

# Risk Factors for Asthma among Preschool Children at Al-Najaf, Iraq: A Case Control Study

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## ABSTRACT

**Objectives:** To study epidemiological and clinical characteristics of asthmatic children, to find possible etiological risk factors, and the associated links to childhood asthma.

**Methods:** A matched case-control study was conducted at Al-Najaf governorate for a six-months period. The study samples were 300 children, 1-5 years old, attending the pediatric outpatient clinic at Al-Zahra Pediatric and Maternity Teaching Hospital. The data were collected through interviewing mothers of one hundred fifty asthmatic patients (case group), and one hundred fifty non-asthmatic children (control group). Data were included and analyzed, using different statistical tests by SPSS (version 20).

**Results:** A multivariate analysis for all significant risk factors, using a binary logistic regression adjusted for different confounders, showed that recurrent upper respiratory tract infections in the first year of life (OR (95% CI)=6.86 (2.89-16.29)), and intake of medication tablets during pregnancy (OR(95% CI)= 3.22(1.29-8.04)), are independent risk factors for asthma; whereas, an exclusive breastfeeding is a protective factor for asthma (OR(95% CI)=0.37 (0.16-0.83)).

**Conclusions:** Any medication intake during pregnancy and recurrent upper respiratory tract infections during the first year of life, increased the risk of childhood asthma, while an exclusive breastfeeding ( $\geq 6$  months) appeared to be a protective factor for asthma.

**Keywords:** Asthma, breastfeeding, preschool children, protective factor, risk factors

## INTRODUCTION

Asthma is the most common chronic disease during childhood [1]. The prevalence of childhood asthma has increased over the past three decades, and it is currently about 10% of a worldwide pediatric population [2]. It is associated with significant consequences, including missed school, limitations in activity, recurrent hospitalizations and emergency unit visits [3]. Both environmental and hereditary factors are important in the pathogenesis of asthma [4]. A family history of asthma and atopy are the major identifiable risk factors, contributing to severe and persistent asthma [5]. Exposure to different risk factors during the critical time of lung development influences the subsequent course of disease in infancy and childhood [6]. Some risk factors, such as impaired intrauterine growth and prenatal tobacco smoke exposure have been firmly established [7]. Other factors like diet and nutrition, use of antibiotics or paracetamol during pregnancy, mode of delivery, prematurity, and low birth weight may also affect the early development of allergy and asthma [8-10]. During infancy, putative risk factors include exposure to allergens; viral respiratory tract infections play an important role in the development of asthma [11]. However, breastfeeding was associated with decreased risk of childhood asthma as reported by meta-analysis study [12]. To the best of our knowledge, no studies conducted in Iraq that have investigated the risk factors of childhood asthma among preschool children. The current study was conducted to describe some epidemiological and clinical characteristics of asthmatic children, to find possible etiological risk factors, and the associated links to childhood asthma.

## PATIENTS & METHODS

**Study design and Setting:** A case-control study was conducted at Al-Zahra Pediatric and Maternity Teaching

Hospital in Al-Najaf governorate, Iraq, for the period of 1<sup>st</sup> of January to the 1<sup>st</sup> of July 2019.

**Subjects and Sampling:** The case group included one hundred fifty asthmatic patients, age 1-5 years, attending a pediatric outpatient clinic during the period of the study. The control group included one hundred fifty children, who were matched to cases by age, sex, and all were coming from the same community.

The sample size was calculated, considering the power of 80%, alpha of 5% and confidence level (CI) of 95%, while taking proportions equal to 0.57, and 0.73. Both case and control groups were selected randomly from an outpatient clinic. Any child who was not accompanied by their biological mothers, and who did not meet the selection criteria for the case and control groups, was excluded from the study. Inclusion criteria for cases were as follows: Diagnosed as asthmatic by consultant pediatrician, positive past history of prior three or more attacks of shortness of breath per year, and should respond well to anti-asthmatic medication; whereas, inclusion criteria for control were healthy or apparently healthy, and with no history of medical problem or chronic diseases.

**Ethical Approval:** An official letter from the Iraqi Board for Medical Specialization was directed to Al-Zahra Pediatric and Maternity Teaching Hospital to take the official agreement from the Research Ethical Committee for performing the research. Confidentiality and privacy were considered, and mothers of the patient were given the right to participate or not in the study, without any reward or, otherwise, penalties; yet neither of them refused to participate.

**Data Collection:** The specific prepared questionnaire form was filled by the investigator through a direct interview with the mothers. The questionnaire included demographic data such as sex, age, place of residence, parent education,

and probable risk factors like family history of asthma or atopy, exposure to passive smoking, any medication during pregnancy, presence of low birth weight, or preterm delivery, early postnatal factors such as exclusive breastfeeding, and recurrent respiratory infections.

**Exposure Assessment:** Exposure to passive smoking was defined as routine exposure, resulting from any family member who smoked daily in the same room(s) at home. Medication tablet intake was defined as any treatments, which were prescribed by an obstetrician, including antibiotics, tocolytic medication, antiemetic, analgesics, hypnotics, and medicine for the gastrointestinal symptoms or a common cold. Preterm delivery was defined as birth before 37 weeks of gestational age [13], and low birth weight was defined as birth weight, lower than 2500 grams [14], depending on mothers' report. For early postnatal exposures, information was gathered about breastfeeding, recurrent respiratory tract infections, which defined as three or more episodes of parental report of chest infections in the first year of life. Atopy is defined as atopic dermatitis or allergic rhinitis as reported by mother.

**Statistical Analysis:** patients' characteristics were described, using numbers, percentage, mean, and standard deviation. The characteristics of subjects with or without asthma were examined by chi-square test. The effect of each risk factor on developing childhood asthma was represented by odds' ratio (OR) and 95% confidence interval (CI); all tests were at 5% significance level. Binary logistic regression was used to assess the risk of childhood asthma for each individual type of exposure. All the models of logistic regression were adjusted for the parents' level of education, mother's age at the birth of this child, exposure of children to passive smoking, personal history of atopy, family history of asthma and atopy. Data were included and analyzed by SPSS version 20.

## RESULTS

The majority of cases and control (243 children) were living in urban areas; about 80.0% of cases, and 82.0% of controls; however, there is no significant association between residency and asthma ( $P = 0.66$ ). It was found that the rate of lower educational years ( $\leq 12$  years) of parents

was higher among parents of asthmatic children than in controls. Statistical analysis showed a highly significant association between maternal and paternal educational years and asthma ( $p < 0.001$ ). Most of cases had a positive family history of asthma (80,53.5%) versus (12,8.0%) of the control group. Similarly, cases were higher than the control group in the presence of a positive family history of atopy (92,61.3%), compared to (41,27.3%). A significant association was shown between family history of asthma, and family history of atopy with asthma ( $P < 0.001$ ). Percentage of children exposed to passive smoking was higher among asthmatic cases (53.3%) than controls (23.3%). A significant association was shown between a history of exposure to passive smoking with asthma ( $P < 0.001$ ), (Table 1). It was found that mean  $\pm$  SD for the mother's age at the birth of her child was  $24.28 \pm 6.110$  years for cases, and  $28.69 \pm 4.973$  years for controls. Statistical analysis, using independent t-test showed a highly significant difference ( $p < 0.001$ ,  $t = -6.85$ ).

This study showed that mothers of asthmatic children received more medication tablets during their pregnancy (53.3%), while in the mothers of controls (22.0%), a statistical significant association was demonstrated between medication intake during pregnancy and asthma ( $p = 0.01$ , OR (95% CI) = 3.22(1.29-8.04)) (Table 2). Further statistical analysis of the duration of the treatment had shown that mean  $\pm$  SD for medication exposure was  $4.87 \pm 4.93$  days for cases versus  $1.19 \pm 2.50$  days, for controls with a highly significant difference ( $p < 0.001$ ,  $t = -8.14$ ).

Mothers of asthmatic children took treatment for a common cold during their pregnancies, more than mothers of controls (50.7% vs 32.0%), adjusting of statistical analysis for different confounders revealed no significant relationship between asthma and gestational exposure to medications for common cold ( $p = 0.12$ , OR (95% CI) = 1.91(0.84-4.33) (Table 2). Analysis of the duration of the treatment had shown that mean  $\pm$  SD for a common cold medication exposure was  $2.33 \pm 2.44$  days for cases versus  $1.01 \pm 1.59$  days for controls, with a high significant difference ( $p < 0.001$ ,  $t = -5.56$ ).

Table 1: Sociodemographic characteristics of the studied children

Risk factors	Cases		Controls		P value
	N=150	%	N=150	%	
Gender					
Male	100	66.7	100	66.7	
Female	50	33.3	50	33.3	
Residency					
Urban	120	80.0	123	82.0	0.66
Rural	30	20.0	27	18.0	
Maternal education					
$\leq 12$ years	114	76.0	37	24.7	<0.001**
>12 years	36	24.0	113	75.3	
Paternal education					
$\leq 12$ years	98	65.3	32	21.3	<0.001**
>12 years	52	34.7	118	78.7	
Animal in the house					
Presence	46	30.7	32	21.3	0.07
Absence	104	69.3	118	78.7	
Family history of asthma					
Yes	80	53.5	12	8.0	<0.001**

No	70	46.7	138	92.0	
Family history of atopy					
Yes	92	61.3	41	27.3	<0.001**
No	58	38.7	109	72.7	
Personal history of atopy					
Yes	84	56.0	34	22.7	<0.001**
No	66	44.0	116	77.3	
Exposure to passive smoking					
Yes	80	53.3	35	23.3	<0.001**
No	70	46.7	115	76.7	

\*\*highly significant p value

Table 2: Antenatal, natal, and post-natal risk factors related to asthma among the children studied

Risk factors	Cases		Control		Unadjusted		Adjusted†	
	N	%	N	%	OR	95% C.I	OR	95% C.I
Medication tablet intake <sup>#</sup>								
Yes	80	53.3	33	22.0	4.05	(2.45-6.70)**	3.22	(1.29-8.04)*
No	70	46.7	117	78.0				
Treatment for a common cold								
Yes	76	50.7	48	32.0	2.18	1.37-3.49)**(	1.91	(0.84-4.33)
No	74	49.3	102	68.0				
Mode of delivery								
Vaginal	99	66.0	95	63.3	1.12	(0.68-1.86)		
Caesarean section	51	44.0	55	46.7				
Low birth weight								
Yes	42	28.0	12	8.0	4.47	(2.25-8.91)**	3.87	(0.27-56.06)
No	108	72.0	138	92.0				
Preterm delivery								
Yes	35	23.3	11	7.3	3.85	(1.87-7.91)**	0.90	(0.80-0.05)
No	115	76.7	139	92.7				
Type of feeding								
Exclusive breast(≥ 6 months)	65	43.3	85	56.7	0.59	(0.37-0.92)*	0.37	(0.16-0.83)*
Others <sup>§</sup>	85	56.7	65	43.3				
Recurrent respiratory infections								
> 3 times/year	121	80.7	61	40.7	6.09	(3.62-10.24)**	6.86	(2.89-16.29)**
≤ 3 times/year	29	19.3	89	59.3				

† All analyses were done using a binary logistic regression adjusted for different confounders

<sup>#</sup>any prescribed medications, <sup>§</sup>Include mixed and bottle-feeding, \*Significant p value

\*\*Highly significant p value, OR= Odds ratio, CI= Confidence interval

## DISCUSSION

Asthma is the most common respiratory disease in children. Several studies propose that the development of childhood asthma occurs primarily in the period between conception and three years old [6,9,10]. In the present study, the relationship between early life exposure to environmental factors and asthma is explored in detail.

Among the risk factors evaluated by different studies, parents' educational level, family history of asthma/atopy, personal history of atopy, and pre or postnatal exposure to passive smoking [15-17], had all significant values ( $P < 0.001$ ) in the current study.

Age of mother at the birth was one of the antenatal factors that was investigated in previous studies, which demonstrated either the greater risk of childhood asthma with younger maternal age [18] or older maternal age was significantly associated with increased risk of childhood asthma [19]. In this study, a significant difference ( $P < 0.001$ ) was found in the mean age of mothers  $24.28 \pm 6.11$  years for cases, and  $28.69 \pm 4.97$  years for controls, this indicate younger age of mothers at birth was significantly associated with risk of asthma in children.

Several meta-analyses have investigated the risk of childhood asthma with maternal paracetamol

(acetaminophen) intake during pregnancy. One study reported that paracetamol use during pregnancy was significantly associated with 1.2 times increased odds of wheeze at the ages of 2.5 years to 7 years [20]. Whereas, another study concluded that the association between gestational use of paracetamol and infant wheezing is, mainly, if not completely explained by confounding [21]. Current study found the same non-significant association ( $P = 0.12$ ).

Recent studies reported that maternal urinary tract infection and maternal use of antibiotic were considered as risk factors for childhood asthma [20,22]. In this study, after adjusting for possible confounders, intake of any medication tablet was associated with 3.2 times increased odds of childhood asthma.

Previous findings regarding the mode of delivery and the risk of asthma are contradictory; while some studies have shown that cesarean section is a risk factor for subsequent asthma [20,22]; others have failed to find an association [17]. Our study showed no significant association ( $P = 0.63$ ) between mode of delivery and childhood asthma.

Earlier studies [10,23] recorded that low birth weight, and preterm birth was associated with higher odds of wheezing disorders or asthma, but there was a wide

heterogeneity across studies. Currently, after adjustment of results for different confounders, we found that low birth weight and prematurity were not significantly associated with childhood asthma ( $P>0.05$ ). This contradiction in findings could be due to various factors, including the method of data collection, sample size, and study design.

Infant breastfeeding is strongly correlated with a reduction of respiratory morbidities in later childhood and adolescence [4]. A meta-analysis studies [12] reported that breastfeeding for six months or more, was associated with reduced odds of recent asthma and recent wheeze by 24 %, and 19%, respectively. Current findings showed that exclusive breastfeeding for at least six months, reduced odds of childhood asthma by 37%. Maternal milk may reduce the risk of asthma by reducing or preventing respiratory infections [24], promoting lung growth and development [25], and promoting maturation of the immune system [26].

Lower respiratory tract infection of infants with rhinovirus or respiratory syncytial virus has increased the risk of childhood asthma [27]. Viral infection stimulates immune responses and can interact with atopy to promote symptoms of asthma [11]. A meta-analysis study showed that hospitalization for respiratory syncytial virus infection in early life has increased the risk of childhood wheeze or asthma by 3.84 times [28]. Current results showed that recurrent respiratory tract infection increased the odds of childhood asthma by 6.86 times.

The main limitation of our study is the recall bias; the mothers of children in the current research were informed that the interview was about the children's health problems, instead of mentioning asthma primarily. Distant recall of prenatal and perinatal factors reported by biological mothers has been regarded as a reliable method [29,30]. Earlier studies demonstrated that maternal recall is mostly a valid measure for perinatal variables ten years after pregnancy. However, caution should be taken about variables such as medical problems, birth length, and substance use [29]. In our state, there are no existing health records, whether during pregnancy or later in life for newborns; therefore, the recall of mother is the only available source for assessment of exposure status.

## CONCLUSIONS

Mother intake of medications during pregnancy and early life recurrent respiratory tract infections are independent risk factors for childhood asthma. Exclusive breastfeeding ( $\geq 6$  months) is protecting from the risk of asthma. Therefore, mothers should be encouraged to breastfeed their babies exclusively, especially in the first months of life. They also should be educated about the risk of self-prescribing any medication during the pregnancy. In conclusion, large-scale studies are recommended to investigate the risk factors in more details, including type, dose of medication, and number of prescriptions during pregnancy, in addition to the type and severity of respiratory tract infection during the first year of life.

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**Conflict of Interest:** None.

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