Scientific Research Publishing

Open Journal of Respiratory Diseases, 2021, 11, 1-18
https://www.scirp.org/journal/ojrd
ISSN Online: 2163-9418
ISSN Print: 2163-940X

The Pattern of Comorbidities of Childhood Asthma as Seen in the Rivers State University Teaching Hospital, Nigeria

Uchenna Onubogu*, Boma West

River State University Teaching Hospital, Portharcourt, Nigeria
Email: *utchayonubogu@yahoo.co.uk

How to cite this paper: Onubogu, U. and West, B. (2021) The Pattern of Comorbidities of Childhood Asthma as Seen in the Rivers State University Teaching Hospital, Nigeria. *Open Journal of Respiratory Diseases*, **11**, 1-18.
https://doi.org/10.4236/ojrd.2021.111001

Received: January 6, 2021
Accepted: February 21, 2021
Published: February 24, 2021

Abstract

Background: Asthma exits with comorbidities which can affect the quality of life of children with asthma. Objective: To identify the common comorbidities with asthma, identify factors associated with the presence of specific comorbidities and evaluate their impact on asthma severity and control among children attending the respiratory clinic in the Rivers State University Teaching Hospital. Materials & Methods: All asthma cases seen in the paediatric respiratory clinic, from 1st November 2014 to 30th October 2019 were consecutively recruited. Results: Of 264 children with asthma, 190 (72.0%) had other comorbidities with a F:M ratio of 1.56:1. Difficulty in breathing, chest pain, and the degree of asthma control were significantly associated with having other comorbidities while SPO_2 at 1st consult was significantly lower in children with comorbidities, P value < 0.05. Allergic rhinitis 116 (43.9%), adenotonsillar hypertrophy 99 (37.5%), atopic dermatitis 54 (20.5%), allergic conjunctivitis 37 (14%), food allergy 27 (10.2) and Gastroesophageal reflux14 (5.3%) were the commonest comorbidities identified. Majority (24, 88.9%) had allergy to one type of food. Children < 3 years and those whose age at diagnosis was <2 years were significantly at lower risk of having atopic dermatitis. Gastroesophageal reflux disease was significantly more likely to be seen in children aged > 11 years, overweight children, and those presenting with chest pain or chest tightness. Presence of various comorbidities increased the odds of having a more severe asthma, and likelihood of which increased with increasing number of coexisting comorbidities. Conclusion: The prevalence of allergic comorbidity is high among asthmatic children with allergic rhinitis being the commonest cause. Most children with asthma have more than one allergic comorbidity. A comprehensive evaluation of these comorbidities is thus essential in the management of asthmatic children for improved outcomes and quality of life.

Keywords

Childhood Asthma, Asthma Comorbidity, Rhinitis, Allergic Conjunctivitis, Food Allergy, Atopic Dermatitis

1. Introduction

Asthma, a major public health problem, is the commonest chronic childhood illness globally affecting more than 300 million people [1] [2]. In Nigeria, the overall prevalence of clinical asthma is 6.4% and 3.1% among children aged 6 - 17 yrs [3]. It is a chronic inflammatory condition of the large lung airways resulting in episodic airway obstruction [4]. World Health Organization estimates Asthma to account for the loss of 15 million disability-adjusted life years annually [2] [5].

A combination of environmental exposures, inherent biologic, and genetic susceptibilities have been implicated in the aetiology of Asthma [4]. Asthma has been observed to co-exist with other conditions which result in difficulty in its control, increase in its case fatality, increased acute exacerbations with an increased cost of health care, reduced work productivity as well as poor quality of life for both the child and caregivers [6] [7] [8]. Some of the comorbid conditions in childhood asthma are allergic rhinitis, sinusitis, atopic dermatitis, allergic conjunctivitis, gastroesophageal reflux disease (GERD), adenotonsillar hypertrophy, obstructive sleep apnea, food allergies, respiratory infections, obesity as well as psychologic disorders [9]. The prevalence of the comorbidities varies with age as well as geographic areas [10].

It has been shown that 20% - 50% of patients with allergic rhinitis have asthma while greater than 80% of patients with asthma have Allergic Rhinitis [11]. It has been observed that such children have poorer asthma control when compared with asthmatic children without allergic rhinitis [12] [13]. Food allergy, atopic dermatitis, and recurrent respiratory tract infections have been observed in about 25%, 45%, and 60% of children with asthma respectively [14] [15] [16] [17] [18]. Asthmatic children with food allergies tend to have increased asthma symptoms with significantly lower lung function [14] [19].

The main goal in the management of asthma is to achieve and maintain asthma control which is defined as the reduction or resolution of various asthma symptoms with treatment [20]. Several studies have shown poor asthma control in children despite the proper use of inhaled corticosteroids [21] [22] [23]. Asthma control among Nigerians in a multicity, population-based study has been reported to be 6.2% using GINA category and 33.8% using ACT category, while among children, it was reported to be 7.1% and 28.6% respectively [24]. The presence of comorbid conditions in patients with asthma increases disease severity, makes asthma control difficult to achieve, and it can also mask the symptoms for assessing control like persistent cough in rhinitis and GERD, thus

making the physician give higher asthma medications and increasing the risk for drug side effect [9] [25]. Patients with comorbid conditions with their asthma have been reported to have more hospital admissions and emergency room visits for asthma-related conditions and treatment of these comorbid conditions reduces the risk of hospitalization and emergency room visits by 50% [9] [25] [26]. In a single-center Nigerian study, children with rhinitis were more likely to have persistent asthma than intermittent asthma 22.5% vs 14.4% [27].

Although studies on common comorbidities in childhood asthma have been done in Nigeria [27] [28], there is a paucity of data in Rivers State, southern Nigeria hence the present study was carried out to identify the common comorbidities with asthma, identify factors associated with the presence of specific comorbidities and evaluate their impact on asthma severity and control among children attending the respiratory clinic in the Rivers State University Teaching Hospital (RSUTH).

2. Materials and Methods

This was a hospital-based descriptive cross-sectional study. All children diagnosed with asthma (two documented previous wheezing episodes within the preceding 12 month period, that responded to a bronchodilator [1] who came for follow up at the paediatric respiratory clinic of the Rivers State University Teaching Hospital, Nigeria from 1st November 2014 to 30th October 2019 were eligible to be recruited into the Paediatric Asthma register of the hospital at their first visit, the scope of information gradually increased over the years. The sample size was adjusted for a finite population, based on the 264 registered asthma patients in the clinic. The prevalence of allergic comorbidities among children with asthma was assumed to be 41.5% [29], using an alpha value of 5% with a 95% confidence interval and 80% power, the minimum sample size was calculated to be 155. Ethical approval was obtained from the Rivers State Health Research Ethics Committee and informed consent was obtained from the parents/caregivers of very young children and the children if older before entering their data into the register. Children whose parents did not give consent were excluded as well as those who were referred to the clinic following their first episode of wheeze with no other risk factor for having asthma. The following pieces of information were retrieved from the asthma register: Age, sex, anthropometric measurements, exposure to passive smoking, type of domestic cooking fuel, presence of comorbidities like allergic rhinitis, adenotonsillar hypertrophy, allergic dermatitis, gastroesophageal reflux disease, food allergies, asthma control test score, family size, social class, asthma severity classification, family history of atopy, presence of cardinal asthma symptoms (cough, difficulty breathing, wheeze, chest pain), baseline SPO_2 at first follow up visit and age at diagnosis.

The severity of asthma was assessed for all children who attended the respiratory clinic for 2 months and who could retrospectively recall symptom frequency. They were then given a symptom diary to prospectively document their

symptoms and a 6 weeks clinic appointment was given to re-confirm the classification after which an asthma action plan was drawn up for each child recruited. The severity of asthma before the commencement of asthma management was assessed and categorized using the frequency of day and night-time symptoms into intermittent, mild persistent, moderate persistent, and severe persistent based on the National Asthma Education and Prevention Program (NAEPP) guidelines [30]. For assessment of impact of asthma comorbidities on its severity, moderate persistent and severe persistent asthma were sub classified as a more severe form of asthma while intermittent and mild persistent were classified as a less severe form of asthma. Allergic rhinitis was defined by recurrent symptoms of rhinorrhoea, nasal blockage, itching, and sneezing caused by exposure to allergens [13], atopic dermatitis was defined according to the UK working party criteria with the presence of itchy skin condition and three or more of the following; a history of flexural involvement, history of asthma or hay fever, generalized dry skin, onset of rashes before 2 years or visible flexural dermatitis [31]. Allergic conjunctivitis was suspected in patients with a history of recurrent itchy eyes, brownish sclera, or periorbital hyperpigmentation. They were then referred to the ophthalmologist for confirmatory diagnosis. Gastroesophageal reflux disease was defined by using a six GerdQ questionnaire to ascertain the presence and severity of reflux using a score of ≥8 diagnostic cut off for GERD [32]. Adenotonsillar hypertrophy was defined as the presence of clinical signs of upper airway obstruction with radiographic evidence of narrowed upper airway by enlarged tonsils and adenoids. Food allergy was defined by repeated allergic reaction within 2 hours of ingesting a particular type of food, the clinical symptom could be either on the skin (urticaria, angioedema in the oropharyngeal airway (throat tightness, difficulty swallowing, choking), lower respiratory system (difficulty breathing, repetitive cough, wheeze, chest tightness), cardiovascular system (dizziness, fainting,) or gastrointestinal system (vomiting) [33].

Asthma control test (ACT) was done using the Childhood ACT (C-ACT) questionnaire [4] for children aged 11 years and below while ACT for adult questionnaire was done for children aged 12 years and above [34]. For both ACTs, patients were classified as well controlled with an ACT of ≥20, partially control with an ACT score of 16 - 19, and poor control with an ACT score of <15. The social class of the parents/caregivers were determined using the classification by Olusannya *et al.* [35]. The total class score ranged from 1 to 5 in order of descending privileges and divided into 3 equal parts to get upper (1 to 1.7), middle (>1.7 to 3.3), and lower (>3.3) socioeconomic classes. Nutritional status of each child was classified using the weight for age Z score (Zs) into overweight (>2 Zs), normal nutrition (2 to −2 Zs), moderate malnutrition (<−2 to −3 Zs), and severe malnutrition (<−3 Zs).

Data collected were entered into an Excel spreadsheet and analyzed using IBM SPSS Statistics version 23. Descriptive statistics were used to express patient's

characteristics while bivariate association test was done using the chi-square test and odds ratio analysis, comparison of means was done for numerical variables using analysis of variance (ANOVA). Any incomplete data were excluded in the final analysis. P-value was set at ≤0.05 with a 95% confidence interval.

3. Result

3.1. Clinical Characteristics of Children Who Have Asthma with Other Comorbidities

A total of 264 children with asthma were seen among whom 190 (72.0%) had other comorbidities. The age range of the children was from 6.96 months to 16 years with a mean age of 7.0 ± 3.9 years. There were more females with comorbidity than males with an F: M ratio of 1.56:1. Patients with asthma comorbidity were mostly aged 8 - 12 years 63 (33.2%), had normal weight 146 (76.8%), lived in households with no adult smoker 181 (95.3%), belonged to upper socioeconomic class, 83 (43.7%), and had a positive family history of atopy 127 (66.8%). A majority had intermittent asthma 59 (31.1%) and partially controlled asthma 67 (35.3%). Compared to those without comorbidities they were significantly more likely to be aged 8 - 12 years (p = 0.04), have symptoms of difficulty in breathing (168 (73.4%): P=0.04), chest pain 85 (73.9%): p = 0.001), have their asthma duration for >6 - 9 years (p = 0.03) and have partially controlled asthma (p = 0.04). The mean baseline SPO_2 at first consult was significantly lower for children with comorbidities (97.1 ± 1.48 Vs 96.6 ± 2.1, P = 0.05), their baseline PEFR was also lower (76.1 ± 19.7.7 vs 73.6 ± 21.21, p = 0.5) although the difference was not statistically significant (Table 1).

3.2. Types of Comorbidity with Asthma in Children

The most frequent comorbidity identified was allergic rhinitis 116 (43.6%) followed by adenotonsillar hypertrophy in 99 (37.5%) while the least common was gastroesophageal reflux (GERD) 14 (5.3%) see Figure 1. Most children had only one comorbidity 88 (46.3%) while multiple comorbidities of 2, 3, and 4 were found in 62 (32.6%), 27 (14.2%), and 13 (6.8%) children respectively.

3.3. Types of Reported Food Allergy

Among the 27 children that reported having food allergy, most of them reported allergy to one type of food 24 (88.9%) while allergy to multiple foods up to a maximum of 3 was reported in only 2 children. Food types in which only one person reported being allergic to were grouped as miscellaneous (Figure 2).

3.4. Impact of Asthma Comorbidity on Asthma Severity and Control

Fifty-eight children whose asthma severity could not be classified due to inadequate information were excluded from the analysis of the impact of asthma comorbidity on asthma severity giving us a sample size of 206. The presence of any

Table 1. Clinical characteristics of children who have asthma with other comorbidities.

Variable	Without Comorbidity n = 74 (28%)†	With Comorbidity n = 190 (72%)†	Total†	P Value
Age (years)				
<4	21 (28.4)	40 (21.1)	61 (23.1)	0.20
4 - 8	22 (29.7)	60 (31.6)	82 (31.1)	0.7
8 - 12	15 (20.3)	63 (33.2)	78 (29.5)	**0.04**
12 - 16	16 (21.6)	27 (14.2)	43 (16.3)	0.14
Gender				
Male	27 (36.5)	74 (38.9)	101 (38.3)	0.29
Female	47 (63.5)	116 (61.1)	163 (61.7)	
Weight for Age Z score				
Overweight	14 (18.9)	42 (22.1)	56 (21.2)	0.56
Normal nutrition	57 (77.0)	146 (76.8)	203 (76.9)	0.97
Moderate malnutrition	1 (1.4)	2 (1.1)	3 (1.1)	0.83
Severe malnutrition	2 (2.7)	0 (0)	2 (0.8)	0.07
Adult smoker in the child's household				
Yes	4 (5.4)	6 (3.2)	10 (3.8)	0.31
No	63 (85.1)	181 (95.3)	244 (92.4)	
Undisclosed	7 (9.5)	3 (1.6)	10 (3.8)	
Cooking fuel used in household*				
Liquified petroleum gas	52 (24.6)	159 (75.4)	211	0.09
Kerosene and Firewood	17 (29.8)	40 (70.2)	57	0.51
Social class Score of families				
Upper	35 (47.3)	83 (43.7)	118 (44.7)	0.5
Middle	32 (43.2)	81 (42.6)	113 (42.8)	0.8
Low	2 (2.7)	16 (8.4)	18 (6.8)	0.1
Undisclosed	5 (6.8)	10 (5.3)	155.7)	
Known Family history of atopy				
Yes	43 (58.1)	127 (66.8)	170 (64.4)	0.2
No	30 (40.5)	62 (32.6)	92 (34.8)	
Unsure	1 (1.4)	1 (0.5)	29 (0.8)	
Symptoms reported*				
Cough	60 (25.8)	173 (74.2)	233	0.2
Difficulty breathing	61 (26.6)	168 (73.4)	229	**0.04**
Wheeze	52 (34.3)	162 (75.7)	214	0.08
Chest pain/chest tightness	30 (26.1)	85 (73.9)	115	**0.001**
Age at first diagnosis of asthma (years)				
<4	34 (45.9)	76 (40.0)	110 (41.7)	0.49

Continued

4 - 8	25 (33.8)	64 (33.7)	89 (33.7)	0.98
8 - 12	9 (12.2)	38 (20.0)	47 (17.8)	0.15
12 - 16	6 (8.1)	12 (6.3)	18 (6.8)	0.49
Duration since 1st asthma diagnosis (years)				
≤3	56 (75.7)	149 (78.7)	205 (77.7)	0.63
>3 - 6	7 (9.5)	24 (12.6)	31 (11.7)	0.47
>6 - 9	9 (12.2)	9 (4.7)	18 (6.8)	**0.03**
>9	2 (2.7)	8 (4.2)	10 (3.8)	0.56
Baseline SPO_2 at first consult	97.1 ± 1.48	96.6 ± 2.1	96.8 ± 1.9	**0.05**
Baseline PEFR% predicted for Age	76.1 ± 19.7.7	73.6 ± 21.21	74.5 ± 20.7	0.5
Classification of asthma				
Intermittent	18 (24.3)	59 (31.1)	77 (29.2)	0.63
Mild persistent	11 (14.9)	25 (13.2)	36 (13.6)	0.41
Moderate Persistent	17 (23.0)	52 (27.4)	69 (26.1)	0.88
Severe Persistent	6 (8.1)	18 (9.5)	24 (9.1)	0.97
Unclassified	22 (29.7)	36 (18.9)	58 (22.0)	
Asthma control				
Controlled	14 (18.9)	38 (20.0)	52 (19.7)	0.49
Partially controlled	13 (17.9)	67 (35.3)	80 (30.3)	**0.04**
Poorly controlled	16 (21.6)	35 (18.4)	51 (19.3)	0.11
Unclassified	31 (41.9)	50 (26.5)	81 (30.7)	

(†) percentages within columns for mutually exclusive variables, (*) percentages across rows.

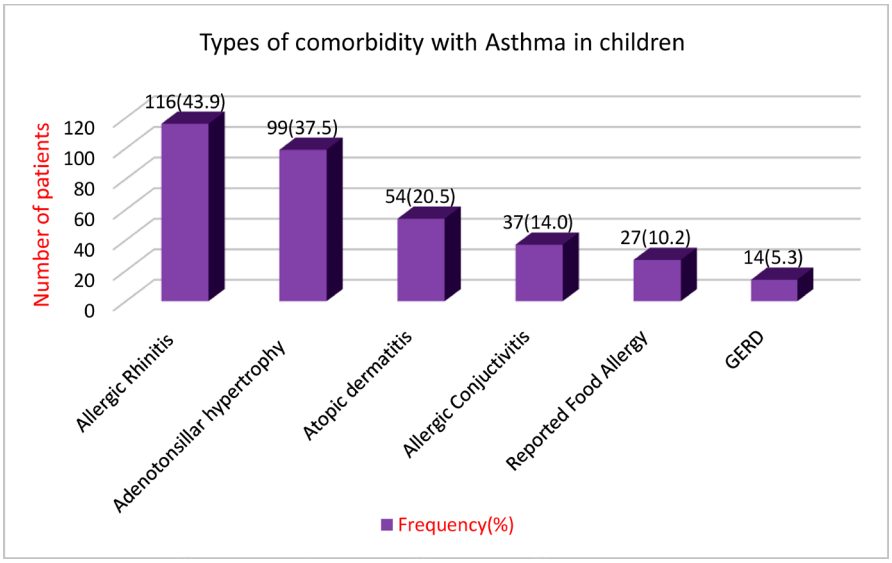

Figure 1. Types of comorbidity with Asthma in children.

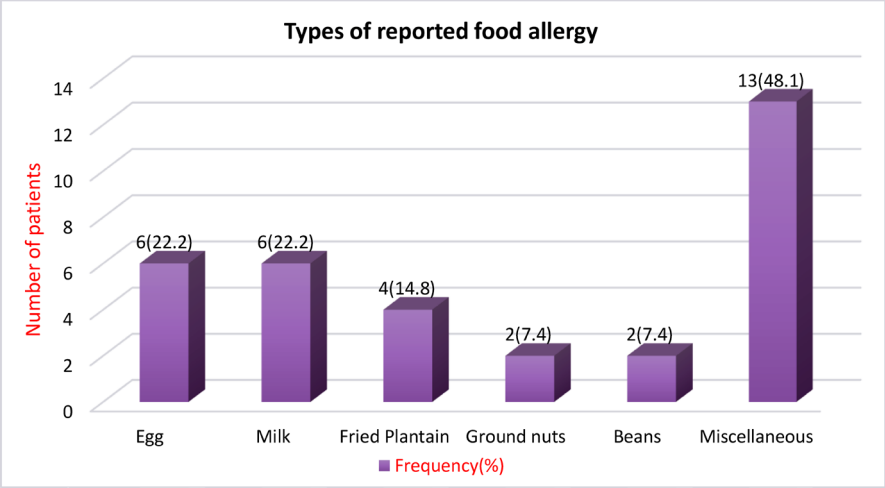

Figure 2. Types of reported food allergy.

comorbidity increased the odds of having severe asthma and the likelihood of having severe asthma also increased with an increasing number of coexisting comorbidities (OR: >1). This increase in the odds of having severe asthma was statistically significant in only those that had coexisting allergic conjunctivitis (OR: 2.2 95% CI; 1.05, 4.7, P = 0.03) and in those with ≥4 comorbidities (OR: 4.4, 95% CI; 1.17, 16.5, P = 0.01), **Table 2**.

Eighty-one children whose level of asthma control could not be ascertained due to inadequate information were excluded from the analysis of the impact of the presence of comorbidity on asthma control, giving a sample size of 183. The presence of any comorbidity increased the odds of having uncontrolled asthma although it was not statistically significant (OD: 1.2, 95% CI; 0.6, 2.71, P = 0.49). In addition, although not statistically significant, the odds of having uncontrolled asthma was highest amongst those with GERD (OD: 3.79 95% CI; 0.46, 0.4, P = 0.18) followed by those with food allergy (OD: 1.95, 95% CI; 0.53, 7.3, P = 0.30) (**Table 3**).

3.5. Factors Significantly Associated with Specific Asthma Comorbidities

Children who were <3 years (OR: 0.18 95% CI: 0.04, 0.77) and those who had their asthma diagnosis at <2 year of age (OR: 0.45 95% CI: 0.20, 0.97) were significantly at lower risk of having atopic dermatitis. GERD was significantly more likely to be seen in children aged > 11 yrs, overweight children, and those presenting with chest pain or chest tightness (OR 6.69, 2.78 and 6.07 respectively). No significant association was found with food allergies. Comorbidities whose presence were significantly associated with each other include allergic rhinitis with adenotonsillar hypertrophy (OR: 1.9, 95% CI, 1.2, 3.06, P = 0.007) and allergic conjunctivitis (OR: 2.3 95% CI, 1.15, 4.8, P = 0.016). Adenotonsillar hypertrophy was significantly associated with atopic dermatitis (OR: 1.9, 95% CI, 1.05, 3.50, P = 0.03) and allergic rhinitis (OR: 1.99, 95% CI, 1.20, 3.33, P = 0.007).

Atopic dermatitis is further associated with allergic conjunctivitis (OR: 3.28 95% CI, 1.57, 6.89 P = 0.0013) see Table 4.

Table 2. Impact of comorbidity on asthma severity.

Variable	Severe Asthma N = 93	Nonsevere Asthma N = 113	Total N = 206	Odds ratio	95% confidence interval		P
					Lower	Upper	
Rhinitis							
Yes	51 (51.5)	48 (48.5)	99	1.64	0.94	2.8	0.07
No	42 (39.3)	65 (60.8)	107				
Adenotonsillar hypertrophy							
Yes	33 (42.3)	45 (57.7)	78	0.83	0.47	1.4	0.52
No	60 (46.9)	68 (53.1)	128				
Atopic dermatitis							
Yes	24 (50)	24 (50)	48	1.2	0.67	2.4	0.44
No	69 (43.7)	89 (56.3)	158				
Gastroesophageal reflux disease							
Yes	8 (66.7)	4 (33.3)	12	2.54	0.74	8.8	0.12
No	85 (43.8)	109 (56.2)	194				
Food allergy							
Yes	10 (50)	10 (50)	20	1.2	0.49	3.12	0.64
No	83 (44.6)	103 (55.4)	186				
Allergic conjunctivitis							
Yes	21 (61.8)	13 (38.2)	34	2.2	1.05	4.7	0.03*
No	72 (41.9)	100 (58.1)	172				
Presence of any comorbidity							
Yes	70 (45.4)	84 (54.6)	154	1.05	0.55	1.99	0.87
No	23 (44.2)	29 (55.8)	52				
Presence of only 1 comorbidity							
Yes	28 (41.8)	39 (58.2)	67	0.82	0.45	1.45	0.50
No	65 (46.8)	74 (53.2)	139				
Presence of 2 comorbidities							
Yes	18 (35.3)	33 (64.7)	51	0.58	0.30	1.1	0.1
No	75 (48.4)	80 (51.6)					
Presence of 3 comorbidities							
Yes	14 (60.9)	9 (39.1)	23	2.04	0.84	4.9	0.10
No	79 (43.2)	104 (56.8)	183				
Presence of 4 comorbidities							
Yes	10 (79.9)	3 (23.1)	13	4.4	1.17	16.5	0.01*
No	83 (43)	110 (57)	193				

Table 3. Impact of asthma comorbidity on asthma control.

Variable	Controlled Asthma N = 52	Uncontrolled Asthma N = 131	Total N = 183	Odds ratio	95% confidence interval		P
					Lower	Upper	
Rhinitis							
Yes	23 (25.6)	67 (74.4)	90	1.31	0.69	2.51	0.39
No	29 (31.2)	64 (68.8)	93				
Adenotonsillar hypertrophy							
Yes	21 (28.8)	52 (71)	73	0.97	0.5	1.9	0.9
No	31 (28.2)	79 (71.8)	110				
Atopic dermatitis							
Yes	13 (29.5)	31 (70.4)	44	0.93	0.41	1.96	0.84
No	39 (28.1)	100 (71.9)	139				
Gastroesophageal reflux disease							
Yes	1 (10)	9 (90)	10	3.76	0.46	30.4	0.18
No	51 (29.5)	122 (70.5)	173				
Food allergy							
Yes	3 (17.6)	14 (82.4)	17	1.95	0.53	7.3	0.30
No	49 (29.5)	117 (70.5)	166				
Allergic conjunctivitis							
Yes	7 (25)	21 (75)	28	1.2	0.48	3.1	0.66
No	45 (29)	110 (71)	155				
Presence of any comorbidity							
Yes	38 (27.1)	102 (72.8)	140	1.2	0.6	2.71	0.49
No	14 (32.6)	29 (67.4)	43				
Presence of only 1 comorbidity							
Yes	17 (28.3)	43 (71.7)	60	1.006	0.5	1.99	0.98
No	35 (28.5)	88 (71.5)	123				
Presence of 2 comorbidities							
Yes	13 (26.5)	36 (73.5)	49	1.13	0.5	2.37	0.73
No	39 (29.1)	95 (70.9)	134				
Presence of 3 comorbidities							
Yes	6 (28.6)	15 (71.4)	21	0.99	0.36	2.7	0.9
No	46 (28.4)	116	162				
Presence of 4 comorbidities							
Yes	2 (20)	8 (80)	10	1.6	0.32	7.9	0.6
No	50 (28.9)	123 (71.1)	173				

Table 4. Factors significantly associated with specific asthma comorbidities.

Comorbidity and Variable	Frequency (%)	Odds ratio	95% Conf. Interval		P-value
			lower	Upper	
Allergic Rhinitis					
Adenotonsillar hypertrophy					
Yes	54 (54.6)	1.9	1.2	3.06	0.007
No	62 (37.6)				
Allergic conjunctivitis					
Yes	23 (62.1)	2.3	1.15	4.8	0.016
No	93 (41.0)				
Adenotonsillar hypertrophy					
Atopic dermatitis					
Yes	27 (50.0)	1.9	1.05	3.50	0.03
No	72 (34.3)				
Allergic Rhinitis					
Yes	54 (46.6)	1.99	1.20	3.33	0.007
No	30 (30.4)				
Atopic Dermatitis					
Age < 3 yrs					
Yes	2 (5.1)	0.18	0.04	0.77	0.01
No	52 (23.1)				
Adenotonsillar hypertrophy					
Yes	27 (27.3)	1.92	1.04	3.50	0.03
No	27 (16.4)				
Allergic Conjunctivitis					
Yes	15 (40.5)	3.28	1.57	6.89	0.001
No	39 (17.2)				
Diagnosed asthma < 2 yrs old					
Yes	9 (12.2)	0.45	0.20	0.97	0.03
No	45 (23.7)				
Allergic Conjunctivitis					
Allergic Rhinitis					
Yes	23 (19.8)	2.3	1.15	4.8	0.02
No	14 (90.5)				
Atopic dermatitis					
Yes	15 (27.8)	3.28	1.57	6.8	0.001
No	22 (10.5)				

Continued

Gastroesophageal reflux					
Age > 11 yrs					
Yes	10 (12.8)	6.69	2.03	22.05	0.0001
No	4 (2.2)				
Overweight					
Yes	6 (10.7)	2.78	1.008	7.69	0.04
No	8 (3.8)				
Chest pain/tightness					
Yes	11 (9.57)	6.07	1.37	26.82	0.006
No	2 (1.57				

4. Discussion

Our study showed that there is a high prevalence of atopic comorbidities among children with asthma. It also outlined the distribution of these comorbidities and highlighted the fact that while they are all interrelated, some have a more intricate relationship in a way that the presence of one increases the likelihood of the other. The prevalence of allergic comorbidities with asthma in this study was high (72.0%). Similar high rates with slight differences have been reported by other Nigerian studies, 85.9%, and 60.2% [27] [28]. Like our study they were both hospital-based although carried out in different geographic locations; the northwestern and southwestern part of Nigeria which could explain the slight difference from our study which was carried out in the southern part of Nigeria. Besides that, the scope of the comorbidities evaluated in these studies was not the same which could account for the variability in prevalence rates reported. There is thus a need to standardize the panel of atopic comorbidities that should be routinely screened for in children with asthma to ensure completeness and be able to compare rates across borders. Other allergic diseases have been known to coexist with asthma as part of the atopic march which is an allergy specific type 2 mediated response in which an early occurrence of one type of atopic manifestation leads to the occurrence of more atopic symptoms in a progressive manner [36].

Comorbid ratios were more among females although the difference was not statistically significant, Lee *et al.* [37] also reported that more females had allergic comorbidities with their asthma among patients with severe or difficult to treat asthma, the reason for this relative higher preponderance of comorbidities among females was because females were more likely to be unable to avoid indoor allergic triggers like house dust mites, molds, and fumes from cooking fuels, also there is a possibility of a gender-based variance in favor of the men, in their response to asthma medications another explanation is the hormonal impact of the female sex steroids which are proinflammatory and can increase susceptibility to atopy [38].

Children who had difficulty in breathing and chest pain as part of their asthma symptoms significantly had a higher likelihood of other allergic comorbidities with their asthma in the present study. Studies have shown that not all the cardinal symptoms of asthma (cough, difficulty breathing, chest pain, and wheeze) are present during asthma exacerbations for every patient [39]. Difficulty in breathing and chest pain is reported in 94.6% and 47.4% of patients with asthma [39]. Perception of dyspnoea in asthma is due to the increase in the work of breathing caused by chronic inflammation of the airways which can lead to increased airway resistance, its' presence does not always correlate with decreased lung function in asthmatic patients [40] [41], but it can be inferred that its' presence as a symptom of asthma in children with allergic comorbidities could be a pointer to more severe disease. The same theory could explain the significant presence of chest pain or chest tightness in children with allergic comorbidity. Chest tightness is caused by smooth muscle bronchoconstriction of the smaller airways and its perception as a symptom could be due to the degree of bronchoconstriction in the patients especially in older children who can report it as a symptom [40] [41]. Although not significantly different, the lower SPO_2 levels and peak expiratory flow rate (PEFR) levels in children with allergic comorbidity when compared to those without comorbidity suggests a relatively higher degree of airway resistance.

Allergic rhinitis was the most common atopic comorbidity seen in children with asthma in the present study which was similar to reports from other studies [27] [42], although with lower prevalence rates when compared to the present study 43% Vs < 25% and 37.6% [27] [42]. A higher prevalence rate of 58% allergic rhinitis has also been reported by Hamouda *et al.* [43]. They used a structured questionnaire with high sensitivity and specificity (>91%) for the diagnosis of rhinitis while in the present study self-reported recurrent symptoms were used which could be less sensitive. The coexistence of allergic rhinitis and asthma could be because both upper and lower respiratory airways have a continuous basal membrane with the same stratified ciliated epithelium covering their mucous membrane as a result they share the same susceptibility to inhalation allergens [44]. This united epithelial covering could also explain the significant coexistence of allergic rhinitis and adenotonsillar hypertrophy in asthma comorbidity. Other allergic comorbidities that usually exist should be sought as highlighted in this study. Children older than 3 years were more likely to have atopic dermatitis compared to older children which was similar to the findings by Feng *et al.* [33] which reported a significant coexistence of atopic dermatitis and allergic conjunctivitis. Allergic conjunctivitis has been described as the ocular manifestation of atopic dermatitis as up to 65% of patients with allergic conjunctivitis have been found to have atopic dermatitis [45].

Suspected food allergy in this study was seen in 10.2% of children with egg and milk allergy being the commonest type of food implicated. Food allergy is rarely reported in Nigeria and there is limited data on types of food allergy

among children with asthma especially in a developing country like Nigeria but for the observant caregiver who identifies a repeated clinical symptom when a child ingests a certain type of food it could be interpreted as suspected food allergy until confirmatory tests are done. In the USA however, the prevalence of food allergy sensitization among inner-city children with asthma using specific Immunoglobulin E (IgE) serology to six common types of food (egg, milk, peanut, wheat, soy, and fish) was 45% (Wang *et al.*). This prevalence rate is much higher than what was reported in the present study although our methodology of using reported clinical symptom from exposure to a particular food to access the presence of food allergy is not very sensitive as a result it would limit the ability of this study to detect the actual prevalence of food allergy sensitization. Diagnostic tests like skin prick test and IgE serology testing however are not available in our facility. The peculiar relationship between food allergy sensitization and asthma is that the presence of asthma increases the likelihood of persistence of food allergy sensitization and there is also a higher risk of severe asthma or fatal outcome from asthma among those with food allergy [46]. In addition, the management of asthma from a food allergy is different from other asthma symptoms exacerbation with the need to give injectable epinephrine first as opposed to short-acting β-agonist in conventional asthma management.

GERD was significantly more in children aged > 11 years old in our study cohort, this relatively high prevalence in older children could be because older children can correctly answer the GerdQ questionnaire while for younger children there is a high dependency on the report of the caregiver whose report may not be as sensitive as self-reported symptoms for identifying GERD [32]. The same maturity is also needed in the ability to report chest pain or chest tightness which is also significantly more in children with GERD. We also found that overweight children with asthma were more likely to have GERD as comorbidity. This is not surprising as obesity causes an increase in transabdominal pressure which lowers the pressure of the esophageal sphincter leading to a backflow of gastric contents to the lower esophagus [47].

Although other comorbidities were associated with an increase in the odds of having a more severe asthma only allergic conjunctivitis was found to be statistically significant and no specific type of comorbidity was associated with poor control. Kuti *et al.* [15] found that allergic rhinitis, adenotonsillar hypertrophy, and obesity increased the likelihood of having a persistent form of asthma while Bilkisu *et al.* [16] did not find any association between asthma severity and the presence of comorbidities. The presence of comorbidities can affect the pathophysiological process of asthma as can be seen in allergic rhinitis in relation to bronchial asthma due to their united airways [9]. Asthma severity can be determined by intrinsic factors like genetic predisposition and phenotypic expression of the disease while asthma control is determined by extrinsic factors like making the correct diagnosis, appropriate treatment, compliance, and screening to treat other comorbidities. In effect, good asthma control is a reflection of the

quality of health care given to treat asthma both of which are physician and patient-related.

5. Conclusion

The prevalence of allergic comorbidities is high among children with asthma. It occurs more in females and the highest prevalence is seen among those aged 8 - 12 years. Allergic rhinitis is the most common comorbidity followed by adenotonsillar hypertrophy, atopic dermatitis, and allergic conjunctivitis. Most children with asthma have more than one allergic comorbidity coexisting with their asthma. Both Allergic rhinitis and atopic dermatitis significantly coexist with adenotonsillar hypertrophy and allergic conjunctivitis. The presence of comorbidity increased the odds of having severe asthma and the likelihood of having severe asthma also increased with an increasing number of coexisting comorbidities. In the management of asthma in children, comprehensive evaluation of other comorbidities is therefore essential in order to improve outcomes of treatment and the patients' quality of life.

6. Study Limitation

The absence of a Lung function test done is a limitation to this study as it would have compared the baseline lung functions of patients with comorbidity and those without comorbidity, to objectively assess the impact of the presence of comorbidity on asthma severity and lung function.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Global Initiative for Asthma (GINA) (2020) Global Strategy for Asthma Management and Prevention (2020 Update). https://ginasthma.org/wp-content/uploads/2020/06/GINA-2020-report_20_06_04-1-wms.pdf

[2] Masoli, M., Fabian, D., Holt, S. and Beasley, R. (2004) Global Initiative for Asthma (GINA) Program. The Global Burden of Asthma: Executive Summary of the GINA Dissemination Committee Report. *Allergy*, **59**, 469-478. https://doi.org/10.1111/j.1398-9995.2004.00526.x

[3] Ozoh, O.B., Aderibigbe, S.A., Ayuk, A.C., Desalu, O.O., Oridota, O.E., Olufemi, O., *et al.* (2019) The Prevalence of Asthma and Allergic Rhinitis in Nigeria: A Nationwide Survey among Children, Adolescents and Adults. *PLoS ONE*, **14**, e0222281. https://doi.org/10.1371/journal.pone.0222281

[4] Liu, A.H., Covar, R.A., Spahn, J.D. and Sicherer, S.H. (2016) Childhood Asthma. In: Kliegman, R.M., Stanton, B.F., St Geme III, J.N. and Behrman, R.E., Eds., *Nelson Textbook of Paediatrics*, 20th Edition, Elsevier, Philadelphia, 1095-1115.

[5] Bousquet, J.K.A. (2007) Global Surveilliance, Prevention and Control of Chronic Respiratory Diseases: A Comprehensive Approach. World Health Organization,

Geneva.

[6] Ledford, D.K. and Lockey, R.F. (2013) Asthma and Comorbidities. *Current Opinion in Allergy and Clinical Immunology*, **13**, 78-86. https://doi.org/10.1097/ACI.0b013e32835c16b6

[7] Ndarukwa, P., Chimbari, M. and Sibanda, E. (2020) Effects of Comorbidities on Asthma Control among Patients Attended to at Chitungwiza Central Hospital in Zimbabwe. *PAMJ-Clinical Medicine*, **2**, 83. https://doi.org/10.21203/rs.2.17794/v1

[8] Peters, S.P., *et al.* (2006) Uncontrolled Asthma: A Review of the Prevalence, Disease Burden and Options for Treatment. *Respiratory Medicine*, **100**, 1139-1151. https://doi.org/10.1016/j.rmed.2006.03.031

[9] Boulet, L. (2009) Influence of Comorbid Conditions on Asthma. *European Respiratory Journal*, **33**, 897-906. https://doi.org/10.1183/09031936.00121308

[10] Yuksel, H., Dinc, G., Sakar, A., Yilmaz, O., Yorgancioglu, A., Celik, P., *et al.* (2008) Prevalence and Comorbidity of Allergic Eczema, Rhinitis, and Asthma in a City in Western Turkey. *Journal of Investigational Allergology & Clinical Immunology*, **18**, 31-35.

[11] Kumar, P., Singh, G., Goyal, J.P., Khera, D. and Singh, K. (2019) Association of Common Comorbidities with Asthma in Children: A Cross-Sectional Study. *Sudanese Journal of Paediatrics*, **19**, 88-92. https://doi.org/10.24911/SJP.106-1544873451

[12] Deliu, M., Belgrave, D., Simpson, A., Murray, C.S., Kerry, G. and Custovic, A. (2014) Impact of Rhinitis on Asthma Severity in School-Age Children. *Allergy*, **69**, 1515-1521. https://doi.org/10.1111/all.12467

[13] Bousquet, J., Khaltaev, N., Cruz, A.A., Denburg, J., Fokkens, W.J., Togias, A., *et al.* (2008) Allergic Rhinitis and Its Impact on Asthma (ARIA) 2008 Update (in Collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy*, **63**, 8-160.

[14] Friedlander, J.L., Sheehan, W.J., Baxi, S.N., Kopel, L.S., Gaffin, J.M., Ozonoff, A.F., *et al.* (2013) Food Allergy and Increased Asthma Morbidity in a School-Based Inner-City Asthma Study. *The Journal of Allergy and Clinical Immunology: In Practice*, **1**, 479-484. https://doi.org/10.1016/j.jaip.2013.06.007

[15] Leynaert, B., Neukirch, F., Demoly, P. and Bousquet, J. (2000) Epidemiologic Evidence for Asthma and Rhinitis Comorbidity. *Journal of Allergy and Clinical Immunology*, **106**, S201-S205. https://doi.org/10.1067/mai.2000.110151

[16] Ballardini, N., Kull, I., Lind, T., Hallner, E., Almqvist, C., Östblom, E., *et al.* (2012) Development and Comorbidity of Eczema, Asthma and Rhinitis to Age 12—Data from the BAMSE Birth Cohort. *Allergy*, **67**, 537-544. https://doi.org/10.1111/j.1398-9995.2012.02786.x

[17] de Oliveira, T.B., Klering, E.A. and da Veiga, A.B.G. (2019) Is Recurrent Respiratory Infection Associated with Allergic Respiratory Disease? *The Journal of Asthma*, **56**, 160-166.

[18] Tay, T.R. and Hew, M. (2018) Comorbid "Treatable Traits" in Difficult Asthma: Current Evidence and Clinical Evaluation. *Allergy*, **73**, 1369-1382. https://doi.org/10.1111/all.13370

[19] Simpson, A.B., Glutting, J. and Yousef, E. (2007) Food Allergy and Asthma Morbidity in Children. *Pediatric Pulmonology*, **42**, 489-495. https://doi.org/10.1002/ppul.20605

[20] Reddel, H.K., Taylor, D.R., Bateman, E.D., Boulet, L.P., Boushey, H.A., Busse, W.W., *et al.* (2009) An Official American Thoracic Society/European Respiratory

Society Statement: Asthma Control and Exacerbations: Standardizing Endpoints for Clinical Asthma Trials and Clinical Practice. *American Journal of Respiratory and Critical Care Medicine*, **180**, 59-99. https://doi.org/10.1164/rccm.200801-060ST

[21] Kuehni, C.E. and Frey, U. (2002) Age-Related Differences in Perceived Asthma Control in Childhood: Guidelines and Reality. *European Respiratory Journal*, **20**, 880. https://doi.org/10.1183/09031936.02.00258502

[22] Rabe, K.F., Adachi, M., Lai, C.K.W., Soriano, B.J., Vermeire, P.A., Weiss, K.B., *et al.* (2004) Worldwide Severity and Control of Asthma in Children and Adults: The Global Asthma Insights and Reality Surveys. *The Journal of Allergy and Clinical Immunology*, **114**, 40-47. https://doi.org/10.1016/j.jaci.2004.04.042

[23] Smith, L.A., Bokhour, B., Hohman, K.H., Miroshnik, I., Kleinman, K.P., Cohn, E., *et al.* (2008) Modifiable Risk Factors for Suboptimal Control and Controller Medication Underuse among Children with Asthma. *Pediatrics*, **122**, 2007-2750. https://doi.org/10.1542/peds.2007-2750

[24] Ozoh, O.B., Ayuk, A.C., Ukwaja, K.N., *et al.* (2019) Asthma Management and Control in Nigeria: The Asthma Insight and Reality Nigeria (AIRNIG) Study. *Expert Review of Respiratory Medicine*, **13**, 917-927.

[25] Solé, D., *et al.* (2005) Is Rhinitis Alone or Associated with Atopic Eczema a Risk Factor for Severe Asthma in Children? *Pediatric Allergy and Immunology*, **16**, 121-125.

[26] Crystal-Peters, J., Neslusan, C., Crown, W.H. and Torres, A. (2002) Treating Allergic Rhinitis in Patients with Comorbid Asthma: The Risk of Asthma-Related Hospitalizations and Emergency Department Visits. *Journal of Allergy and Clinical Immunology*, **109**, 57-62. https://doi.org/10.1067/mai.2002.120554

[27] Kuti, B.P. (2020) Asthma Co-Morbidities in Nigerian Children: Prevalence, Risk Factors and Association with Disease Severity and Symptoms Control. *Pan African Medical Journal*, **35**, 91. https://doi.org/10.11604/pamj.2020.35.91.18470

[28] Garba, B.I., Sani, U.M., Isezuo, K.O., Waziri, U.M., Ugege, M.O., Adamu, A., *et al.* (2019) Pattern of Allergic Co-Morbidities in Children with Asthma in Sokoto, North Western Nigeria. *International Journal of Biomed Research*, **10**, e5282. https://doi.org/10.22270/jddt.v10i4.4158

[29] Ayuk, A., Eze, J., Edelu, B. and Oguonu, T. (2018) The Prevalence of Allergic Diseases among Children with Asthma: What Is the Impact on Asthma Control in South East Nigeria? *The Nigerian Journal of Clinical Practice*, **21**, 632-638. https://doi.org/10.4103/njcp.njcp_343_17

[30] Colice, G.L. (2004) Categorizing Asthma Severity: An Overview of National Guidelines. *Clinical Medicine & Research*, **2**, 155-163. https://doi.org/10.3121/cmr.2.3.155

[31] Williams, H.C., Burney, P.G., Pembroke, A.C. and Hay, R.J. (1994) The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent Hospital Validation. *British Journal of Dermatology*, **131**, 406-416. https://doi.org/10.1111/j.1365-2133.1994.tb08532.x

[32] Jones, R., Junghard, O., Dent, J., Valkil, N., Halling, K., Wernersson, B., *et al.* (2009) Development of the GerdQ, a Tool for the Diagnosis and Management of Gastro-Oesophageal Reflux Disease in Primary Care. *Alimentary Pharmacology & Therapeutics*, **30**, 1030-1038. https://doi.org/10.1111/j.1365-2036.2009.04142.x

[33] Schroeder, A., Kumar, R., Pongracic, J.A., Sullivan, C.L., Caruso, D.M., Costello, J., *et al.* (2009) Food Allergy Is Associated with an Increased Risk of Asthma. *Clinical and Experimental Allergy*, **39**, 261-270. https://doi.org/10.1111/j.1365-2222.2008.03160.x

[34] Liu, A.H., Zeiger, R., Sorkness, C., Mahr, T., Ostrom, N., Burgess, S., *et al.* (2007) Development and Cross-Sectional Validation of the Childhood Asthma Control Test. *The Journal of Allergy and Clinical Immunology*, **119**, 817-825. https://doi.org/10.1016/j.jaci.2006.12.662

[35] Olusanya, O., Okpere, E. and Ezimokhai, M. (1985) The Importance of Social Class in Voluntary Fertility Control in a Developing Country. *West African Journal of Medicine*, **4**, 205-212.

[36] Paller, A.S., Spergel, J.M., Mina-Osorio, P. and Irvine, A.D. (2019) The Atopic March and Atopic Multimorbidity: Many Trajectories, Many Pathways. *The Journal of Allergy and Clinical Immunology*, **143**, 46. https://doi.org/10.1016/j.jaci.2018.11.006

[37] Lee, J., Haselkorn, T., Chipps, B., Miller, D. and Wenzel, S. (2006) Gender Differences in IgE-Mediated Allergic Asthma in the Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens (TENOR) Study. *The Journal of Asthma*, **43**, 179-184. https://doi.org/10.1080/02770900600566405

[38] Martinez-Moragón, E., Plaza, V., Serrano, J., Picado, C., Galdiz, J.B., López-Viña, A., *et al.* (2004) Near-Fatal Asthma Related to Menstruation. *The Journal of Allergy and Clinical Immunology*, **113**, 242-244. https://doi.org/10.1016/j.jaci.2003.11.002

[39] Onubogu, U.C. and West, B.A. (2020) Childhood Asthma-Pattern, Severity and Control among Children Seen in an Outpatient Respiratory Clinic in River State University Teaching Hospital, Port Harcourt, Nigeria. *Journal of Pediatrics, Perinatology and Child Health*, **4**, 73-85.

[40] Yeh, S.Y. and Schwartzstein, R. (2009) Asthma: Pathophysiology and Diagnosis. In: Harver, A. and Kotses, H., Eds., *Asthma, Health and Society: A Public Health Perspective*, Springer, Berlin, 19-42. https://doi.org/10.1007/978-0-387-78285-0_2

[41] Moy, M.L., Lantin, M.L., Harver, A. and Schwartzstein, R.M. (1998) Language of Dyspnea in Assessment of Patients with Acute Asthma Treated with Nebulized Albuterol. *American Journal of Respiratory and Critical Care Medicine*, **158**, 749-753. https://doi.org/10.1164/ajrccm.158.3.9707088

[42] Heck, S., Al-Shobash, S., Rapp, D., Le, D.D., Omlor, A., Bekhit, A., *et al.* (2017) High Probability of Comorbidities in Bronchial Asthma in Germany. *NPJ Primary Care Respiratory Medicine*, **27**, 28. https://doi.org/10.1038/s41533-017-0026-x

[43] Hamouda, S., Karila, C., Connault, T., Scheinmann, P. and DeBlic, J. (2008) Allergic Rhinitis in Children with Asthma: A Questionnaire-Based Study. *Clinical & Experimental Allergy*, **38**, 761-766. https://doi.org/10.1111/j.1365-2222.2008.02953.x

[44] Bergeron, C. and Hamid, Q. (2005) Relationship between Asthma and Rhinitis: Epidemiologic, Pathophysiologic, and Therapeutic Aspects. *Allergy, Asthma, and Clinical Immunology*, **1**, 81-87. https://doi.org/10.1186/1710-1492-1-2-81

[45] Bielory, L., Delgado, L., Katelaris, C.H., Leonardi, A., Rosario, N. and Vichyanoud, P. (2019) ICON: Diagnosis and Management of Allergic Conjunctivitis. *Annals of Allergy, Asthma & Immunology*, **124**, 118-134.

[46] Wang, J. and Liu, A.H. (2011) Food Allergies and Asthma. *Current Opinion in Allergy and Clinical Immunology*, **11**, 249-254. https://doi.org/10.1097/ACI.0b013e3283464c8e

[47] Emerenziani, S., Paola Rescio, M., Luca Guarino, M.P. and Cicala, M. (2013) Gastro-Esophageal Reflux Disease and Obesity, Where Is the Link? *World Journal of Gastroenterology*, **19**, 6536-6539. https://doi.org/10.3748/wjg.v19.i39.6536