



## Association between wheezing and sleep disturbance in Lebanese asthmatic school-aged children

Ahmad Chahal<sup>1</sup>, Rose Al Bacha<sup>2</sup>, Kim Charro<sup>3</sup>, Bassem Abou Merhi<sup>4</sup>, Nada Sbeiti<sup>5</sup>

<sup>1</sup> Department of Radiology and Medical Imaging, Lebanese University-Faculty of Medical Sciences, Beirut, Lebanon

<sup>2,3</sup> Department of Internal Medicine, Lebanese University-Faculty of Medical Sciences, Beirut, Lebanon

<sup>4</sup> Associate Professor of Clinical Pediatrics, Department of Pediatric, Lebanese University-Faculty of Medical Sciences, Beirut, Lebanon

<sup>5</sup> Department of Pediatric Hematology and Oncology, Lebanese University-Faculty of Public Health, Beirut, Lebanon

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### Abstract

**Background:** Asthma is the most common chronic illness in childhood, affecting approximately 7.53% of children in the Middle East. Symptoms that asthmatic children experience include coughing, chest tightness, dyspnea, and recurrent wheezing, with nightly and early morning symptoms being more prevalent. On the other hand, many studies have shown that children with insufficient, fragmented, or poor-quality sleep are prone to impulsivity, hyperactivity, and aggression, as well as problems with mood, academic performance, and neurocognitive functioning.

**Objective:** To determine whether an association exists between wheezing as a symptom of asthma on one hand and disturbed sleep on the other hand in Lebanese children aged 5 to 15 years.

**Methods:** This is a cross-sectional study done on school-aged children recruited in different schools across Lebanon. Two surveys were filled by their parents or guardians: the first one is the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire to investigate wheezing and asthma, and the second is the Pediatric Sleep Questionnaire (PSQ) to evaluate sleep quality.

**Results:** 235 children were enrolled from five different schools in two regions in Lebanon. Of those diagnosed with asthma according to their parents/guardian (n=32), 16 had 1 to 3 nocturnal wheezing attacks during the last 12 months, 7 had 4 to 12 nocturnal wheezing attacks and the remaining 9 experienced no wheezing attacks during the last year. Delayed sleep onset latency, night waking's and restless sleep were found to be associated with nocturnal wheezing attacks.

**Conclusion:** An increased number of nocturnal wheezing attacks in asthmatic children are related to sleep disturbance and poor sleep quality. Future trials on how asthma treatment could improve sleep behavior in children are needed in Lebanon.

**Keywords:** NREM: non-rapid eye movement. Rem: rapid eye movement. SDB: sleep disordered breathing

### Introduction

Asthma is the most common chronic disease during childhood, affecting approximately 7.53% of children in the Middle East <sup>[1]</sup>. It is a chronic disorder of the bronchial tree, occurring by airway hyper-responsiveness to a variety of stimuli, such as allergens, nonspecific triggers and infections leading to activation of many different inflammatory cells which in turn produce a variety of mediators that act on target cells of the airways. This complex process eventually leads to the abnormal pathophysiological features typical of asthma such as airway obstruction, mucus hyper-production and airway wall remodeling. Symptoms that asthmatic children experience include chest tightness, cough, dyspnea, and recurrent wheezing, with symptoms being more prevalent during the night and early morning <sup>[2, 3]</sup>. On the other hand, it is widely recognized that sleep is essential for children's health and well-being, and that sleep interruption can have a detrimental influence on the different aspects of a child's life, such as school achievement, social activities and family life. In fact, many studies have shown that children with insufficient, fragmented, or poor-quality sleep have increased impulsivity, hyperactivity, and aggression, as well as problems with mood, academic performance, and neurocognitive functioning <sup>[4]</sup>. In addition to nocturnal awakening, which is starting to be recognized as a common problem, asthmatic children are largely

confronted by other sleep disturbances such as resisting going to bed at bedtime, difficulty falling asleep, restlessness and very early morning awakening. In childhood, the different aspects of sleep disturbance as a consequence of wheezing has been a poorly-addressed subject, and no large correlational studies exist to investigate the possible relationship between wheezing and sleep disturbance in school-aged children <sup>[5]</sup>. In this manuscript we present a review of the literature of asthma and sleep disturbed breathing followed by the method of data collection in five different schools in Lebanon and its interpretation. Then we discussed our results to end with a conclusion whether wheezing due to asthma is associated to poor sleep habits.

### Literature Review

#### Asthma in children

Asthma is an important health problem worldwide. It is one of the most common chronic diseases of childhood in many countries. The prevalence is not the same around the world and it ranges from 1 to 18 percent. In the United States, for example, more than nine million kids have been ever told they had asthma, and over six million still have asthma. In the Middle East, Asthma affects approximately 7.53% of children <sup>[1]</sup>. Establishing a diagnosis of asthma involves a careful process of history taking, physical

examination, and diagnostic studies that should focus on the presence of typical symptom patterns, precipitating factors or conditions (i.e., Atopy), and known asthma risk factors. The differential diagnosis of wheezing must be carefully considered, particularly in infants and very young children, for whom testing for reversible airflow obstruction is not usually done routinely [6]. Additional history that should be obtained in a child with established asthma who presents for disease monitoring includes previous and current therapy (controller and quick-relief medication use), exposure to triggers, utilization of health care services (emergency department [ED], hospital, unscheduled clinic visits), school attendance and performance, and participation in physical activity [7].

**Symptoms: Wheezing:** is a high-pitched, musical sound produced when air is forced through airways that are narrowed. The wheezing of asthma is usually varied in pitch, characterized as being polyphonic, reflecting the heterogeneous distribution of affected airways. When airflow obstruction becomes severe, wheezing lasts during both inspiration and expiration [8]. In contrast to asthma, central airway obstruction such as in case of tracheomalacia can cause a harsh expiratory monophonic wheeze. Upper airway obstruction (e.g., vocal cord dysfunction) should be suspected if an inspiratory monophonic (of single pitch) wheeze (typically called stridor) is the only audible sound during an exacerbation [9, 10]. A silent chest in the context of an asthma exacerbation implies airflow limitation of such severity that audible wheezes cannot be produced and this represents a medical emergency [11].

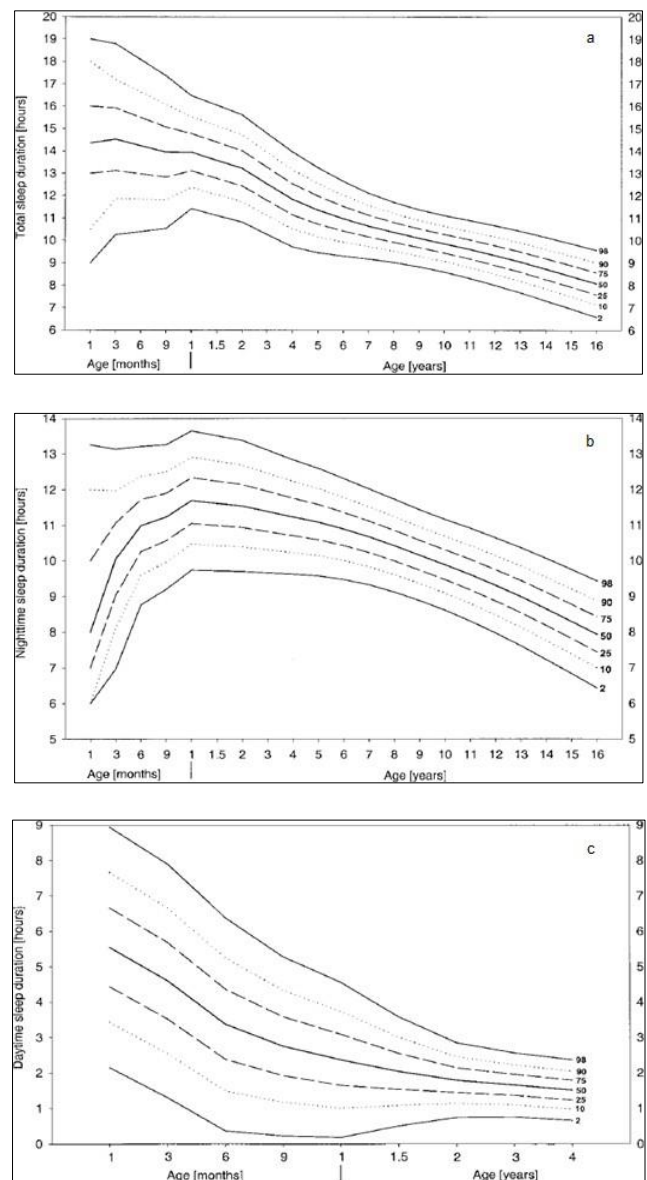
**Cough:** Although wheezing is considered the hallmark of asthma in children, cough can be frequently the sole presenting complaint. The presence of a nocturnal cough, a cough that recurs seasonally, a cough triggered by specific exposures (e.g. exercise, cold air, allergens, laughing or crying), or a cough that lasts more than three weeks should raise the suspicion for asthma [12]. The most common cause of chronic cough in children older than three years is asthma, even in the absence of wheezing. The cough in asthma is typically dry and hacking but may sometimes be productive; when this is the case, clear or whitish sputum may be expectorated (which often contains eosinophils). It is not unusual for chronic cough lasting more than three weeks to be labeled "bronchitis" and to be treated with cough suppressants, decongestants, or even antibiotics. However, such types of cough may actually be manifestations of asthma and consequently respond to asthma therapy [13].

**Current status:** Wheezing, despite being most commonly related to asthma, is not a pathognomonic finding of this condition. The lack of objective measures of pulmonary function in very young children and the relatively high prevalence of congenital and inherited disorders that present with wheezing make it imperative to consider the differential diagnosis of wheezing illnesses before making a diagnosis of asthma solely on the basis of wheezing [10, 14, and 15]. In case of failure to respond to asthma therapy or in case the history and physical examination suggest alternative diagnoses, other causes of wheezing in children must be excluded. Cough can be the primary manifestation in some children with asthma; therefore, the differential diagnosis for chronic cough in children should also be considered [16].

**Sleep disturbance in children:** Identification of sleep problems

in children is of a very important value because of the growing body during this stage of life. Evidence states that sleep disorders can actually interfere with physical, cognitive, emotional and social development. Building on this, clinicians should incorporate questions about sleep behavior into health assessment for children of all ages [17].

**Sleep stages:** Sleep is an active and dynamic physiologic process that undergoes several important developmental changes during the first few years of life leading to the expected adult sleep-wake pattern [18]. Sleep-wake patterns become more nocturnal and sleep times gradually decrease from infancy through adolescence, as shown in figure 1. Consolidation of nocturnal sleep occurs during the first year of life with a decreasing trend of daytime sleep duration [19]. Sleep time of children in a given age group varies by as much as two hours. In addition, sleep patterns are affected by sociocultural factors and have changed over time in a way that sleep duration in equivalent age groups has declined [18].



**Fig 1:** Sleep duration per 24 hours from infancy to adolescence [19]. Percentile curves for total sleep duration (a), nighttime sleep duration (b), and daytime sleep duration (c).

Sleep in the healthy, full-term newborn is distinguished from that of older individuals by longer sleep duration (16 to 18 hours per 24 hours), rapid eye movement (REM) sleep occurring at sleep onset, increased proportion of REM sleep and REM-nonrapid eye movement (NREM) cycle much shorter in duration as compared with older individuals. With maturation of the child's central nervous system, predictable changes occur, including gradual decrease in total sleep time and the proportion of REM sleep, progressive lengthening of the REM-NREM cycle, and shift to the adult pattern of sleep onset via NREM sleep<sup>[20]</sup>. In normal older children and adolescents, sleep is characterized by onset via NREM sleep, NREM sleep occupying approximately 75 percent of total sleep time and progressive lengthening of the duration of REM sleep periods in the final one-third of the night<sup>[21]</sup>.

### **Changes in respiratory physiology during sleep**

Sleep-related breathing disorders in children occur along a wide scope of severity, ranging from primary snoring to obstructive sleep apnea on the serious end of the spectrum<sup>[22]</sup>. In a normal child there is a modest increase in upper airway resistance during sleep and a small decrease in nocturnal ventilation is tolerated. Overnight polysomnography (PSG) studies in normal children have quantified these changes, establishing norms for nocturnal ventilation in children: a small decrease in oxygen saturation (0 to 7 percent) and a rise in end-tidal PCO<sub>2</sub> (0 to 13 mmHg). Brief central apneas are also common in children and are especially related with movements, obstructive apneas however are never normal in this age group<sup>[23]</sup>. The decrease in ventilation is related to both an increase in upper airway resistance and a decrease in central respiratory drive, as detailed below.

### **Increased upper airway resistance**

Although the nose is the site of greatest resistance in the upper airway, the pharynx is the site of the greatest increase in airway resistance during sleep. This increase in resistance is due to the decreased size of the pharynx associated with relaxation of the pharyngeal dilators<sup>[24]</sup>. During sleep in individuals without a sleep-related breathing disorder, there is a decrease in activity of the pharyngeal dilators that results in a decrease in pharyngeal size and a concomitant increase in upper airway resistance. Their activity during sleep is managed by the respiratory control center of the medulla, which receives input from the pharyngeal mechanoreceptors. These reflexes likely play an even more important role during sleep in adults and children with sleep-disordered breathing<sup>[25, 26]</sup>. Decreased central respiratory drive if the increased upper airway resistance is reversed by nasal continuous positive airway pressure (CPAP), a small decrease in ventilation persists, suggesting an independent decrease in central respiratory drive during sleep. This decrease has been attributed to the loss of a "wakefulness respiratory drive," the nature of which is not completely understood<sup>[27]</sup>.

### **Sleep disordered breathing**

Diagnostic classification of sleep disorders is important because it standardizes definitions, improves awareness of the conditions, and facilitates an understanding of symptoms, etiology, and pathophysiology that paves the way for appropriate treatment<sup>[28]</sup>. Breathing disorders are a well-known culprit in sleep disturbance, in fact the International Classification of Sleep Disorders (ICSD),

the most widely used classification system for sleep disorders, and divides sleep disorders into seven categories with Sleep-related breathing disorders being one of them. The remaining six categories cover Insomnia, Central disorders of hyper somnolence, Circadian rhythm sleep-wake disorders, Parasomnias, Sleep-related movement disorders and other sleep disorders<sup>[29]</sup>. Sleep-related breathing disorder is the disruption of normal respiratory patterns and ventilation during sleep. It has a broad clinical presentation, ranging from primary snoring to obstructive sleep apnea (OSA)<sup>[30]</sup>. Its relation to asthma has been well-established in the literature, often described as being bi-directional<sup>[31-33]</sup>. Several studies proved that children with SDB were more likely to have a history of asthma/wheezing: A study done by Lu *et al.* in New South Wales, Australia with a total of 974 pre-school children recruited reported that 42.2% of children who snored had asthma<sup>[34]</sup>. Sulit *et al.* in a US community-based cohort study of 788 participants between the ages of 8 and 11 years found that children with SDB had nearly twice the odds of wheezing compared with those without SDB<sup>[35]</sup>. A large Chinese epidemiological study of 20,672 children with a mean age 9.0±1.61 years concluded that snoring and OSA is a significant predictor of asthma<sup>[36]</sup>.

### **Underlying medical conditions**

Sleeplessness may cause a child to have problems with daytime performance, behavior or mood regardless of the underlying cause<sup>[37, 38]</sup>. Problem sleeplessness in children is a manifestation of a vast group of disorders that include but are not limited to behavioral, social, environmental, circadian rhythm, and medical causes. The causes and clinical presentation of sleeplessness in children with underlying medical conditions differ from those in adults, and as a result, approaches to diagnosis and management are not the same. Little substantive literature however exists exploring the association between medical conditions and sleeplessness in childhood<sup>[39]</sup>.

### **Objectives**

#### **Primary objective**

The primary objective of this study is to determine whether an association exists between nocturnal wheezing as a symptom of asthma on one hand and sleep disturbance on the other hand in Lebanese children aged 5 to 15 years.

#### **Secondary objectives**

To determine whether a difference in demographic distribution of asthma in the study sample (age, gender) exists between different regions across the country. To determine whether a more severe asthmatic profile manifested as more frequent wheezing attacks translates into a more profound sleep disturbance. To try and indicate specific sleep habits that are most affected in case a correlation between nocturnal wheezing and sleep disturbance does exist.

### **Subjects and Methods**

#### **Study Design**

We implemented this correlational study over the period of 6 months to children in five different schools in Lebanon located in the North and South governorates: Saint Antonios Al Bedwani School in Karm Saddeh-North Lebanon, Collège De La Salle

Kfaryachit in Zgharta-North Lebanon, Fursan al Azraa School in Harf Mezyara-North Lebanon, Al Farah High School in Tebnin-South Lebanon and Tyr public School in Tyr-South Lebanon. We intended to enroll at least 100 Lebanese asthmatic and non-asthmatic children who are 5 to 15 years of age.

**Subjects**

**Inclusion criteria**

Children aged 5 to 15 years. Children are of Lebanese nationality.

**Exclusion criteria**

Presence of any respiratory disorder other than asthma (emphysema, bronchiectasis, bronchitis and tuberculosis). Presence of any comorbidity that could adversely affect quality of life (e.g. severe cardiac, hepatic, renal, psychiatric illness) and patients who could not or refused to complete the questionnaire.

**Data Collection**

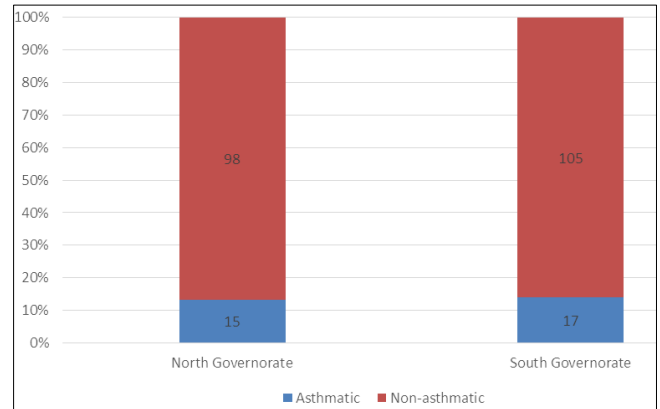
We obtained a written informed consent from the parents/guardians of every child included in the study. We used the core questionnaire for wheezing and asthma of the International Study of Asthma and Allergies in Childhood (ISAAC) to investigate wheezing. The main parameters targeted in this questionnaire were whether the child has been previously diagnosed as being asthmatic by a specialist, whether he/she had any whistling or wheezing during the 12 months preceding the study and whether nocturnal wheezing attacks, divided if existent into 1 to 3, 3 to 4 and 4 to 12 attacks, were experienced by the child during the past year. Sleep habits were evaluated based on The Children’s Sleep Habits Questionnaire (CSHQ). For the sake of simplicity, answer choices to most of the questions in the sleep habit questionnaire were changed into simple yes or no answers. The questionnaire covers a large panel of different sleep habits such as bedtime (having a constant bedtime, taking a long time to fall asleep, needing someone else or a special object around to fall asleep, etc.), sleep behavior (sleeping the same amount every day, being restless during sleep, snoring loudly, etc.), waking during the night and morning wakeup including daytime napping and falling and being tired during the day. Arabic and English versions of both questionnaires were made available for parents/guardians to fill out. The average time to complete both questionnaires was expected to be around 10 minutes.

**Statistical Analysis**

Collected data was organized in an excel sheet and was then analyzed by running a bivariate (Pearson) correlation analysis using the Statistical package for Social Sciences Software (SPSS). A regression was done and a P-value less than 0.05 were considered significant.

**Results**

We enrolled 235 children from five different schools in North and South Lebanon. The age of the children that were included in this study ranged from 5 to 15 years with a mean of 9.7 years (SD=2.3). Participants were divided into three age groups: 5 to 8 years old, 8 to 12 years old and 12 to 15 years old. Parent report was used to designate asthma versus no asthma. The percentage of kids who had asthma (n=32) was 13.6 % with no significant difference between the North and South governorates (15.3% and 16.1% respectively).



**Fig 2:** Percentage of enrolled asthmatic kids in the North and South governorates

No significant age difference was found between asthmatic (n=32) and non-asthmatic children (n=203) with respective means of 9.3 years (SD=2.7) and 9.7 years (SD=2.25). Of those who were previously diagnosed with asthma: 20 had wheezing or whistling in the chest during the last 12 months, 9 of them had no nocturnal wheezing attacks in the last 12 months, 16 had 1 to 3 nocturnal attacks, 7 had 4 to 12 nocturnal attacks and the remaining 1 had whistling without any nocturnal wheezing attacks. Of the non-asthmatic children, 4 had whistling in the chest during the last 12 months without any wheezing attacks. None of the asthmatic kids had more than 12 wheezing attacks during the last year so we divided the asthmatic kids into three groups only based on the frequency of their wheezing attacks: Group 1 (n=9) had no nocturnal wheezing attacks in the last 12 months, Group 2 (n=16) had 1 to 3 attacks and Group 3 (n=7) had 4 to 12 attacks. This classification was based on the fact that the frequency of asthma attacks is one of the main criteria in assessing asthma severity and efficacy of treatment [40-42]. The differences between genders were small in the asthmatic groups. Demographic data for the three groups are showed in Table 1.

**Table 1:** Demographic characteristics of study sample

|                   | Group 1 (n=9) | Group 2 (n= 16) | Group 3 (n=7) | No asthma (n=203) |
|-------------------|---------------|-----------------|---------------|-------------------|
| Age               |               |                 |               |                   |
| 5 to 8 year-old   | 5             | 5               | 5             | 67                |
| 9 to 12 year-old  | 3             | 10              | 2             | 111               |
| 13 to 15 year-old | 1             | 1               | 0             | 23                |
| Gender            |               |                 |               |                   |
| Male              | 4             | 7               | 2             | 40                |
| Female            | 5             | 9               | 5             | 161               |

### Sleep Behavior Parameters

Several elements of sleep behavior are represented in table 2. Enrolled kids were divided into non-asthmatic, asthmatic without nocturnal wheezing attacks in the last 12 months and asthmatic children with at least one nocturnal attack in the last 12 months (Groups 2 and 3). Several sleep behavior parameters showed no statistically-significant difference between asthmatic and non-asthmatic children as well as between asthmatic children without and with nocturnal wheezing attacks. This included going to bed every night at the same time (p-value=0.12), waking up very early in the morning (p-value=0.81), falling asleep alone in own

bed (p-value=0.66), needing a special object (p-value=0.81) or a parent in the room (p-value=0.92) to fall asleep, being afraid of sleeping in the dark (p-value=0.78). Other parameters of particular importance that showed no significant association to asthma and nocturnal wheezing attacks were waking up during the night sweating, screaming and being inconsolable (p-value=0.63), grinding teeth during sleep (p-value=0.059), being tired during daytime (p-value=0.23), taking daily naps (p-value=0.82) and falling asleep while involved in activities (p-value=0.79).

**Table 2:** Sleep behavior in asthmatic and non-asthmatic children

|   | Asthmatic with nocturnal wheezing (n=23) | Asthmatic without nocturnal wheezing (n=9) | Non-asthmatic (n= 203) | Total (n=235) | P-value |
|---|--|--|------------------------|---------------|---------|
| Same bedtime every night                  | 9  | 6  | 151                    | 166           | 0.12    |
| Sleep onset latency (20 minutes)          | 10                                       | 5  | 154                    | 169           | 0.04    |
| Night wakings, once                       | 7  | 2  | 12                     | 21            | 0.001   |
| Night wakings, more than once             | 6  | 3  | 8                      | 17            | 0.0011  |
| Wake time (very early in the morning)     | 1  | 2  | 9                      | 12            | 0.81    |
| Tired during daytime                      | 1  | 1  | 5                      | 7             | 0.23    |
| Daily naps                                | 4  | 0  | 36                     | 40            | 0.87    |
| Falls asleep while involved in activities | 1  | 0  | 3                      | 4             | 0.052   |
| Restless sleep                            | 11                                       | 5  | 153                    | 169           | 0.04    |

Questionnaires were coded and analyzed by running a bivariate correlation analysis using the SPSS software. Variables included being non asthmatic, asthmatic without nocturnal wheezing and asthmatic with nocturnal wheezing on one side and several sleep behavior parameters on the other side. Compared to children with no asthma and asthmatic children with no nocturnal wheezing attacks, asthmatic children that experienced nocturnal wheezing attacks during the last 12 months (Groups 2 and 3) had longer sleep onset latency, more than 20 minutes. The same thing applies for having a restless night sleep. Compared to children without asthma, asthmatic children without and with nocturnal wheezing attacks had more frequent night waking's. The number of night waking's was higher in asthmatic kids that experienced more nocturnal wheezing attacks (Group 3) compared to asthmatic kids with fewer attacks (Group 2) (p-value=0.001). Asthmatic children with 4 to 12 nocturnal wheezing attacks in the last 12 months (Group 3) napped more frequently compared to non-asthmatic children and asthmatic children with no or fewer nocturnal attacks (Groups 1 and 2), Total nighttime sleep duration did not differ between groups (p-value=0.68). The duration of daytime sleep was also not significantly different between groups (p-value=0.87). There was no significant difference in going to bed at the same time every night and waking up very early in the morning between groups (p=0.81).

### Discussion

Sleep is very important during childhood as it impacts mental and physical growth, and sleep disturbance can have detrimental consequences on the different aspects of a growing child's life [43, 44]. One of the common causes that can lead to insufficient or fragmented sleep in asthmatic children is nighttime wheezing [45]. This subject is of particular importance since previous longitudinal research around the world has indicated that poor asthma control is associated with poor sleep quality [46]. Our study focused on wheezing as a symptom of asthma to find out whether

it has an impact on sleep quality in school-aged children. Asthma is in fact the most common chronic disease of childhood still causing considerable morbidity and mortality worldwide imposing an increasingly consistent burden on health systems [47, 48]. In this random sample of school-aged children the prevalence of wheezing was 13.6%, a little bit higher than what has been reported in the Middle East [1]. No significant difference in prevalence was noted between the North and South governorates with respective values of 15.3% and 16.1%, likely since the bulk of the participants in both regions came from private schools located in rural areas with very similar environmental and socio-economic statuses. No significant age difference was found between asthmatic and non-asthmatic groups. This was expected considering the narrow age range targeted in our study. Asthma is in fact a chronic disease with cumulative years' effect [49] and clinical manifestations that prompt an expert's diagnosis can become more overt with age. No significant differences were found between genders either although it has been shown in the literature that male sex is predominant in asthma population in the first decade of life [50].

Concerning sleep habits, our results showed that nocturnal wheezing in asthmatic school-aged children is in fact associated with poorer sleep quality, paralleling those found in the literature [45, 51-54]. Particularly, one meta-analysis conducted by Brockmann *et al* reviewed seventeen studies involving 45155 children to conclude that children with asthma had a significantly higher risk of SDB and thus poorer sleep quality [55]. As for sleep habits parameters that were specifically affected, kids with asthma have shown difficulty falling asleep at night with prolonged sleep onset latency, more than 20 minutes, and had more than one nocturnal waking compared to non-asthmatic kids. This is consistent with the hard evidence found in previous studies [56-58], and as expected, asthmatic children with frequent recurrent nocturnal wheezing attacks had more frequent nocturnal awakenings than young children with only few attacks.

Nocturnal wheezing in asthma was also found to relate to restless sleep, defined in the used CSHQ as frequent moving during sleep. This has also been solidly proven in the literature [45], with one chief explanation, the fact that asthmatics suffer bronchoconstriction during REM sleep [59], a sleep stage that is already characterized by a normally irregular shallow breathing and hypoxemia [60]. This makes them prone to micro-arousals and shallow sleep with frequent movements. Furthermore, concerning sleep terrors that have been previously linked to severe nocturnal symptoms of asthma [46], no significant relation was found in our study, only two children had sleep terrors and none of them was asthmatic. In fact, the trigger for sleep terrors is insufficient sleep or poor sleep quality, that's why sleep disruptions in young children with asthma are likely to cause more sleep terrors. Since sleep terrors have been clearly defined in the questionnaire we used as waking up during the night sweating, screaming and being inconsolable leaving very little margin for misunderstanding, one plausible explanation for the discordant result is that sleep disturbance in recruited children was possibly not profound enough to cause sleep terrors, a type of parasomnia located on the more severe end of sleep disturbance spectrum [61]. Another parameter that was not found to correlate to nocturnal wheezing is bruxism, the habit of grinding one's teeth in non-functional activities. In fact, no previous studies associating nighttime bruxism and asthma were found in the literature and one possible explanation for the lack of significant bruxism in our study sample of asthmatics is the fact that such a subtle habit may be easily missed by the parents of young children, and the only reference to its presence may be the development of dental caries later on. As for daytime symptoms such as frequent napping, being tired during the day and sleeping during activities, although clearly proven as a consequence of poor sleep quality due to asthma [62-65], no statistically-significant difference was found neither between asthmatics and non-asthmatics nor between asthmatics with nocturnal wheezing attacks and asthmatics without nocturnal attacks. The rationale behind this can be the fact that sleep disturbance in the asthmatic kids of our sample was not severe or chronic enough to have repercussions on daytime functioning, which underlines the importance of future studies inquiring daytime symptoms specifically in our country.

### Study Limitations and Perspectives

There are several study limitations that need to be addressed. First, only five schools in two out of eight governorates were included in this study mainly due to logistical factors, and four of them were in rural areas, two elements that can render our study sample incompletely representative of the entire population of school-aged children in Lebanon. Second, this study is a questionnaire-based one relying on parents' statements to classify children as being asthmatic or not, posing problems in recall deficiency and over or under evaluation of symptoms. Although the ISAAC questionnaire we used is an internationally-validated questionnaire in the definition of asthma [66-68], lung function tests can help in standardizing case definition since these tests are less influenced by recognition or awareness of symptoms. No pulmonary function tests were conducted and no specialized physicians or professional caregivers were contacted to confirm the diagnosis of asthma. Similarly, another challenge in

questionnaire-based studies was to obtain an objective definition of sleep problems. We also relied on parents' statements to characterize a child's sleep habits and no polysomnographic studies, the gold-standard in the diagnosis of sleep problems [69], were done. Third, because of the cross-sectional study design, no conclusions can be drawn about the causality between asthma, sleep disturbance and other confounding factors which is beyond the scope of our work. Future research is needed to address the methodological limitations of this study. In order to determine the possible underlying mechanism through which nocturnal wheezing leads to impaired sleep in asthmatic school-aged children, the relation of other asthma-related variables such as chronic cough and chronic rhinitis to sleep disturbance needs to be targeted. Other causes of nocturnal wheezing such as the presence of gastro-esophageal reflux disease (GERD) also need to be addressed. Other studies specifically querying daytime symptoms in children and the repercussions of asthma-related sleep disturbance on behavioral and academic functioning are needed in Lebanon. Similarly, studies reflecting on the effect of treatment in asthmatic children with disturbed sleep are also important. Furthermore, referral to specialists is needed to classify the severity of sleep disorder based on the yield of the sleep behavior variants that turned out to be related to nighttime wheezing attacks (i.e. nighttime waking's, sleep onset latency, restless sleep, etc.) and to offer treatment options to keep consequences of poor sleep to a minimum.

### Conclusion

The characterization of sleep in children with asthma and recurrent nocturnal wheezing attacks is a new contribution to the literature in Lebanon. The results of our study are in line with the findings in the literature and nocturnal wheezing due to asthma has in fact detrimental effects on several aspect of a child's sleep. These findings are relevant for clinicians working with the young population, suggesting the importance of addressing sleep problems in every asthmatic child and trying to identify the treatable risk factors to limit the consequences of poor sleep not only on the growing child's life but also on his close family members.

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