# NOCTURNAL ASTHMA IN SCHOOL CHILDREN OF SOUTH PUNJAB, PAKISTAN

### Ghulam Mustafa, Pervez Akber Khan, Imran Iqbal

Department of Paediatrics, Nishtar Medical College & Hospital, Multan. Pakistan

**Background:** At the present time, the epidemiology of the childhood asthma is of considerable interest. There is an understandable concern that changes in the geographical area, lifestyle, and environment. This study was conducted to find the prevalence of nocturnal asthma, in school children of south Punjab, Pakistan. **Methods:** It was a cross sectional, questionnaire based, descriptive survey of the children aged 3–18 years, in randomly selected primary and secondary schools, from October 2002 to March 2003. The data was analysed with Statistical Analysis System (SAS). **Results:** Of 6120 questionnaire sent to the parents/guardians, we received 3180 back (52%). Of the 3180 respondents, 1767 (56%) were for boys and 1413 (44%) were for girls. The median age was 8.25 years. Around 71% of children were between 4 to 11 years of age. The parents reported nocturnal asthma in 177 (6%) of their children with an equal prevalence in boys and girls, i.e., (3% each, rounded off to nearest whole number). Of these 177 children with nocturnal asthma, 99 (56%) were boys and 78 (44%) were girls. Of the 1767 boys and 1413 girls, the nocturnal asthma reported by parents was 6% each (99 and 78 respectively). The nocturnal asthma was not reported in 14–18 years age group of females. **Conclusion:** The asthma is taken as a stigma in our society and as such is not reported or disclosed rather denied. An extensive educational media campaign is required for awareness of the masses.

Keywords: Childhood asthma, Nocturnal asthma, Pakistan.

#### INTRODUCTION

At the present time, the epidemiology of the childhood asthma is of considerable interest and concern to all, dealing with it, because of an increase in the use of health services<sup>1</sup> for asthma, a possible increase in its prevalence<sup>2,3</sup> and severity<sup>4</sup>. There is an understandable concern that changes in the geographical area<sup>5</sup>, lifestyle,<sup>6,9</sup> and environment<sup>10–12</sup> may be having an adverse effect on its incidence, prognosis and severity<sup>13</sup>.

Night time awakening is a common symptom in asthmatic children.<sup>14</sup> The children with nocturnal awakenings also had demonstrated an increased number of days of school missed, increased symptom severity and an increased use of reliever medications. The parents of the children with nocturnal asthma had an increased frequency of missed work days.<sup>15</sup> The nocturnal asthma is associated with increased asthma severity<sup>16</sup>, but several well controlled studies have argued that nocturnal asthma may be a distinct entity<sup>17</sup>. Whether or not nocturnal asthma may be a distinct entity, the clinical association among gastro-oesophageal reflux disease<sup>18</sup>, increased morbidity<sup>19</sup>, obesity<sup>20</sup>, and impairment in psychometric and quality of life indexes<sup>15</sup>, for the child & parents, are clear and they provide a compelling rationale for a comprehensive study of this disorder.

In Pakistan the existing studies do not provide adequate information about the epidemiology of nocturnal asthma in children and there remains an important gap in our knowledge of its descriptive epidemiology. <sup>2,6,21,22</sup>

We have tried to focus the epidemiology of nocturnal asthma in children of the south Punjab (central Pakistan). This opportunity arose from two initiatives: first, a desire to know the epidemiological variables of asthma in the 'central Pakistan' (south Punjab) and second, development of a questionnaire for the epidemiological study of asthma in school children of this area. In this questionnaire, we also asked if the child had episodes of dry cough at night when there was no flu or cold, during the last one year. We made the diagnosis of nocturnal asthma on a parent/caregiver's positive response to this question. This is one of the standard methods and has been employed worldwide in various studies. 9,13 The resultant study, being reported, describes the prevalence of nocturnal asthma in various groups of the school children of the central Pakistan.

#### MATERIAL & METHODS

It is a cross sectional, questionnaire based, descriptive survey of the children aged 3–18 years, in randomly selected primary and secondary schools, from October 2002 to March 2003. We obtained school lists from the Department of Education in the District Multan of the Punjab, Pakistan. The list was used as a sampling frame of the schools that included all the socioeconomic and geographical strata of the society. The total number of students studying in government and private schools were approximately 258,000. With a power of 99% and a confidence interval of 2.5, a sample size of 2635 was calculated to be sufficient to be representative of the target population. A total of 6120 questionnaire were sent to the parents/guardians and we received 3180 back with an average response rate of 52%.

At first stage we randomly selected 9 schools to represent each socioeconomic and geographical category of schools of the region. The socioeconomic groups were defined by the level of school fee that the parents were affording for a particular school. Stratified random sampling with proportional allocation was used for this purpose. The questionnaires were sent to the selected schools proportional to their enrolment, i.e., proportional allocation was used again. The individual respondents within a school were selected using stratified random sampling where due consideration was given to gender and age/class.

Before distributing the questionnaire, the teachers and students were told about the objectives of the study and a need to bring the questionnaire back after duly filled. As the initial response rate was very poor so we had to pursue the parents through class teachers for cooperation in the larger interest of the community. Also we gave reminders to the parents through the teachers. Few of the children lost or tore the questionnaires and we had to issue the new ones to take home and get them completed by the parents/guardians. The efforts really brought fruit with a response rate of 52%.

We modified the International Study of Asthma & Allergies in Childhood (ISAAC) protocol to conduct this cross-sectional, school-based survey of school children. The ISAAC was a multinational collaborative project developed to investigate variations in childhood asthma and allergies at the population level.<sup>2,3,6</sup> Our study protocol was approved by the Institutional Review Board of our hospital, and it complied with the principles outlined in the Helsinki Declaration. The questionnaire was taken home by the students and answered by the parents or the guardians. The definition of 'nocturnal asthma' used in this study was determined by a positive response to the question, 'In the last 1 year, has your child had a bout of dry cough at night when there was no flu or cold?' The question was also translated in local language and was validated by the reverse translation. The parents or the guardians had the choice to answer in either language.

The data obtained was entered and then cleaned for removing possible typing-in errors and to ensure the internal consistency of the data. The data then was analysed with Statistical Analysis System (SAS).

#### RESULTS

Of the 3180 respondents, 1767 (56%) were for boys and 1413 (44%) were for girls. The median age of students was 8.25 years while average age was 9.04 years. Around 71% of children were between 4 to 11 years of age. The parents reported nocturnal asthma only in 177 (6%) of their children without any gender predominance, i.e., 3% in each. Of the 177 reported children with nocturnal asthma, 56% were boys and 44% were girls. Of the 1767 boys and 1413 girls, the nocturnal asthma was reported by parents in 6% each (99 and 78 respectively).

The nocturnal asthma reported in males and females of all age groups is not very much different. The significant point is that the parents of 14–18 years age group of girls have denied any nocturnal asthma in their children (Table-1). They have rather not liked even to respond to the questionnaire or were hesitant to do so as is evident by the one third of the response in comparison to the boys in this age groups. The response rate in other age groups was comparable for boys and girls.

The intra age group percentage of the children that were reported to have nocturnal asthma in the last one year is comparable (around 7%) in all age groups except 7–9 years age where it is low (3%). Also boys are affected more than girls in 9–11 years age group (5% vs 3%).

#### **DISCUSSION**

Asthma is the single most common chronic childhood disease in developed world<sup>3</sup> and its prevalence and severity is increasing in many developing countries<sup>2,3</sup>. The change has been too rapid to be accounted for by the changes in gene frequencies only or to the environmental factors only. This suggests, at least, that the prevalence changes with the environmental exposure especially geographical variation. Therefore it is necessary to study the epidemiology of asthma in various geographical areas.

In childhood, sleep disturbance as a consequence of asthma has been a neglected area. Lack of awareness of asthma-sleep association and its clinical implications can lead to a vicious cycle of poor control of asthma and impaired daytime activity. The nocturnal awakening is beginning to be recognized as a common problem among asthmatic children. 25,26

Table-1: Age distribution and	l nocturnal asthma in sch	ool children of south Puniab

Age groups	# (%)	Nocturnal Asthma # (%)	Males #(%)	Nocturnal Asthma # (%)	Females # (%)	Nocturnal Asthma # (%)
<4 yrs	187 (6)	16 (9)	111 (3)	9 (0)	76 (2)	7 (0)
>4-7 yrs	950 (30)	68 (7)	533 (17)	37 (2)	417 (13)	31 (1)
>7–9 yrs	801 (25)	26 (3)	449 (14)	14 (0)	352 (11)	14 (1)
>9–11 yrs	501 (16)	33 (7)	295 (10)	23 (1)	206 (7)	10 (0)
>11-13 yrs	540 (17)	31 (6)	283 (9)	15 (0)	257 (8)	16 (1)
14–18 yrs	201 (6)	1 (0)	96 (3)	1 (0)	105 (3)	0
Total	3180 (100)	177 (6)	1767 (56)	99 (3)	1413 (44)	78 (3)

Percentage has been rounded off to nearest whole number.

Lung function in a healthy individual varies in a circadian rhythm, with peak lung function occurring near 4:00 PM and minimal lung function occurring near 4:00 AM. An episode of nocturnal asthma is characterized by an exaggeration in this normal variation in lung function from daytime to night-time, with diurnal changes in pulmonary function generally of >15%.<sup>27</sup>

Nocturnal asthma is recognized as an indicator of uncontrolled asthma, but it also has important effects on quality-of-life (QOL) and psychometric indexes. A study by Diette et al<sup>15</sup> at Johns Hopkins University of 400 asthmatic children and their parents demonstrated that 40% of children had experienced night-time awakening within the previous 4 weeks. Moreover, those children with nocturnal awakenings also had demonstrated an increased number of days of school missed, increased symptom severity, and an increased use of reliever medications. In addition, the parents of these children with nocturnal asthma had an increased frequency of missed work days. Thus, nocturnal asthma impacts the QOL of both the patients and their families having a clinical importance. An earlier study by Weersink et al<sup>17</sup> made related observations. More than 40 asthmatic subjects underwent psychometric testing before and after randomized treatment with inhaled fluticasone, inhaled salmeterol, or a combination of the two agents. At baseline, asthmatic subjects demonstrated a variety of psychometric abnormalities compared to a control group. However, each treatment strategy was associated with an improvement in psychometric indices (to the normal range of findings) and an improvement in pulmonary function. No differences among the three strategies were observed for the outcomes measured. These data provide yet another important rationale for identifying and treating nocturnal asthma.

There are data emerging from the literature suggesting that the diurnal variation in lung function, and perhaps in the occurrence of nocturnal asthma, may be age-related.<sup>28</sup> Studies of asthmatic children who ranged in age from 8 to 13 years demonstrated minimal diurnal variation in respiratory system compliance and resistance, and suggested that the frequency of significant diurnal variation is only about one third. Furthermore, the magnitude of the changes was relatively small (20%). These data suggest that age, independent of asthma severity, may be an important determinant of the prevalence of nocturnal asthma. 6,29

The mechanisms by which nocturnal asthma develops remain unclear and may vary from patient to patient. Mechanisms suggested to be related to development of night time symptoms are listed in Table-2.<sup>29</sup>

Table-2: Postulated Mechanisms of Nocturnal Asthma

- Airway cooling
- Allergen exposure
- Gastroesophageal reflux
- Obesity
- Increased tissue inflammation
- Decreased plasma epinephrine
- Decreased plasma cortisol
- Increased circulating eosinophils
   Increased cholinergic tone
- Polymorphisms of adrenergic receptor

Newer data have shed light on physiologic and immunologic mechanisms that underlie the nocturnal development of airway obstruction. It remains controversial whether nocturnal asthma is a distinct entity or is a manifestation of more severe asthma. The current data do not resolve these two alternatives, as wellcontrolled studies have reached opposite conclusions.<sup>29-31</sup> Thus, although the literature does not at present distinguish between nocturnal asthma as distinct entity vs. a marker of severity, it is clear that asthmatic subjects with more severe asthma also may have a prominent nocturnal component to their disease.

According to current US guidelines<sup>32</sup>, nocturnal symptoms of asthma occurring more often than once weekly may indicate inadequate control of asthma. Because most patients with nocturnal asthma have symptoms at least this frequently, it follows that most patients with nocturnal asthma have persistent asthma of moderate or severe levels of severity, as determined by the guidelines. Furthermore, the preferred treatment for persistent asthma of these levels of severity is inhaled corticosteroids. Thus, most patients with clinically important nocturnal asthma should probably be receiving an inhaled steroid as the primary controller agent.

Finally, newer data suggest that many available asthma treatments can improve nocturnal asthma symptoms. 14 Head-to-head comparisons now suggest that treatment with inhaled corticosteroids, followed by longacting bronchodilators if needed, can reduce considerably the symptoms and consequences of nocturnal asthma.

Our cross-sectional modified questionnaire survey of 3-18 years old school children about nocturnal asthma was part of a broader survey that was looking into the epidemiology of asthma in children in the 'central part' (south Punjab) of Pakistan. The aim of one question in our study was to know the prevalence of nocturnal asthma in a school based sample of primary and secondary school children.

The gender analysis does not reveal susceptibility for boys that have been a case in many reported studies from outside the Pakistan<sup>33,34</sup> except for 9–11 years age group.

The parents have denied the presence of nocturnal asthma in the adolescent girls. This is an understandable and expected response. The asthma is taken as a stigma in our society.<sup>21</sup> As the community is not well aware of this disease so such a diagnosis lowers the chances for a female to receive a good proposal for marriage. The parents of girls in this age group have shown minimal interest to respond even, though the response was comparable in other age groups for boys and girls.

## **CONCLUSION**

We suggest, to doctors dealing with asthmatic children that answer to question: "In the last 1 year, has your child had a bout of dry cough at night when there was no flu or

cold?" must be sought. This may be more meaningful in the context of our society as they usually deny the diagnosis of asthma. This is especially important in case of female adolescent children. There is also a need to plan studies that can objectively do lung function tests in children and validate and correlate the parental reports of symptoms of asthma.

# **REFERENCES**

- Lara M, Akinbami L, Flores G, Morgenstern H. Heterogeneity of Childhood Asthma among Hispanic Children: Puerto Rican children bear a disproportionate burden. Pediatrics 2006;117:43–53.
- ISAAC. Worldwide variation in prevalence of symptoms of asthma, allergic rhino conjunctivitis, and atiopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Lancet 1998;381:1225–32.
- Asher MI, Montefort S, Björkstén B, Christopher KW, Strachan DP, Weiland SK, WillianH, the ISAAC Phase Three Study Group. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 2006;368:733–43
- Innes MA, Montefort S, Björkstén B, Christopher KW, Strachan DP, Stephan K, Williams, and the ISAAC Phase Three Study Group; Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 2006;368:733–43.
- Weiland SK, Husing A, Strachan DP, Rzehak P, Pearce N, and the ISAAC Phase One Study Group. Climate and the prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in children. Occup Environ Med 2004;61:609–15.
- Burr M, Emberlin J, Treu R, Cheng S, Pearce N, ISAAC Phase One Study Group. Pollen counts in relation to the prevalence of allergic rhinoconjunctivitis, asthma and atopic eczema in the International Study of Asthma and Allergies in Childhood (ISAAC). Clin Exp Allergy 2003;33:1675–80.
- Björkstén B. Effects of intestinal microflora and the environment on the development of asthma and allergy. Springer Semin Immunopathol 2004;25:257–7.
- Devenny A, Wassall H, Ninan T, Omran M, Khan SD, Russell G. Respiratory symptoms and atopy in children in Aberdeen: questionnaire studies of a defined school population repeated over 35 years. BMJ 2004;329:489–90.
- Higgins PSH, Wakefield D, Cloutier MM. Risk Factors for Asthma and Asthma Severity in nonurban Children in Connecticut. Chest, 2005;128:3846–53.
- Hijazi N, Abalkhail B, Seaton A. Diet and childhood asthma in a society in transition: a study in urban and rural Saudi Arabia. Thorax 2000:55:775–9.
- Platts TA, Carter MC, Heymann PW. Specific and non-specific obstructive lung disease in childhood: causes of changes in the prevalence of asthma. Environ Health Perspect 2000;108(suppl 4):725–31.
- Mutius E. Infection: friend or foe in the development of atopy and asthma? The epidemiological evidence. Eur Respir J 2001;18:872–81.
- Akinbami LJ, Rhodes JC, Lara M. Racial and Ethnic Differences in Asthma Diagnosis among Children Who Wheeze. Pediatrics, 2005;115:1254–60.
- 14. Calhoun WJ. Nocturnal Asthma. Chest, 2003;123:399-405.
- 15. Diette GB, Markson L, Skinner EA, Nguyen TT, Algatt-Bergstrom

- P, Wu AW. Nocturnal asthma in children affects school attendance, school performance, and parents' work attendance. Arch Pediatr Adolesc Med. 2000;154:923–8.
- ten Hacken NHT, Timens W, Smith M, Drok G, Kraan J, Postma DS. Increased peak expiratory flow variation in asthma: severe persistent increase but not nocturnal worsening of airway inflammation. Eur Respir J 1998;12:546–50
- Weersink EJM, Postma DS. Nocturnal asthma: not a separate disease entity. Respir Med. 1994;88:483–91
- Gislason T, Janson C, Vermeire P, Plaschke P, Björnsson E, Gislason D, et al. Respiratory symptoms and nocturnal gastroesophageal reflux. Chest 2002;121:158–63.
- Weersink EJM, van Zomeren EH, Koeter GH, POSTMA DS. Treatment of nocturnal airway obstruction improves daytime cognitive performance in asthmatics. Am J Respir Crit Care Med 1997;156:1144–50
- Hakala K, Stenius-Aarniala B, Sovijarvi A. Effects of weight loss on peak flow variability, airways obstruction, and lung volumes in obese patients with asthma. Chest 2000;118:1315–21.
- Hazir T, Das C, Piracha F, Waheed B, Azam M. Carers perception of childhood asthma and its management in a selected Pakistani community. Arch Dis Child. 2002;87:287–90.
- Rathore AW, Miraj P, Ahmed TM. Childhood Asthma: Emerging patterns and precipitating factors. Ann King Edward Med Coll 2002;8:233–6.
- Kristine ND, Vera N, Joost J J, Weyler, Wilfried AD. Sleep disturbance and daytime symptoms in wheezing school-aged children. J. Sleep Res 2005;14:77–82.
- Fitzpatrick MF, Engleman H, Whyte KF, Deary IJ, Shapiro CM, Douglas NJ. Morbidity in nocturnal asthma: sleep quality and daytime cognitive performance. Thorax 1991;46:569–73.
- Sadeh A, Horowitz I, Wolach-Benodis L, Wolach B. Sleep and pulmonary function in children with well-controlled, stable asthma. Sleep 1998;21:379–84.
- Stores G, Ellis A J, Wiggs L, Crawford C, Thomson A. Sleep and psychological disturbance in nocturnal asthma. Arch Dis Child 1998;78:413–9.
- Tomalak W, Elbousefi A, Kurzawa R, Doniec Z. Diurnal variations of respiratory system resistance and compliance derived from input impedance in asthmatic children. Respir Physiol 2000;123:101–8.
- Bellia V, Cuttitta G, Cibella F, Vignola AM, Crescimanno G, D'Accardi P, et al. Effect of ageing on peak expiratory flow variability and nocturnal exacerbations in bronchial asthma. Eur Respir J 1997;10:1803–8.
- Desjardin JA, Sutrarik JM, Suh BY, Ballard RD. Influence of sleep on pulmonary capillary volume in normal and asthmatic subjects. Am J Respir Crit Care Med 1995;152:193–8.
- Irvin CG, Pak J, Martin RJ. Airway-parenchyma uncoupling in nocturnal asthma. Am J Respir Crit Care Med 2000;161:50–6.
- Kraft M, Pak J, Martin RJ, Kaminsky D, Irvin CG. Distal lung dysfunction at night in nocturnal asthma. Am J Respir Crit Care Med 2001;163:1551–6.
- National Asthma Education and Prevention Program. Expert panel report 2: guidelines for the diagnosis and prevention of asthma. Bethesda, MD: National Institutes of Health, April 1997; Publication No. 97-405.
- Basagan´a X, Sunyer J, Zock JP, Kogevinas M, Urrutia I, Maldonado JA, et al. Incidence of asthma and its determinants among adults in Spain. Am J Respir Crit Care Med 2001;164:1133–7.
- Lee YL, Lin YC, Hsiue TR, Hwang BF, Guo YL. Indoor and Outdoor Environmental Exposures, Parental Atopy, and Physician-Diagnosed Asthma in Taiwanese Schoolchildren. Pediatrics 2003;112:e389–e395.

#### **Address for Correspondence:**

Dr. Ghulam Mustafa, 12-A, Gilani Colony, Court Road, Multan, Pakistan. Tel: +92-61-4541851/454,

Cell: +92-300-8635452

Email: falahchild@hotmail.com