Age- and gender-specific trends in respiratory outpatient visits and diagnosis at a tertiary pediatric hospital in China: a 10-year retrospective study

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Abstract

Background: Respiratory infections are one of three leading causes of childhood mortality, and worldwide increase and recent plateau in childhood asthma has been reported. However, data on respiratory disease trends over long period of time is limited. This study aimed to determine trends in respiratory disease outpatient visits (ROVs) and diagnoses (RODs) amongst attendants to one of the largest children's teaching hospitals in China between 2009 and 2018.

Methods: A retrospective study of routine administrative data was designed and reported according to the RECORD statement. Demographic details and diagnoses of patients <18 years attended the respiratory disease clinic were extracted from the Hospital Information System. Age and gender-specific trends were analyzed by comparing change in number of clinic attendants and different diagnoses over time.

Results: There were 698054 ROVs involving 285574 children (59.6% male and 40.4% female). Average growth rate of ROVs was 15.2% and children aged 4 to <7 years had a faster increase than other age groups. Lower respiratory infections (LRI) (29.6%), influenza and pneumonia (17.9%), asthma and allergic diseases (13.2%), and diseases of upper respiratory tract (12.1%) accounted for 72.8% of all RODs. Gender-specific trend in diagnoses showed the percentage of asthma and allergic diseases increased with ages, especially among the group aged between 4 to <7 years. Gender-specific trend in ROVs showed a greater increase of asthma and allergic diseases than other RODs for males and females. The percentage of asthma and other allergic diseases was greater for males but the growth rate was faster for females. Asthma and allergic diseases were evaluated as co-morbidities to LRI and associated to 25.5% of LRI patients.

Conclusion: The sustainable upward trend in ROVs was observed among children at different ages and a gender differential effect was also seen. In contrast to what has been reported, asthma and allergies diseases burden continued to increase in our locally.

Background

Respiratory infections are still one of three leading causes of child mortality worldwide [1-3]. Each year childhood respiratory infections bring along a significant burden to our healthcare system in terms of manpower and resource utilization [4-7]. However, little is known about secular trends in respiratory outpatient visits (ROVs) and diagnoses (RODs) over a longer term period. Increasing incidence of respiratory infections and prevalence of asthma is reported according to the National Surveillance for Asthma in the United State from 1980 to 2013 [8-10]. Compared with the report from the US, study in Shanghai also showed the prevalence of asthma among children in China has increased almost five-fold, from 2.1% in 1990 to 10.2% in 2011 and boys had a higher prevalence of asthma than girls in the age group of 3-7 years [11]. These studies suggested age and gender differential effects on the increasing asthma prevalence. However, the full picture of ROVs and RODs, especially the age- and gender-specific trends, has not been well documented, partly related to a lack of computerized databases containing

diagnosis-specific outpatient data. In this study, we used 10-year routine administrative data and reported age- and gender-specific trends in ROVs and RODs among children attending one of the largest tertiary-level pediatric hospitals in China.

Methods And Materials

Study design

This was a retrospective study in a single center and reported according to the RECORD statement [12]. The primary objectives were to describe age and gender-specific trends in ROVs and RODs over a 10-year period and analyze associations between respiratory diseases and the common co-morbidities.

Population and setting

The study population included children, <18 years of age and visited the respiratory medicine clinic between January 1, 2009, and December 31, 2018 at a tertiary pediatric hospital in Shanghai, China.

Data source and extraction

The data were extracted from the hospital information system, which contains administrative data from 2008 when the hospital moved to the new campus area. The selection of participants and data linkage process is shown in Fig. 1.

Definitions

-*Age categories*: age was categorized as < 1 year, 1 to <4 years, 4 to <7 years, 7 to <12 years, and 12 to <18 years. A child could contribute data to multiple age groups as he or she may have visited at different time points.

-*Diagnosis classification*: Principal diagnosis was analyzed for trend in spectrum of respiratory diagnosis according to *International Classification of Diseases, 10th Revision* and categorized based on the category codes (Appendix 1). All respiratory system diagnoses(ICD-10 codes J00-J99) classified as “Other upper respiratory infections”(J00-J06,J32-J39),“Influenza and pneumonia”(J09-J18), “Other lower respiratory infections”(J20-J22, J40-J44,J47 and J85-J86),“Asthma and other allergic diseases”(J30-31,J45-J46,J67),and “Other respiratory disease”(J60-J66,J68-J70,J80-J84,J90-J94,J95-J99). Other system diseases were categorized as “Non-respiratory system diseases”.

- *Co-morbidity*. Secondary diagnoses were classified under ICD-10 suborder codes (5 digital codes, e.g. J20.0 indicated diagnosis of acute bronchitis due to streptococcus) and were defined as co-morbidities associated with the principal diagnosis.

Statistical methods

Data was analyzed descriptively on python platform. The frequency and percentage were calculated to illustrate the structural change of age-specific trend in ROVs and RODs. The visits per year and the growth rate were used to show the trend in quantity of visits. The growth rate each year was calculated by dividing the visit in the same period of last year and the average growth rate (AGR) was calculated by the geometric method. Statistical test was conducted by using Stata 11.0. Chi square test for trend was used to test whether there is a systematic increase or decrease in proportion across categories. Chi square test or Z-test was using to compare the difference between two groups for categorical variable and continuous variable. $P < 0.05$ was considered as statistically significant.

Results

Patient characteristics

Total of 285574 patients attended to the respiratory outpatient department of this hospital during the 10-year study period. Pre-school children aged < 7 years old accounted for 88.0% of all children and number of children aged 1 to < 4 years were twice than that aged < 1 years and 4 to < 7 years. Male patients accounted for 59.6% of the study sample, 39.4% were covered by government insurance and 60.6% were self-finance. Respiratory specialist clinic provided medical service for 46.5% patients mainly attended with specialized respiratory diseases. The doctors with associate professor or above degree in expert-clinic provided medical service for 52.3% patients. The average number of visit per patient for each RODs was 2.44, and the number of visits was not significantly different between patients covered by government insurance and those who were self-finance (2.94 vs 2.12). (Tab 1)

Overall and age-specific trend in ROVs

During the 10-year study period, the overall ROVs were 698 054 with an average growth rate (AGR) of 15.2%. The growth rate became stable around 10% after 2013 (Fig. 2). The percentage of growth for different age groups varied significantly during the study period ($P_{\text{trend}} < 0.0001$). The percentage for children aged < 1 year declined from 24.3% in 2013 to 17.4% in 2018 ($P < 0.001$), while for those aged 4 to < 7 years increased from 22.8% to 28.4% ($P < 0.001$), compared with 22.6% and 24.1% in total, respectively. Children aged 1 to < 4 years, 7 to < 12 years, and 12 to < 18 years remained stable around 43%, 9% and 1%, respectively (Fig. 3). The increasing visits varied considerably among different age groups. Children aged

4 to <7 years had a rapid increase than the AGR of all visits (16.9% vs 15.2%, $P<0.0001$), while age of 7 to <12 years had a slower increase (13.1% vs 15.2%, $P<0.001$). Other age categories had no statistically difference compared with the AGR of all visits (< 1 year: 14.7% vs 15.2%, $P=0.118$; 1 to <4 years: 15.0% vs 15.2%, $P=0.235$; 12 to <18 years: 13.9% vs 15.2%, $P=0.275$) (Fig.4).

Overall trend in RODs and according to age

Overall trend in diagnosis are shown in Fig. 5 and Fig. 6. “Other lower respiratory infections” (29.6%), influenza and pneumonia (17.9%), asthma and other allergic diseases (13.2%), and “Other diseases of upper respiratory tract” (12.1%) accounted for 72.8% of all respiratory diagnoses. The percentage of respiratory diagnosis varied during the 10-year study period ($P_{\text{trend}}<0.0001$). The percentage of asthma and other allergic diseases increased slightly from 13.9% in 2013 to 15.6% in 2018, compared with 13.2% in total. The same trend was in the percentage of other diseases of upper respiratory tract (from 9.3% to 10.0%), other respiratory diseases (from 3.0% to 12.7%), and non-respiratory system diseases (from 7.1% to 12.0%), compared with 12.1%, 17.0%, and 10.2% in total, respectively. The percentage of other lower respiratory infections decreased greatly from 42.4% to 29.3%, compared with 29.6% in total, as well as influence and pneumonia that declined slightly from 24.2% to 20.3%, compared with 17.9% in total. The growth rate of four main categories of respiratory diagnosis showed different trend patterns in visits. Influenza and pneumonia had a rapid increase than the AGR of all visits (22.7% vs 15.2%, $P<0.0001$), as well as asthma and other allergic diseases (16.9% vs 15.2%, $P=0.0001$), “Other lower respiratory infections” (16.0% vs 15.2%, $P=0.0073$). The AGR of other lower respiratory infections had a slower increasing trend than average level of all visits (9.0% vs 15.2%, $P<0.0001$).

Trend in diagnosis according to age is shown in Fig. 7. With increasing age, the proportion of asthma and other allergic diseases increased from 8.1% of patients aged <1 year to 27.4% of patents aged of 12 to <18 years ($P<0.0001$). The proportion of influenza and pneumonia decreased from 27.5% to 11.9% ($P<0.0001$) between the same age categories above, as well as of other lower respiratory infections from 30.6% to 18.5% ($P<0.0001$).

Age-specific trend in RODs

Fig. 8 showed age-specific trend in percentage and visits of respiratory diagnosis. Lower respiratory infections (30.6% in total) and influenza and pneumonia (27.5% in total) were the most common diagnoses for children aged < 1 year. The percentages of these two types of diagnosis changed little from 38.5% in 2013 to 32.8% in 2018 and form 33.5% to 33.9% in the same years, respectively. The increasing trend in visits of lower respiratory infections and influenza and pneumonia was similar with an AGR of 16-21%, far more than an AGR of 6-9% of asthma and other allergic diseases and upper respiratory tract diseases.

Among children aged 1 to < 4 years, lower respiratory infections (31.9% in total) was the most common diagnosis and the percentage of influenza and pneumonia (18.2% in total) was less than the children age <1 year. The percentage of visits for lower respiratory infections was nearly unchanged from 34.1% in 2009 to 33.4% in 2018 with an AGR of 16%, while the percentage of visits for pneumonia increased from 12.7% in 2009 to 21.6% in 2018 with an AGR of 23%. The other diagnosis had an AGR of 8-15%.

For children aged 4 to 7 years, the percentage of asthma and other allergic diseases was significantly higher than children aged 1 to < 4 years (18.2% vs 10.4%, $P<0.001$). The diagnosis of lower respiratory infections was still the commonest diagnosis (28% in total) with a decreasing trend. The AGR of asthma and other allergic diseases was 21% and lower respiratory infections was 17%, as well as the similar increasing rate of other diagnosis of diseases of upper respiratory tract and influenza and pneumonia (11% and 23%, respectively).

With the age of children increasing to 7 and <12 years, the percentage of asthma and other allergic diseases was 22.4% in total with a steadily increase from 15.6% in 2014 to 25.7% in 2018. The percentage of lower respiratory infections showed a concomitant decrease to 21.2% in total with the same trend between 2014 and 2018 (from 34.6% to 17.9%). The trend in visits of asthma and other allergic diseases remained a high AGR of 26% after 2016, while the other three diagnoses became slow down with an AGR below 10.0%.

In the last age category of children, 12 to < 18 years, the percentage of asthma and other allergic diseases reached 27.4% with continuing increase from 2014. The increasing trend of other three respiratory diagnosis was continuing to slow down to a growth rate around 7.0%.

Gender-specific trend in RODs

Fig. 8 showed gender-specific trend in percentage and visits of RODs. Lower respiratory infections and influenza and pneumonia remained the most common diagnoses for males (29.6% and 17.8% respectively) and females (29.6% and 18.0% respectively). The percentage of asthma and other allergic diseases was 14.3% for males and 11.4% for females in total ($P<0.001$) and in 2018 the percentage of that increased to 16.7% for males and 14.2% for females. The increasing trend in visits of lower respiratory infections, influenza and pneumonia, and asthma and other allergic diseases for males was less rapid than females (AGR after 2009: 15.3% for males vs 17.2% for females, 22.1% for males vs 23.5% for females vs 15.8% for males vs 19.1% for females, respectively.). The AGR after 2015 showed a faster increase for asthma and other allergic diseases (23.2% for males and 27.4% for females) than lower respiratory infections (10.1% for males and 11.2% for females) and influenza and pneumonia (16.8% for males and 15.1% for females).

Co-morbidities of Asthma and other allergic diseases, lower respiratory infections

Table 2 showed the top 10 secondary diagnoses defined as the co-morbidity associated with the principal diagnosis of the patients. Asthma and other allergic diseases were associated with 25.5% lower respiratory infection patients, and respiratory infections were associated with 18.8% asthma and other allergic diseases patients.

Discussion

Our study provided real life data of secular trends in out-patient visits and diagnosis amongst children attended one of the largest children's hospitals in China. Detailed computer records of this large sample population allowed stratification into age and gender-specific trends over a period of 10 years.

During the past 10 years, the trend in ROVs increased rapidly in the early part of this decade and slowed substantially after 2013. The result suggested the demand of specialist medical service of respiratory diseases increased greatly in the early years and the supply of respiratory outpatient service nearly reached the full level in the subsequent years.

Among the total ROVs, per-school children were the consumers receiving specialist medical services. Children aged 1 to < 4 years accounted for 43.0% of ROV in total, and 4 to < 7 years accounted for a further 24.2%, <1 year accounted for 22.6%, respectively. This is understandable as pre-schoolers, with their relatively naïve immune system are most susceptible to respiratory diseases and different environmental triggers.

When we further analyzed the age-specific trend in RODs, we found the percentage of asthma and other allergic diseases increased with the age consistently. The AGR of asthma and other allergic diseases ranked first at 16.86% amongst total visits of all age groups, and reached 20-27% in children aged 4 to <7 especially after 2014, with the concomitant decreasing trend in the percentage of respiratory infectious diseases. Our findings of overall trend in ROVs of asthma and other allergic diseases were in contrast to the national surveillance of asthma in the United States from 2001 to 2010[9] and UK from 2006 to 2016[13]. The US survey showed there was no significant trend in the number of asthma hospital outpatient department visits from 2001 to 2009, so did the population-based rate and risk-based rate of hospital outpatient department visits [9]. The similar trend in the prevalence of current asthma was 7.2% in 2006, gradually falling to 6.5% in 2016 in UK [13]. However, the age-specific trend in ROVs of asthma and allergic disease was in accordance with the study in US and Europe. The prevalence of asthma across all ages was 21.8% in Philadelphia, with an increase of prevalence after 6-10 ages (22.9%) to the peak prevalence between 14 and 17 years of age (23.0%) from 2001 to 2013[14]. In Northern Sweden, the prevalence of physician-diagnosed asthma increased from 5.7% at age of 7-8 to 7.7% at age of 11-12 ($P<0.001$) [15]. Our findings also were in accordance with the prevalence of childhood asthma in

Shanghai, which showed the greatly increasing from 1990 to 2011 and asthma is more reliably diagnosed than in younger children among 6-year old children [11]. In China, asthma and allergic diseases were in the process of increasing and the age of 4 to <7 years is a critical period for pediatric physicians to take an early action on the treatment of asthma and allergic diseases.

Considering the gender-specific trend in asthma and allergic diseases, our study showed similar findings with the latest report in the US from 2001 to 2013. The US survey suggested asthma prevalence is higher among males in 5-9 years of age and increases among females compared to males in 10-17 years of age [10]. Our study showed a sharp increase of visits of asthma and other allergic diseases after 2015 compared to lower respiratory infections and influenza and pneumonia. And the percentage of asthma and other allergic diseases was higher for males than females, while faster growth rate of visits among females. This gender-specific trend suggested the 'adolescent switch' observed in other studies. Asthma mostly affects boys in childhood and women in adulthood[16], with many factors contributing to its frequency and severity, including that shift in sex hormone[17-19], genetic factors[20], maternal asthma[21], and environmental exposure[22]. Gender-specific trend for asthma and allergic diseases should be taken into account in asthma management and it is relevant to consider gender differences in the daily clinical practice [23].

The results of co-morbidities indicated the high relation between asthma and other allergic diseases and lower respiratory infections. Of total ROVs, 25.5% asthma and other allergic diseases often accompanied with lower respiratory infections. The results were in consistent with the guideline of asthma diagnosis and management, the long-term prevention to control inflammation and airway hyperactivity play an import role in asthma management [24].

Strengths and limitations

Strengths of our study were huge sample size of 10-year administrative data and reported according to the RECORD statement. And we used the ICD-10 classification system to analyze the age-specific trend in RODs, which can make comparison with other studies possible.

We admitted limitations of our study. Firstly, this is a hospital-bases study in a single center. We cannot calculate the prevalence of pediatric RODs in the population. Secondly, the nature of retrospective study has a risk of report bias. The diagnosis recorded in HIS system may have a higher occurrence of unspecified diagnosis and use of the ICD-10 category symptoms, signs and abnormal clinical and laboratory findings in the early of the decade. Thirdly, the effect of missing data of diagnosis cannot be excluded. We noticed that the age-specific trend had an obvious decline in 2013 and 2014 and then increased after 2015. It may contribute to the high rate of missing data of diagnosis in 2013 and 2014, which was 58% and 42%, respectively. A sensitive analysis was conducted and no systematic bias of missing data was found (Appendix 2). Lastly, our findings are based on data from a tertiary pediatric hospital, which may not be generalized to all the providers of pediatric medical service.

Conclusion

Our findings suggest that the upward trend in pediatric ROVs among children at different ages in the past 10 years. More attention should be given to the children aged more than 4 years and the 'adolescent switch' with the increasing trend of asthma and other allergic diseases for both males and females. Gender differences and long-term prevention to control inflammation should be concerned in the daily clinical practice.

Abbreviations

ROVs:respiratory outpatient visits; RODs:respiratory outpatient diagnoses; RD: respiratory disease; LRI:lower respiratory infections; HIS:Hospital Information System; AGR:average growth rate

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Tables

Table 1 Characteristics of patients, 2009-2018

	Patients visited the respiratory outpatient department
<i>n</i> of patients	285574
Age, year	
<1	74034(23.0)
1 to <4	132178(41.1)
4 to <7	76818(23.9)
7 to <12	33825(10.5)
12 to <18	4512(1.4)
Total ^[1]	321368
Sex	
Male	170192(59.6)
Female	115382(40.4)
Payer type	
Government insurance	112495(39.4)
Self-finance	173079(60.6)
Clinic types	
Specialist Clinic	170808(46.5)
Expert-clinic	192081(52.3)
Disease-specific Clinic	4434(1.2)
Total ^[2]	367323
Average visits per patients	2.4
Government insurance	2.9
Self-finance	2.1

Note[1] A child could contribute data to multiple age groups as he or she visited the clinic of respiratory disease in different year.

[2] A child could contribute data to multiple clinic types as he or she visited the clinic of respiratory disease in different type.

Table 2. Co-morbidities of Asthma and other allergic diseases, lower respiratory infections

Rank	Most common co-morbidities [#]	Asthma and other allergic diseases (patients= 6737)	Most common co-morbidities	Lower respiratory infections* (patients= 10448)
1	Allergic rhinitis(J30.4)	1981(29.4)	Bronchitis(J40)	3543(33.9)
2	Asthma(J45.9)	1073(15.9)	Asthma(J45.9)	1361(13.0)
3	Acute upper respiratory infection(J06.9)	461(6.8)	Allergic rhinitis(J30.4)	986(9.4)
4	Bronchitis(J40)	450(6.7)	Respiratory disorder [J98.9]	638(6.1)
5	Cough (R05)	382(5.7)	Chronic nasopharyngitis (J31.1)	409(3.9)
6	Predominantly allergic asthma(J45.0)	377(5.6)	Predominantly allergic asthma(J45.0)	323(3.1)
7	Respiratory disorder [J98.9]	283(4.2)	Acute laryngitis (J04.0)	228(2.2)
8	Bronchopneumonia (J18.0)	236(3.5)	Noninfective gastroenteritis and colitis(K52.9)	210(2.0)
9	Other pneumonia, organism unspecified (J18.8)	119(1.78)	Acute tonsillitis[J03.9]	154(1.5)
10	Chronic nasopharyngitis (J31.1)	109(1.6)	Chronic obstructive pulmonary disease (J44.8)	135(1.3)
	Others	1266(18.8)	Others	2461(23.6)

*not including influenza and pneumonia.

[#]co-morbidity indicated the secondary diagnosis of outpatient.

The words with black front indicated the secondary diagnosis were different from the category of principal diagnosis.

Declarations

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manuscript. Dr Liu assisted in data clearing, interpretation of the results and revised the manuscript. Ms J. Li designed the data collection instruments, collected data, carried out the initial analyses. Drs A.M. Li, Wang, Xu, and Huang critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work. Consent for publication Not applicable Competing interest The authors declare that they have no competing interests.

Figures

Figure 1

Flowchart illustrating selection of participants and data linkage process

Figure 2

Trend in respiratory outpatient visits, 2009-2018

Figure 3

Age-specific trend in percentage of respiratory outpatient visits, 2009-2018

Figure 4

Age-specific trend in respiratory outpatient visits, 2009-2018

Figure 5

Trend in percentage of respiratory outpatient diagnosis, 2009-2018

Figure 6

Trend in visits of respiratory outpatient diagnosis, 2009-2018

Figure 7

Trend in respiratory outpatient diagnosis according to age, 2009-2018

Figure 8

Age-specific trend in percentage and visits of respiratory outpatient diagnosis, 2009-2018

Figure 9

Gender-specific trend in percentage and visits of respiratory outpatient diagnosis, 2009-2018

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