

BRIEF COMMUNICATION

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Associations of Behavioral Disorders with Asthma in Iranian Children

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ABSTRACT

Asthma is a common respiratory disease with huge economic burden leading to activity limitations, morbidity, and mortality. In this study, we aim to investigate the prevalence of Oppositional Defiant Disorder (ODD), Attention Deficit Hyperactivity Disorder (ADHD) and Conduct Disorder (CD) among children with asthma.

This case-control study was performed in a pediatric referral health care center (Children's Medical Center in Tehran University of Medical Sciences) in 2017. With random selection, the 80 children with asthma and 92 controls with age range of 5 to 11 years were enrolled in this study. In addition to the demographic information and family history of allergy, asthma symptoms, and control quality evaluated with a validated Childhood Asthma Control Test (C-ACT). The mode of measurement for ADHD, ODD and CD was based on Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) psychiatric scales from clinical interviews conducted by child psychiatrists.

Totally, 42.5% and 25% in the case and control groups had ADHD respectively with significant difference ($p=0.01$). Also, 25% and 5.4% in the case and control groups had ODD respectively with significant difference ($p=0.001$). But conduct disorder was 10% and 10.9% in case and control groups respectively without significant difference ($p=0.8$).

Children with asthma were associated with exhibiting ADHD and ODD but not CD. Therefore, appropriate evaluation and treatment are needed for asthmatic children with attention-deficit and ODD symptoms. Besides, further research is needed to determine the etiological approach towards ADHD, ODD and asthma.

Keywords: Asthma; Attention deficit disorder with hyperactivity; Conduct disorder; Child; Oppositional defiant disorder

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INTRODUCTION

Asthma is one of the most common chronic childhood diseases in the respiratory system which is

characterized by the obstruction and hyper-responsiveness of the trachea bronchial system.¹ Asthma is a major burden worldwide, for patients and their caregivers and remains a common cause of death in many countries. It is affecting up to 20% of children aged 6–7 years experiencing severe wheezing episodes within a year.² Asthma with increasing rate and various endotypes caused by genetic susceptibility and environmental factors.³ Recently, it has been suggested that asthma may be a risk factor for Oppositional Defiant Disorder (ODD), Attention Deficit Hyperactivity Disorder (ADHD) and Conduct Disorder (CD), that cause physical and emotional problems, long-term school absence, and social problems.^{4,5}

Psychological comorbidities and behavioral conditions are increasingly recognized as important determinants of asthma management and prognosis as these are associated with inadequate disease control, higher health care use, and poor quality of life.⁶⁻⁸ Moreover, the recurrent exacerbations of asthma are associated with specific co-morbidities that require additional therapeutic interventions.⁹ Uncontrolled ADHD and ODD may result in several complications, including the persistence of symptoms into adolescence or adulthood, poor social skills, depression, or even criminal activity.⁵

Although a considerable number of studies have documented the prevalence of comorbidities in asthma patients, the data of the Iranian population is scarce. Therefore, the current study assessed the prevalence of psychopathology in children with asthma focusing on ODD, ADHD, and CD using research diagnostic interviews according to the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) scales.¹⁰

MATERIALS AND METHODS

Participants

This case-control study was conducted in Children's Medical Center, a pediatric referral health care center at Tehran University of Medical Sciences. During a period of 12 months (February of 2017 to February of 2018), 234 children were invited to study which 171 ones were accepted to participate in the current study. The study was approved by the local ethical committee (approval code: 931168002) and the Helsinki Declaration was respected across the course of the study.

The inclusion criteria for the case group were the age range of 5 to 11 years, certified asthma diagnosis, and parental consent. The patients with chronic respiratory or somatic disease, mental retardation, epilepsy, visual/auditory disorders, and lack of parental satisfaction for incorporation of children were excluded. Their characteristics are shown in Table 1 and 2. The control group consisted of 92 children matched for age and gender selected from schools by cluster sampling method. The control children had no a family history of atopic diseases and self-history of severe or chronic diseases such as atopic, respiratory, infectious, autoimmune, neurological and psychiatric disorders.

Procedure

The demographic information and self and family history of allergy were recorded. The respiratory function tests were assessed with hand-held spirometer (ZAN 100, Obertulba, Germany) in the case group. Also, a validated Childhood Asthma Control Test (C-ACT) questionnaire was used to assess asthma symptoms and control. Uncontrolled asthma was defined as those with the ACT score of 19 or less. The Child Symptom Inventory-4 (CSI-4) questionnaire¹¹⁻¹³ was answered by parents to assess behavioral disorders, and those with abnormal results were recorded and also referred to psychiatrists.

Statistical Analysis

Data analysis was performed by SPSS (version 22.0) [Statistical Procedures for Social Sciences; Chicago, Illinois, USA]. Independent-Sample-T, ANOVA, and Logistic regression tests were used and at P values less than 0.05 were considered statistically significant.

RESULTS

Demographic Characteristics of the Participants

Demographic and respiratory function tests data of 79 asthmatic patients with mean disease duration of 4.047 years (1.6–10.2 years) have been shown in Tables 1 and 2. Mean age of patients and control groups were 7.54 years (5.5–11.8 years) and 7.74 years (5.8–13.5) respectively. The 63.3% and 51.6% in the case and control groups were males respectively (p Value > 0.05). There were no significant differences between case and control groups in age and sex factors.

Table 1. Respiratory characteristics of children with asthma in a study on their behavioral disorders (n=79)

Parameters	Mean(SD)
Age at onset	3.77 (± 2.32)
FEV1%	85.7 (± 14.25)
FEV1/FVC%	87.16 (± 14.16)
MEF.25_75%	78.4 (± 15.18)
MEF.25_75%.rising	14.9 (± 9.63)
ACT Score	19.83 (± 4.44)

FEV1: forced expiratory volume 1, FVC: forced vital capacity, MEF: mid-expiratory flow, ACT: Asthma Control Test, MEF.25_75.rising means increase of 25% in response to Bronchodilators: SD, standard deviation

Table 2. Characteristics of children with asthma in a study on their behavioral disorders (n=79)

Parameters related to asthma	Status	Frequency (%)
Exposure to parental smoking	Yes	30 (37.9)
	No	49(62)
Parental relativeness	Yes	24(30.3)
	No	55(69.6)
Family History of Atopy	Yes	55(69.6)
	No	24(30.3)
Bronchodilators Response (increase of FEV1 \geq 12%)	Negative	16(20.2)
	Positive	62(78.4)
Inhalational Steroids	fluticasone	52(65.8)
	beclomethasone	5(0.06)
	budesonide	22(27.8)
Rhinitis History	Yes	59(74.6)
	No	20(25.3)
Eczema History	Yes	21(26.5)
	No	58(73.4)
Emergency attending in past year	Disease uncontrolled (2 and more)	5(0.06)
	Disease controlled (< 2)	74(93.6)
Steroid use times in past year	Disease uncontrolled (3 and more)	15(19)
	Disease control (< 3)	64(81)
Attack times in past 6 months	Disease uncontrolled (2 and more)	32(40.5)
	Disease controlled (< 2)	47 (59.4)
School Absences Times in past year	<3	34(43)
	≥ 3	45(57)

FEV1: forced expiratory volume 1

The Prevalence of ADHD in Asthma

Totally 42.5% (34 cases) and 25% (23 cases) in the case and control groups had ADHD respectively with significant difference ($p=0.01$). This difference also was seen in all ADHD subtypes including attention deficit ($p=0.005$), hyperactivity ($p=0.006$) and combined

($p=0.01$). Among respiratory and demographic factors FEV1/FVC ($p=0.007$), steroid use frequency ($p=0.04$) and school absence times in the past year ($p=0.01$) associated with hyperactivity type. Also, Logistic regression test among respiratory function tests showed MEF.25-75% ($p=0.004$), MEF.25-75% rising

($p=0.003$) and steroid use frequency ($p=0.006$) could predict attention deficit type, and MEF.25-75%.rising ($p=0.04$) and male gender ($p=0.01$) could predict hyperactivity type of ADHD.

The Prevalence of ODD and CD in Asthma

The 25% (20 cases) and 5.4% (5 cases) in the case and control groups respectively had ODD with significant difference ($p=0.001$). Among respiratory and demographic factors, school absence times in the past year ($p=0.024$) and emergency attending in the past year ($p=0.042$) could predict ODD in asthma patients.

Totally, 10% (8 cases) and 10.9% (10 cases) in case and control groups had conduct disorder respectively without significant difference ($p=0.8$).

DISCUSSION

To the best of our knowledge, this is the first study of psychiatric and behavioral disorders in Iranian asthmatic children. Asthma is an important cause of morbidity and disability in individuals and the control of this disease worsens at alter age, which is also associated with increased emergency medicine as well as hospitalizations.¹⁴ Psychiatric and mental symptoms would result in the higher severity of asthma, further health care costs, functional impairments, and non-optimal asthma control.⁶⁻⁸ Also, comorbidity would result in a higher recurrence rate.⁹ This study demonstrated the high prevalence of ADHD and ODD in asthma patients in comparison to controls. But conduct disorder frequency was not significantly different between the two groups.

Over the last decades, the hypothesis has been raised that an atopic response could result in the development of attention-deficit/hyperactivity disorder (ADHD).¹⁵ Both ADHD and atopic disorders (i.e., asthma, atopic eczema, and allergic rhinitis) are complex disorders in which genetic factors, as well as environmental factors, play a major role.^{16,17} Currently, the etiologic pathways of the possible association between atopic diseases like asthma and ADHD are still not well understood. Several cross-sectional studies determined an association between asthma and ADHD. A systematic review by Schmitt et al¹⁸ concluded that only eczema was independently associated with ADHD among the atopic diseases and positive association between asthma and ADHD was

at least partly confounded by eczema which precedes asthma and allergic rhinitis in the atopic procession. However, after this review, several studies found a positive association between asthma and ADHD independent of eczema.¹⁹⁻²² Recently a comprehensive systematic review and meta-analyses by Schans et al.¹⁵ found overall odds ratio of children having asthma compared to the children without asthma and the odds of ADHD onset was 1.34 (95% CI 1.24–1.44).

It has been demonstrated that asthmatic children exhibit more symptoms of hyperactivity/impulsivity in adolescence than controls.²³ Holmberg et al²⁴ studied multiple types of asthma and ADHD concluded that asthma was associated equally with attention and hyperactivity and the association was not restricted to either of the two dimensions of ADHD. Also, Yi-Tsen et al⁵ demonstrated that children (aged 9–10 y old) having symptoms of asthma within the past 1 y were associated with having all dimensions of symptoms of ADHD. In our study asthma associated with attention and hyperactivity but not combined type. This discrepancy may be due to sampling size, asthma control quality, and age range. Additionally, these differences especially sample size may be a reason that the prevalence of ADHD in our control group is higher than the local²⁵⁻²⁷ and global reports.²⁸

Children with ODD show an ongoing pattern of extreme negativity, hostility, and defiance lasting for at least 6 months. Without appropriate management, ODD may progress to conduct disorder, law-breaking, and illicit substance usage. It has been documented that parental marital conflicts, low socioeconomic status, household second-hand smoke or prenatal tobacco exposure, and preterm birth are related to ADHD or ODD. Uncontrolled ADHD and ODD may result in several complications, including the persistence of symptoms into adolescence or adulthood, poor social skills, depression, or even criminal activity.⁵

Saricoban et al²⁹ in a study of 409 patients with a mean age of 9.0 ± 2.67 years did not find significant prevalence difference in hyperactivity, ADHD, and ODD between the study and control groups, however, they suggested that rather than asthma itself, adjunctive use of leukotriene antagonist (LA)+inhaled corticosteroids (ICS) therapy appears to be related with symptoms of common behavioral problems, including hyperactivity, attention deficit, ADHD, and ODD and to increase the risk of ODD. Two cross-sectional studies of children aged 5–15 years³⁰ and 3-15 years³¹

found an increased risk of conduct problems among children with asthma. These studies were population-based on parent report or self-report of both asthma and mental health problems using Strengths and Difficulties Questionnaire (SDQ). A population-based birth cohort study on children at ages 5–17 years⁴ and a population-based sample of children with mean age 10.4 years³² found similar associations between asthma and conduct problems. Our study found an association between asthma and ODD but not conduct disorder. This might be explained by relatively small samples, lack of adjustment for potential confounders, cultural differences and the quality of control in the patients.

Our limitations were low cooperation of families, small sample size, difficulties to attain socioeconomic data, and lack of data about the quality of care from patients in the past year. Moreover, parent relatedness may affect the incidence of inherited psychological disorders in a population. Unfortunately, this study did not cover this issue. Additionally, behavioral problems in patients with asthma may be partly because of the side effects of therapeutic interventions.²⁹ However, the reason for this process is not completely understood, but it appears that these treatments shrink the hippocampus volume.³³

In the end, according to the obtained results, it may be concluded that ADHD and ODD are related to asthma, but there is no significant association between CD and asthma. However, further studies with larger sample size and with the consideration of socioeconomic status and the quality of care from patients in past year and also an assessment of asthma severity in addition to assessment of atopy in control subjects with laboratory methods are suggested.

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