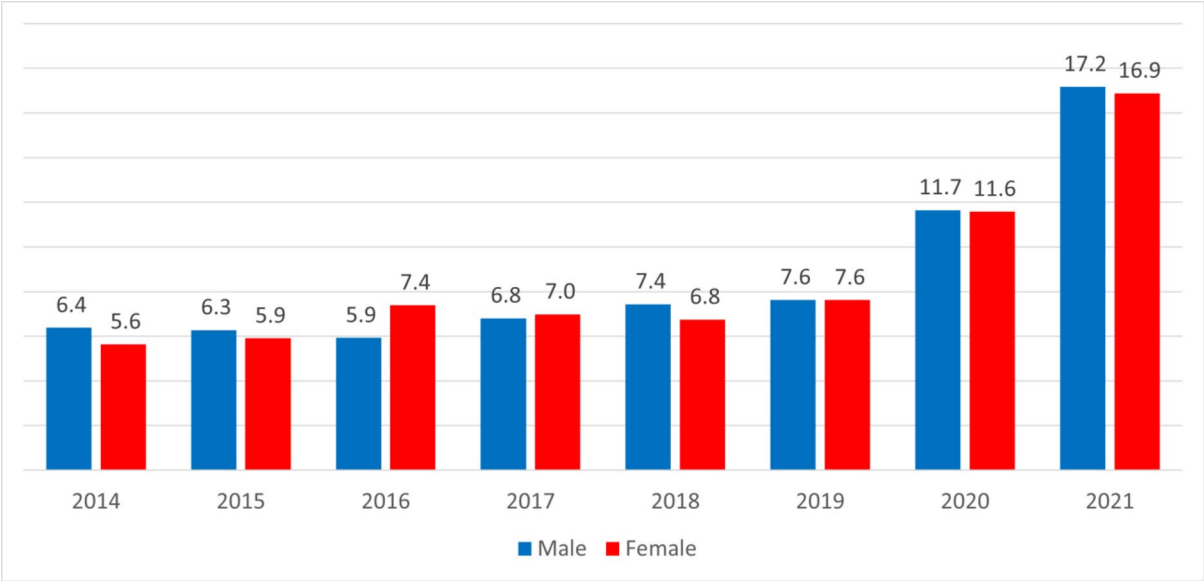

Fig. 4. Incidence rates of all-cause hospitalization per 1,000 person-years stratified by sex & year of diagnosis.

factors associated with all-cause hospitalizations in this subgroup. This is Kazakhstan's first study on this topic, which was performed nationally, utilizing extensive administrative health data from the UNEHS.

Compared to a similar retrospective pediatric cohort study conducted in the USA in 2008–2011, the percentage of male patients in our cohort (63.7%) was identical to theirs (61.1%), and the largest age group was 5–11 years (47.9%) in our cohort, similarly to theirs (46.5%)[12]. The incidence of asthma has been observed to be higher among boys in the age category of 0–17 years[13]. However, the incidence and severity of asthma tend to be higher among women compared to men in adult populations[14]. The mechanisms underlying these differences are not fully understood but are linked to sex hormones, where ovarian hormones increase, and testosterone decreases airway inflammation in asthma[14]. Additionally, pre-adolescent boys tend to have smaller airways relative to lung size than girls. This pattern reverses during adolescence and is possibly associated with the differences in the incidence of asthma in these groups[15]. In terms of age, the higher incidence of asthma in the category of 5–11 years compared to 12–17 years may be attributed to a weaker immune system and lower self-management abilities in younger children, making them more vulnerable to upper respiratory infections, which significantly contribute to childhood asthma[16]. Compared to the age category of 0–4 years, the higher incidence in the 5–11 years category may be more attributable to diagnostic challenges. In the youngest age

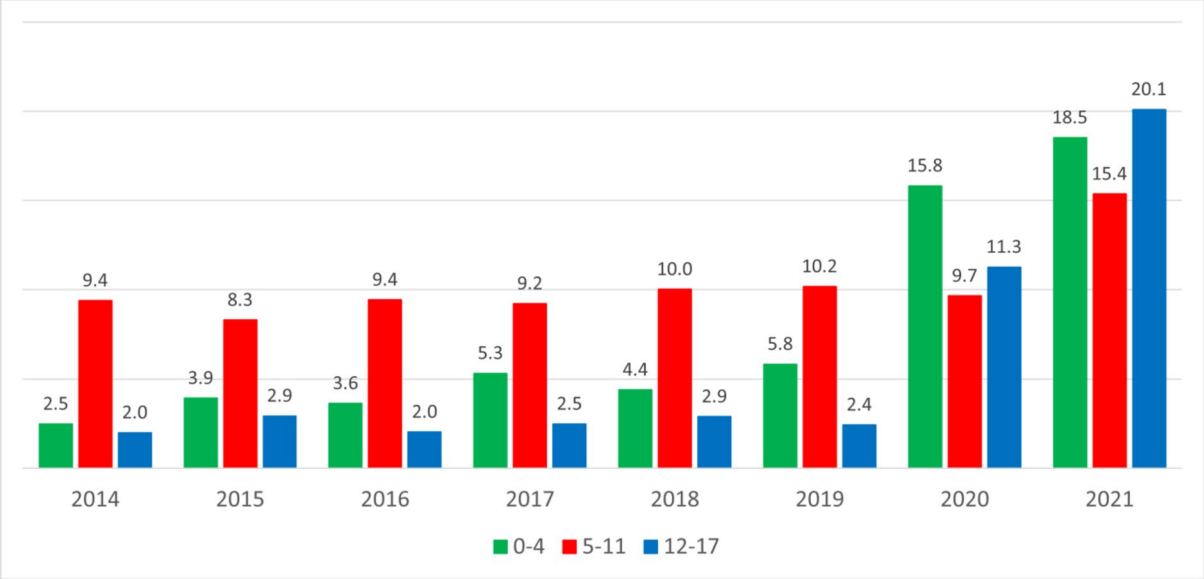

Fig. 5. Incidence rates of all-cause hospitalization per 1,000 person-years stratified by age & year of diagnosis.

	Crude HR (95% CI)	*p*-value	Adjusted HR (95% CI)	*p*-value
Sex				
Male	Ref.		Ref.	
Female	0.99 (0.87–1.14)	0.915	1.06 (0.91–1.23)	0.471
Age category				
0–4	Ref.		Ref.	
5–11	1.98 (1.67–2.35)	< 0.001	2.59 (2.10–3.19)	< 0.001
12–17	0.61 (0.46–0.81)	< 0.001	0.83 (0.59–1.17)	0.293
Residence				
Urban	Ref.		Ref.	
Rural	1.20 (1.01–1.43)	0.038	1.16 (0.97–1.39)	0.095
Associated conditions				
Respiratory infections (J09-J21)	14.29 (12.49–16.35)	< 0.001	14.48 (12.34–16.98)	< 0.001
Allergic rhinitis (J30)	9.86 (8.13–11.95)	< 0.001	12.95 (10.41–16.11)	< 0.001
Acute rhinosinusitis (J01)	56.26 (40.27–78.60)	< 0.001	7.28 (4.65–11.39)	< 0.001
Atopic dermatitis (L20)	0.98 (0.51–1.88)	0.944	1.59 (0.79–3.20)	0.193

Table 2. Cox regression model for the risk of all-cause hospitalization among the outpatients in the pediatric asthma cohort registered in UNEHS in 2014–2021.

group, the diagnosis is primarily based on clinical judgment and assessment of the symptoms, especially because episodic respiratory symptoms like wheezing and cough are also common in children without asthma in this age group[17]. As such, the difficulty of reliably diagnosing asthma at this age may result in a substantial portion of children presenting the symptoms to be assigned diagnoses other than asthma. Urban residents were more prevalent, constituting 74.1% of the cohort. This may be attributed to the higher levels of air pollution in urban settings, such as traffic-related air pollution and indoor pollutants, as well as prolonged exposure, which is a notable risk factor for the development of asthma[18,19].

Our cohort's most common associated conditions were respiratory infections, allergic rhinitis, acute rhinosinusitis, and atopic dermatitis. In other studies, allergic rhinitis was estimated to affect up to 60% of patients with asthma[4]. In our cohort, allergic rhinitis affects a considerably lower estimate of 5.9% of patients. Respiratory infections are strongly correlated with asthma since upper (URTI) and lower respiratory tract infections (LRTI) are diagnosed in 42.8% and 16.5% of patients within 1 year preceding a diagnosis of asthma[12]. Our study found that a respiratory infection diagnosis was made for 20.2% of asthma patients over the follow-up period. High rates of respiratory infections among younger patients can be attributed to immature immune systems, which translate into susceptibility to infections and exacerbate asthma symptoms[16]. Approximately 4–7% of asthma patients require intensive care unit (ICU) admission, a significant cause of which is respiratory failure[20]. In our study, a diagnosis of respiratory failure was made for 6.7% of patients. Acute rhinosinusitis, while potentially an

independent condition, can be a complication in the context of asthma that further exacerbates the symptoms and leads to a higher risk of subsequent hospitalization.

The relatively consistent trends in asthma incidence rates in 2014–2019, followed by a considerable decline in 2020–2021, likely reflect the impact of the COVID-19 pandemic[21,22]. Public health measures implemented at that time, such as lockdowns, wearing of masks, and reduced exposure to allergens and other environmental triggers, may have contributed to the decline in asthma diagnoses. Additionally, lower availability and lower utilization of healthcare services may have contributed to the lower estimates.

The observed increase in the rate of all-cause hospital admissions during 2020–2021 is likely linked to the COVID-19 pandemic. Numerous studies indicate that asthma is a significant risk factor for increased hospitalization due to COVID-19[23,24]. In settings with early strict lockdowns, a decrease in hospital visits and a potential decline in the effective management of chronic conditions like asthma may have resulted in a surge in admissions as restrictions were lifted and postponed care was sought, thus contributing to the increased hospitalization risk among asthmatic children.

The risk of all-cause hospital admissions was significantly associated with age and the presence of respiratory infections, allergic rhinitis, and acute rhinosinusitis. Children with asthma receiving outpatient care at the age of 5–11 years are at 2.59 times higher risk of subsequent all-cause hospital admissions compared to the age category of 0–4 years. This may be due to the higher exposure to environmental triggers and respiratory infections at that age while still having less than fully mature immune systems. In patients with respiratory infections, allergic rhinitis, and acute rhinosinusitis, the risks of hospitalization are 14.48 times, 12.95 times, and 7.28 times higher, respectively. These associated conditions can cause inflammation and obstruction in the airways, leading to a higher likelihood of a child with asthma requiring hospitalization.

This study has several limitations. Firstly, it relies on secondary data, which is subject to measurement accuracy and documentation practices outside the researchers` control. Another significant issue is the lack of information on therapies, clinical data, and instrumental data, which restricts the methodological approaches available for data analysis. Although efforts were made to account for potential confounders, it is recognized that there may still be residual confounding from unmeasured or unknown factors. As this is an observational study, we cannot draw any conclusions about causality.

Despite these limitations, this study offers valuable insights into asthma incidence among children in Kazakhstan. It lays the groundwork for additional research to tackle these limitations and enhance our understanding of the subject.

Conclusion

The incidence of asthma was higher among boys aged 5 to 11 years and remained relatively consistent from 2014 to 2019, decreasing substantially in 2020 and 2021, potentially reflecting the impact of the COVID-19 pandemic. Respiratory infections, allergic rhinitis, acute rhinosinusitis, and atopic dermatitis were the most common associated conditions in the cohort. The risk of all-cause hospitalizations in the outpatient subgroup was significantly elevated in the 5 to 11 age group and among patients with comorbid conditions. Acute sinusitis, allergic rhinitis, and respiratory infections were associated with the highest risk of hospital admissions in children with asthma. These findings underscore the need for targeted asthma management strategies that address demographic factors and associated condition-related risks. The insights from this study enhance our understanding of asthma in Kazakhstan and offer valuable lessons that can be applied to similar contexts globally. Effective pediatric asthma care requires comprehensive approaches that integrate the management of commonly associated conditions to reduce hospitalization risks and improve overall outcomes. Ongoing research is essential to refine asthma care strategies and ensure that children in Kazakhstan and elsewhere receive optimal, evidence-based care. This will help mitigate the burden of asthma and enhance the quality of life for affected children worldwide.

Data availability

All data related to this study are available from the Republican Center for Electronic Health of the Ministry of Health of the Republic of Kazakhstan, but restrictions apply to the availability of these data, which were used under the contract agreement for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission from the Ministry of Health of the Republic of Kazakhstan. Queries should be directed to the PI of the project – D.G. (d.galiyeva@nu.edu.kz).

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Author contributions
D.S. – dataset preparation, data analysis, and manuscript writing, K.M. – assistance with dataset preparation and data analysis, D.P. – participation in developing the study design and manuscript revision, A.G. – acquisition of data and supervision, D.G. – primary investigator, corresponding author, development of study design, revisions.

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Declarations

Competing interests
The authors declare no competing interests.

Ethics approval and consent to participate
Nazarbayev University Institutional Research Ethics Committee (NU-IREC) approved this project to be exempt from further NU IREC oversight (NU-IREC 505/06122021). The NU-IREC waived the need for informed consent as the study involved the analysis of anonymized secondary data from the Unified National Electronic Health System (UNEHS). The study was performed according to international local ethics guidelines and regulations and the Declaration of Helsinki.

Additional information
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