Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
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ORIGINAL ARTICLE

OPEN ACCESS

Prevalence of self-reported asthma in type 1 diabetes children and its associated predictors

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Received 25 September 2024; Accepted 28 November 2024
Available online 1 January 2025

KEYWORDS
asthma;
asthma symptoms;
type 1 diabetes;
children;
prevalence;
predictors

Abstract
Background: Asthma is considered one of the most common and serious noncommunicable diseases, with high morbidity and mortality rates in both children and adults.
Objectives: To estimate the frequency and to determine the associated factors of self-reported asthma among children diagnosed with type 1 diabetes.
Methods: A cross-sectional study design was employed, and 175 subjects having type 1 diabetes for more than 1 year were included from the pediatrics endocrine clinic. Validated questionnaires from the International Study of Asthma and Allergies in Childhood (ISAAC) were used for data collection. Statistical analysis was performed using SPSS version 23.0.
Results: The study included 175 participants (48% boys, 52% girls) with a mean age of 10.9 ± 3.76 years. The majority were of high socioeconomic status, that is, with a monthly family income >15,000 Saudi Riyal (SR) . Notably, 78 participants (44.6%) were diagnosed with type 1 diabetes (2–5 years' duration, and the average age at diagnosis was 7.4 ± 3.27 years). Hospital admissions due to diabetes in the past year were reported in 101 (57.7%) patients. Moreover, 143 (81.7%) participants reported hyperglycemic symptoms, while 125 (71.4%) experienced hypoglycemic symptoms. About 36 (20.6%) participants had self-reported asthma, with wheezing reported in 46 (26.3%) participants. Other sociodemographic and diabetes factors showed no significant associations. The prevalence of self-reported asthma was noted in 36 children with type 1 diabetes (20.6%). The presence of a family history of asthma was the only significant variable associated with self-reported asthma in children with type 1 diabetes ($p<0.001$).

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https://doi.org/10.15586/aei.v53i1.1223

The odds of developing asthma increased by almost 11 times among children with type 1 diabetes who had a positive family history of asthma (p=0.002). Middle-income status also showed increased odds of risk for developing asthma by 4.4 times, but it did not reach the level of statistical significance (p=0.21).
Conclusion: A higher prevalence of self-reported asthma was found among children with type 1 diabetes. Those with a family history of asthma may be considered for screening and educational programs.

Introduction

Asthma is considered one of the most common and serious noncommunicable diseases with high morbidity and mortality rates in both children and adults.[1,2] In the study conducted by the International Study of Asthma and Allergies in Childhood (ISAAC), the prevalence of childhood asthma was estimated to be 10.8% worldwide, with the lowest rates in Northern and Eastern Europe (4.5%) and the highest rates were found in North America (20%) and Oceania (29.2%).[3] Chronic inflammation of the respiratory tract and airway hyperresponsiveness are the hallmarks of asthma, which can be triggered by allergen exposure mostly through immunoglobulin (Ig) type E (IgE)-mediated mechanism. The autoimmune hypothesis is further, indirectly, supported by the response to immunosuppressive drugs.[4]

Both asthma and type 1 diabetes are autoimmune diseases thought to be caused by disorders in regulation of immune responses, and their pathogenesis has been conventionally regarded as mutually exclusive. Autoimmunity can be viewed as an exaggerated Th1 response, although asthma with a Th2 basis is consistent with the well-regarded Th1-/Th2-mediated mechanisms.[5]

Type 1 diabetes is an autoimmune disease characterized by high glucose levels in the blood, caused by deficiencies in either insulin production or insulin function, or both. This can be caused by a variety of reasons, resulting in disorders of carbohydrate, protein, and lipid metabolism.[6] Type 1 diabetes can be classified into three stages based on a new staging classification system; stage 1 is distinguished by the presence of ß-cell autoimmunity as evidenced by two or more islet cell autoantibodies along with normoglycemia and presymptomatic diabetes mellitus. Stage 2 is associated with ß-cell autoimmunity and dysglycemia but is not symptomatic. Stage 3 is when affected children with type 1 diabetes begin to exhibit symptoms of insulin deficiency.[7] In type 1 diabetes, there is an abnormal T-cell-mediated autoimmune response causing destruction in the ß-cells of the pancreas, thought primarily to be caused by T helper type 1 (Th1) cells.[8]

The presence of T helper type 2 (Th2) cells is predominant in allergic diseases as in asthma. Many other trials have previously addressed this issue in attempting to clarify the nature of any association at the level of the patient, others have reported inverse associations between the two conditions; however, there has been conflicting evidence.[9] A positive association has been found between allergies and autoimmune diseases in certain patients. Previous diagnosis of asthma was linked to an increased risk of developing type 1 diabetes mellitus. Also, there is evidence for the co-occurrence, sequential appearance of asthma and type 1 diabetes in children and their siblings.[10,11]

Despite evidence suggesting the association between asthma and type 1 diabetes, as both conditions are closely related to autoimmune diseases resulting from defective or overactive immune responses, there are contradictory findings between the studies. Furthermore, there is paucity of data from Saudi Arabia linking the two autoimmune diseases. Therefore, the aims of the current study were to estimate the frequency of self-reported asthma among children diagnosed with type 1 diabetes mellitus, and to determine the possible associated factors.

Methods

Study design and study population

A cross-sectional study was conducted at a tertiary hospital from July to December 2021. The study population included children aged 1–18 years, diagnosed with type 1 diabetes for at least 1 year, and attending pediatric endocrine clinics. Children with type 1 diabetes for less than 1 year, and those who had other autoimmune diseases were excluded. A convenience sampling technique was used to select the study participants.

Sample size estimation

Based on the results of a study conducted in Sweden,[10] the prevalence of asthma among diabetic children was reported to be 13%. Using the following formula: n=z^2*p*(1-p)/e^2, where z is the confidence level at 95%, alpha 0.05=1.96, proportion size of 13%, and precision of 5%, the estimated sample size of the current study was175 participants.

Data collection

The data were collected mainly through a survey distributed to the parents of eligible diabetic children. Also, the same survey was sent to the target population using SMS to maximize the response rate. Asthma and asthma symptoms were assessed using the ISAAC questionnaire.[12] Sociodemographic and diabetes characteristics were assessed by a questionnaire developed by investigators and reviewed by experts in the field. The study variables were

age, gender, family income, and diabetes details including age of the diagnosis, presence or absence of symptoms of high blood sugar or low blood sugar, hospitalization due to diabetes, adherence to prescribed diabetic treatment, and family history of type 1 diabetes. The outcome variable intended to measure was the presence or absence of asthma and the asthma symptoms among the study participants.

Statistical analysis

The data were analyzed using the Statistical Package for Social Science (SPSS) version 23. Descriptive data were represented by mean and standard deviation for continuous variables, while categorical data were presented as frequency and percentages. To test association and statistical significance between two proportions, the chi-square test was used. Furthermore, logistic regression analysis was done to identify the predictors significantly associated with reporting asthma in children with type 1 diabetes. Odds ratios (OR) with 95% confidence intervals (CI) were estimated. P-value of <0.05 was considered statistically significant.

Results

Participant characteristics

A total of 175 participants were included in the study, of which 84 (48%) were boys and 91 (52%) were girls. The mean age of the participants was 10.9 ± 3.76 years, and the majority of them were aged between 10 and 15 years. Most of the participants (65 (37.1%)) were of high socioeconomic status, with an average monthly family income of more than 15,000 SR. Around 78 (44.6%) of the participants have been diagnosed with type 1 diabetes with 2–5 years' duration, and the average age of initial diagnosis was 7.4 ± 3.27 years (range: 1–16 years).

Details of diabetes symptoms

More than half of the participants (101(57.7%)) have been admitted to the hospital due to diabetes-related causes in the last 12 months, and almost 91 (90%) have been admitted three times or less. Around 124 (70.9%) of the participants reported that they were strictly adherent to their prescribed medications, 48 (27.4%) were partially adherent, and only 3 (1.7%) were nonadherent. Less than half of the participants (77(44%)) reported a family history of diabetes affecting their first-degree relatives (Table 1).

Approximately, 125 (71.4%) participants experienced hypoglycemic symptoms while 143 (81.7%) developed hyperglycemic symptoms during the past 12 months, and most of them reported less than 10 episodes.

Frequency of asthma and asthma symptoms

The overall frequency of self-reported asthma among the study participants was 36 (20.6%). Around 46 (26.3%) participants reported that they had experienced wheezing at any point of time, of which 36 (78.3%) reported to have experienced it in the last 12 months. Of these, 21 (46%) had one to three wheezing attacks in the last 12 months, and 32 (69.6%) did not have sleep disturbance due to wheezing. Of those who had wheezing, 12 participants (26.1%) experienced severe symptoms that limited their ability to speak.

Of the total 175 participants, 33 (18.9%) reported wheezing during physical activity in the last 12 months, and 44 (25.1%) had dry cough at night, apart from a cough associated with a cold or a chest infection. Around 39 participants (22.3%) had first-degree relatives diagnosed with asthma. Prevalence of asthma-associated symptoms was not significantly different between boys and girls (Table 2).

Furthermore, children with a family history of asthma had significantly higher frequency of asthma ($p<0.001$) compared to those without a family history of asthma. Other sociodemographic variables and symptoms and management of diabetes did not show significant differences between the groups (Table 3).

Predictors for asthma

The odds of risk of developing asthma increased by 11 times in children with type 1 diabetes who had first-degree

Table 1 Distribution of sociodemographic and diabetes characteristics of study participants (N=175).

Characteristics	N (%)
Gender	
Male	84 (48)
Female	91 (52)
Age (years)	
1-3	6 (3.4)
4-6	20 (11.4)
7-9	38 (21.7)
10-12	43 (24.6)
13-15	50 (28.6)
16-18	18 (10.3)
Family income (Saudi riyal (SR))	
<5,000	20 (11.4)
5,000 to <10,000	35 (20)
10,000 to <15,000	55 (31.4)
≥15,000	65 (37.1)
History of hospital admission due to diabetes	
Yes	101 (57.7)
No	74 (42.3)
Positive first-degree relative history of diabetes	
Yes	77 (44)
No	98 (56)
Duration of having diabetes	
<2 years	56 (32)
2-5 years	78 (44.6)
>5 years	41 (23.4)
Adherence to the prescribed diabetic treatment	
Strict adherence	124 (70.9)
Partial adherence	48 (27.4)
Nonadherence	3 (1.7)

Table 2 The prevalence of asthma-associated symptoms and its comparison between boys and girls.

Asthma-associated symptoms	All (N = 175) n (%)	Boys (N = 84) n (%)	Girls (N = 91) n (%)	*P*-value
Lifetime wheezing	46 (26.3)	26 (31)	20 (22)	0.18
Wheezing in the chest in the last 12 months	36 (78.3)	19 (73.1)	17 (85)	0.33
Number of wheezing attacks in the last 12 months				
0	10 (21.7)	7 (26.9)	3 (15)	0.59
1–3	21 (45.7)	12 (46.2)	9 (45)	
4–12	8 (17.4)	3 (11.5)	5 (25)	
>12	7 (15.2)	4 (15.4)	3 (15)	
Sleep disturbance due to wheezing in the last 12 months				
0	32 (69.6)	19 (73.1)	13 (65)	0.84
≤night/week	12 (26.1)	6 (23.1)	6 (30)	
>night/week	2 (4.3)	1 (3.8)	1 (5)	
Severe wheezing limiting speech in the last 12 months	12 (26.1)	7 (26.9)	5 (25)	0.88
Ever had asthma	36 (20.6)	21 (25)	15 (16.5)	0.16
Exercise included wheezing in the last 12 months	33 (18.9)	18 (21.4)	15 (16.5)	0.40
Dry cough at night in the last 12 months	44 (25.1)	25 (29.8)	19 (20.9)	0.18

Table 3 Differences in asthma prevalence according to demographic and diabetic characteristics of the participants.

Characteristics	**Ever had asthma**		***P*-value**
	Yes N (%)	**No N (%)**	
Gender			
0.16	0.16	0.16	0.16
Female	15 (41.7)	76 (54.7)	
Family income (SR)			
<5,000	4 (11.1)	16 (11.5)	0.99
5,000–10,000	7 (19.4)	28 (20.1)	
10,000–15,000	11 (30.6)	44 (31.7)	
>15,000	14 (38.9)	51 (36.7)	
Duration of having diabetes			
<2 years	12 (33.3)	44 (31.7)	0.29
2–5 years	19 (52.8)	59 (42.4)	
>5 years	5 (13.9)	36 (25.9)	
Low blood sugar symptoms in the past 12 months			
No	9 (25)	41 (29.5)	0.59
Yes	27 (75)	98 (70.5)	
High blood sugar symptoms in the past 12 months			
No	4 (11.1)	28 (20.1)	0.21
Yes	32 (88.9)	111 (79.9)	
Admission due to diabetes			
No	18 (50)	56 (40.3)	0.29
Yes	18 (50)	83 (59.7)	
Adherence to the prescribed diabetes treatment			
Strict adherence	26 (72.2)	98 (70.5)	0.67
Partial adherence	10 (27.8)	38 (727.3)	
Nonadherence	0 (0)	3 (2.2)	
First-degree relatives with type 1 diabetes			
No	20 (55.6)	78 (56.1)	0.95
Yes	16 (44.4)	61 (43.9)	
First-degree relatives with asthma			
No	18 (50)	118 (84.9)	**<0.001**
Yes	18 (50)	21 (15.1)	

relatives with asthma compared to those who did not, OR = 10.94 (95% CI; 2.41–49.74; p=0.002). Other variables did not show any significant effect on asthma in patients with diabetes. The number of hospital admissions due to diabetes and symptoms of high blood sugar showed an increased risk of wheezing by 1.4 and 1.8 times, respectively, but they were not statistically significant (Table 4).

Discussion

The current study investigated the frequency and the associated factors of self-reported asthma among children with type 1 diabetes. Asthma and type 1 diabetes mellitus are two of the most frequent chronic diseases in children, representing a model of the atopic and autoimmune diseases, respectively.

The prevalence of self-reported asthma in children with type 1 diabetes was around 20.6%. This finding was in concurrence with reports from other studies. A previous study from Germany demonstrated a positive correlation between the incidence of type 1 diabetes and asthma/wheezing.[13] Another retrospective study from Finland reported 1.5 times higher risk of asthma in children with type 1 diabetes.[14] Furthermore, a Taiwanese cohort study reported a higher incidence of 47% of asthma in the type 1 diabetes cohort, than in the control cohort, with an adjusted hazard ratio (HR) of 1.34 (95% CI =1.11–1.62).[15]

Another important finding from the current study was the strong association and increased risk of asthma in children with type 1 diabetes who have a positive family history of asthma. An earlier Swedish study found links between type 1 diabetes in children and a variety of immune-mediated diseases in their parents, including asthma.[10] In developed countries, the prevalence of type 1 diabetes and asthma has been steadily increasing.[5,16] The link between type 1 diabetes and asthma is debatable, but it has sparked renewed research in the two diseases. However, epidemiological studies are inconclusive showing conflicting results regarding the prevalence of asthma in patients with type 1 diabetes.[17] A possible explanation can be attributed to methodological differences, errors in assessment, and tools associated with the diagnosis of asthma in children. The study had certain limitations. First, the diagnosis of asthma was primarily based on surveys and self-reported questionnaires; some of the participating parents might not recall precisely the history and symptoms of their children which is not as precise as clinical diagnosis. The recall bias and

Table 4 Predictors for asthma in children with type 1 diabetes mellitus.

Variable	Odds ratio	95% C.I. for odds ratio	*P*-value
Gender			
Boys	1	-	-
Girls	0.93	0.26–3.39	0.91
Family income (SR)			
<5,000	1	-	
5,000 to <10,000	2.09	0.19–23.58	0.55
10,000 to <15,000	4.46	0.44–44.95	0.21
≥15,000	2.94	0.30–28.99	0.36
Duration of having diabetes			
<2 years	1	-	-
2–5 years	0.93	0.21–4.17	0.92
>5 years	0.32	0.04–2.56	0.28
Low blood sugar symptoms in the past 12 months			
No	1	-	-
Yes	0.41	0.08–2.12	0.29
High blood sugar symptoms in the past 12 months			
No	1	-	-
Yes	1.78	0.16–19.50	0.64
Number of admissions due to diabetes			
0–3	1	-	-
4– 7	1.38	0.16–12.24	0.77
Adherence to the prescribed diabetes treatment			
Strict adherence	1	-	-
Partial adherence	0.60	0.14–2.53	0.49
Nonadherence	0.00	0.00	1.00
First-degree relatives with type 1 diabetes			
No	1	-	-
Yes	1.64	0.45–5.97	0.45
First-degree relatives with asthma			
No	1	-	-
Yes	10.94	2.41–49.74	**<0.001**

the compromised diagnostics accuracy might potentially lead to overestimation or underestimation of the disease. To strengthen and stabilize the findings, we used a standardized validated questionnaire, the ISAAC questionnaire; however, using electronic medical records or objective investigations like pulmonary function tests is more reliable. Second, the study population was from a single tertiary hospital which could lead to limitations in generalizability. Multiple centers in Saudi Arabia should be included with a wider and more diverse population to truly generalize the findings. Third, children with less than 1 year duration of type 1 diabetes were excluded which could have possibly undermined the understanding of the relation between newly onset diabetes and asthma. Fourth, the study did not explore the confounders that might influence the association between type 1 diabetes and asthma. Factors such as environmental exposure, lifestyle, and other comorbidities could play a confounding role in the development of asthma. Hence, further research is recommended to include data from multicentric sites along with measuring confounders.

Conclusion

The present study showed higher prevalence of self-reported asthma among children with type 1 diabetes. First-degree relatives with asthma are significantly associated with the development of asthma in children with type 1 diabetes.

Further research exploring the complexities and associations between asthma and type 1 diabetes in children is recommended. Population-based studies examining the interactions of external, environmental, genetic, and immunological factors are much needed. Understanding the causal mechanism linking the two diseases may be useful in the future, particularly in terms of disease prevention.

Acknowledgments

The authors extend their appreciation to the researchers supporting project number RSP2024R506 at King Saud University, Riyadh, Saudi Arabia.

Authors Contribution

Conceptualization, SAA and FMA.; methodology, SAA, FMB, RKA, AFB, WKA, MMA and FAA; formal analysis, FMB, RKA, AFB, WKA, MMA and FAA; investigation, SAA, FMB, RKA, AFB, WKA, MMA and FAA; resources, S.A.A. and F.M.A.; data curation, FMB, RKA, AFB, WKA, MMA and FAA; writing—original draft preparation, SAA, FMB, RKA, AFB, WKA, MMA and FAA; writing—review and editing, SAA, FMA, FMB, RKA, AFB, WKA, MMA, FAA and ST; supervision, SAA; funding acquisition, SAA and FMA. All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Institutional Review Board Statement

The study was approved by the Institutional Review Board (IRB) Committee of King Saud University Research (Approval number: 21-0636).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

Data Availability Statement

Not applicable.

Funding

This study was funded by the researchers supporting project number RSP2024R506 at King Saud University, Riyadh, Saudi Arabia.

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