Postprint: Etiology of pediatric chronic cough in Lanzhou area, 2014-2023

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Abstract

Background Chronic cough is a common reason for pediatric visits, and the etiology of chronic cough in children varies across different regions. Lanzhou is located in the inland northwest of China, with a dry climate, frequent sand and dust weather, and high pollen concentrations in autumn; however, there is currently a lack of etiological studies on chronic cough in children in this region.

Objective To investigate the etiological composition of chronic cough in children and changes in its main causes in Lanzhou region from 2014 to 2023.

Methods A retrospective analysis was conducted on the clinical data of 944 children with chronic cough who received outpatient and inpatient treatment at Gansu Provincial Maternity and Child-care Hospital (Gansu Provincial Central Hospital) from 2014 to 2023, and the etiological composition of chronic cough in children and its relationship with gender, age, season, and year were explored.

Results From 2014 to 2023, the etiological distribution of chronic cough in children was as follows: cough variant asthma in 314 cases (33.26%), upper airway cough syndrome in 259 cases (27.44%), post-infectious cough in 221 cases (23.41%), protracted bacterial bronchitis in 34 cases (3.60%), gastroesophageal reflux-related cough in 9 cases (0.95%), and cough due to other causes in 107 cases (11.34%). Among the 107 children with cough due to other causes, 80 had multiple etiologies (accounting for 8.47% of total cases), and among these children with multiple etiologies, upper airway cough syndrome combined with post-infectious cough accounted for 30.00% (24/80). Comparison of the etiological distribution of chronic cough in children of different genders showed no statistically significant difference (2=0.894, P=0.971). Comparisons of the etiological distribution of chronic cough in children of different ages and seasons showed statistically significant differences (2=361.544, P<0.001; 2=31.793, P=0.007). Trend 2 test results showed that with increasing years, cough variant asthma

gradually decreased (2=43.252, P<0.001), while upper airway cough syndrome gradually increased (2=30.431, P<0.001).

Conclusion Cough variant asthma, upper airway cough syndrome, and post-infectious cough were the main causes of chronic cough in children in Lanzhou region from 2014 to 2023. Among multiple etiologies, upper airway cough syndrome combined with post-infectious cough was the leading cause. Age and season affect the composition of chronic cough in children in this region. With changes in years, cough variant asthma gradually decreased, while upper airway cough syndrome showed a significant upward trend.

Full Text

Study on the Etiology of Chronic Cough in Children in Lanzhou, 2014-2023

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Abstract

Background: Chronic cough is a common reason for pediatric consultations, and its etiology varies across different regions. Lanzhou is located in the inland northwest of China, characterized by a dry climate, frequent dusty weather, and high pollen concentrations in autumn. However, research on the etiology of chronic cough in children is lacking in this region.

Objective: To investigate the etiological composition of chronic cough and changes in its major causes among children in Lanzhou from 2014 to 2023.

Methods: We retrospectively analyzed clinical data from 944 children with chronic cough treated in outpatient and inpatient settings at Gansu Provincial Maternal and Child Health Hospital (Gansu Provincial Central Hospital) between 2014 and 2023. The study explored the etiology of chronic cough in children and its relationship with gender, age, season, and year.

Results: The etiological distribution of chronic cough in children from 2014-2023 was as follows: cough variant asthma (CVA) in 314 cases (33.26%), upper airway cough syndrome (UACS) in 259 cases (27.44%), post-infectious cough (PIC) in 221 cases (23.41%), protracted bacterial bronchitis (PBB) in 34 cases (3.60%), gastroesophageal reflux cough (GERC) in 9 cases (0.95%), and other causes in 107 cases (11.34%). Among the 107 children with other causes, 80

had multiple etiologies (8.47% of total cases), with UACS combined with PIC accounting for 30.00% (24/80) of multiple-etiology cases. No statistically significant difference was found in etiological distribution between genders (^{2}=0.894, P=0.971). However, significant differences were observed across age groups and seasons (^{2}=361.544, P<0.001; ^{2}=31.793, P=0.007). Trend ^{2} tests revealed that CVA gradually decreased over the years (^{2}=43.252, P<0.001), while UACS gradually increased (^{2}=30.431, P<0.001).

Conclusion: CVA, UACS, and PIC were the leading causes of chronic cough in Lanzhou children from 2014-2023. Among multiple etiologies, UACS combined with PIC was the most common combination. Age and season influenced the etiological composition of chronic cough in this region. Over time, CVA showed a decreasing trend while UACS demonstrated a significant upward trend.

Keywords: Chronic cough; Etiology; Lanzhou; Child; Cough variant asthma; Upper airway cough syndrome; Post-infectious cough

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Chronic cough is a common reason for pediatric visits and can involve multiple diseases within and beyond the respiratory system. Cough is a protective defense mechanism that helps clear harmful pathogens and reduces the risk of respiratory infections. However, prolonged chronic cough can negatively impact children's daily life, learning, physical activity, and social interactions, adversely affecting their physical and mental well-being. Compared with adults, children have relatively narrower airways, more pronounced cough reflexes, and developing immune systems, resulting in different etiological patterns of chronic cough [1]. Geographic environment, lifestyle habits, and economic factors contribute to regional and age-related variations in the etiology of chronic cough among children [2-3]. Currently, few studies have investigated the etiology of chronic cough in Lanzhou children, and obtaining follow-up data for revised diagnoses presents certain challenges. This study analyzed data from 944 children with chronic cough at Gansu Provincial Maternal and Child Health Hospital (Gansu Provincial Central Hospital) to provide scientific evidence for etiological diagnosis of chronic cough in the Lanzhou region.

Methods

Study Subjects

After screening with inclusion and exclusion criteria, we retrospectively selected 944 children with chronic cough treated in pediatric outpatient and inpatient departments at Gansu Provincial Maternal and Child Health Hospital (Gansu Provincial Central Hospital) from 2014 to 2023. The cohort included 509 males (53.92%) and 435 females (46.08%), aged 0.3–13.0 years. The patient selection flowchart is shown in [Figure 1: see original paper].

This retrospective study was approved by the Ethics Committee of Gansu Provincial Maternal and Child Health Hospital (Gansu Provincial Central Hos-

pital) (Approval No.: (2023) GSFY Lun Shen [57]). Informed consent was waived due to the retrospective nature of the study.

Inclusion Criteria

1. Met diagnostic criteria from the "Guidelines for the Diagnosis and Treatment of Chronic Cough in Chinese Children (2013 Revision)" [4];
2. Had complete clinical data with follow-up records ($ $1 visit);
3. Aged 0.3–13.0 years;
4. Born and residing in the Lanzhou area.

Exclusion Criteria

1. Abnormal chest X-ray or routine chest CT findings;
2. Definitive systemic diseases such as hematologic disorders or congenital heart disease;
3. Incomplete clinical data or missing follow-up records;
4. Unclear etiology.

Data Collection

Cough-Related Clinical Data We collected data on cough duration, timing, characteristics, associated symptoms, allergy history, family history of allergies, and foreign body aspiration history. Common causes of chronic cough in children included: cough variant asthma (CVA), upper airway cough syndrome (UACS), post-infectious cough (PIC), protracted bacterial bronchitis (PBB), and gastroesophageal reflux cough (GERC).

Physical Examination This included assessment of growth and development, chest wall deformities, cardiopulmonary signs, and nasopharyngeal findings.

Auxiliary Examinations All patients underwent chest X-ray or routine chest CT. Based on medical history, symptoms, and physical signs, selective tests were performed including complete blood count, C-reactive protein (CRP), total IgE, allergen skin prick test (SPT), fractional exhaled nitric oxide (FeNO), pulmonary function and bronchodilator tests, nasopharyngeal lateral radiograph or CT, and respiratory pathogen testing.

Statistical Analysis

SPSS 24.00 software was used for statistical analysis. Categorical data were expressed as cases (%) and compared using ^{2} tests for intergroup comparisons and linear trend analysis of etiology changes over years. $P<0.05$ was considered statistically significant.

Results

Overall Etiological Distribution

Among the 944 children with chronic cough, the etiological distribution from 2014–2023 was: CVA in 314 cases (33.26%), UACS in 259 cases (27.44%), PIC in 221 cases (23.41%), PBB in 34 cases (3.60%), GERC in 9 cases (0.95%), and other causes in 107 cases (11.34%). Among the 107 children with other causes, 80 had multiple etiologies (8.47% of total cases). Within the multiple-etiology group, UACS combined with PIC accounted for 30.00% (24/80) of cases. See and for details.

Relationship Between Chronic Cough and Gender

No statistically significant difference was found in etiological distribution between genders (^{2}=0.894, P=0.971). See .

Relationship Between Chronic Cough and Age

Children were divided into age groups: infancy (68 cases, 7.20%), toddler (150 cases, 15.89%), preschool (404 cases, 42.80%), and school age (322 cases, 34.11%). Etiological distribution differed significantly across age groups (^{2}=361.544, P<0.001). PIC and PBB predominated in infancy; PIC and UACS in toddlerhood; and CVA and UACS in preschool and school-age children. See .

Relationship Between Chronic Cough and Season

The 944 cases were distributed across seasons: spring (215 cases, 22.78%), summer (180 cases, 19.07%), autumn (282 cases, 29.87%), and winter (267 cases, 28.28%). Seasonal differences in etiological distribution were statistically significant (^{2}=31.793, P=0.007). CVA and UACS were predominant in summer and autumn, while CVA and PIC were more common in spring and winter. See .

Temporal Trends in Major Causes of Chronic Cough

The top three causes were CVA, UACS, and PIC. Trend ^{2} tests showed that CVA gradually decreased over the years (^{2}=43.252, P<0.001), while UACS gradually increased (^{2}=30.431, P<0.001). No significant trend was observed for PIC (P>0.05). See .

Discussion

This study demonstrated that the top three causes of chronic cough in Lanzhou children from 2014–2023 were CVA (33.26%), UACS (27.44%), and PIC (23.41%), consistent with findings from the "Multicenter Study on the Etiological Composition of Chronic Cough in Chinese Children" [5]. Xu et al. [6] analyzed 202 children with chronic cough in Chongqing, reporting the

top three causes as PIC (40.1%), CVA (35.1%), and UACS (21.3%). Su et al. [7] reported UACS (51.9%), CVA (24.3%), and PIC (18.3%) as the leading causes in Xuzhou. These regional differences likely relate to Lanzhou' s unique geographic and seasonal characteristics. Adjacent to parts of Inner Mongolia, Lanzhou experiences high pollen concentrations in summer and autumn, particularly in fall when pollen levels rank among the highest nationally. Studies show that *Artemisia sieversiana*, willow, sunflower, and *Chenopodium* pollen are major inhalant allergens in Lanzhou [23]. Pollen irritates airways and increases nasal secretions, directly or indirectly stimulating cough receptors and elevating UACS prevalence. In contrast, spring and winter feature low temperatures, large diurnal temperature variations, and prolonged cold spells—peak seasons for respiratory infections—thereby increasing PIC proportions.

CVA was the leading cause of chronic cough in Lanzhou children during 2014-2023. Lifestyle changes, environmental pollution, and industrialization have contributed to rising CVA incidence [8-9]. Without proper treatment, approximately 30–40% of CVA patients develop bronchial asthma (BA) [10]. Diagnosing CVA in children over 6 years is relatively straightforward, but remains challenging in younger children who cannot complete pulmonary function and bronchodilator tests. Studies suggest impulse oscillometry (IOS) has diagnostic value for pediatric CVA, with IOS parameters showing strong discriminatory potential [11]. Therefore, dynamic observation of disease evolution and treatment response is crucial for diagnosing CVA in children.

UACS has attracted increasing attention due to its rising incidence. Investigations in Xuzhou, Shanghai, Tianjin, Guangzhou, and other regions show UACS has become the leading cause of chronic cough [7,12-14]. In this study, UACS ranked second (27.44%). Research indicates UACS incidence is higher in school-age children, with adenoid hypertrophy being the main cause in preschoolers [15]. While children with typical symptoms are easily diagnosed, some present with atypical manifestations requiring specialist consultation, potentially underestimating true incidence. As diagnostic capabilities improve, more UACS cases will be identified. In this study, preschool children had the highest UACS prevalence, likely due to rapid sinus development and adenoid proliferation at this age, combined with expanded activity spaces and increased exposure to microorganisms and allergens.

PIC refers to persistent cough following infection by various pathogens, typically lasting no more than 8 weeks. Diagnosis is aided by typical irritative dry cough and clear respiratory infection history, with further observation and follow-up being essential. PIC ranked third (23.41%) in Lanzhou, with higher proportions in infancy and toddlerhood. After the Beginning of Autumn each year, large temperature fluctuations coincide with rising respiratory infections involving *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, influenza virus, respiratory syncytial virus, adenovirus, and bacteria. Young children' s relatively weak immune function increases their susceptibility to PIC.

PBB refers to persistent infection of the bronchial mucosa causing productive

(wet) cough for more than 4 weeks [5]. First described by Australian scholars in 2006, it is common in children under 6 years [16]. Diagnostic clues include: productive cough >4 weeks after excluding other causes, high-resolution CT showing bronchial wall thickening with suspected bronchiectasis, effective response to 2 weeks of antibiotic therapy, and elevated neutrophils or positive bacterial culture in bronchoalveolar lavage fluid. This study identified 34 PBB cases (3.60%), substantially lower than rates reported in China' s "Multicenter Study on Chronic Wet Cough in Children" [17] and Australian specialist clinics (10.24%, 41%) [18]. Studies show infants are most susceptible to PBB, with *Haemophilus influenzae* (42.2%) being the most common isolate, followed by *Streptococcus pneumoniae* (22.2%) and *Klebsiella pneumoniae* (20.0%) [19]. In this study, 85.29% of PBB cases occurred in infants and toddlers, highlighting the need for heightened awareness of PBB in this age group, particularly in children with persistent productive cough, to enable early diagnosis and effective treatment.

GERC is a clinical syndrome where gastroesophageal reflux causes cough as the main manifestation [20]. Only 9 cases (0.95%) were identified in this study. CHEN et al. [21] reported GERC accounted for 3.5% of chronic cough in children, while a Chinese multicenter study reported 0.62% [5]. The gold standard for GERC diagnosis—24-hour distal esophageal pH monitoring—is invasive and difficult to obtain parental consent for, likely leading to underdiagnosis. Clinically, infants with suggestive symptoms require careful evaluation for this condition.

Foreign body aspiration is an important cause of accidental injury in children. The diversity of foreign bodies and occult history often lead to misdiagnosis. This study identified 18 aspiration cases, 16 (88.89%) in infants and toddlers, mostly involving peanuts, sunflower seed shells, and walnuts. Due to immature laryngeal reflexes, young children cannot effectively expel foreign bodies through coughing or vomiting; therefore, children under 3 years should avoid such foods. Six cases of congenital airway disease were identified, including 5 in infants (4 congenital tracheoesophageal fistulas, 1 congenital vascular malformation) and 1 toddler with mediastinal tumor-related cough, suggesting greater vigilance for congenital airway diseases is needed in younger children.

Gender did not influence etiological distribution, consistent with previous findings [5-7,12-14,22]. Age-related differences were observed: infancy was dominated by PIC and PBB; toddlerhood by PIC and UACS; and preschool and school age by CVA and UACS. Seasonal variations also affected etiology, with CVA and UACS predominating in summer/autumn and CVA and PIC in spring/winter.

Analysis of temporal trends from 2014–2023 revealed decreasing CVA and increasing UACS. This may relate to lifestyle and environmental changes, improved medical care, and rising prevalence of sinusitis and adenoid hypertrophy in children.

This single-center retrospective study of Lanzhou children from 2014–2023 in-

cluded a large sample size with extensive geographic coverage and comprehensive follow-up, yielding representative results. However, limitations include incomplete implementation of bronchial provocation tests, 24-hour esophageal pH monitoring, and induced sputum eosinophil counts due to objective constraints, potentially introducing bias in etiological analysis.

In summary, this study analyzed the characteristics and trends of chronic cough etiology in Lanzhou children over the past decade, providing valuable reference for clinical practice. These findings can help clinicians employ targeted investigations, implement effective interventions, reduce medical costs, minimize misdiagnosis and missed diagnosis, and improve quality of life for children with chronic cough. Given the complex etiology of chronic cough in children, diagnostic workup should proceed from simple to complex, common to rare, to maximize etiological clarification and optimize treatment.

Author Contributions: NA Feiyang and WANG Yannan designed the study, wrote the manuscript, and handled submission and revisions. YANG Yi and WANG Yong implemented the study and collected and organized data. NA Feiyang and WANG Yannan supervised quality control.

Conflict of Interest: The authors declare no conflict of interest.

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Note: Figure translations are in progress. See original paper for figures.