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Unmasking the Link: Maternal Anxiety and Allergic Rhinitis in Offspring Based on a Case-Control Study

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Abstract

Background: Prenatal mental state is related to offspring health and disease occurrence. However, research concerning the relationship between prenatal anxiety and the incidence of allergic diseases in offspring remains limited. This study tried to explore the potential link between prenatal anxiety, adverse events, and the development of allergic rhinitis in children. **Methods:** The study employed a case-control design incorporating a total of 303 children diagnosed with allergic rhinitis and an age and gender matched control group of 303 healthy children. Comprehensive data regarding the children, their mothers, and maternal pregnancy details were collected from both groups. The Odds Ratio for allergic rhinitis in children was determined using multivariate logistic regression analysis. **Results:** After considering relevant confounding factors, logistic regression analysis showed that maternal anxiety during pregnancy increased the risk of children's allergic rhinitis by 1.689 times (OR = 2.689, $P < 0.001$). Additionally, the total number of negative events during pregnancy increased the risk of allergic rhinitis in children by 0.482 times (OR = 1.482, $P < 0.001$), particularly when mothers experienced injury, illness, inexplicable irritation, or abnormal fetal development was detected during pregnancy. **Conclusions:** The study demonstrated that prenatal anxiety and negative life events could increase the development of children's allergic rhinitis. These findings suggest

that implementing strategies to mitigate prenatal anxiety could be beneficial in reducing the incidence of childhood allergic rhinitis.

Keywords

Prenatal Anxiety, Negative Events during Pregnancy, Children's Allergic Rhinitis

1. Introduction

Allergic rhinitis is a common chronic disease in children [1]. Global studies indicate an approximate worldwide incidence rate of 12.66% in children [2]. The prevalence of children's allergic rhinitis significantly influences the learning and developmental processes of children. If left uncontrolled, it may escalate into severe conditions such as asthma, nasal polyps, sinusitis, and in extreme cases, pose a threat to their lives [3]. The primary causes of pediatric allergic rhinitis are typically hereditary factors and exposure to environmental elements. But current research increasingly indicates that the onset of these conditions can be traced back to the earliest stages of life.

Maternal mental health represents a significant global health burden. Maternal psychological issues during pregnancy have been linked to a variety of adverse health outcomes in offspring. For instance, prenatally distressed women are more likely to have a low birth weight baby as well as a preterm birth baby [4]-[6]. Some studies reported that exposure to severe life events may increase the risk ratio of congenital malformations and small gestational age in very preterm babies [7] [8]. Children born to mothers who experience high levels of psychological distress during pregnancy are at a heightened risk for cognitive, emotional, and physical health issues, which often persist throughout their lives [9]-[11]. Recently, the correlation between maternal stress during pregnancy and offspring allergic diseases has also attracted attention. The study by Li *et al*. [12] suggested a correlation between maternal depression symptoms, both antenatal and postnatal, and the incidence of allergic rhinitis in offspring. Study indicated that children born to mothers who underwent stressful events during gestation have a heightened risk of developing allergic rhinitis during their childhood in Italy [13]. Nevertheless, the children physician-diagnosed allergic rhinitis in 0 - 24 months was not associated with maternal prenatal anxiety [14].

Therefore, literature addressing the relationship between prenatal anxiety and the incidence of allergic disease in offspring is limited and inconsistent so far. This retrospective case-control study is going to fill the gap and investigate the correlation between maternal anxiety and negative life events during pregnancy and the incidence of allergic rhinitis, covering the whole age of childhood. Our study would helpfully provide a theoretical framework for implementing appropriate clinical interventions for expectant mothers and to establish relevant health edu-

cation for the prevention of allergic rhinitis in offspring, which holds significant practical implications.

2. Methods

2.1. Study Design and Population

This case-control study was conducted at the First Affiliated Hospital of Hunan Normal University between May and October 2021. A total of 303 children who were diagnosed with allergic rhinitis and their parents were invited to participate in the case group, while 303 children of the same sex and age who received physical examinations in the hospital and their parents were included in the control group. The study received approval from the Ethics Committee of Hunan Normal University (approval number: 2021-238), and informed written consent was obtained from all participants.

2.1.1. Inclusion Criteria for Case Group

Children have been diagnosed with allergic rhinitis based on the diagnostic criteria of allergic rhinitis by an otolaryngologist. The diagnosis of allergic rhinitis in children was based on 1) typical symptoms (nasal itching, sneezing, watery rhinorrhea, and nasal congestion) for at least 1 year; 2) positive skin prick tests; and 3) positive serum total IgE test. Inclusion criteria are: singleton infants and children aged 1 - 14 years. The children's mothers were normal in language, communication, and thinking.

2.1.2. Exclusion Criteria for Case Group

Children have other major diseases, such as leukemia, epilepsy, congenital heart disease, etc. The child's mothers had mental, consciousness, and communication disorders.

2.1.3. Inclusion Criteria for Control Group

Children have no allergic rhinitis. Children with no typical symptoms (nasal itching, sneezing, watery rhinorrhea, and nasal congestion) for at least 1 year were considered to have no allergic rhinitis by a doctor from the physical examination department. The inclusion criteria were singleton children, and the children's mothers were normal in language, communication, and thinking.

2.1.4. Exclusion Criteria for Control Group

Children have other allergic diseases, such as contact dermatitis, urticaria, eczema, etc. Children have other major diseases, such as leukemia, epilepsy, congenital heart disease, etc. The child's mothers had mental, consciousness, and communication disorders.

2.2. Research Tools

Based on established diagnostic guidelines for children with allergic rhinitis [15], a review of pertinent literature, and consultations with domain experts, the ques-

tionnaire was meticulously designed to align with the research objectives. It encompasses sections on general demographic information and maternal pregnancy conditions. Psychological conditions were assessed using the Pregnancy-Related Anxiety Scale and the Maternal Life Events Scale.

The Pregnancy Anxiety Scale was initially developed by Burstein in 1974 [16]. This study utilized the Pregnancy-related Anxiety Scale, which is derived from the PAS and was specifically adapted by researcher Xiao Limin [17] to reflect the characteristics of pregnant women in China. The scale comprises 13 items, and each has 4 levels of rating: "No worries" (score 1), "Occasionally worried" (score 2), "Often worried" (score 3), and "Always worried" (score 4). The scale has demonstrated good reliability and validity [17] [18]. According to the findings of Jingli Zhang [19], a total score of 24 points is employed to assess the presence of pregnancy-related anxiety in pregnant women. A final score of ≥24 points indicates the presence of pregnancy-related anxiety, whereas a score of ≤24 points suggests the absence of such anxiety.

The Maternal Life Events Scale [20] is designed to identify significant life events experienced by women during any stage of pregnancy. It covers 53 events across various stress categories like work, study, family, and society. Research by Wei Pang and Mali Jiang has confirmed the scale's reliability and validity. Negative events experienced by each individual are assigned a value of one point. The cumulative total of these points for each individual constitutes their total negative event score during pregnancy.

2.3. Clinical Data Collection

2.3.1. General Demographic Information

1) Mother: nationality, educational level, personal monthly income, allergy history, and allergic disease.

2) Children: gender, age, height, weight, nationality, place of residence, allergy history, and allergic diseases.

2.3.2. Mother's Pregnancy Condition

1) General information: gestational age, gestational history, exercise, and occupation.

2) Disease status: including whether to suffer from allergic diseases, infections, colds, and pregnancy diseases (hypertension, diabetes, and heart disease, etc.).

3) Psychological status: Pregnancy-related Anxiety Scale and Maternal Life Events Scale were used to evaluate the psychological status of the participants.

2.4. Statistical Analysis

Continuous variables with normally distributed data are expressed as means and standard deviations, and a t-test was used to compare variables between two groups. The median and quartiles (Q1-Q3) were utilized for non-normally distributed continuous variables, and the Mann-Whitney non-parametric test was used to compare the variables between groups. Cases (n) and percentages (%) were employed to rep-

resent categorical variables, while the chi-square test was utilized to compare between groups. Adjusted odds ratios for the association between prenatal psychological factors and children's allergic rhinitis were generated with regression modeling using the SPSS binary logistic regression (SPSS Inc, Chicago, IL). A *P* value less than 0.05 was considered statistically significant. Data were analyzed using SPSS 27.0.

3. Results

3.1. Children's General Characteristics

As shown in Table 1, the average age in the two groups is 8.3 years old. The rate for boys in both groups was 66%. There was no significant difference in age, gender, or nationality between the two groups. Upon comparison, it was determined that there were no significant differences in age, gender, and nationality between the two groups ($P > 0.05$), suggesting that the groups were well-balanced and suitable for comparative analysis. However, a statistically significant difference was observed in terms of residence between the two groups ($P < 0.05$). The relevant parameters are detailed in Table 1.

Table 1. Characteristics of children in cases and controls.

Variables		Case Group (%) (n = 303)	Control Group (%) (n = 303)	χ^2/Z	*P*
Nationality	Han	294 (97.0)	286 (94.4)	2.572	0.109
	Minority	9 (3.0)	17 (5.6)		
Age (Year)		8.32 ± 2.74	8.10 ± 2.99	−0.935	0.350
Gender	Boy	200 (66.0)	200 (66.0)		
	Girl	103 (34.0)	103 (34.0)		
Place of Residence	Country	39 (12.9)	61 (20.1)	5.797	0.016
	Urban	264 (87.1)	242 (79.9)		

3.2. Maternal General Characteristics

Analysis shows that there were no significant differences in nationality, educational level, personal monthly income, or history of drug allergy between the two groups ($P > 0.05$). But 27.4% participants had a family history of allergies, 34.0% participants had allergic diseases, and 12.5% participants had a history of food allergy in the case group. These three items were significantly higher than the control group ($P < 0.05$) (Table 2).

3.3. Maternal General Condition during Pregnancy

The statistical results showed that there were no significant differences in age, par-

ity, and exercise during pregnancy between the two groups ($P > 0.05$). But 12.2% participants participants pursued high-risk occupations, and 16.5% participants had pregnancy complicating disease in the case group. These four items were significantly higher than the control group ($P < 0.05$) (Table 3).

Table 2. Mother's characteristics of cases and controls.

Variables		Case Group (%) (n = 303)	Control Group (%) (n = 303)	χ^2/Z	*P*
Nationality	Han	295 (97.4)	291 (96.0)	0.827	0.363
	Minority	8 (2.6)	12 (4.0)		
Educational Level	Elementary School	1 (0.3)	6 (2.0)	3.756	0.447
	Middle School	30 (9.9)	30 (9.9)		
	High School	61 (20.1)	65 (21.5)		
	Junior College	81 (26.7)	77 (25.4)		
	Bachelor or Above	130 (42.9)	125 (41.3)		
Personal Monthly Income (RMB)	No	44 (14.5)	49 (16.2)	4.790	0.309
	≤3000	15 (5.0)	23 (7.6)		
	3000 - 4999	61 (20.1)	72 (23.8)		
	5000 - 7999	105 (34.7)	87 (28.7)		
	≥8000	78 (25.7)	72 (23.8)		
History of Drug Allergy	No	276 (91.1)	289 (95.4)	4.421	0.035
	Yes	27 (8.9)	14 (4.6)		
Allergic Disease	No	200 (66.0)	294 (97.0)	96.779	<0.001
	Yes	103 (34.0)	9 (3.0)		
Family History of Allergy	No	220 (72.6)	294 (97.0)	70.175	<0.001
	Yes	83 (27.4)	9 (3.0)		
History of Food Allergy	No	265 (87.5)	292 (96.4)	16.186	<0.001
	Yes	38 (12.5)	11 (3.6)		

Table 3. Maternal general condition during pregnancy between the two groups.

Variables		Case Group (%) (n = 303)	Control Group (%) (n = 303)	χ^2/Z	*P*
Age (Year)	≤25	101 (33.3)	98 (32.3)	0.509	0.775
	25 - 30	151 (49.8)	159 (52.5)		
	>30	51 (16.8)	46 (15.2)		
Parity	1	171 (56.4)	188 (62.0)	1.975	0.160
	≥1	132 (43.6)	115 (38.0)		
Exercise	No	13 (4.3)	20 (6.6)	2.181	0.336
	Sometimes	134 (44.2)	140 (46.2)		
	Frequently	156 (51.5)	143 (47.2)		
High-Risk Occupations*	No	37 (12.2)	300 (99.0)	30.942	<0.001
	Yes	37 (12.2)	3 (1.0)		
Pregnancy Complicating Disease#	No	253 (83.5)	293 (96.7)	29.597	<0.001
	Yes	50 (16.5)	10 (3.3)		

*: High-risk occupations during pregnancy (chemistry & chemical industry, rubber and plastic production, paint or decoration, wood processing and production, agriculture, leather and fur manufacturing, building materials production). #: Hypertension, diabetes, heart disease, viral hepatitis, and iron deficiency anaemia.

3.4. Maternal Psychological Condition during Pregnancy

According to the Pregnancy-Related Anxiety Scale, 24.8% of patients in the case group and 5.9% participants in the control group experienced anxiety during pregnancy. The difference between the two groups was statistically significant ($P < 0.05$). Among the 53 identified negative events, four items were significantly more prevalent in the case group compared to the control group. By categorizing participants based on the third quartile of total negative events experienced during pregnancy, it was observed that 44.6% of patients in the case group and 23.4% participants in the control group exhibited a high total negative event score. This difference between the two groups was statistically significant ($P < 0.05$) (Table 4).

Table 4. Comparison of maternal anxiety and negative events during pregnancy between the two groups.

Variables		Case Group (%) (n = 303)	Control Group (%) (n = 303)	χ^2	*P*
Anxiety	No	228 (75.2)	285 (94.1)	41.269	<0.001
	Yes	75 (24.8)	18 (5.9)		
Question 3	No	195 (64.4)	259 (85.5)	35.969	<0.001
	Yes	108 (35.6)	44 (14.5)		
Question 9	No	237 (78.2)	268 (88.4)	11.418	0.001
	Yes	66 (21.8)	35 (11.6)		
Question 12	No	275 (90.8)	297 (98.0)	15.081	<0.001
	Yes	28 (9.2)	6 (2.0)		
Question 36	No	230 (75.9)	272 (89.8)	20.475	<0.001
	Yes	73 (24.1)	31 (10.2)		
Total Score	<Q3	168 (55.4)	232 (76.6)	30.123	<0.001
	≥Q3	135 (44.6)	71 (23.4)		

Question 3: I have sustained an injury or an illness; Question 9: I have encountered multiple miscarriages or prolonged infertility; Question 12: Abnormal fetal development has been detected; Question 36: I occasionally experience inexplicable irritation; Q3: The third quartile of total negative event score during pregnancy (Figure 1).

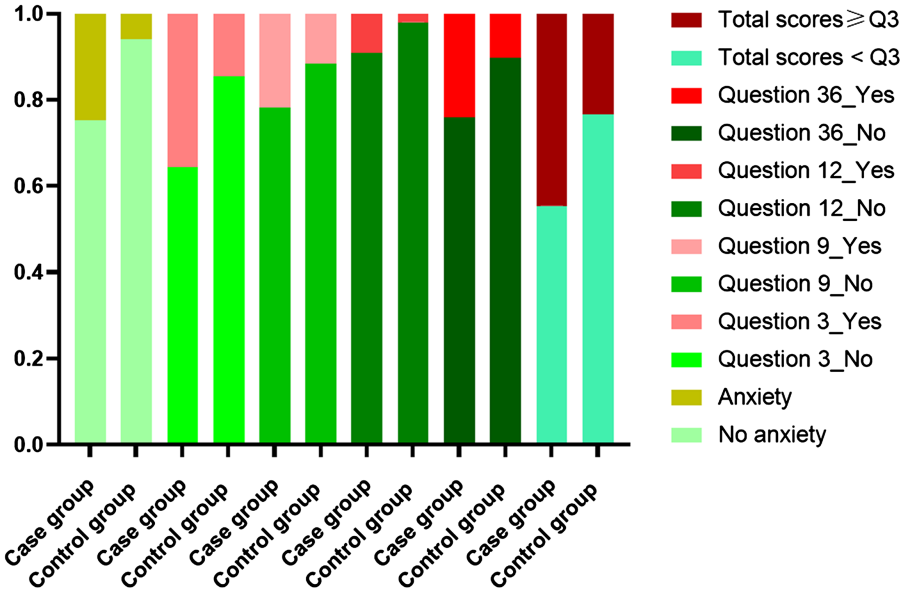

Figure 1. Comparison of maternal anxiety and negative events during pregnancy between the two groups.

3.5. Logistic Analysis of Maternal Psychological Condition during Pregnancy with Children's Allergic Rhinitis

Maternal high-risk occupations, pregnancy-complicating diseases, history of drug allergies, allergic diseases, family history of allergies, history of food allergies, and place of residence were considered as confounding factors. Logistic regression analysis revealed that maternal anxiety during pregnancy increased the risk of allergic rhinitis in children by 1.689 times (OR = 2.689, $P < 0.001$). Additionally, the total number of negative events during pregnancy increased the risk of allergic rhinitis in children by 0.482 times (OR = 1.482, $P < 0.001$), particularly when mothers experienced injury, illness, inexplicable irritation, or abnormal fetal development was detected. After considering the confounding factors, the Q9 item was no longer a risk factor but a protective factor. This exception might be because of a sample size problem (Table 5).

Table 5. Logistic analysis of the link between maternal anxiety and negative pregnancy events with children's allergic rhinitis.

		B	SE	Wald	*P*	OR (95% CI)
Anxiety	No					1
	Yes	0.989	0.140	50.154	<0.001	2.689 (2.045, 3.536)
Question 3	No					1
	Yes	0.459	0.166	7.652	0.006	1.582 (1.143, 2.189)
Question 9	No					1
	Yes	−0.315	0.150	4.371	0.037	0.730 (0.544, 0.981)
Question 12	No					1
	Yes	0.649	0.194	11.176	0.001	1.913 (1.308, 2.798)
Question 36	No					1
	Yes	0.852	0.134	40.414	<0.001	2.344 (1.802, 3.047)
Total Score	<Q3					1
	≥Q3	0.393	0.145	7.345	0.007	1.482 (1.115, 1.969)

Logistic statistic analysis was used, and confounding factors include maternal high-risk occupations, pregnancy complicating disease, history of drug allergy, allergic disease, family history of allergy, history of food allergy, and place of residence (Figure 2).

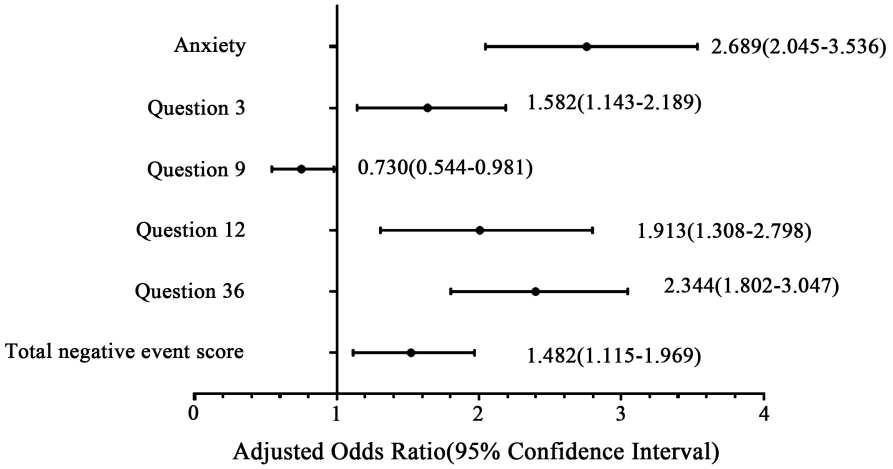

Figure 2. Forest plot of logistic analysis assessing the association between maternal anxiety and negative events during pregnancy and children's allergic rhinitis.

4. Discussion

The findings of this study, which involved a Chinese population, provide compelling evidence linking maternal prenatal anxiety and negative pregnancy events to the development of allergic rhinitis in children. This association underscores the importance of maternal mental health during pregnancy and its potential long-term implications for child health.

Maternal anxiety during pregnancy is an area of growing concern. Research has shown that elevated levels of anxiety in expectant mothers are directly linked to increased rates of developmental disorders and respiratory issues in their children [21] [22]. In the present study, we found the increased risk of children's allergic rhinitis among women with more life event stress and anxiety during pregnancy, which was consistent with previous studies [13] [23]. This highlights the critical need to address psychological well-being in pregnant women, as anxiety can manifest in various forms, impacting not just the immediate health of the mother but also the long-term health prospects of the child.

The underlying mechanisms through which maternal anxiety affects offspring health are complex and multifactorial. Stress-induced alterations in maternal hormone levels, such as cortisol [24], can lead to significant changes in the intrauterine environment. Several animal studies have demonstrated that prenatal stress exerts an adaptive programming effect on the healthy development of offspring, influencing aspects such as growth, development, and immune function [25] [26]. Furthermore, maternal anxiety may influence prenatal behaviors, including diet and substance use, further exacerbating the risk of developmental issues [24]. Additionally, genetic and epigenetic factors activated by maternal stress may play a crucial role, contributing to the expression of susceptibility to conditions like allergic rhinitis and other chronic diseases. Understanding these mechanisms is essential for developing effective interventions aimed at mitigating the risks associated with maternal anxiety during pregnancy.

There are some limitations in this study. First, this was a single-center case-control study, and the sample size was not very large. Secondly, the mother's condition during pregnancy was reviewed retrospectively. Hence, recall bias might exist. Therefore, multicenter prospective studies with larger sample sizes are needed in the future.

5. Conclusion

Given the extensive prevalence of allergic rhinitis, it is vital for public health initiatives to understand the factors contributing to the onset of allergic disorders. Developing strategies to cope with prenatal anxiety may reduce the incidence of childhood allergic rhinitis. A variety of strategies can be employed to promote mental wellness among expectant mothers, such as stress management programs, psychiatric support, and community-based interventions. There is a need for further research into the specific interventions most effective in reducing maternal anxiety and, therefore, reducing the risk of allergic rhinitis in their children. The goal would be to formulate targeted health policies that prioritize mental health during pregnancy, which would result in improved child health outcomes.

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Authors' Contributions

Conceptualization: Yunpeng Dong, Jian Li. Funding acquisition: Jian Li. Investigation: Yaqian Zhou, Junrong Chen. Methodology: Yunpeng Dong, Yide Yang, Jian Li. Supervision: Yunpeng Dong, Jian Li. Validation: Yunpeng Dong, Yide Yang, Jian Li. Writing-original draft: Yaqian Zhou, Jian Li. Writing-review & editing: Yunpeng Dong, Jian Li.

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Conflicts of Interest

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

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