SHORT REPORT

Clinical syndrome of childhood asthma based on key indicators detection

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Abstract

This study was conducted to investigate the clinical syndromes of asthma in children based on the detection of key indicators. A total of 50 children with asthma were selected based on the asthma diagnostic methods categorised according to cough, wheezing, sputum and wheezing sound. The levels of D-dimer (DD) and fibrinogen (Fg) in plasma and blood gas analysis were also measured. The diagnostic symptoms were divided into TCM diagnostic statistics and western medicine diagnostic scores. The analysis showed male children to be affected much more than female children, and the age of 2-5 years was more common. Blood tests showed that the plasma levels of DD and Fg in children with acute asthma increased significantly. The onset of asthma in children was closely related to history of allergy and family inheritance. More than half of the children had a history of allergy. Respiratory tract infection caused by cold air was the most important cause of asthma in children. Most children with asthma were febrile with cough (moderate to severe) and sputum. The syndromes in this study included wind-heat syndrome, lung-qi deficiency syndrome and wind-cold syndrome, which could lay a foundation for the prevention, diagnosis and treatment of asthma in children.

Keywords: Childhood Asthma, Clinical Syndromes, Detection of Traditional Chinese and Western Medicine.

Introduction

Bronchial asthma is one of the most common chronic respiratory diseases in children, and also an important cause of morbidity and mortality of chronic diseases worldwide. Over the past 10 years, the incidence of childhood asthma has risen all over the world.[1] The mortality rate of asthma is also high which has been reported in hospitalized children in China as 0.13%~0.14%. The epidemiological survey of asthma in China in 2002 showed that the prevalence rate of asthma was 0.5%~3% in two years, and it was as high as 5% in some areas.[2] Active prevention is therefore important to reduce the incidence of asthma. Asthma has a serious impact on children' s normal physical and mental development. Due to the chronic nature of the illness and repeated attacks, the child becomes frail with a low resistance. The treatment costs bring enormous economic and mental pressure on the families.[3] The pathogenesis of childhood asthma includes environmental, genetic, emotional, infection and other factors.[4-6] If asthma in children is not treated early, and adequately, it can become a lifelong disease.[7] In modern medicine, bronchial asthma, referred to as asthma, is a chronic inflammatory disease of the airway involving a variety of cells, such as eosinophils, mast cells, T lymphocytes, neutrophils and other cellular components. The main signs include chronic airway inflammation, airway hyperresponsiveness to multiple stimuli, extensive and variable reversible airflow limitation, and airway remodelling due to prolonged illness.[8] Clinical manifestations are recurrent wheezing, chest tightness, shortness of breath or cough, which usually occurs at night and aggravates in the morning.[9,10] Since children cannot express themselves adequately it can be a challenge for the health care providers. The family plays an important role in the management of Asthma which is closely related to the progress of the child's disease.[11-16]

Fibrin dissolving system is the most important anticoagulant system in human body. During the dissolving process, fibrin is hydrolysed to release fibrin monomer, which further forms cross-linked fibrin.[17,18] After being degraded by plasmin, the cross-linked fibrin released fragments, which are further degraded into D-dimer (DD).[19] When the balance between coagulation system and fibrinolysis system is destroyed, the tendency of coagulation in blood vessels is enhanced, fibrin is aggregated, and the degradation products are increased, so the content of DD and fibrinogen (Fg) is increased.[20-22] DD is an intermediate product in the process of blood coagulation and micro-thrombosis. It can be used as an indicator of hypercoagulability and hyperfibrinolysis, and has important clinical diagnostic value.[23] Mohamed et al. (2019) showed that compared with mild asthma patients and control group, the level of DD in patients with moderate and severe asthma was higher, and they considered that DD was a key indicator of clinical

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symptoms in patients with asthma.[24] A good clinical history along with a physical examination revealing bilateral wheezing with a prolonged expiratory phase along with a family history provides an accurate diagnosis.

The family history, allergic history and inducing factors of the patients should be enquired, to determine the diagnosis and provide the correct therapy.[25-29] This report aims to study the clinical syndromes of asthma in children in China based on the detection of key indicators.

Methods and Results

Fifty children with asthma tested and treated in Dezhou People's Hospital from February 2018 to February 2019 were selected for the study. Written consent was obtained from all patients or their guardians for participating. Based on the age, trigger, personal history, allergic history, family history, symptoms, signs, treatment before admission and laboratory examination results after admission (such as routine blood tests, immunity, Mycoplasma pneumoniae antibody, inhalation/ingestion allergen screening) of children with asthma, the characteristics of children with asthma were analysed. The common clinical syndromes of acute attack of asthma in children were also summarised. This study was approved by the Ethics Committee of Dezhou People's Hospital.

Inclusion criteria: Children between one and 15 years with asthma who met the above diagnostic criteria were selected. Exclusion criteria: Children older than 15 years or younger than 1 year, children with other serious complications or primary diseases, and/or did not provide complete answers to the case observation questions for determining the syndrome. In addition, children with poor compliance were excluded. Children whose family members requested to withdraw from the clinical trial were also excluded. If serious adverse events occurred during the treatment, such as allergies to medicines, the children were removed from the study. Moreover, included children who did not follow the prescribed medication and treatment or incomplete case reports were not continued in the study.

Table-1: Comparison of main symptoms and signs between the two groups before treatment (x±s).

Symptoms/signs	Before treatment	After treatment
Cough	1.79±0.65	0.09±0.41
Wheezing	1.45±0.67	0.08±0.26
Phlegm	1.78±0.59	0.34±0.44
Wheezing sound	2.03±0.72	0.12±0.35

Diagnosis of asthma was based on the symptoms of wheezing, coughing, shortness of breath and chest tightness recurring repeatedly. If wheezing sounds were heard in the lungs, any of the following bronchodilation tests were used to assist in the diagnosis: inhalation of quick-acting β 2 receptor agonist nebulized solution or aerosol, and subcutaneous injection of 0.1% epinephrine 0.01ml/kg. If the result was positive, asthma was diagnosed. It was also noted that if within 15 to 30 minutes after any of the above tests, wheezing continued or was significantly reduced or alleviated. If conditions permitted, PEF or FEV1 were performed before and after treatment in children over 5 years age. If PEF and FEVI increased by 15% after treatment, asthma was considered confirmed. If there was no wheezing sound in the lungs

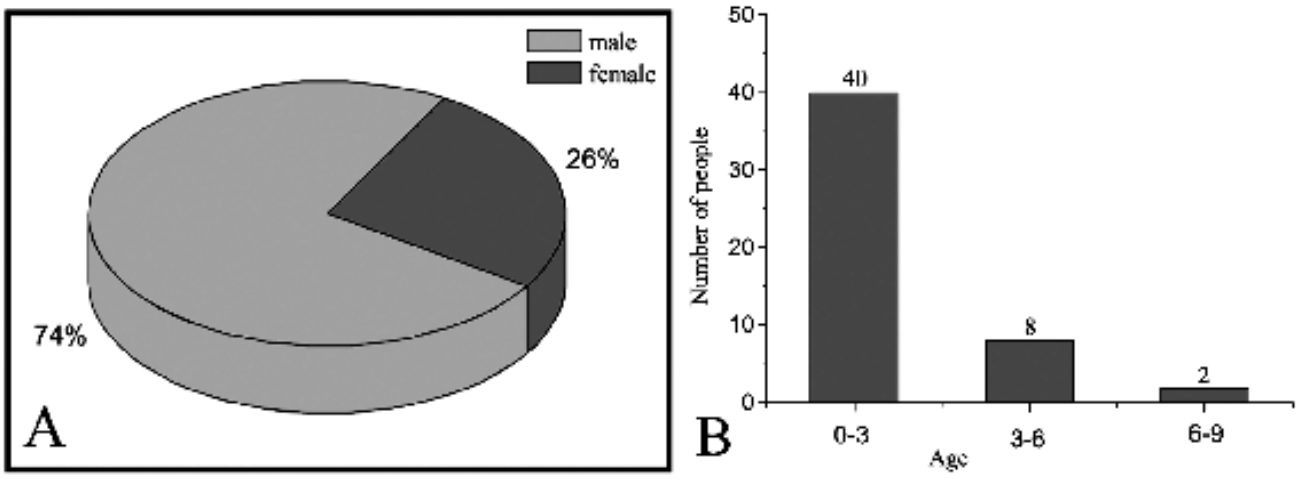

Figure-1: Statistical chart of basic situation of children (A: Gender composition of children B: Age composition of children).

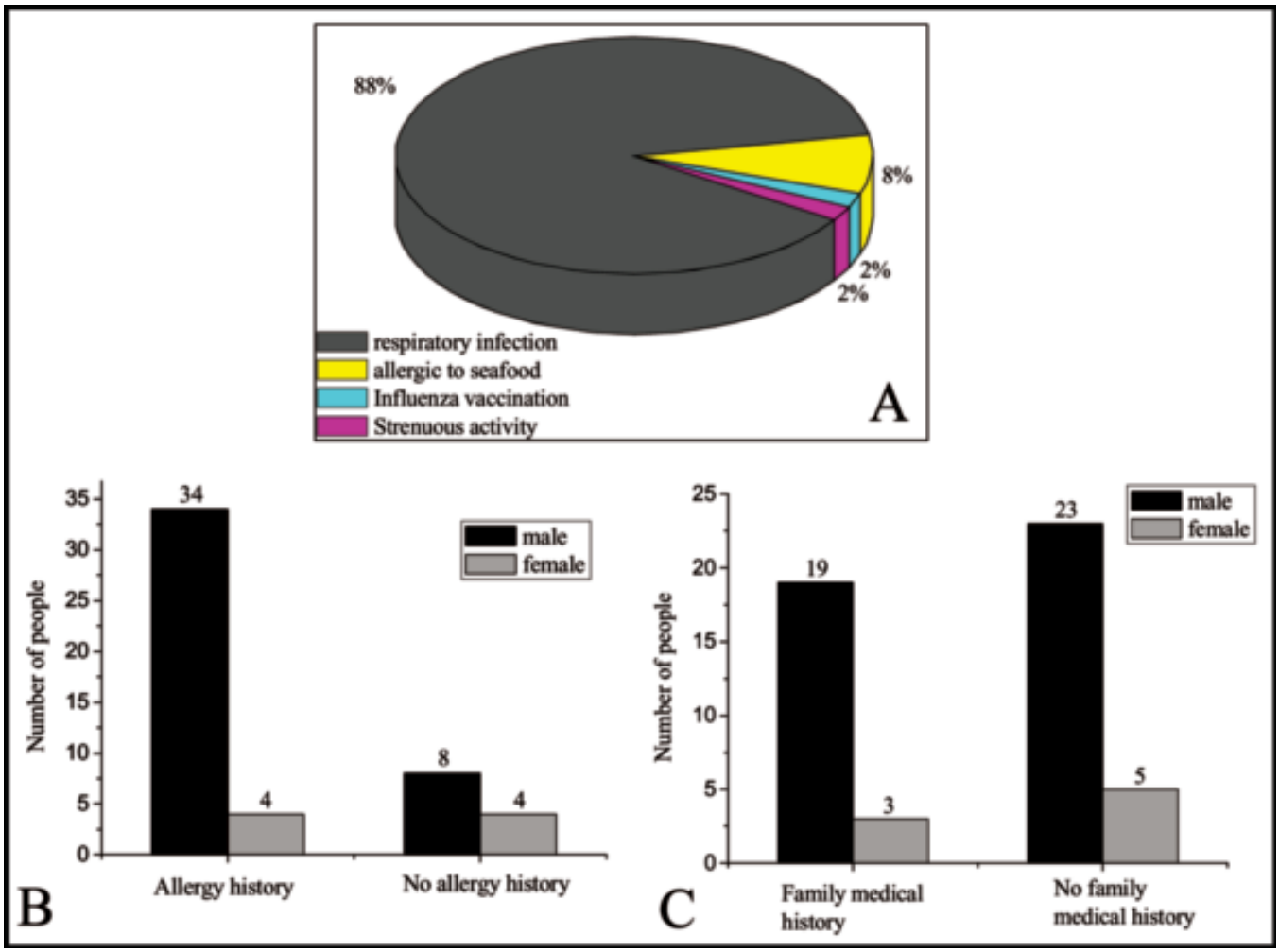

Figure-2: Relevant causes of asthma in children (A: The proportion of predisposing factors of childhood asthma; B: The proportion of allergic history; C: The proportion of family history).

and FEV1 > 75%, bronchial provocation test was done. If positive, asthma was diagnosed.

The main symptoms and signs scoring criteria were as follows.

Cough: no (0 points); mild (1 point) occasional attack of cough, moderate (2 points): cough more, cough a few times, but does not affect normal life, between mild and severe; severe (3 points): cough frequently day and night, affecting sleep and activity. Asthma: no (0 point); mild (1 point): wheezing occasionally attacks, does not affect sleep and activity; moderate (2 points): wheezing attacks more frequent, can lie flat, between mild and severe; severe (3 points): wheezing obvious, cannot lie flat, affecting sleep and activity. Phlegm ringing: no (0 points); mild (1 point): mild phlegm ringing in larynx; moderate (2 points): phlegm ringing in larynx between mild and severe; severe (3 points): phlegm roaring in larynx; Breathing sound: no (0 points); less (1 points): occasionally audible, or appear after deep breathing; medium (2 points): scattered; more (3 points): always audible; Symptom scoring criteria: There are no symptoms during the day or night (0 points). There are a few symptoms during the day, which lasts for a short time, such as waking up once or waking up early at night (1 point). There are two or more symptoms during the day, such as waking up twice or more at night, including early awakening (2 points). There are slight symptoms during most hours of the day, such as waking up several times at night, but it has little impact on normal life (3 points). The symptoms are more serious in most time of the day, which has an impact on normal life and patient cannot fall asleep at night (4 points).

According to the clinical practice and the evaluation method of general curative effect index, the scores of

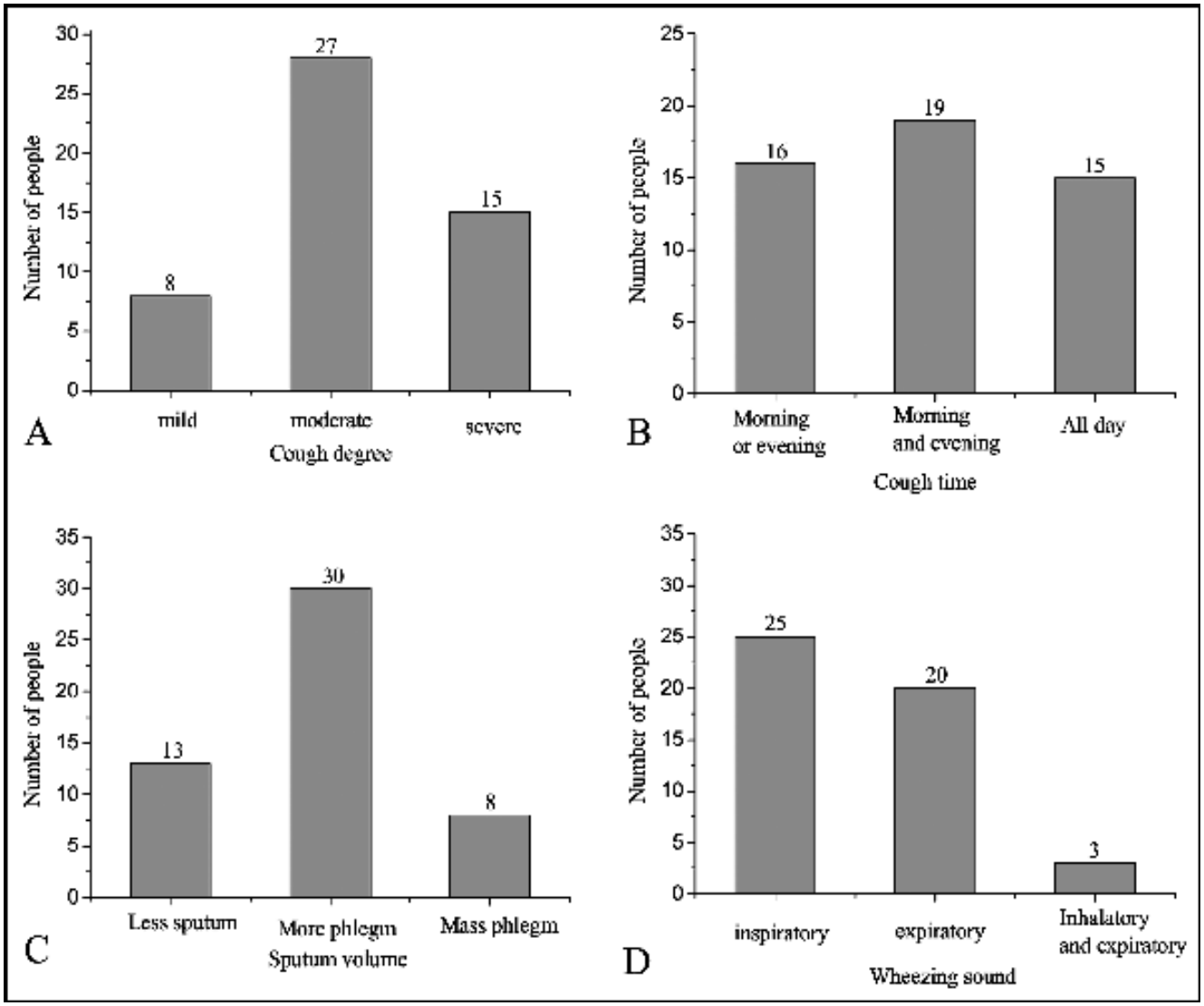

Figure-3: Contrastive analysis of main symptoms in children (A: Children's symptoms are counted according to the degree of cough; B: Children's symptoms are counted according to the time of cough; C: Children's symptoms are counted by sputum amount D: Children's symptoms are counted by wheezing sound or not).

main symptoms and signs before and after treatment, the comprehensive curative effect was judged by the integral improvement rate. The improvement rate of integral= (total integral before treatment-total integral after treatment)/total integral before treatment. The score was considered100% clinical control, if the total integral of the syndrome after treatment decreased by more than 90% compared with the before treatment score. Significant effect: After treatment, the score of syndrome decreased by more than 67-89% compared with that before treatment. Effective: After treatment, the score of syndromes decreased by more than 34-67% compared with that before treatment. Invalid: After treatment, the score of syndromes decreased by less than 34% compared with before treatment.

Determination of DD: 8 mL cubital vein blood was extracted and placed in a vacuum container (containing 10 mmol/L sodium citrate, mixed with blood at a ratio of 1:9 to anticoagulate) and was sent to the Laboratory for testing. The method was determined by immunofiltration and the normal value was < 200 ug/L. Determination of Fg: 2 mL cubital vein blood was extracted and placed in a vacuum blood vessel (containing 10 mmol/L sodium citrate, mixed with blood in a ratio of 1:9 to anticoagulate). The blood was tested in the laboratory and determined by thrombin turbidimetry, and the normal value was 2-4 g/L. All the data were processed by

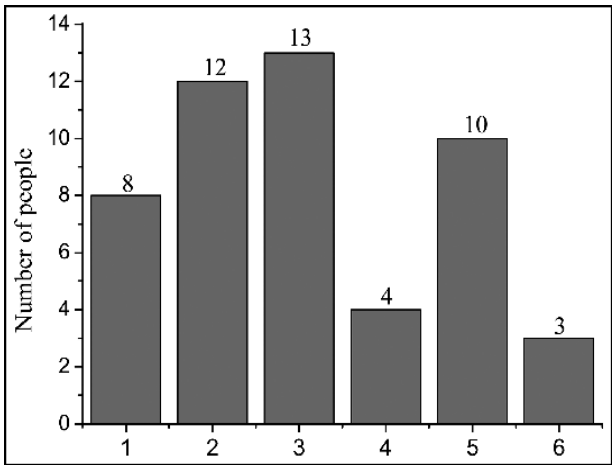

Figure-4: Contrast chart of clinical syndromes (The abscissa is 1. Wind and cold invade the lung. 2. Wind and heat invade the lung. 3. Phlegm and dampness obstruct the lung. 4. Lung and spleen are qi deficiency. 5. Spleen and kidney are yang deficiency. 6. Lung and kidney are yin deficiency).

SPSS version13.0 statistical software. The t-test and chi-square test were carried out for measurement data and counting data, respectively, while Ridit was used to analyse the grade data.

A total of 50 children with asthma were observed. Among them, there were 42 males (74%) and 8 females (26%). The age of the children ranged from 0.5 to 9 years. The age distribution is shown in Figure-1A. Among the children, the age of first attack was 0-3 years (80%), 3-6 years (16%) and (4%) in 6-9 years, as shown in Figure-1B. The results revealed that, 44 (88%) cases were caused by respiratory tract infection, 4(8%) children had consumed seafood, one case was caused by influenza vaccine injection and one case by intense activity. It could be seen that respiratory tract infection was an important inducing factor of the asthma attack, as shown in Figure-2A. The wheezing sound could be divided into exhalative wheezing sound and wheezing sound both in inhalation and exhalation, as shown in Figure-3.

Figure-4 depicts that number of patients suffering from different syndrome types such as wind-cold invading lung, wind-heat invading lung, phlegm-dampness obstructing lung, lung-qi deficiency, spleen-kidney Yang deficiency and lung-kidney Yin deficiency. Statistical analysis of t-test showed that the main symptoms and signs of the children before and after treatment had a significant difference ($P > 0.05$), and the condition of the children improved remarkably as shown in Table-1. The levels of plasma DD and Fg in patients with acute attack of bronchial asthma were (258.47±24.81) ug/L and (3.71±1.48) g/L, respectively; the levels of plasma DD and Fg in patients with remission of bronchial asthma after treatment were (64.15±5.13) ug/L and (2.68±0.55) g/L; the levels of DD and Fg in patients with acute attack of bronchial asthma were significantly different from those in patients with remission ($P<0.05$).

Discussion

Although there are national, regional and ethnic differences in the prevalence of asthma, the incidence and mortality of asthma (especially children) are increasing at an alarming rate in most parts of the world in the past 20 years.[20] In the epidemiological survey of asthma carried out in some areas of China, there are at least 20 million asthmatic patients and infants in China.[30] The prevalence of asthma in children has been increasing for the last 10 years.[31] WHO reported that the social

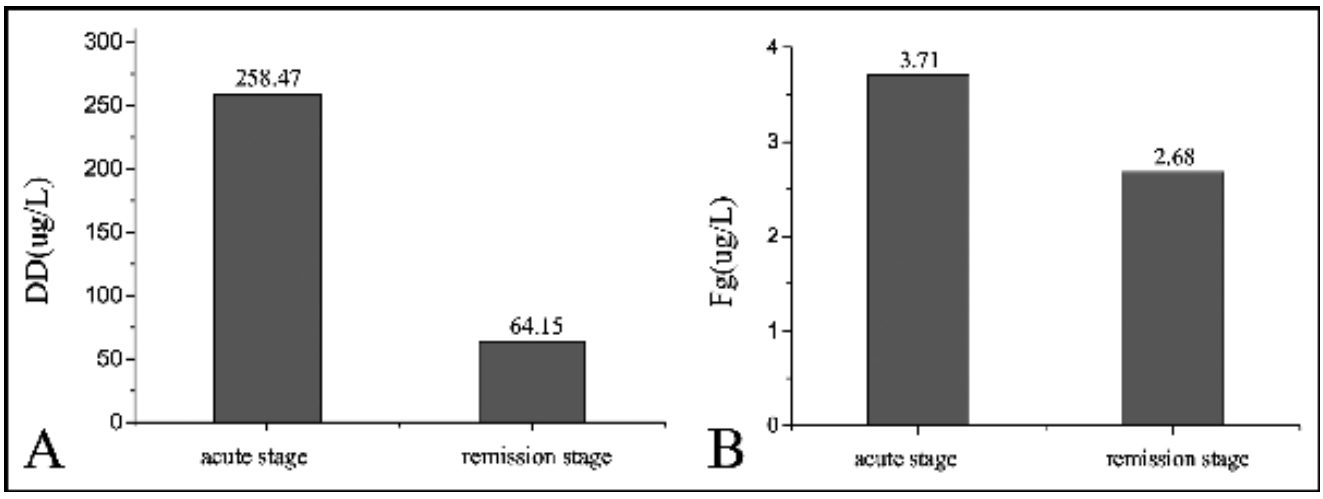

Figure-5: Comparison of DD and Fg in acute attack and remission (A: Comparison of DD between acute attack and remission; B: Comparison of Fg between acute attack and remission).

burden and economic loss caused by asthma is higher than the total loss of tuberculosis and AIDS.[32] The repeated attacks of asthma not only consume huge health resources, but also cause serious physical and mental damage to patients, and cause heavy economic burden to individuals, families and society.[33]

In this study, a history of allergy was found to be closely related to the onset of asthma in children. More males (36%) were affected than females. This has been reported by another study which found that the majority of children with asthma were boys, in the age group 3-8-years, pre-school and school-age children, with the first episode at the age within 4 years.[34]

It has also been found that asthma is prone to occur at night and in autumn. Infection, allergen contact and excessive exercise, can induce an acute attack of asthma. Timely diagnosis of asthma and systematic and standardized treatment can control asthma and reduce the acute attack which was supported by our study also.[35] Another study showed that serum allergens of the elderly were usually inhaled allergens, while those of the infants were mainly ingested allergens.[36] In our study, there were 2 cases of drug allergy, 3 cases of food allergy, 28 cases of allergic rhinitis and 5 cases of urticarial showing serum allergens to be a major cause.

Other studies have shown that family history of asthma and allergies, personal history of allergies, respiratory tract infection in infancy, early addition of inappropriate complementary food, passive smoking, environmental and allergen exposure are risk factors for asthma.[37] In our study, there were 22 cases with a family history, including 19 males and 3 females.

In addition, it has been found that the protective factors of asthma are childbirth, breastfeeding, high education of parents and health education during pregnancy.[38] To sum up, there are many factors affecting children's asthma. Indoor odour, humidity, new furniture purchase and redecoration, tobacco smoke and pet keeping have significant effects on children's asthma and allergic diseases.[39]

It was another research focus to introduce the constitution of traditional Chinese medicine into the prevention and treatment of children's asthma and to explore the distribution of constitution and syndrome types of children with asthma in different stages.[40,41] On the other hand, sounds were divided into mild and heavy coughs. The amount of sputum was divided into a small amount, more sputum and a large amount of sputum. In the investigation, syndrome types were studied according to six syndrome types, including wind-cold invading lung, wind-heat invading lung, phlegm-dampness obstructing lung, lung-qi deficiency, spleen-kidney Yang deficiency and lung-kidney Yin deficiency. Among them, 8 cases suffered from wind-cold. There were 12 cases of wind-heat invading the lung, 13 cases of lung-spleen deficiency, 4 cases of phlegm-dampness obstructing the lung, 10 cases of spleen-kidney Yang deficiency and 3 cases of lung-kidney Yin deficiency. The main symptoms and signs (cough, wheezing, phlegm and wheezing) during the acute attack of asthma were selected as the main indicators to observe the severity of asthma.

A close relationship between syndrome types and physical characteristics in children with asthma attack has been shown by researchers.[42] Studies have also proved that the children developing asthma had qi deficiency, cold drink and stop lung syndrome, phlegm heat dampness and heat dampness. External cold lung heat syndrome is mainly characterized by qi deficiency and heat dampness, and deficiency and excess are mixed with Yang deficiency, heat dampness, Qi deficiency, blood stasis, phlegm dampness and heat dampness.[43]

At present, there is no single drug for effective treatment of children's asthma. Modern medicine often gives a combination of drugs according to different individuals. Attention should be given to the prevention and treatment of asthma. Besides parents should be guided to choose a good life style and acquire health education to protect their children from developing asthma.

Conclusion

The selected 50 children were diagnosed and categorized according to cough, wheezing, sputum ringing and wheezing sound. The diagnostic symptoms were divided into TCM diagnostic statistics and western medicine diagnostic scores. The results showed that the main cause of asthma in Chinese children was respiratory tract infection caused by cold air. By comparing symptomatology it was observed that most children had moderate to severe symptoms. The lung-qi deficiency was the most common syndrome type, followed by wind-heat invading the lung, spleen-kidney yang deficiency, and lastly wind-cold invading the lung. After treatment, there was significant improvement observed in the study children.

Disclaimer: This work has not been submitted to any other journal for consideration.

Conflict of Interest: We declare that all contributing authors of this paper has no conflict of interest and all have contributed equally for this research work.

Funding Disclosure: This work was supported by contributing authors University through internal research grant Heilongjiang Provincial Health and Health Commission.

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