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Ministry of Higher Education and Scientific Research

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College of Medicine



Clinical & Epidemiological aspects of Childhood Asthma in Thi-Qar 2018

A retrospective Study



Supervisors:

**Prof. Dr. Moyaed Naji Majeed**

Pediatrics department, Thi-Qar college of medicine

M.B.Ch.B. D.O. H F.I.C.M.S. (Ped)

**Dr. Mudher Zaki Al-khairalla**

Respiratory Diseases Consultant, Al-Hussien Teaching Hospital

M.B.Ch.B. M.R.C.P.(UK) C.C.T (Resp & GI) F.R.C.P.E

By:

* **Hassan AG. Aziz**
* **Adyan Ridha Mutlak**
* **Hussien Ali Abd-Al-Wahid**

Thi-Qar University / College of medicine / 6th years students 2018-2019

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# Dictation

We wish to thank the guardians who irrigates the ground with their blood for us to draw the pencils on papers. May Allah Bless you, your families and beloved ones.

We also wish to thank the candles who melt themselves to enlighten our roads, our teaches and masters.

We also wish to thank the journey mates, without the path could not be bared, our colleagues and friends.

We also wish to thank the two’s who raised us and we’re owed to them for our apparent existence, our parents.

We wish and have to thank our creator, who amazes us with miracles in the far prospects and within the near spirits, thanks to Allah for every blessing was or is being.

# Abstract

**Background:** Asthma is a leading cause of illness in childhood responsible for significant proportion of morbidity and school-days lose. It is a complex heterogeneous disease that likely comprises several distinct disease phenotypes. Allergy and asthma are important causes of wheezing and probably generate the most questions by the parents of a wheezing infant.

**Aim of this study:** The aim of this study is to shed some light on the clinical & epidemiological aspects of childhood asthma in Thi-Qar in 2018.

**Methodology:** A retrospective clinical study were conducted on 70 patients whose ages were from 1 year to 15 years over the period from 1st of January 2018 to 31st of December 2018.

**Results:** The study showed that most of the cases were in the 7-12 years age group (57.2%), and male to female was nearly 1.9:1. Majority (71.4%) of the children were from Nasiriyah. Highest proportion of cases (36.2%) presents with cough only, and season of presentation was highest in Spring (38.6%).

**Conclusion:** Prevalence of asthma was higher among 10-12 years children. Most of children had family history of allergic diseases. Viral upper respiratory tract infection & cold exposure were recognizable triggering factor for precipitating of attacks and worsening of symptoms. The cough at night and at exertion was the most presenting complaint among our patients.

**Keywords:** childhood asthma, phenotypes, wheeze

# Abbreviations

AHR: Airway hyper-reactivity

BMI: Body Mass Index

CBC: complete blood count

CT: Computed tomography

FEV: Forced expiratory volume

FVC: Forced vital capacity

IgE: Immunoglobulin E

NO: Nitric Oxide

PVM: Perfusion Ventilation Mismatch

RSV: Respiratory Syncytial Virus

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# Chapter 1: Introduction

## Definition:

Asthma is the most common chronic condition and the most frequent cause of hospital admission in childhood. Determining a precise definition of asthma has been difficult, particularly in infancy. However, the operational definition proposed in the Third International Pediatric Consensus Statement on the Management of Asthma for Infancy is “*Recurrent wheezing and/or persistent coughing in a setting where asthma is likely and other rare conditions have been excluded*.” [[1]](#endnote-1)

For older children, the National Heart, Lung and Blood Institute's definition describes asthma in terms of airway inflammation with a predominance of eosinophils and mast cells, bronchial hyperresponsiveness, and reversible airflow limitation resulting in recurrent cough and wheeze.[[2]](#endnote-2)

*Wheezing*, the production of a musical and continuous sound that originates from oscillations in narrowed airways is heard mostly on expiration as a result of critical airway obstruction, and it is the hallmark of asthma.[[3]](#endnote-3)

Asthma is a heterogeneous, multifactorial disease with variable and mostly reversible respiratory pathway obstruction based on a chronic bronchial inflammatory reaction. The symptoms are variable and correlated with expiratory flow limitation. Although bronchial hyperresponsiveness (BHR) is often present, the current GINA Guidelines no longer include it as a necessary or sufficient criterion for diagnosis.[[4]](#endnote-4)

## Etiology:

Although the cause of childhood asthma has not been determined, a combination of environmental exposures and inherent biologic and genetic susceptibilities has been implicated. In the susceptible host, immune responses to common airways exposures (e.g. respiratory viruses, allergens, tobacco smoke, air pollutants) can stimulate prolonged, pathogenic inflammation and aberrant repair of injured airways tissues. Lung dysfunction (AHR, reduced airflow) and airway remodeling develop. These pathogenic processes in the growing lung during early life adversely affect airways growth and differentiation, leading to altered airways at mature ages. Once asthma has developed, ongoing inflammatory exposures appear to worsen it, driving disease persistence and increasing the risk of severe exacerbations.

Other Causes of wheeze that should be excluded:

* *Acute bronchiolitis***:** is predominantly a viral disease. RSV is responsible for more than 50% of cases. Other agents include parainfluenza, adenovirus, rhinovirus, and Mycoplasma.
* *Anatomic Abnormalities*: Laryngomalacia, vascular ring.
* *Mucociliary Clearance Disorders*: cystic fibrosis.
* *Aspiration*
* *Other*: Bronchopulmonary dysplasia, heart failure and inhalation injuries. [[5]](#endnote-5)

## Epidemiology:

Asthma is the most common chronic disease of childhood in industrialized countries, affecting nearly 7 million children younger than 18 years of age in the United States. The number of people with asthma continues to grow. One in 11 children (7 million) had asthma, and 1 in 12 (18.7 million) adults (totaling over 25 million or 8% of U.S. population) had asthma in 2010 compared to 1 in 14 people (about 20 million, or 7%) in 2001. One in 5 children went to the emergency department for an asthma-related visit in 2009. Women are more likely than men to have asthma, and boys are more likely than girls to have asthma.[[6]](#endnote-6)

Because there are many definitions to diagnose asthma in Pediatrics age group, about sixty different definitions were identified in PubMed, in which the prevalence estimates varied between 15.1% and 51.1%.[[7]](#endnote-7)

 Asthma was less prevalent in developing countries, and the highest prevalence was observed in Anglo-Saxon countries.[[8]](#endnote-8)

## Pathophysiology:

Infants are more likely to wheeze than older children and adults as a result of a differing set of lung mechanics. The obstruction to flow is affected by the airway caliber and compliance of the infant lung. Resistance to airflow through a tube is inversely related to the radius of the tube to the 4th power. In children younger than 5 years old, small-caliber peripheral airways can contribute up to 50% of the total airway resistance. Marginal additional narrowing can cause further flow limitation and a subsequent wheeze.

With the very compliant newborn chest wall, the inward pressure produced in expiration subjects the intrathoracic airways to collapse. Differences in tracheal cartilage composition and airway smooth muscle tone increase the collapsibility of the infant airways in comparison to older children. These mechanisms combine to make the infant more susceptible to airway obstruction, increased resistance, and subsequent wheezing. Many of these conditions are outgrown in the 1st year of life.

Immunologic and molecular influences can contribute to the infant’s propensity to wheeze. In comparison to older children and adults, infants tend to have higher levels of lymphocytes and neutrophils, rather than mast cells and eosinophils, in bronchoalveolar lavage fluid.

## Clinical Manifestations:

Children with asthma have symptoms of coughing, wheezing, shortness of breath or rapid breathing, and chest tightness.

Intermittent dry coughing and expiratory wheezing are the most common chronic symptoms of asthma. Older children and adults report associated shortness of breath and chest congestion and tightness; younger children are more likely to report intermittent, non-focal chest pain. Respiratory symptoms can be worse at night, associated with sleep, especially during prolonged exacerbations triggered by respiratory infections or inhalant allergens. Daytime symptoms, often linked with physical activities (exercise-induced) or play, are reported with greatest frequency in children. Also, there may be general fatigue (possibly resulting from sleep disturbance). [[9]](#endnote-9)

Monophonic wheezing refers to a single-pitch sound that is produced in the larger airways during expiration, as in distal tracheomalacia or bronchomalacia. Wheezing is polyphonic when there is widespread narrowing of the airways, causing various pitches as air moves through different levels of obstruction to flow, as seen in asthma. When obstruction occurs in the extra thoracic airways during inspiration, the noise is referred to as *stridor*.[[10]](#endnote-10)

During acute episodes, tachypnea, tachycardia, cough, wheezing, and a prolonged expiratory phase may be present. Physical findings may be subtle. Classic wheezing may not be prominent if there is poor air movement from airway obstruction. As the attack progresses, cyanosis, diminished air movement, retractions, agitation, inability to speak, tripod sitting position, diaphoresis, and pulsus paradoxus (decrease in blood pressure of >15 mm Hg with inspiration) may be observed. Physical examination may show evidence of other atopic diseases such as eczema or allergic rhinitis.

Rhonchi and crackles (or rales) can sometimes be heard, resulting from excess mucus production and inflammatory exudate in the airways. The combination of segmental crackles and poor breath sounds can indicate lung segmental atelectasis that is difficult to distinguish from bronchial pneumonia and can complicate acute asthma management. In severe exacerbations, the greater extent of airways obstruction causes labored breathing and respiratory distress, which manifests as inspiratory and expiratory wheezing, increased prolongation of exhalation, poor air entry, suprasternal and intercostal retractions, nasal flaring, and accessory respiratory muscle use. In extremis, airflow may be so limited that wheezing cannot be heard.[[11]](#endnote-11)

## Exacerbating factors & Risk factors:

Exacerbating factors include viral infections, exposure to allergens and irritants (e.g., smoke, strong odors, fumes), exercise, emotions, and change in weather/humidity. Rhinosinusitis, gastroesophageal reflux, and nonsteroidal anti-inflammatory drugs (especially aspirin) can aggravate asthma. Treatment of these conditions may lessen the frequency and severity of the asthma. [[12]](#endnote-12)

Family history of asthma and allergy is a recognizable risk factor for developing asthma.[[13]](#endnote-13) The childhood wheezing phenotype has been linked to many early exposures including fetal nutrition, maternal smoking, prenatal and birth maternal complications, prenatal and neonatal exposure to anti-biotics, exposure to high levels of environmental allergens, and high infant adiposity. Infections during infancy have been cited as risk factors for later wheezing, including respiratory syncytial virus (RSV), rhinovirus, cytomegalovirus, human metapneumovirus, bocavirus, adenovirus, and Chlamydia \ pneumoniae.

A variety of inflammatory mediators have also been implicated in the wheezing infant such as histamine, cytokines, leukotrienes, and interleukins. Taken together, these fetal and/or early postnatal exposures may cause a “programming” of the lung that ultimately affects structure and function.[[14]](#endnote-14)

## Classifications:

The National Asthma Education and Prevention Program has classified asthma as (Box 1-1):

* Intermittent.
* Mild persistent.
* Moderate persistent.
* Severe persistent.

These classifications are based on severity, which is determined by symptoms and lung function tests. You should be assigned to the most severe category in which any feature occurs.[[15]](#endnote-15)

With noting the following:

* Classification is based on symptoms before treatment.
* Classification may change over time.
* A person in any category can have severe asthma attacks (exacerbation).
* Asthma in children younger than age 4 can be hard to diagnose. And its symptoms may be different from asthma in older children or adults.

There are also classifications based on symptoms control *(Box 1-2)* and attack/exacerbation severity *(Box 1-3)*.[[16]](#endnote-16)

Box 1-1: Classification of asthma

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Intermittent | Persistent-mild | Persistent-moderate | Persistent-severe |
| Symptoms | ≤ 2 days per week | > 2 days per week, but not daily | Daily | Throughout the day |
| Nighttime awakenings | ≤ 2 times per month | 3 to 4 times per month | > Once per week, but not nightly | Often 7 times per week |
| Short-acting beta agonist use for symptom control | ≤ 2 days per week | > 2 days per week, but not more than once per day | Daily | Several times per day |
| Interference with normal activity | None | Minor limitation | Some limitation | Extremely limited |
| Lung function | Normal FEV1between exacerbations; FEV1 >80 percent of predicted; FEV1/FVC normal | FEV1 ≥ 80 percent of predicted; FEV1/FVC normal | FEV1 > 60 percent but < 80 percent of predicted; FEV1/FVC reduced 5 percent | FEV1 < 60 percent of predicted; FEV1/FVC reduced >5 percent |

Box 1-2: Classification of asthmatic patients according to level of control, based on frequency of symptoms

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Domain | Component | Level of Control | | | |
| **Complete** | **Good** | **Partial** | **None** |
| Impairment | Symptoms – Daytime | None | ≤2/week | >2/week | Continuous |
| Symptoms – Night- time/awakenings | None | ≤1/month | >1/month | Weekly |
| Need for rescue medication | None | ≤2/week | >2/week | Daily |
| Limitation of activities | None | None | Some | Extreme |
| Lung function - FEV1, PEF (predicted or personal best) | >80% | ≥80% | 60%-80% | <60% |
| Risk | Exacerbations (per year) | 0 | 1 | 2 | >2 |
| Medication side effects | None | Variable | | |

Box 1-3: Classification of asthma attack according to severity of exacerbation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Mild | Moderate | Severe | Very severe |
| Wheeze | Variable | Moderate to loud | Loud – both on inhalation and exhalation | Often quiet |
| Breathlessness | Walking | At rest | At rest/sits upright | |
| Speaks in | Sentences | Phrases | Words | Unable to speak |
| Accessory muscle use | No | common | marked | paradoxical |
| Consciousness | Not affected | Not affected | Agitated, confused | |
| Respiratory rate | Slightly increased | Increased | Highly increased | Undetermined |
| Pulse | <100 | <140 (depending on age) | >140 | bradycardia |
| PEF (% of predicted or personal best) | >60-70% | 40-70% | <40% | <25% |
| SaO2 (% on air) | >94-95% | 90%-95% | <90% | |
| PCO2 (mmHg) | <42 | <42 | >=42 | |

Also, asthmatic children can be classified based on wheezing pattern, or what’s call wheezing phenotype.

Three identified patterns of childhood wheezing are the transient early wheezer, the persistent wheezer, and the late-onset wheezer. These patterns are seen in 19.9%, 13.7%, and 15% of the general population, respectively, with the remaining 50% of the population never wheezing prior to age 6 years.[[17]](#endnote-17)

*Transient early wheezers***:** Transient early wheezers wheeze at least once with a lower respiratory infection before the age of 3 years, but never wheeze again (i.e. resolved by 6 years of age):

* Initial risk factor is primarily diminished lung size.

*Persistent wheezers***:** The persistent wheezer has wheezing episodes before age 3 years and is still wheezing at 6 years of age (persists beyond 6 years of age)

* Initial risk factors include parental asthma history, atopic dermatitis, allergen sensitization, peripheral eosinophilia (>4%) and wheezing unrelated to colds in the 1st year of life.
* At increased risk of developing clinical asthma

*Late-onset wheezer***:** does not wheeze before age 3 years (symptoms begin after age 3 years and persist)[[18]](#endnote-18)

## Phenotypes & Endotypes Concept:

It is widely believed that the clinical variability of asthma signifies not one disease but many, united by some common clinical features, such as intermittent wheezing and reversible airways obstruction. This has given rise to the concept of different phenotypes of asthma, each of which may arise from different pathological processes (endotypes) and which may respond differently to asthma treatments. [[19]](#endnote-19)

A disease *phenotype* is described by clinical characteristics, which can include biochemical and other measured variables as well as physical features, without reference to an underlying pathophysiological process.

The term ‘‘*endotype’’* is used to describe a disease sub-type based on distinct pathological mechanisms.

Therefore, a clinical phenotype of asthma may be underpinned by a number of discrete endotypes, each of which leads to a final common pathway of disease manifestations that characterize that particular phenotype.

Conversely, a discrete endotype, for example, one classified by a particular inflammatory pathway such as eosinophilic airway inflammation, could be extant in a number of different clinical phenotypes.

The importance of disentangling the various phenotypes and endotypes of asthma is two-fold: asthma prevention and treatment.

## Laboratory findings:

Objective measurements of pulmonary function (spirometry) help establish the diagnosis and direct the treatment of asthma. Spirometry is used to monitor response to treatment, assess degree of reversibility with therapeutic intervention, and measure the severity of an asthma exacerbation. The FEV1 (forced expiratory volume in 1 sec) should be reproducible within 5% on 3 measurements, and the highest value taken as the reported measure effort of the 3 is used. Generally, *an FEV1:FVC* ratio *<0.80* indicates significant airflow Obstruction. [[20]](#endnote-20) Such measures of airflow alone are not diagnostic of asthma, because numerous other conditions can cause airflow reduction. [[21]](#endnote-21)

*Bronchodilator response* to an inhaled β-agonist (e.g., albuterol) is greater in asthmatic patients than non-asthmatic persons; an improvement in FEV1 ≥12% or >200 mL is consistent with asthma.[[22]](#endnote-22) Bronchoprovocation challenges can be helpful in diagnosing asthma and optimizing asthma management.

*Allergy skin testing* should be included in the evaluation of all children with persistent asthma but not during an exacerbation of wheezing. Positive skin tests results, identifying immediate hypersensitivity to aeroallergens (e.g. as tree and grass pollens, and dust), correlate strongly with bronchial allergen provocative challenges. [[23]](#endnote-23)

A *chest radiograph* should be performed with the first episode of asthma or with recurrent episodes of undiagnosed cough or wheeze to exclude anatomic abnormalities. Repeat chest radiographs are not needed with new episodes unless there is fever (suggesting pneumonia) or localized findings on physical examination (Asthma masqueraders: aspiration pneumonitis, hyperlucent lung fields in bronchiolitis obliterans) and complications during asthma exacerbations (atelectasis, pneumomediastinum, pneumothorax)). [[24]](#endnote-24)

*High-resolution, thin-section chest CT* scans can show bronchiectasis, which is sometimes difficult to appreciate on chest radiograph but is clearly seen on CT scan, implicates an asthma masquerader such as cystic fibrosis, allergic bronchopulmonary mycoses (aspergillosis), ciliary dyskinesias, or immune

deficiencies. [[25]](#endnote-25)

Two *novel forms* of monitoring asthma and airway inflammation directly include *exhaled nitric oxide analysis* and quantitative analysis of expectorated *sputum for eosinophilia*.[[26]](#endnote-26)

## Preventive Measures:

Education plays an important role in helping patients and their families adhere to the prescribed therapy and needs to begin at the time of diagnosis. Successful education involves teaching basic asthma facts, explaining the role of medications, teaching environmental control measures, and improving patient skills in the use of spacer devices for metered dose inhalers and peak flow monitoring. Families should have an asthma management plan for daily care and for exacerbations.

So, instructions that should be given to asthmatic child who is aware and to his family:

* Follow your asthma action plan.
* Get vaccinated for influenza and pneumonia.
* Identify and avoid asthma triggers
* Identify and treat attacks early.
* Take your medication as prescribed.
* Pay attention to increasing quick-relief inhaler use.

# Aim of the study

The aim of this study is to obtain data about clinical & epidemiological aspects of childhood asthma in Thi-Qar 2018.

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# Chapter 2: Methodology

## Design:

A retrospective study, utilizing patient’s data of Thi-Qar Lung Diseases center.

The data was from Consultants reviews, Laboratory results & Registration/Booking details.

## Inclusion & Exclusion criteria:

The data was filtered with the following:

* Key words: Asthma, allergic bronchitis.
* Age: More than or equal to 1 years, and less than or equal to 15 years.
* Residence: in Thi-Qar.
* Presentation Date: in 2018

The result was 103 records, those were furthered filtered and some (33 records) were excluded by:

* Absent of patient data (Deleted files).
* Absent data about clinical presentation (Complaint & Physical Finding).
* Absent data about any performed investigation.
* Duplicated patient presentation (Only the recent was included).

All the rest (70) records were included.

## Ethical Consideration:

Authority to access the data bank in Thi-Qar Lung Diseases center was given from *Dr.Mudher ZH Al-khairalla* & *Eng. Muwaffaq*, with acceptance to protect the patient privacy & avoid excessive system utilization in a way that affect the center daily work.

## Data Collection:

Data collection was performed as 1-2 visits per week to the center, from the period of 25th of November 2018 to 23rd of March 2019 (about 16 weeks). The visit lasts 20-40 minutes, where in each a data was collected from about 3-6 records.

## Material & Variables:

The variables that could be obtained from the archives are:

* Age
  + Arranged in groups of 3 years Interval.
* Sex
* Residence
* Date of presentation, was interpreted as:
  + Spring: from March 1 to May 31;
  + Summer: from June 1 to August 31;
  + Fall (Autumn) runs from September 1 to November 30; and.
  + Winter: from December 1 to February 28 (February 29 in a leap year).[[27]](#endnote-27)
* Body Mass Index, was represented as:
  + < 18.5 – underweight
  + 18.5 to 24.9 – normal.
  + 25.0 to 29.9 – overweight.
  + Over 30 or greater – obese.
* Presenting Complain
* Physical Findings
* Personal history of atopy
* Personal history of allergic rhinitis
* Family History of asthma
* Family History of atopy
* Family history of allergic rhinitis
* Complete blood count with differential i.e. Neutrophils and/or Eosinophils (Not all).
  + Using *Mindray BC-5000.*
  + Neutrophils count was represented as:
    - Raised (neutrophilia): >8 (10^9/L)
    - Normal: <= 8 (10^9/L)
  + Eosinophils count was represented as:
    - Raised (eosinophilia): >0.8 (10^9/L)
    - Normal: <= 0.8 (10^9/L)
* Immunoglobulin E
  + Using *TOSAA1A360.*
  + Was represented as:
    - Positive: >= 295
    - Negative: < 295
* C-Reactive Protein
  + Using *Genrui PA64.*
  + Was represented as:
    - Positive: >= 10
    - Negative: < 10
* FEV1/FVC Ratio with Bronchodilator response
  + Using *MIR Spirolab.*
  + FEV1/FVC Ratio was represented as:
    - Normal: >= 80%
    - Decreased: <80%
  + Bronchodilator response in FEV1 was represented as:
    - Asthmatic range: >= 12%
    - Non asthmatic range: <12%
* Chest X-Ray
* Oxygen Saturation.

## Data Collection & Analysis:

Data was collected using Microsoft Excel 2019, and statistical analysis was performed with IBM SPSS Statistics Version 23.

# Results

Epidemiological aspects:

Table 1: Sociodemographic criteria of cases.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | **Count** | **Percent %** | **Goodness of Fit** | |
| ***χ2*** | ***p value*** |
| **Age** | **1-3** | 8 | 11.4% | 11.211 | .024 |
| **4-6** | 12 | 17.1% |  |  |
| **7-9** | 16 | 22.9% |  |  |
| **10-12** | 24 | 34.3% |  |  |
| **13-15** | 10 | 14.3% |  |  |
| **Gender** | **Male** | 46 | 65.7% | .681 | .409 |
| **Female** | 24 | 34.3% |  |  |
| **Residence** | **Nasiriyah** | 50 | 71.4% |  |  |
| **Jibayish** | 1 | 1.4% |  |  |
| **Shatra** | 9 | 12.9% |  |  |
| **Souq Al-Shoyokh** | 4 | 5.7% |  |  |
| **Rifayi** | 6 | 8.6% |  |  |
| **Total** |  | 70 | 100% |  |  |
| Table 1: Sociodemographic criteria of cases. shows that number of cases was highest in 10-12 years age group (34.3%), followed by 7-9 years age group (22.9%). Also shows that majority (71.4%) of the children reside in Nasiriyah where Thi-Qar Lung Diseases center is located, the remaining (28.6%) reside outside Nasiriyah within Thi-Qar province. Utilizing Goodness of Fit Chi-Square to compare the age and gender with standardized criteria in [[28]](#endnote-28), the p-value was (0.024) for age which is lower than (0.05), thus the difference is statically significant and observed data nearly differs from expected data significantly. the p-value was (0.409) for gender which is higher than (0.05), thus the difference is not statically significant and observed data nearly similar to expected data. | | | | | |

Figure 1) shows that study group consisted of 46 (65.71%) male and 24 (34.29%) female. The ratio of male to female was nearly 1.9:1.

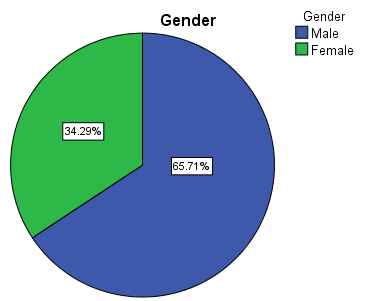


Figure 1: Gender distribution of cases.

Clinical Aspects:

Table 2: Presenting complaint/s.

|  |  |  |  |
| --- | --- | --- | --- |
|  | | **Count** | **Percent %** |
| **Presenting Complain/s** | **Cough** | 25 | 36.2% |
| **Dyspnea + Cough** | 9 | 13.0% |
| **Dyspnea** | 8 | 11.6% |
| **Cough + Disturbed Sleep** | 4 | 5.8% |
| **Dyspnea + Cough + Fever** | 4 | 5.8% |
| **Dyspnea + Wheeze + Cough** | 3 | 4.3% |
| **Dyspnea + Wheeze + Runny Nose** | 2 | 2.9% |
| **Cough + Fever** | 1 | 1.4% |
| **Cough + Fever + Disturbed Sleep** | 1 | 1.4% |
| **Cough + Hemoptysis** | 1 | 1.4% |
| **Cough + Poor Feeding** | 1 | 1.4% |
| **Dyspnea + Cough + Runny Nose** | 1 | 1.4% |
| **Dyspnea + Cough + Runny Nose + GERD** | 1 | 1.4% |
| **Dyspnea + Fever** | 1 | 1.4% |
| **Dyspnea + Infection (pneumonia)** | 1 | 1.4% |
| **Dyspnea + Nasal Blockage** | 1 | 1.4% |
| **Dyspnea + Sore Throat** | 1 | 1.4% |
| **Dyspnea + Wheeze** | 1 | 1.4% |
| **Dyspnea + Wheeze + Cough + Runny Nose + Sneezing** | 1 | 1.4% |
| **Fever + Chest Tightness** | 1 | 1.4% |
| **Wheeze** | 1 | 1.4% |
| **Total\*** | 69 |  |
| Table 2) shows that highest percent of cases (36.2%) presents with *cough* only. *Dyspnea + Cough* was the second complaint in frequency (13%). *Cough + Disturbed Sleep* symptoms were demonstrated in 4 (5.8%) cases. *Wheeze* only as the presenting symptom was found in 1 (1.4%) case only.  \*One case (of the total 70 cases) presented as follow up with physical findings without presenting complaint. | | | |

Table 3: Physical Findings & Body Mass Index.

|  |  |  |  |
| --- | --- | --- | --- |
|  | | **Count** | **Percent %** |
| **Physical Findings** | **Wheeze** | 38 | 54.3% |
| **Normal** | 7 | 10.0% |
| **High Pitch Sounds** | 7 | 10.0% |
| **Wheeze + Prolonged Expiratory Phase** | 3 | 4.3% |
| **Wheeze + Pigeon Chest** | 3 | 4.3% |
| **Wheeze + Crackles** | 3 | 4.3% |
| **Wheeze + Tight Chest** | 1 | 1.4% |
| **Wheeze + High Pitch Sounds** | 1 | 1.4% |
| **Wheeze + Harsh Lung Sounds** | 1 | 1.4% |
| **Wheeze + Bronchial Breathing** | 1 | 1.4% |
| **Prolonged Expiratory Phase + Rhonchi** | 1 | 1.4% |
| **Prolonged Expiratory Phase** | 1 | 1.4% |
| **Pansystolic Murmur** | 1 | 1.4% |
| **High Pitched Sounds** | 1 | 1.4% |
| **Crackles** | 1 | 1.4% |
| **Body Mass Index** | **Normal** | 20 | 31.3% |
| **Underweight** | 35 | 54.7% |
| **Overweight** | 8 | 12.5% |
| **Obese** | 1 | 1.6% |
| Table 3) shows that *wheeze*, as the only auscultatory finding in chest examination, was found in 38 (54.3%) cases. A *high pitch sounds* only was found in 7 (10%) cases. *Pigeon chest*, *prolonged expiratory phase* and *crackles*, all with *wheeze*, were found in 3 (4.3%) of cases for each. Rest of demonstrated findings, as a combination, were found in 1 (1.6%) of cases. 7 (10%) of cases were with *normal* chest examination. Body mass index was underweight in 35 (54.7%) of cases, overweight in 8 (12.5%) of cases and obese in 1 (1.6%) of cases, the remained 20 (31.3%) cases were normal. | | | |

Table 4: Season of presentation & triggering factors.

|  |  |  |  |
| --- | --- | --- | --- |
|  | | **Count** | **Percent %** |
| **Season of presentation** | **Spring** | 27 | 38.6% |
| **Summer** | 15 | 21.4% |
| **Autumn** | 15 | 21.4% |
| **Winter** | 13 | 18.6% |
| **Timing/Triggering Factor** | **Non specific** | 40 | 57.1% |
| **at night** | 18 | 25.7% |
| **at exertion** | 4 | 5.7% |
| **at viral infection** | 3 | 4.3% |
| **at night + at exposure to inhalants** | 2 | 2.9% |
| **at winter** | 1 | 1.4% |
| **at night + at exertion** | 1 | 1.4% |
| **at exposure to fumes** | 1 | 1.4% |
| **Total** | | 70 | 100.0% |
| Table 4) shows that season of presentation of cases was highest in Spring (38.6%), while was lowest in Winter (18.6%). Though most cases (57.1%) were without recognizable timing/triggering factors, the remaining were occurring *at night* only in about 18 (25.7%) cases, and *at exertion* only in about 4 (5.7%) cases. *Viral infection* alone was responsible for 3 (4.3%) cases. | | | |

Table 5: Comorbid allergic conditions and family history of allergic diseases.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | **Count** | **Percent %** | **Goodness of Fit** | |
| ***χ2*** | ***p value*** |
| **Comorbid allergic conditions** | **Negative** | 58 | 82.9% | 23.143a | .000 |
| **Allergic Rhinitis** | 9 | 12.9% |  |  |
| **Atopic Dermatitis** | 2 | 2.9% |  |  |
| **Atopic Dermatitis + Allergic Rhinitis** | 1 | 1.4% |  |  |
| **Family history of allergic diseases** | **Negative** | 17 | 24.3% | 1.370 | .242 |
| **Asthma** | 27 | 38.6% |  |  |
| **Atopic Dermatitis** | 20 | 28.6% |  |  |
| **Allergic Rhinitis** | 1 | 1.4% |  |  |
| **Asthma + Atopic Dermatitis** | 2 | 2.9% |  |  |
| **Asthma + Allergic Rhinitis** | 1 | 1.4% |  |  |
| **Asthma + Atopic Dermatitis + Allergic Rhinitis** | 2 | 2.9% |  |  |
| **Total** | | 70 | 100.0% |  |  |
| Table 5) shows that comorbid *allergic rhinitis* alone was found in 9 (12.9%) cases and comorbid *atopic dermatitis* alone was found in 2 (2.9%) cases. Co-existence of both *allergic rhinitis + atopic dermatitis* (alongside with current asthma diagnosis) was found in 1 (1.4%) cases. The remaining 58 cases (82.9%) had none of the described comorbid allergic diseases. Also shows that family history of *asthma* alone was found in 27 (38.6%) cases, family history of *atopic dermatitis* was found in 20 (28.6%) cases, family history of *allergic rhinitis* alone was found in 1 (1.4%) case, family history of *asthma + atopic dermatitis* was found in 2 (2.9%) cases, family history of *asthma + allergic rhinitis* was found in 1 (1.4%) case, family history of all three allergic diseases (*asthma + atopic dermatitis + allergic rhinitis*) was found in 2 (2.9%) cases and the remaining 17 (24.3%) cases had negative family history of allergic diseases. Utilizing Goodness of Fit Chi-Square to compare the family history of allergic diseases with standardized criteria in [[29]](#endnote-29), the p-value was (0.242) which is higher than (0.05), thus the difference is not statically significant and observed data nearly similar to expected data.   1. Chi-Square result may be invalid because cell frequencies less than minimum expected frequency. | | | | | |

Figure 2) shows that 32 (45.7%) cases had family history of asthma, 23 (32.9%) cases had family history of atopic dermatitis and 4 (5.7%) cases had family history of allergic rhinitis. Also shows that personal history of atopic dermatitis was found in 3 (4.3%) cases and personal history of allergic rhinitis was found in 10 (14.3%) cases.

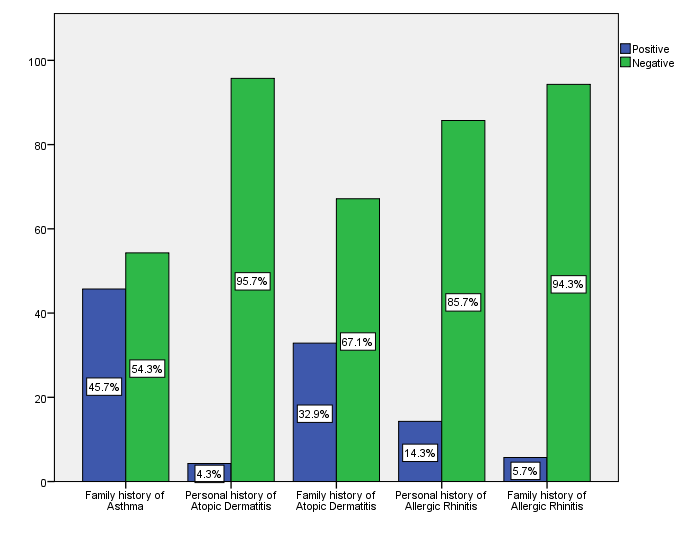


Figure 2: Family and personal history of allergic diseases.

Table 6: Laboratory findings.

|  |  |  |  |
| --- | --- | --- | --- |
|  | | **Count** | **Percent %** |
| **Neutrophils** | **Raised** | 2 | 16.7% |
| **Normal** | 10 | 83.3% |
| **C-Reactive Protein** | **Positive** | 6 | 19.4% |
| **Negative** | 25 | 80.6% |
| **Eosinophils** | **Raised** | 5 | 38.5% |
| **Normal** | 8 | 61.5% |
| **Immunoglobulin E** | **Elevated** | 27 | 42.2% |
| **Normal** | 37 | 57.8% |
| **FEV1/FVC Ratio** | **Decreased** | 11 | 44.0% |
| **Normal** | 14 | 56.0% |
| **Bronchodilator response** | **Positive** | 7 | 28.0% |
| **Negative** | 18 | 72.0% |
| **X-Ray** | **Normal** | 28 | 71.8% |
| **Bronchiectasis** | 7 | 17.9% |
| **Hyperinflation** | 3 | 7.7% |
| **Increased PVM** | 1 | 2.6% |
| Table 6) shows that neutrophils count was high in 2 (16.7%) of cases who performed CBC (12 in total) and normal in the remaining 10 (83.3%) of them. C-Reactive protein was positive in 6 (19.4%) of cases who performed C-RP assay and negative in the remaining 25 (80.6%) of them. Eosinophils count was high in 5 (38.5%) of cases who performed eosinophils differential count (13 in total) and normal in the remaining 8 (61.5%) of them. IgE level was elevated in 27 (42.2%) of cases who performed IgE level assay (64 in total) and normal in the remaining 37 (57.8%) of them. FEV1/FVC ratio was decreased in 11 (44%) of cases who performed lung function test (25 in total) and normal in the remaining 14 (56%) of them. Bronchodilator response was positive in 7 (28%) of cases who had bronchodilator challenge (25 in total) and normal in the remaining 18 (72%) of them. Also, from 39 cases who performed chest x-ray, 28 (71.8%) of them was normal, 7 (17.9%) for them had bronchiectasis changes, 3 (7.7%) had hyperinflated chest changes and 1 (2.6%) of them had increased PVM. | | | |

Table : Spirometer parameters according to age

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Age** | | | | | | | | | | |
| **1-3** | | **4-6** | | **7-9** | | **10-12** | | **13-15** | | **Total** |
| **%** | **#** | **%** | **#** | **%** | **#** | **%** | **#** | **%** | **#** |  |
| **Decreased FEV1/FVC Ratio** | 0.0% | 0 | 0.0% | 0 | 0.0% | 0 | 63.6% | 7 | 36.4% | 4 | 11 |
| **Positive Bronch-odilator response** | 0.0% | 0 | 14.3% | 1 | 0.0% | 0 | 57.1% | 4 | 28.6% | 2 | 7 |

Table 7) shows that decreased FEV1/FVC ratio and positive reversibility appear to be more frequent in 10-12 years age group than younger age groups.

Table : State of Immunoglobulin E level in various parameters

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | | **Immunoglobulin E** | | | | ***χ2*** | ***p value*** |
| **Positive** | | **Normal** | |
| **Count** | **Percent %** | **Count** | **Percent %** |
| **Age** | **1-3** | 2 | 25.0% | 6 | 75.0% | *2.206* | *.698a* |
| **4-6** | 3 | 30.0% | 7 | 70.0% |  |  |
| **7-9** | 7 | 46.7% | 8 | 53.3% |  |  |
| **10-12** | 10 | 47.6% | 11 | 52.4% |  |  |
| **13-15** | 5 | 50.0% | 5 | 50.0% |  |  |
| **Gender** | **Male** | 19 | 46.3% | 22 | 53.7% | *.807* | *.369* |
| **Female** | 8 | 34.8% | 15 | 65.2% |  |  |
| **Eosinophils** | **Raised** | 3 | 75.0% | 1 | 25.0% | *2.213* | *.137 a* |
| **Normal** | 2 | 28.6% | 5 | 71.4% |  |  |
| **Family history of allergic diseases** | **Positive** | 20 | 41.7% | 28 | 58.3% | *.021* | *.884* |
| **Negative** | 7 | 43.8% | 9 | 56.3% |  |  |
| **Personal history of other allergic diseases** | **Positive** | 8 | 66.7% | 4 | 33.3% | *3.629* | *.057* |
| **Negative** | 19 | 36.5% | 33 | 63.5% |  |  |
| Table 88) shows that IgE state is positive more frequently when age is older (p-value is *.698*), gender is male (p-value is *.369*), eosinophils is raised (p-value is *.137*), family history of allergic diseases is negative (p-value is *.884*) and personal history of other allergic diseases is negative (p-value is *.057*).   1. More than 20% of cells in this sub-table have expected cell counts less than 5. Chi-square results may be invalid. | | | | | | | |
|  | | | | | | | |

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# Chapter 3: Discussion

## Strength:

This study has presented data on the sociodemographic aspects, clinical aspects regarding presentation, physical findings and laboratory investigations that included hematological investigations in form of CBC, C-RP and IgE assay, lung function parameters and radiology imaging of childhood asthmatics in 70 cases who visited Thi-Qar lung diseases center in Thi-Qar, Iraq in 2018, and the association of the IgE level with various parameters that is suspected to be associated with allergic/familial origin.

Solid data was obtained from advanced patient achieving system, that is highly reliable and useful for further studies.

Utilizing computerized systems limit errors that can occurs from manual typing, and ease further edition, addition and organization of data.

A greater understanding of the etiopathological mechanisms underpinning different disease phenotypes could reveal modifiable factors that initiate disease or influence its natural history enabling development of primary or secondary prevention strategies.

Alternatively, drug-targetable pathways, applicable only in certain sub-types of asthma, could be discovered, opening the way for personalized medicine in asthma treatment.

## Limitations:

As this study was a retrospective, some important data couldn’t be obtained, that was intended to be included in the research. Either because they were not taking during usual consultation, or require follow up to be obtained. Some patients were consulting other centers/clinics and this perhaps limit the archiving of data from their past years.

This data that could not be obtained included: age of diagnosis, weather rural or urban living, breast feeding & prematurity, consanguinity status, school performance, frequency & severity of attacks.

The location of the Medical Center where research data were obtained in the center of Thi-Qar province, yet Thi-Qar is a large geographic area with multiple distincts, and economic status of families are high in most of cases, thus there may be some deflection of data towards nearby areas.

One of the challenges of classifying clinical phenotypes of asthma in children arises from the practical and ethical difficulties of obtaining biological material from the disease end-organ, the pediatric airway. Which is an important data if could be obtained to compare with laboratory findings & radiology.

## Comparison and explanation:

Overall, male preponderance was noticed among the children with a male-to-female ratio of 1.9:1, compared with 1.6:1 in other studies. Yet the difference was not statistically significant. This can be attributed to the fact that boys are more active than girls and get exposure to cold and environmental factors more.

The age distribution of the children with asthma revealed that 34.3% were 10-12 years old, and majority of the children with asthma were school age (57.2%). This age distribution is similar to reports in other studies[[30]](#endnote-30). Worthy of note from this study is that 11.4% of the children with asthma were <3 years. This underscores the need to have a high index of suspicion and promptly diagnosed asthma in infants and young children if present to ensure good asthma control and improve quality of life in both the child and caregivers.

One of the pillars of adequate management of childhood asthma included early recognition and management of comorbid allergic conditions to ensure optimal asthma control.[[31]](#endnote-31) In the present study, comorbid conditions found in the children with asthma included allergic rhinitis, atopic dermatitis, or both allergic rhinitis + atopic dermatitis in (17.1% ) of patient, with most being with allergic rhinitis (75% of them), this is similar to findings in previous studies. Children with allergic rhinitis are at increased risk of asthma exacerbation probably due to the fact that increased oral breathing often seen in children with allergic rhinitis due to impaired filtering and humidification functions of the nose leads to increased exposure of the lower airway to allergens and other triggers of asthma exacerbation.[[32]](#endnote-32)

Obstructive ventilatory pattern was observed in (44%) children who were able to perform acceptable and useable Spirometry. Expectedly, the abnormalities in ventilation were seen more among the late school and early adolescent ages than in the younger age groups. This is in keeping with the fact that it takes time for airway remodeling and abnormalities to set in in children with uncontrolled asthma for ventilatory abnormalities to be detected on lung Spirometry.[[33]](#endnote-33)Although the FEV1-FVC ratio might be normal in many patients with asthma (on the basis of a normal FVC value), this does not exclude the possibility that FEV1 will improve substantially with bronchodilator challenge.[[34]](#endnote-34)

And also, children older than 5 years of age can perform spirometry maneuvers. But for younger children who cannot perform spirometry maneuvers or peak flow, a therapeutic trial of controller medications helps in the diagnosis of asthma.[[35]](#endnote-35)

The findings of chest radiographs (posteroanterior and lateral views) in children with asthma often appear to be normal, aside from subtle and nonspecific findings of hyperinflation. This goes with our finding of normal chest x-ray in 71.8% and hyperinflation in only 7.7% of patients who had chest radiographs. Surprisingly bronchiectasis changes were found in 17.9% of them, which can be due to incompliance with treatment or delay in diagnosis.

When IgE is elevated, a positive family history of allergic disease is more common (74%), this can go with what SHIELDS et al. in Belfast found in their study.[[36]](#endnote-36)

Also, eosinophilia was found, when CBC with differential performed, to be elevated in (38.5%) of cases, this is close to the (41%) that was found in FLEMING et al. study.[[37]](#endnote-37)

Classically, asthma in children has been regarded as a Th-2 mediated disease that is strongly associated with sensitization to allergens and other allergic disease manifestations, including eczema and allergic rhinitis. This has been conceptually encapsulated in the allergic march.

However, many children with one allergic disease do not progress to another so there may be specific phenotypes of asthma with eczema or hay fever.

Alternatively, a common pathway such as induction of allergic sensitization through skin barrier defects, could promote the development of allergic airway inflammation; for example, children who are deficient in filagrin have a higher risk of asthma but only in the presence of eczema.[[38]](#endnote-38)

Atopy is certainly more strongly associated with persisting wheezing phenotypes than with transient viral-triggered wheezing and the classification of asthma into an atopic and non-atopic phenotype is relatively straightforward from a clinical perspective. However, this approach may be to fall into a trap of regarding atopy as a single disease entity analogous to the previous concept of asthma, several groups have now applied clustering methods to atopy and have reported discrete phenotypes that differ in their associations with asthma.[[39]](#endnote-39)

Therefore, it seems likely that multidimensional and sophisticated statistical approaches will be needed to untangle the component phenotypes of even seemingly straightforward clinical categories.

Other clinical phenotypes (e.g., it has been suggested that a discrete obesity-asthma phenotype exists) could well be subject to the same complexities of association, which may explain some of the discrepancies that exist in the literature relating these two increasingly common phenomena.

# Conclusions

Childhood asthma in Thi-Qar, Iraq was found to be more common in males than females. About one-tenth of the children with asthma were <3 years and majority of the children were in school ages. Allergic conditions were observed in about one-half of the children.

Presenting complain can vary grossly and mimic other causes of respiratory illness. Also, it varies according to age group and gender.

Viral upper respiratory tract infection & cold exposure were recognizable triggering factor for precipitating of attacks and worsening of symptoms. The cough at night and at exertion was the most presenting complaint among our patients.

The need for prompt diagnosis, appropriate assessment, and monitoring as well as management of children with asthma is important to improve the quality of life of these children and their caregivers.

# Recommendations

**Research Recommendations:**

* Identify biomarkers for airway inflammation that are both informative for initial and ongoing treatment decisions and are also practical for clinical use.
* Diagnostic and prognostic markers for asthma and/or specific phenotypes are clearly needed.
* Indirect, non-invasive measures of airway pathology will help the diagnostic investigation in young children
* Development of easy to use lung function tests for young children will improve diagnosis.
* Study of lung function cut-off points (FEV1, bronchodilator response) in children is needed.
* Whether phenotype-specific management strategies can be more effective than currently used ones, should be investigated.
* Educational programs largely depend upon local culture, therefore, local versions, based on these principles should be developed.

**Guideline Update Recommendations:**

* Newer lung function tests (e.g. oscillometry) may be included as aid to asthma diagnosis in young children.
* Pediatric lung function cut-off points should be considered as data becomes available.
* Peripheral airway parameters may be helpful in the diagnostic evaluation.
* The role of FENO in diagnosis and monitoring can be reevaluated.
* The role of AHR assessment in clinical practice should be clearly defined.
* Phenotype-specific management principles can be useful.
* Probabilistic models, taking into account future risk, may be helpful in guideline design.

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