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Risk Factors for Asthma Among Preschool Children Attending Allergy Clinic at Benghazi Children' Hospital, Libya

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Abstract **Original Research Article**

Introduction: Bronchial asthma is a common heterogeneous chronic inflammatory disorder of the lower respiratory airways in childhood. ***Aim:*** This study aimed to examine different recognized risk factors of asthma. ***Methods:*** A total of 420 children sample of case-control groups of matched age (1-5 years) and gender were randomly selected and recruited in this study. The number of children in each group was (210). The cross-sectional study was conducted at Benghazi children's hospital for six months period from 1st of June 2021 to 31st of December 2021. The data were collected using a self-administrated. The collected data were analyzed using SPSS (version 22). The chi-square test used to compare proportions. Whereas, the binary logistic regression was used to calculate the odds ratios (OR) and 95% confidence intervals (CI). ***Results:*** The result of cross-tabulation using chi-square of all different recognized factors showed a statistically significant different of p-value>0.05 were age, the family history of asthma and atopy, personal history of asthma, pet in the house, maternal medication intake, maternal treatment for the common cold, mode of delivery, preterm delivery, low birth weight, and recurrent respiratory tract infections. On other hand, the analysis of all substantial risk factors for asthma using a binary logistic regression showed age (being older (>3-5 Years)) had a protective effect against asthma (OR=0.800, (95% CI)=(0.492-1.302)), gender (being female had a protective effect against asthma (OR=0.886, (95% CI) = (0.544-1.443)), paternal (OR=0.698, (95% CI) = (0.400-1.217), not maternal educational levels had a protective against asthma, none of the personal and environmental factors affected the development of asthma in our studied children. While, the greatest contribution in this study was from natal and post natal factors including mode of delivery (OR= 0.621, (95% CI) = (0.383-1.006), and type of feeding (OR=0.854, (95% CI) = (0.515-1.416) that are a protective factor against asthma. Whereas, preterm delivery (OR=1.462, (95% CI) = (0.429-4.987), and recurrent upper respiratory tract infections (OR=5.144, (95% CI)= (3.199-8.271) had increased the odds of asthma. ***Conclusion:*** The recognized risk and protective factors of asthma indicated the combined effects of demographic, natal, and postnatal factors but not the personal and environmental factors in the development of asthma in our studied groups of children.

Keywords: Asthma, preschool children, risk factors, paternal, maternal, history, Benghazi.

INTRODUCTION

Bronchial asthma in childhood is a common diverse chronic inflammatory illness of the lower respiratory airways in childhood. Frequently characterized by respiratory symptoms including breathlessness, wheezing, cough, and chest tightness together wheezing, breathlessness, chest tightness, and cough, together with inconstant expiratory airflow obstruction (Hargreave and Nair., 2009; Bush and Fleming., 2015). Asthma frequently begins in early childhood, and in the first six years of the life of half of the children with asthma at minimum one episode of wheezing occurs (Dharmage *et al*., 2019). The prevalence of asthma in school-aged children and infants is lower than that in preschool children (Zhonghua and Ke. (2013; Croisant, 2014) with an increased prevalence over the last few decades in all sex, ages, and racial groups, especially in children (Hao *et al*., 2022). Asthma is the most common chronic pediatric disease. Symptoms can occur several times a day if the disease is not controlled. Uncontrolled symptoms considerably decrease the quality of life for patients and family members because of reduced activity levels, daytime fatigue, sleeplessness, and absences from school or work (BinSaeed *et al*., 2014). In addition, children with asthma are significantly burdened by asthma morbidity, with higher rates of emergency department visits, hospitalizations, and deaths. A large proportion of the asthma burden is the

consequence of poor asthma control. Children with poorly controlled asthma report a decreased health-related quality of life. Asthma guidelines emphasize the importance of achieving asthma control to minimize or prevent exacerbations (Hao *et al*., 2022). Also, the diagnosis and treatment of asthma in preschool children are challenging due to confusion with other diseases such as bronchitis and bronchiolitis (Dharmage *et al*., 2019). Since the 1970s, the worldwide incidence and prevalence of asthma have increased markedly, with an estimated 334 million cases worldwide in 2014 (Zhonghua and Ke. 2013; Croisant, 2014).

The best-known risk factors and triggers that lead to allergic diseases, especially asthma and related bronchopathies in children are different, such as genetic, pulmonary immaturity, viral infections, environmental pollution (Williams *et al*., 2000) or environmental insults (both pre-and post-birth), acting in a critical window of development in early life. According to recent evidence, some conditions such as genetic factors, maternal infections and drugs, birth characteristics, and environmental exposures give information about the complex mechanisms shaping the immune and pulmonary systems of neonates and infants, and the later possible development of asthma in children and adult life (García-Serna *et al*., 2021).The current study aimed to identify the possible risk and protective factors for asthma in preschool children at the age of 1–5 years, to determine the risk of childhood asthma for each individual type of exposure, and to assess the relationships between the demographic, personal and environmental, and natal and postnatal variables.

METHODOLOGY

Study Design

A hospital-based cross-sectional study was carried out in a period from the 1st of June 2021 to the 31st of December 2021 using a self-administrated questionnaire, at Benghazi children's hospital

Subjects and Sampling

The study population consisted of 420 children divided into two groups. The first group is a case that included 210 asthmatic patients attending an outpatient allergy clinic during the time of the study. A second group is a control group that included 210 patients attending other outpatients' clinics for different illnesses except for chronic diseases and asthma. The two groups matched ages from 1 to 5 years and gender. The samples of both groups were selected randomly from outpatient clinics.

Ethics approval

Consent was taken from the head of the outpatient clinic to fill out the questionnaires by the researchers. Consent was also taken from the parents to participate in the study.

The questionnaire and data collection

The self-administrated questionnaires were filled by the researchers through a direct interview with the parents. The questionnaire consisted of sixteen questions and was divided into three parts. The first part covers the demographic data of participants including age, gender, residency, and parent education. The second part covers the personal and environmental factors including a family history of asthma or atopy, and personal history of atopy, the presence of pets in the house, exposure to passive smoking, and the third part covers the natal and postnatal factors including maternal medication intake, maternal treatment for the common cold, mode of delivery, presence of low birth weight, preterm delivery, early postnatal factors such as type of feeding either exclusive breastfeeding for six months or bottle feeding, any medications for baby and recurrent upper respiratory infections. Most of the risk factors mentioned were coded as binary variables by "yes/no" questions

Statistical analysis

The filled questionnaires were sorted into case and control groups, then the data were coded, entered, checked for accuracy, and finally analyzed using the SPSS version 22.0 software package. There was no missing data. The descriptive statistics including frequencies and percentages were used to display the categorical variables in form of tables and figures. The chi-squared ($\chi 2$) test was used to test the significance of differences between children in case (asthmatic) and control (without asthma) groups. The effect of eighteen risk factors possibly associated with developing asthma were examined using Binary logistic regression. The results of regression were expressed by odds ratio (OR) and 95% confidence interval (CI) (all tests were at 5% significance level) for each risk factor. The level of significance (P-value $\leq$ 0.05) was considered statistically different for all tests.

RESULTS

The sociodemographic characteristics of the studied children

The sociodemographic characteristics of the studied groups were illustrated in table (1). There were no significant association ($p>0.05$) between gender, area of residency, maternal and paternal education and asthma ($p=0.765$, $p=1$, $p=0.716$ and $p=0.111$) respectively. While, there is a significant association between age and asthma ($p=0.048$, $p\leq0.05$). Totally, the average age of studied children was (3.27years), the number of studied children in the age group (1-3 years) was (244, 58.1%) and the children in age group (>3-5years) was (176, 41.9%), which were nearly close to each other. In the asthmatic group, the distribution of children in two age groups (1-3years) and (>3-5years) were (112, 53.3%) and (98, 46.7%) respectively. Meanwhile, the children in the age group (1-3years)

were (132, 62.9%) and the children in the age group (>3-5years) were (78, 37.1%).

In total, nearly three third of the studied children were male (253, 60.24%) and the rest were female (176, 39.76%). The same was for the case group and control group. In which, the males were (128, 60.95%) and (125, 59.52%) and females were (82, 39.05%) for case and control groups respectively, meeting the condition of matched age and gender. In total, the majority (396, 93.3%) of the studied children were from Benghazi city which is marked as urban and the rest only 28 children representing (6.67%) were from different towns and villages in the eastern part of Libya. The area of residency distribution of studied children in both groups is the same. Nearly all the asthmatic and control children from Benghazi city represent (196, 93.3%) for each and the rest are from different towns and villages in the eastern part of Libya representing (14, 6.67%) each.

In the asthmatic children group, most of the mothers were educated for <15 (166, 79.1%) and only 44 mothers (20.9 %) were educated for >15 years. Nearly the same distribution was found for mothers of studied children in total, the number of mothers educated for <15 (335, 79.7%), and only 85 mothers (20.2 %) were educated for >15 years. Similarly, the number of mothers of control children educated for <15 years and <15 years were (169, 80.5%) and (41.5, 19.5%) respectively. In total, almost seventy percent (69.8%) of fathers of studied children in both groups were educated for <15 years and the rest (127, 30.2%) were educated for >15 years. Almost two-thirds (139, 66.2%) of asthmatic children's fathers were educated for <15 years and only one-third were (71, 33.8%) educated for >15 years. Whereas, about three-quarters of control children's fathers were educated for <15 years, and one-quarter were (56, 26.7%) educated for >15 years.

Table 1: The sociodemographic characteristics of the studied children

Risk factors	Asthmatic		Control		Total		p-value
	N	%	N	%	N	%	
Age (years)							
1-3	112	53.3	132	62.9	244	58.1	P value=0.048
>3-5	98	46.7	78	37.1	176	41.9	
Gender							
Male	128	60.95	125	59.52	253	60.24	P value=0.765
Female	82	39.05	85	40.48	167	39.76	
Residency							
Urban*	196	93.3	196	93.3	396	93.3	P value=1
Rural**	14	6.67	14	6.67	28	6.67	
Maternal education							
<15 years	166	79.1	169	80.5	335	79.7	P value=0.716
>15 years	44	20.9	41	19.5	85	20.2	
Paternal education							
<15 years	139	66.2	154	73.3	293	69.8	P value=0.111
>15 years	71	33.8	56	26.7	127	30.2	

*Benghazi city/ **Towns and villages in the eastern part of Libya (Five children from Suluq, four from Qaminis, three children from Marj, three children from Kufra, three from Ajdabiya, two from Abyar, two from Deriana, two from Tocra, one from Sabha, one from Bayda, one from Al-Kwayfiya and one from Makzaha

The personal and environmental risk factors of asthma

The personal and environmental risk factors of asthma were summarized in Table 2.

A family history of asthma

Totally, a few above one-third of families had a history of asthma (148, 35.2%) and nearly three third of studied children's families had no history of asthma (272, 64.8%). Among the asthmatic children group, a few above half of the families had a history of asthma (111, 52.9%) and the rest (99, 47.41%) had a history of asthma. Conversely, only 49 normal children representing (35.2%) had a family history of asthma and most of them had no history of asthma (272, 64.8%).There is a significant association between a family history of asthma and having asthma (p=0.00, p≤0.05) that (47.1%) of asthmatic children's families had a history of asthma versus only (35.2%) of control children's families had a history of asthma.

The family history of atopy

Among the studied children, three third of families had a family history of atopy (280, 66.7%) and only one-third of families had no history of atopy. A family history of atopy was found in the majority of asthmatic children families (170, 81%) and the rest of the families had no history of atopy (40, 19%). In contrast, the history of atopy and no history of atopy were found in (110, 52.4%) and (100, 47.6%) of the control children's families respectively. There is a

significant association between a family history of atopy and asthma (p=0.00, p≤0.05).

The personal history of atopy

In case and control groups the personal history of atopy was only found in 53 children representing (12.6%). While, the majority of children (367, 87%) had no personal history of atopy. The majority of asthmatic children had no personal history of atopy (169, 80.5%) and only (41, 19.5%) had no history of personal atopy. Yet, almost all control children had no history of personal atopy (198, 94.3%), and only twelve children (5.7%) had a personal history of atopy. There is a significant association between a personal history of atopy and having asthma (p=0.000, p≤0.05).

The presence of pets in the house

In general, only (99, 23.57%) of the studied children had pets in their house and a few above quarters (321, 76.43%) had no pets in their house. Yet, less than one-third (65, 30.95%) of the asthmatic children had pets in their house and the rest (145, 69.05%) had no pets. In the control group, the pets were present only in 34 (16.19%) houses. While, the majority (176, 83.81%) had no pets in the house. There is a significant association between the presence of pets in the house and having asthma (p=0.001, p≤0.05). The percentage of control children who had pets is the half of percentage of asthmatic children who had pets in the house.

Exposure to passive smoking

Totally, a few above halve (228, 54.3%) of studied children were exposed to passive smoking, and (192, 45.7%) were not exposed to passive smoking. Similarly, one hundred and nineteen asthmatic children were exposed to passive smoking (56.7%), and (91, 43.3%) were not exposed to passive smoking. Nearly half of normal children were exposed to passive smoking (109, 51.9%). There is no significant association between exposure to passive smoking and having asthma (p=0.327, p>0.05).

Table 2: The personal and environmental risk factors of asthma

Risk factors	Asthmatic		Control		Total		P value
	N	%	N	%	N	%	
A family history of asthma							
Yes	99	47.1	49	23.3	148	35.2	P value=0.000
No	111	52.9	161	76.7	272	64.8	
A family history of atopy							
Yes	170	81.0	110	52.4	280	66.7	P value=0.000
No	40	19.0	100	47.6	140	33.3	
The personal history of atopy							
Yes	41	19.5	12	5.7	53	12.6	P value=0.000
No	169	80.5	198	94.3	367	87.4	
The presence of pets in the house							
Yes	65	30.95	34	16.19	99	23.57	P value=0.000
No	145	69.05	176	83.81	321	76.43	
Exposure to passive smoking							
Yes	119	56.7	109	51.9	228	54.3	P value=0.327
No	91	43.3	101	48.1	192	45.7	

The bold values were statistically significant (p≤0.05)

The natal and postnatal factors

Maternal medication intake

Totally, out of 420 mothers, 258 (61.4%) were taken medications during pregnancy. While 162 mothers (38.6%) were not taken medications. Correspondingly, nearly the same proportion of mothers of asthmatic and control were taken medications during pregnancy representing (131, 62.4%) and (127, 60.5%) respectively. Yet, the mothers of asthmatic and control children not taken medications were represented as (79, 37.6%) and (83, 39.5%) respectively. There is no significant association between maternal medication intake and asthma (p=0.688, p>0.05). The types of medications consumed during pregnancy by mothers of all children were presented in (Figure 1). The tonic was taken by (160, 38.1%) mothers, antibiotics were taken by (94, 22.4%) mothers, aspirin was only taken by two mothers (0.47%), also antibiotic for urinary tract infection was only taken by two (0.47%) mothers.

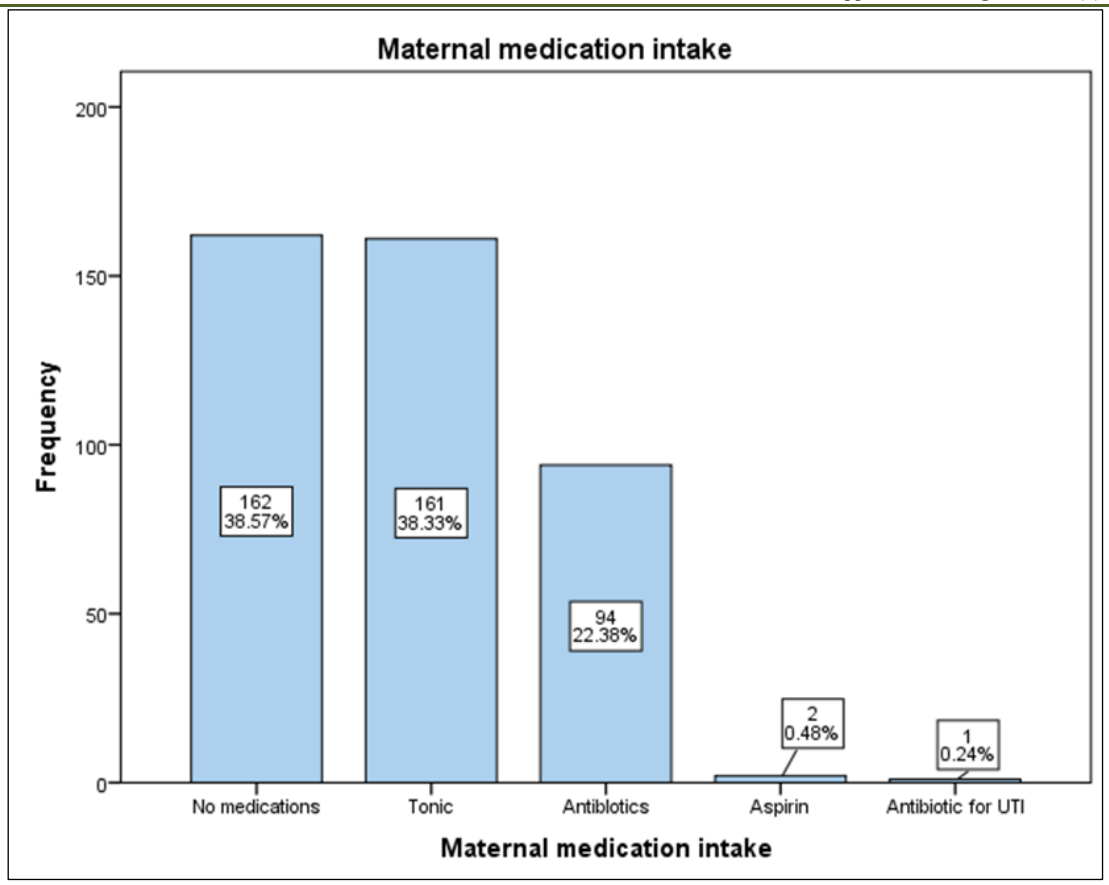

Figure 1: The maternal medication intake by mothers of case and control groups ((UTI)=antibiotic for urinary tract infection)

Maternal treatment for the common cold

In total, the majority (358, 85.2%) of mothers had not taken treatment for the common cold during pregnancy. Only 62(14.8%) mothers had taken treatment for the common cold. The majority (169, 80.5%) of mothers of Asthmatic children had not taken treatment for the common cold and almost all the mothers of control children had not taken treatment for the common cold (189, 90%). There is a significant association between maternal treatment for the common cold and having asthma (p=0.006, p≤0.05).

Mode of delivery

Generally, a few above halves of children in both groups were normally delivered (222, 52.9%), and (198, 47.1%) were born by cesarean section. The proportion of normally delivered asthmatic children is low (98, 46.7%) versus the proportion of normally delivered control children (124, 59). The opposite is for the proportion of asthmatic children born by cesarean section is higher (112, 53.3%) versus the proportion of control children born by cesarean section (86, 41%). There is a significant association between the mode of delivery and asthma (p=0.011, p≤0.05).

Preterm delivery

Among both groups, almost all children were delivered full-term (388, 92.4%) as only 32 children were born preterm (7.6%). The same for asthmatic children that only 22 (10.2%) were preterm and only 5(32%) of control children were preterm. There is a significant association between preterm delivery and having asthma (p=0.027, p≤0.05). The distribution of mode of delivery among studied children was also specified in which, full term normal delivery (FTND) was predominant in control and asthmatic groups (122, 29.05% and 95, 22.62%) respectively. Followed by a full caesarian section (FTC/S) presented (80, 19.05%) in control and (103, 24.52%) in asthmatic. respectively. While, the preterm term normal delivery (PTND) was the least common type of delivery in control and asthmatic groups (2, 0.48% and 3, 0.71%) respectively. Yet, the preterm caesarian section (PTC/S) was slightly higher in asthmatic (9, 2.14%) than in control (6, 1.34%).

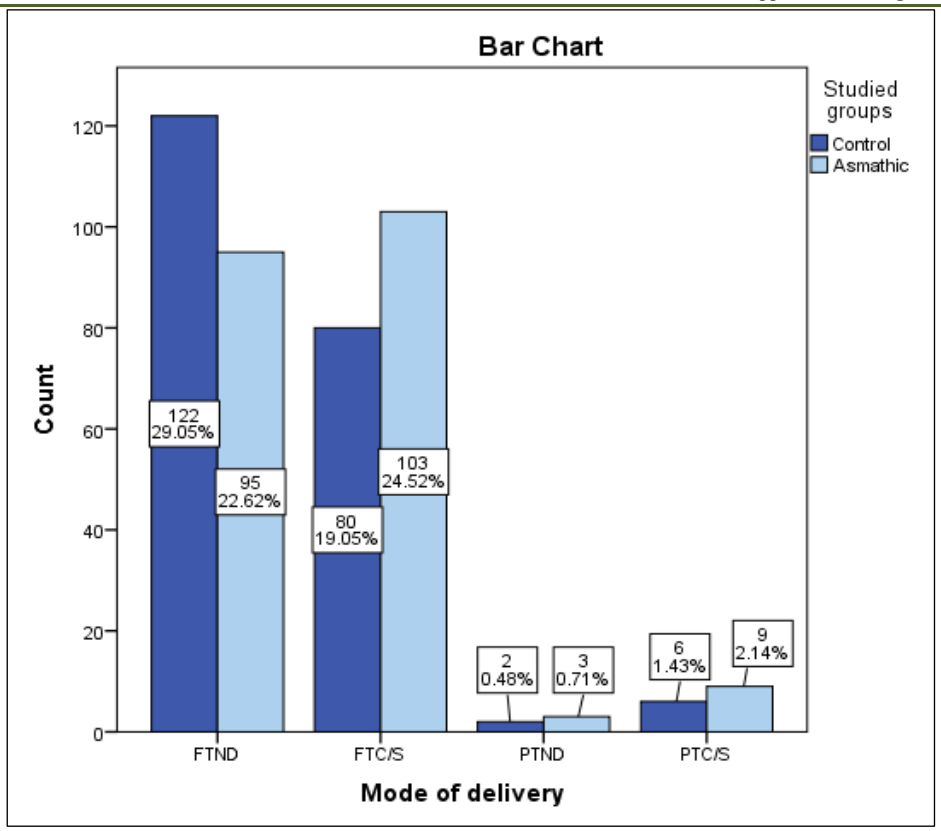

Figure 2: The distribution of mode of delivery among studied children in case and control groups (FTND=Full term normal delivery, FTC/S= Full term caesarian section, PTND=Preterm term normal delivery, PTC/S=Preterm caesarian section)

Presence of low birth weight

In general, most (360, 85.7%) of the studied children had no low birth weight and only 60(14.3) had low birth weight. The majority of asthmatic children had no low birth weight (171, 81.4%) and the rest (39, 18.6%) had low birth weight. Almost all of the control children had no low birth weight (189, 90%) and only 21 children (10%) had low birth weight. There is a significant association between low birth weight and having asthma (p=0.012, p≤0.05).

Type of feeding

In general, two-thirds of studied children were exclusively breastfed and the rest (143, 33.8%) were mixed and bottle-feeding. Likewise, the numbers of breastfed children in asthmatic and control groups were nearly similar around three-thirds accounting (for 137, 65.2%) and (141, 67.1%) respectively. The rest were mixed and bottle-feeding accounting (73, 34.8%) and (69, 32.9%) for asthmatic and control children respectively. There is no significant association between the type of feeding and having asthma (p=0.68, p>0.05).

Recurrent upper respiratory tract infections

Totally, the recurrent upper respiratory tract infection among all studied children was nearly equally distributed between less than three times a year (216, 51.4%) and more than three times a year (204, 48.6%). though, three-quarters of asthmatic children had more than three times respiratory tract infections a year (148, 70.5%) and only 62(29.5%) had less than three times respiratory tract infections. In contrast, more than three-quarters (154, 73.3%) of control children had less than three times respiratory tract infections and the rest (56, 26.7%) had more than three times infections a year. There is a significant association between recurrent upper respiratory tract infection during a year and having asthma (p=0.00, p≤0.05).

Table 3: The natal and postnatal factors

Risk factors	Asthmatic		Control		Total		P value
	N	%	N	%	N	%	
Maternal medication intake							
Yes	131	62.4	127	60.5	258	61.4	P value=0.688
No	79	37.6	83	39.5	162	38.6	
Maternal treatment for the common cold							
Yes	41	19.5	21	10	62	14.8	P value=0.006

Risk factors	Asthmatic		Control		Total		P value
	N	%	N	%	N	%	
No	169	80.5	189	90	358	85.2	
Mode of delivery							
Normal delivery	98	46.7	124	59	222	52.9	P value=0.011
Cesarean section	112	53.3	86	41	198	47.1	
Preterm delivery							
Yes	22	10.5	10	5	32	7.6	P value=0.027
No	188	89.5	200	95	388	92.4	
Low birth weight							
Yes	39	18.6	21	10	60	14.3	P value=0.012
No	171	81.4	189	90	360	85.7	
Type of feeding							
Exclusive breastfeeding (≥ 6 months)	137	65.2	141	67.1	278	66.2	P value=0.68
Others*	73	34.8	69	32.9	142	33.8	
Recurrent upper respiratory tract infections							
<3 times a year	62	29.5	154	73.3	216	51.4	P value=0.000
>3 times a year	148	70.5	56	26.7	204	48.6	

The bold values were statistically significant (p≤.0.05), *Include mixed and bottle-feeding,

Associations between all the risk factors and asthma using binary logistic regression.

The results of binary logistic regression were illustrated in Table 3:

Age

The children aged more than three years up to five years were significantly associated with lower odds of asthma by (OR=0.800, (95% CI) =(0.492-1.302)).

Gender

The female gender in comparison to the male gender was significantly associated with lower odds of asthma, this means the female gender had a protective effect against asthma (OR=0.886, (95% CI) = (0.544-1.443)).

Area of residency

The results showed there is no association between the area of residency and asthma (OR=0.685, (95% CI) = (0.268-1.752)).

Maternal education

The results showed there is no association between maternal educational years and asthma (OR=1.131, (95% CI) = (0.601-2.131)).

Paternal education

The results showed there is a strong association between paternal educational level and asthma. Paternal education for >15 years was associated with lower odds of asthma as compared to maternal education for >15 years (OR=0.698, (95% CI)=(0.400-1.217)).

Family history of asthma and atopy

In our studied children, the results showed there is no association between a family history of asthma and atopy and asthma (OR=0.396, (95% CI) = (0.236-0.664)) and (OR=0.263, (95% CI) = (0.155-0.446)) respectively.

Personal history of atopy

The results showed there is no association between a personal history of atopy and asthma (OR=0.302, (95% CI) = (0.134-0.677)).

Pets in the house

The results showed there is no association between the presence of pets in the house and asthma (OR=0.492, (95% CI) = (0.274-0.884)).

Exposure to passive smoking

The results showed there is no association between the exposure of children to passive smoking and asthma (OR=0.743, (95% CI) = (0.457-1.205)).

Maternal medication intake

The results showed there is no association between maternal medication intake during pregnancy and asthma (OR=0.885, (95% CI) = (0.536-1.462)).

Maternal treatment for the common cold

Our study showed no significant association between maternal treatment for the common cold and asthma (OR= 0.782, (95% CI) = (0.386-1.586)).

Mode of delivery

Our study showed is a strong association between the mode of delivery of children and asthma. The normal delivery of children had a protective factor and a decreased odds of asthma (OR=0.621, (95% CI) = (0.383-1.006).

Preterm delivery

The results showed there is a strong association between preterm delivery of children and asthma. The preterm children had increased odds of asthma (OR=1.462, (95% CI) = (0.429-4.987)).

Low birth weight

The results showed there is no association between the low birth weight of children and asthma (OR=0.428, (95% CI) = (0.173-1.059)).

Feeding type

The results showed there is a strong association between the types of the feeding of children and asthma. Exclusive breastfeeding for (≥ 6 months) showed a protective effect against asthma (OR=0.854, (95% CI) = (0.515-1.416)).

Recurrent upper respiratory tract infections

The results showed there is a strong association between recurrent upper respiratory tract infections of babies for > 3 times as compared to respiratory tract infections for < 3 times. The children who had a respiratory tract infection > 3 times had higher odds of asthma (OR=5.144, (95% CI)= (3.199-8.271)).

Table 4: Associations between risk factors and asthma using binary logistic regression

Risk factor	OR	95% CI
Demographic data		
Age		
1-3 Years	1	
>3-5 Years	0.800	(0.492-1.302)
Gender		
Male	1	
Female	0.886	(0.544-1.443)
Area of residency		
Rural	1	
Urban	0.685	(0.268-1.752)
Maternal education		
>15 years	1.131	(0.601-2.131)
<15 years	1	
Paternal education		
>15 years	0.698	(0.400-1.217)
<15 years	1	
Personal and environmental factors		
Family history of asthma		
No 0	1	
Yes 1	0.396	(0.236-0.664)
Family history of atopy		
No	1	
Yes	0.263	(0.155-0.446)
Personal history of atopy		
No	1	
Yes	0.302	(0.134-0.677)
Pets in house		
No	1	
Yes	0.492	(0.274-0.884)
Exposure to passive smoking		
No	1	
Yes	0.743	(0.457-1.205)
Natal and post natal factors		
Maternal medication intake		
No	1	
Yes	0.885	(0.536-1.462)
Maternal treatment for the common cold		
No	1	
Yes	0.782	(0.386-1.586)
Mode of delivery		
Normal delivery	0.621	(0.383-1.006)
Cesarean section	1	

Risk factor	OR	95% CI
Preterm delivery		
No	1	
Yes	1.462	(0.429-4.987)
Low birth weight		
No	1	
Yes	0.428	(0.173-1.059)
Feeding type		
Exclusive breastfeeding (≥ 6 months)	0.854	(0.515-1.416)
Others*	1	
Recurrent upper respiratory tract infections		
<3 times a year	1	
>3 times a year	5.144	(3.199-8.271)

*Include mixed and bottle-feeding, Values in bold were significantly associated with asthma. OR= Odds ratio, CI= Confidence interval

DISCUSSION

To the best of our knowledge, this study is the first to be done at Benghazi children's hospital to assess the risk factors of asthma among preschool children. The results of this study showed that the average age of our studied group was (3.27years), with the predominance of males (235, 60.24%) on females (167, 39.76%). Regarding age, this result came in line with the study of Cho *et al.* (2014) that done among preschool asthmatic children in Korea, which found the average age of children was 3.68 years. Also, the gender distribution was almost identical numbers of boys and girls. Which is different from our study's gender distribution. Yet, Indinnimeo *et al*. (2016) did a study in Italy among children with atopic disease and they found that girls had a lower risk of developing asthma with respect to boys (OR, 0.50; 95% CI, 0.27–0.90). This result was comparable to our study in that the female gender compared to the male gender was significantly associated with lower odds of asthma (OR=0.886, 95% CI= (0.544-1.443). Conversely, a study done to study asthma-related outcomes in Boston by Taveras *et al*. (2006) found that boys had a higher incidence of asthma-related outcomes than girls (OR=1.52, 95% Cl=1.10-2.12)

In this study, the maternal educational levels were not related to the risk of asthma. This is not compatible with the result of Lewis *et al*. (2017) cohort study done across all of European, which found children born to mothers in the lowest tertile of education were 46% more likely to develop asthma than children born to mothers in the highest tertile (95% CI 1.26, 1.71). Also, they concluded in general the relative and absolute asthma risk are inversely related to maternal education. In regard to parental education, this study showed paternal education for >15 years was associated with lower odds of asthma (OR=0.698, 95% CI=0.400-1.217). These results were comparable to Mendes *et al.* (2011) study who found that paternal but not maternal educational levels are significantly associated with asthma severity in children (aOR=2.49, 95% CI=1.04-5.99). Patients whose fathers have less than a high school education (<9 years of schooling) are more likely to have persistent asthma. Also, they stated the association between parental education and child health outcomes has been well recognized. The pathways through which parental education positively impacts child health remains to be clarified; however, two hypotheses have been proposed.

First, more educated parents may be more efficient "producers" of child health from given health inputs because they are more likely to adhere to medical advice and to adopt better child care practices or higher hygiene standards (productive efficacy). Alternatively, more educated parents may choose better health input mixes that generate more health outputs (allocative efficacy). It is generally believed that maternal education is the more critical determinant of child health; however, the relative roles of mothers' and fathers' education on child health outcomes vary substantially across countries with different social and cultural backgrounds. This may explain the difference between the results of different studies (Mendes *et al.*, 2011). A study by Cho *et al*. (2014) reported that the parental history of allergic diseases has increased the risk of the development of asthma and allergic diseases in their children. An increase in risk is seen to be higher in cases where both parents had a history of these diseases than in cases where only one of the parents had the history. They also found that parental medical history of allergic diseases increased the risk of the development of allergic diseases for their children. For a child whose parents had a history of allergic disease, the OR of ''ever'' having asthma was (OR=1.60, 95% CI = (0.95–2.67) and the OR for current asthma was 1.86 (95% CI 0.97–3.56) this result was opposite to our results that there is no association between a family history of asthma and asthma (OR=0.396, 95% CI=0.236-0.664). Whereas, the work of Pinto. (2021) found the parental history of asthma showed a protective effect on asthma control that was not reported elsewhere. As no differences in the rate of adherence to therapy were found, this effect might be

related to genetic and epigenetic factors that could have an influence on disease severity and responsiveness to the preventive therapy. This finding is comparable to our study finding.

In addition, the data of meta-analysis by Lim *et al*. (2011) showed that both maternal and paternal disease state affects offspring disease, and based on individual studies, maternal asthma is the more potent contributor. When analyzing all studies and comparing the two summary odds ratios, maternal asthma confers a greater risk of disease than does paternal asthma (OR 3.04 and 2.44, respectively). Also, children of non-asthmatic fathers are less likely to develop asthma than those of asthmatic fathers (summary OR 2.44, 95%CI: 2.14–2.79). This study result is not compatible with our results. In our studied children, the results showed there is no association between a family history of atopy and asthma (OR= 0.263, 95% CI=0.155-0.446). These results are inconsistence with the results of Indinnimeo *et al*. (2014) work that the diagnosis of atopy was positively associated with the mother's history of atopy (OR, 2.09; 95% CI, 1.15–3.77). Also, the current study result is different from the results of a study by Taveras *et al*. (2014) who reported that child with a parental history of allergic disease, the significant ORs were 2.86 (95% CI=2.20–3.72) for ''ever'' having asthma and 2.14 (95% CI=1.62–2.82) for ''current'' having asthma. Specifically, in families where both parents had allergic disease history; there was a higher risk of children developing asthma and allergic diseases.

The results of our study showed there is no association between the presence of pets in the house and asthma (OR =0.492, 95% CI= 0.274-0.884), which agrees with the results of Karunasekera *et al*. (2001) work concluded that pet at the home of different types such cat and dogs showed no association with asthma (OR=0.9, 95% Cl=0.7-1.3) and (OR=0.9, 95% Cl= 0.7-1.4) respectively. Our study results showed there is no association between the exposure of children to passive smoking and asthma (OR=0.743, 95% CI=0.457-1.205). This result came in agreement with the result of Burke *et al*. (2012) study, which reported the exposure to household passive smoke was not significantly associated with the incidence of wheeze in children aged 3 to 4 years (OR = 1.06, 95% CI = 0.88–1.27). On other hand, the same study found in children aged 2 years increased exposure to passive smoking was associated with an increased risk of persistent wheeze (OR per hour per week exposed = 1.14, 95% CI = 1.02–1.27), which is different from our result. They explain that the moderate levels of heterogeneity were partly attributable to study quality.

The results showed there is no association between maternal medication intake during pregnancy and asthma (OR=0.885, (95% CI) = (0.536-1.462)). This result is not comparable with the result of Al Fadhul & Al Dabbagh (2020) study who found that the increased odds of asthma were associated with the intake of medication tablets during pregnancy (OR(95% CI)= 3.22(1.29-8.04)). Also, a study by Indinnimeo *et al*. (2014) examined the association between prenatal treatment with antibiotics and the consequent development of atopic disease in two ways: by the number of courses of antibiotics during pregnancy and with treatment as a dichotomous predictor (i.e., any antibiotic use). Our study showed no significant association between maternal treatment for the common cold and asthma (OR=0.782, (95% CI)=(0.386-1.586)), which is comparable to the results of Al Fadhul & Al Dabbagh (2020) study which found there is no association between the mothers' treatment for a common cold during their pregnancies and the development of asthma OR (95% CI) =2.18 (1.37-3.49).

Our study showed the normal delivery of children had a protective factor and a decreased odds of asthma (OR= 0.621, 95% CI=0.383-1.006), which came in line with the study of Subbarao *et al*. (2009) who found that development of atopy was 2 to 3 times more likely among infants delivered by emergency cesarean section, although no such association occurred with elective cesarean section. Potential reasons for these findings include maternal stress and differences in the infant's gut microflora associated with different modes of delivery. Although some studies suggest lower birth weight is a risk factor for childhood asthma, others do not. For example, a study done by He *et al*. (2015) revealed that children born preterm had a significantly higher prevalence (P, 0.001) of asthma than children born to term. This finding was comparable to our study results that the preterm children had increased odds of asthma (OR=1.462, 95% CI=0.429-4.987).

This association has suggested may be due primarily to preterm births. Although others have observed increased asthma prevalence among full-term infants with low birth weight. Few previous studies have adjusted for gestational age in an attempt to isolate the effect of fetal growth from prematurity. The work of Taveras *et al*. (2006) stated there is no any definitive association between length of gestation and asthma-related outcomes. This finding is opposite to our study findings. The effect of breastfeeding on the risk of childhood asthma remains debated. A number of researchers have stated higher rates of asthma and allergy among children fed breast milk. While others have reported a protective effect of breastfeeding. In the meta-analysis study of Lim *et al*. (2010), they showed that exclusive breastfeeding for at least three months was connected with lower rates of asthma in children aged 2 to 5 years of age (preschool age), with the extreme effect happening among those with a parental history of atopy. This work is different from our study finding that showed a significant association between the feeding type of children and asthma. The exclusive breastfeeding for (≥ 6 months) showed a protective effect against asthma (OR=0.854, (95% CI) = (0.515-

1.416). On other hand, in a longitudinal birth cohort study by Gdalevich *et al*. (2001), they found breastfeeding was associated with a higher risk of atopic asthma in later childhood, with the greatest influence occurring among those with a maternal history of atopy.

In this study, a respiratory tract infection > 3 times was associated with higher odds of asthma (OR=5.144, 95% CI=3.199-8.271). This finding is consistent with De Benedictis & Attanasi (2008) study who stated that lower respiratory tract infections in the first years of life are associated with recurrent upper wheezing and later asthma. Led to a focus on the role and pathogenetic mechanisms of viral agents such as rhinoviruses and respiratory syncytial virus in asthma development. The role of bacterial agents in eliciting asthmatic symptoms in young children and in increasing the risk of asthma development has been emphasised as well. Indeed, the normal microbiota exerts profound effects on the mucosal immune system and may be determinant in human physiology and disease.

CONCLUSION

To conclude, the recognized risk and protective factors proposed that the development of asthma in preschool children is a result of combined demographic, natal, and postnatal factors. In which, being older (>3-5 Years) and being female had a protective effect against asthma. Also, the paternal, not maternal educational levels had a protective effect against asthma. None of the personal and environmental factors affected the development of asthma in our studied children. While, the greatest contribution in this study was from natal and post-natal factors in which mode of delivery, and type of feeding had a protective effect against asthma. Whereas, recurrent upper respiratory infections of more than three times a year increased the odds of asthma.

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