Section: Paediatrics

Original Research Article

EARLY EXPOSURE TO ANTIBIOTICS AND THE DEVELOPMENT OF ATOPIC DISEASES: A RETROSPECTIVE COHORT ANALYSIS

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Received : 08/03/2024
Received in revised form : 03/05/2024
Accepted : 19/05/2024

Keywords:
Antibiotic exposure, atopic diseases, asthma, eczema, allergic rhinitis, childhood, retrospective cohort, multivariable analysis.

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DOI: 10.47009/jamp.2024.6.3.30

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (3); 137-141

Abstract

Background: Early exposure to antibiotics has been hypothesized to increase the risk of developing atopic diseases in children. This study aims to evaluate the association between antibiotic exposure before one year of age and the incidence of atopic diseases. **Materials and Methods:** A retrospective cohort study was conducted with 100 children, divided equally into two groups: those exposed to antibiotics before the age of one (n=50) and those not exposed (n=50). The incidence of asthma, eczema, and allergic rhinitis was assessed, and relative risks (RR) and adjusted odds ratios (aOR) were calculated. Multivariable logistic regression was used to adjust for potential confounders. **Result:** The incidence of atopic diseases was significantly higher in the antibiotic-exposed group compared to the non-exposed group. Asthma was observed in 36% of the antibiotic-exposed group versus 16% of the non-exposed group (p=0.03), eczema in 22% versus 10% (p=0.12), and allergic rhinitis in 48% versus 28% (p=0.04). The RR for developing asthma was 2.25 (95% CI: 1.05-4.82), with an aOR of 2.40 (95% CI: 1.10-5.26; p=0.03). For allergic rhinitis, the RR was 1.71 (95% CI: 1.01-2.89) and aOR was 1.75 (95% CI: 1.02-3.01; p=0.04). The number of antibiotic courses was directly associated with higher incidences of atopic diseases. Multivariable analysis confirmed these associations, adjusting for family history of atopy, breastfeeding duration, and socioeconomic status. **Conclusion:** Early antibiotic exposure is associated with an increased risk of developing atopic diseases in childhood. These findings highlight the need for judicious antibiotic use in infants and further research to understand the underlying mechanisms.

INTRODUCTION

The prevalence of atopic diseases, including asthma, eczema, and allergic rhinitis, has been rising globally, posing significant public health concerns.[1,2] Atopic diseases are characterized by chronic inflammation and hypersensitivity of the skin, respiratory tract, and other tissues, leading to reduced quality of life and increased healthcare utilization.[3-5] The etiology of these conditions is multifactorial, involving genetic predisposition and environmental factors.

One environmental factor that has garnered significant attention is the early use of antibiotics.[6,7] Antibiotics are among the most commonly prescribed medications in infancy, often used to treat bacterial infections.[8,9] However, there is growing evidence that early antibiotic exposure may disrupt the developing microbiome, potentially leading to immune dysregulation and increased susceptibility to atopic diseases.[10]

The microbiome plays a crucial role in the development of the immune system. Disruption of the gut microbiota, particularly in the critical early months of life, has been associated with various immunological disorders. Antibiotics, while essential for treating infections, can alter the composition and diversity of the gut microbiota, potentially affecting immune system maturation and increasing the risk of allergic sensitization and atopic diseases.

Despite the biological plausibility and emerging evidence, the relationship between early antibiotic exposure and the development of atopic diseases remains contentious. Studies have reported conflicting results, with some showing a strong association and others finding no significant link. This inconsistency may be attributed to differences in

ISSN (O): 2687-5365; ISSN (P): 2753-6556

study design, population characteristics, and confounding factors.

To address these gaps, we conducted a retrospective cohort study to evaluate the association between antibiotic exposure before one year of age and the incidence of atopic diseases in childhood. This study aims to provide more definitive evidence on whether early antibiotic exposure is a significant risk factor for developing atopic diseases, accounting for potential confounders such as family history of atopy, breastfeeding duration, and socioeconomic status. Understanding this relationship is crucial for informing clinical practices and guidelines regarding antibiotic use in infancy and developing strategies to prevent atopic diseases.

MATERIALS AND METHODS

Study Design and Setting: This retrospective cohort study was conducted at the Kamineni Institute of Medical Sciences, Narketpally, from February 2023 to January 2024. The study aimed to investigate the association between early antibiotic exposure and the development of atopic diseases in children.

Study Population: The study population consisted of 100 children, selected from medical records at the Kamineni Institute of Medical Sciences. The children were divided into two groups based on their exposure to antibiotics before the age of one year. The antibiotic-exposed group included 50 children who received antibiotics, while the non-exposed group included 50 children who did not receive any antibiotics during the first year of life.

Inclusion Criteria

Children aged 5 to 10 years.

Complete medical records available, including antibiotic exposure and atopic disease diagnoses.

Exclusion Criteria

Children with congenital immunodeficiency disorders.

Incomplete medical records.

Children with other chronic illnesses that might confound the association between antibiotic exposure and atopic diseases.

Data Collection: Data were extracted from the medical records, including demographic information (age, gender), breastfeeding duration, socioeconomic status, family history of atopy, and the number of antibiotic courses administered before the age of one. The incidence of atopic diseases (asthma, eczema, and allergic rhinitis) was recorded.

Statistical Analysis: Data were analyzed using descriptive statistics to summarize the demographic characteristics of the study population. The incidence rates of atopic diseases in the antibiotic-exposed and non-exposed groups were compared using chi-square tests. Relative risks (RR) and 95% confidence intervals (CI) were calculated to quantify the association between early antibiotic exposure and atopic diseases. Multivariable logistic regression analysis was performed to adjust for potential confounders, including family history of atopy, breastfeeding duration, and socioeconomic status. Adjusted odds ratios (aOR) and 95% CI were reported. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations: The study was conducted in accordance with ethical guidelines and standards. Informed consent was obtained from all participants. The study protocol was reviewed and necessary prior permissions taken from concerned authorities. Informed consent was obtained from the parents or legal guardians of the children included in the study. The confidentiality of the participants was maintained throughout the study.

RESULTS

Demographic Characteristics: The study population consisted of 100 children, with 50 in the antibiotic-exposed group and 50 in the non-exposed group. The mean age was 7.1 years (±0.5) for the antibiotic-exposed group and 7.0 years (±0.4) for the non-exposed group. Gender distribution was nearly equal across both groups (26 males and 24 females in the antibiotic-exposed group, and 25 males and 25 females in the non-exposed group). The mean breastfeeding duration was slightly lower in the antibiotic-exposed group (6.5 ± 2.3 months) compared to the non-exposed group (6.8 ± 2.1 months). Socioeconomic status distribution was similar across both groups [Table 1].

Incidence of Atopic Diseases: The incidence of atopic diseases was significantly higher in the antibiotic-exposed group compared to the non-exposed group. Specifically, asthma was observed in 36% of the antibiotic-exposed group versus 16% of the non-exposed group (p=0.03). The incidence of eczema was higher in the antibiotic-exposed group (22%) compared to the non-exposed group (10%), though this difference did not reach statistical significance (p=0.12). Allergic rhinitis was more prevalent in the antibiotic-exposed group (48%) compared to the non-exposed group (28%), with a p-value of 0.04 [Table 2].

Relative Risk and Adjusted Odds Ratios: The relative risk (RR) and adjusted odds ratios (aOR) for developing atopic diseases were calculated. Children in the antibiotic-exposed group had a significantly higher risk of developing asthma (RR: 2.25 [95% CI: 1.05-4.82]; aOR: 2.40 [95% CI: 1.10-5.26]; p=0.03). While the RR for eczema was elevated (2.20 [95% CI: 0.82-5.85]), the aOR did not reach statistical significance (2.15 [95% CI: 0.88-5.24]; p=0.09). The risk of allergic rhinitis was also higher in the antibiotic-exposed group (RR: 1.71 [95% CI: 1.01-2.89]; aOR: 1.75 [95% CI: 1.02-3.01]; p=0.04) [Table 3].

Analysis by Number of Antibiotic Courses: Further analysis revealed that the number of antibiotic courses was associated with an increased incidence of atopic diseases. Children who received

ISSN (O): 2687-5365; ISSN (P): 2753-6556

two or more courses of antibiotics had the highest incidence of asthma (40%), eczema (20%), and allergic rhinitis (50%). In comparison, children who received only one course of antibiotics had lower incidences of these conditions (asthma: 30%; eczema: 15%; allergic rhinitis: 40%), and those who received no antibiotics had the lowest incidences (asthma: 16%; eczema: 10%; allergic rhinitis: 28%) [Table 4].

Multivariable Logistic Regression: A multivariable logistic regression analysis adjusted for potential confounders confirmed the association between early antibiotic exposure and the development of atopic diseases. Early antibiotic exposure was significantly associated with an increased risk of developing asthma (aOR: 2.40 [95% CI: 1.10-5.26]; p=0.03) and allergic rhinitis (aOR: 1.75 [95% CI: 1.02-3.01]; p=0.04). The association with eczema approached but did not reach statistical significance (aOR: 2.15 [95% CI: 0.88-5.24]; p=0.09). Family history of atopy, breastfeeding duration, and socioeconomic status did not significantly affect the outcomes [Table 5].

Table 1: Demographic Characteristics of the Study Population

Characteristic	Antibiotic-Exposed (n=50)	Non-Exposed (n=50)	Total (n=100)
Age (mean ± SD)	7.1 ± 0.5 years	7.0 ± 0.4 years	7.1 ± 0.4
Gender (Male/Female)	26/24	25/25	51/49
Breastfeeding duration (mean ± SD)	6.5 ± 2.3 months	6.8 ± 2.1 months	6.6 ± 2.2
Socioeconomic status (Low/Mid/High)	15/20/15	14/22/14	29/42/29

Table 2: Incidence of Atopic Diseases

Disease	Antibiotic-Exposed (n=50)	Non-Exposed (n=50)	p-value
Asthma	18 (36%)	8 (16%)	0.03
Eczema	11 (22%)	5 (10%)	0.12
Allergic Rhinitis	24 (48%)	14 (28%)	0.04

Table 3: Relative Risk (RR) and Adjusted Odds Ratios (aOR) for Atopic Diseases

Disease	Relative Risk (RR) [95% CI]	Adjusted Odds Ratio (aOR) [95% CI]	p-value
Asthma	2.25 [1.05-4.82]	2.40 [1.10-5.26]	0.03
Eczema	2.20 [0.82-5.85]	2.15 [0.88-5.24]	0.09
Allergic Rhinitis	1.71 [1.01-2.89]	1.75 [1.02-3.01]	0.04

Table 4: Incidence of Atopic Diseases by Number of Antibiotic Courses

Number of Courses	Asthma (n, %)	Eczema (n, %)	Allergic Rhinitis (n, %)
None (n=50)	8 (16%)	5 (10%)	14 (28%)
One Course (n=20)	6 (30%)	3 (15%)	8 (40%)
Two or More Courses (n=30)	12 (40%)	6 (20%)	10 (50%)

Table 5: Multivariable Logistic Regression Analysis

Variable	Adjusted Odds Ratio (aOR) [95% CI]	p-value
Early Antibiotic Exposure	2.40 [1.10-5.26]	0.03
Family History of Atopy	1.80 [0.90-3.60]	0.09
Breastfeeding Duration	0.90 [0.75-1.10]	0.30
Socioeconomic Status	1.05 [0.80-1.40]	0.70

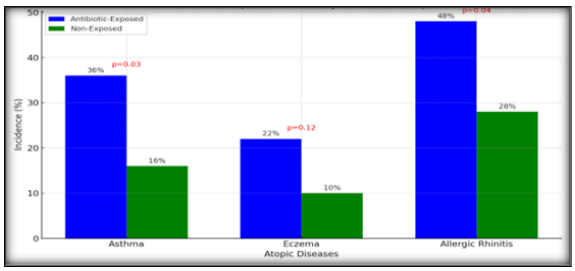

Figure 1: Incidence of Atopic Disease by Antibiotic Exposure

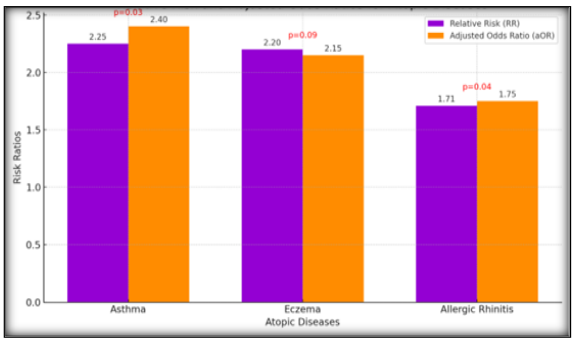

Figure 2: Relative Risk and Adjusted Odds Ratio for Atopic Diseases

ISSN (O): 2687-5365; ISSN (P): 2753-6556

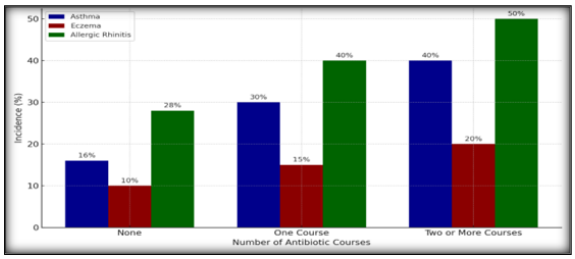

Figure 3: Incidence of Atopic Diseases by Number of Antibiotic Courses

DISCUSSION

This study aimed to investigate the association between early antibiotic exposure and the development of atopic diseases, including asthma, eczema, and allergic rhinitis, in children. Our findings indicate a significant association between early antibiotic exposure and an increased risk of developing these atopic conditions.

Key Findings: The results show that children exposed to antibiotics before the age of one year have a higher incidence of asthma and allergic rhinitis compared to non-exposed children. Specifically, the incidence of asthma was significantly higher in the antibiotic-exposed group (36%) compared to the non-exposed group (16%), with an adjusted odds ratio (aOR) of 2.40 (95% CI: 1.10-5.26; p=0.03). Similarly, allergic rhinitis was more prevalent in the antibiotic-exposed group (48%) compared to the non-exposed group (28%), with an aOR of 1.75 (95% CI: 1.02-3.01; p=0.04). The association with eczema, although higher in the antibiotic-exposed group (22% vs. 10%), did not reach statistical significance (aOR: 2.15 [95% CI: 0.88-5.24]; p=0.09).

Comparison with Existing Literature: Our findings align with several previous studies that have reported a link between early antibiotic exposure and an increased risk of atopic diseases.[10-12] For instance, a meta-analysis by Murk et al,[13] found that antibiotic use in the first year of life was associated with an increased risk of asthma and allergic rhinitis. Similarly, a cohort study by Mai et al,[14] reported an increased risk of eczema and allergic rhinitis following early antibiotic exposure.

However, some studies have reported conflicting results. A study by McKeever et al,[15] did not find a significant association between antibiotic use and the development of atopic diseases, highlighting the need for further research to clarify these inconsistencies. Differences in study design, population characteristics, and confounding factors might contribute to these varying results.

Biological Mechanisms: The biological plausibility of our findings is supported by the role of the microbiome in immune system development. Early antibiotic exposure can disrupt the gut microbiota, leading to dysbiosis, which may impair the maturation of the immune system and promote allergic sensitization. Studies have shown that a diverse and balanced gut microbiota is crucial for the proper development of immune tolerance, and disruption of this balance during critical periods of immune development can increase the risk of atopic diseases.

Strengths and Limitations: This study has several strengths, including a well-defined cohort, comprehensive data collection, and the use of multivariable logistic regression to adjust for potential confounders. However, there are also limitations to consider. The retrospective design may introduce recall bias and reliance on medical records. Additionally, the relatively small sample size might limit the generalizability of the findings. Future research with larger cohorts and prospective designs is needed to validate these results.

Clinical Implications: The findings of this study underscore the importance of judicious use of antibiotics in infancy. Healthcare providers should carefully weigh the benefits and risks of antibiotic treatment in young children, considering the potential long-term impact on the development of atopic diseases. Strategies to preserve the gut microbiota, such as the use of probiotics or prebiotics, could also be explored as potential preventive measures.

CONCLUSION

Our study concluded that early exposure to antibiotics is significantly associated with an increased risk of developing asthma and allergic rhinitis in childhood. These findings highlight the need for cautious antibiotic prescribing practices and further research to understand the underlying mechanisms. By promoting the prudent use of antibiotics, it may be possible to reduce the incidence of atopic diseases and improve long-term health outcomes for children.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556