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Original Article

Mode of delivery and risk of asthma in children 5-14 years old in Tabriz, Iran

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Abstract

Introduction: It has been suggested that a cesarean section increases risk of developing asthma due to lack of exposure to maternal microflora during birth. To investigate the association between the mode of delivery and the risk of asthma in children aged 5-14 years in Tabriz, Iran.

Methods: A case-control study was performed on 233 (case = 81, control = 152) children aged 5-14 years referred to outpatient clinics of Tabriz Children's Hospital and Sheikhorraiz Clinic in 2014. Clinical asthma diagnosis was done according to Global Initiative for Asthma Criteria. A questionnaire was administered to obtain a demographic, environmental, and clinical history. Age-sex frequency matching with cases was carried out during sampling for controlling of possible confounding effects of age and sex for asthma.

Results: Of 233 children, 53.6% of them were male (case group = 54.3% and control group = 53.3%). Over half (54.5%), the participants had been delivered by caesarian section. Cases were not significantly more likely to have been delivered by caesarian section as compared to controls [adjusted odds ratio (AOR) = 0.69; 95% confidence interval (CI) = 0.34-1.42]. However, more frequent episodes of common cold [$\beta = 0.094$; standard error (SE) (β) = 0.031, $P < 0.001$], birth order (second born children compared to firstborns) (AOR = 2.54; 95% CI = 1.18-5.46), high maternal education levels: 12 years (AOR = 3.76; 95% CI = 1.10-12.9), collegiate (AOR = 6.12; 95% CI = 1.43-26.20), and intra-family marriage (AOR = 2.89; 95% CI = 1.21-6.89) were associated with childhood asthma.

Conclusion: Delivery mode was not associated with risk of developing childhood asthma in our study. Intra-family marriage increased the odds of childhood asthma. Further study on the relationship between maternal education and the odds of asthma is proposed.

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Introduction

Asthma is a chronic inflammatory disorder of the airways, in which the inflamed airways are hyper-responsive chronically and become obstructed. Airflow is restricted by

bronchoconstriction, mucus plugs, and increased inflammation when airways are exposed to various risk factors. Asthma is the main cause of chronic morbidity worldwide, and its prevalence has increased extremely

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for past 20 years, especially in children. It is estimated that 300 million individuals are affected all over the world.¹

In a descriptive meta-analysis survey based on the International Study of Asthma and Allergies in subjects under 18 years old in Iran, the least prevalence was in Kerman (2.7%), Iran, and the highest prevalence was in Tehran (35.4%), Iran, and the prevalence in Tabriz, Iran, was 3.95%, the average prevalence at a national level in Iran was estimated 13.14%.² However, the prevalence of asthma among middle school students (average age = 12.56 years was 2%) in Tabriz.³ The causes of asthma are still unknown, and it is likely to be multifactorial. Many genetic and environmental factors and complex interactions are involved in it.⁴

Asthma risk factors include tobacco smoke, pollens and molds, cockroaches, house dust mites, having pets, air pollution, chemical irritants and drugs, occupational irritants, foods and additives, respiratory (viral) infections, exercise, and strong emotional expressions.¹ Furthermore, a possible association between caesarean section and asthma has been investigated in preceding studies with conflicting results.⁵⁻¹⁸ An incipient microbiological colonization may vary among infants born by vaginal delivery and infants born by caesarean section, and this has been deemed as a possible determinant of asthma. It is hypothesized that the microbial flora may affect the immune system in early childhood and alter the equilibrium between Th1 and Th2 helper cells and that imbalance may be associated with allergic asthma. The caesarean section rate has increased during the past 20-30 years in the world.¹³

In a survey conducted in Iran, the average prevalence of caesarian section was estimated 33.1%,¹⁹ and it was estimated 45.6% in Tabriz.²⁰ The aim of this study is to investigate the association between the mode of delivery and the risk of asthma in children 5-14 years old in the presence of potential confounding variables in Tabriz.

Methods

A case-control study was carried out in 2014

among Iranian children 5-14 years of age referred to outpatient clinics of Tabriz Children's Hospital and Sheikhorrais Clinic. Since the definitive diagnosis of asthma in children under 5 is difficult, we did not include these children in the study. Study eligibility criteria included the following: Non-Iranian Children, the ones who suffered from congenital diseases, allergies, and any other diseases related to asthma were excluded. Assuming a significance level of $P = 0.050$, a confidence interval (CI) of 95%, prevalence of cesarean in Tabriz = 45.6%,²⁰ prevalence of cesarean section in mothers of children with asthma 65.6% (based on likelihood of 20% more),²¹ Using PS software (version 3.0.43), a sample size of 213 children (cases = 71 controls = 142) was estimated by simple random sampling. We chose a ratio of 1-2 for cases and controls to enhance the power of the study.

Considering the likelihood of missing cases, 233 children (cases = 81, controls = 152) were involved in the study. First, cases were diagnosed by a pediatric pulmonary specialist based on Global Initiative for Asthma Criteria¹ according to patient's history, physical examination, and pulmonary function test, and if the consent was obtained from children and their parents, a face to face interview was conducted to fill out a questionnaire by a trained interviewer. Weight and height were measured to calculate body mass index (BMI), and BMI status was determined using WHO's (World Health Organization) BMI table for 5-19 years old boys and girls separately.²² The validity and reliability of the questionnaire had been confirmed by specialists and researchers. The questionnaire consisted of demographic, environmental, and clinical history information.

After the selection of cases, we started to choose controls. Children aged 5-14 years referred to the outpatient clinics of Tabriz Children's Hospital and Sheikhorrais Clinic and who did not have asthma or any other upper respiratory illness including common cold, tonsillitis, or cough were eligible to be considered for the control group. Causes for

referral could include other diseases such as food poisoning (diarrhea and vomiting), high fever, chronic headache, stomach ache, backache, otitis, and anemia. If the consent was obtained from children and their parents, they included in the study after a physical examination by the pediatric pulmonary specialist.

A face-to-face interview was conducted to fill out a questionnaire by the trained interviewer age-sex frequency matching with cases was performed during sampling for controlling of possible confounding effects of age and sex for asthma. We used Independent sample t-test to examine age-sex frequency matching with cases and there were no statistically significant differences between sex and age in case and control groups. Descriptive statistics were used for description of data. Univariate and multiple logistic regressions were used for analysis. We used odds ratio (OR) to report categorical variables and used standard error (β) [SE (β)] for continuous variables. We opted $P < 0.050$ as significance level. The statistical analysis was performed using PS software (version 3.0.43).

Results

Of 233 children in the study, 81 subjects (34.8%) were cases of asthma and 152 subjects (65.2%) were controls. 53.6% of children ($n = 125$) were male [case group = 54.3% ($n = 44$), control group = 53.3% ($n = 81$)] and 46.4% ($n = 108$) were female [case group = 45.7% ($n = 37$), control group = 46.7% ($n = 71$)]. The overall average age was 94.3 months [standard deviation (SD) = 26.47], [case group = 92.9 (SD = 29.2), control group = 95 (SD = 24.9)]. All in all, 127 children (54.5%) had been delivered by caesarian section, [case group = 49 (60.5%), control group = 78 (51.3%)] and 106 children (45.5%) had been delivered by vaginal section, [case group = 32 (39.5%), control group = 74 (48.7%)]. Results for BMI indicated that the prevalence of normal, overweight, and obese children was 50.6% ($n = 41$), 13.6% ($n = 11$), and 9.9% ($n = 8$) in the case group and were 61.7% ($n = 92$), 14.1% ($n = 21$), and 2.7% ($n = 4$) in the control group, respectively, (Table 1). The

family history of Asthma was 11.1% ($n = 9$) in cases and 7.2% ($n = 11$) in controls. Demographic, environmental, and clinical history information is available in table 1.

In univariate analysis, although there were no significance seen between asthma and mode of delivery ($P = 0.180$) significance was seen in maternal education level, birth order, history of a severely negative event during life (having a chronic disease, hospitalization or surgery, and the death of a family member), family history of allergy and frequent episodes of common cold ($P < 0.050$) (Table 2), thus, children whose mothers had a collegiate education level were more likely to have asthma than children whose mothers had elementary or less than elementary education level [OR = 2.91, 95% CI = 1.21-6.86; $P = 0.010$]. Odds of asthma was also higher for the second born children compared to firstborns (OR = 2.12, 95% CI = 1.15-3.89; $P = 0.010$). Children who had a history of a severely negative event during life had a higher odds of asthma (OR = 1.81, 95% CI = 1.04-3.12; $P = 0.030$). Odds of asthma was lower for children who didn't have a Family history of Allergy (OR = 0.52, 95% CI = 0.28-0.88; $P = 0.010$). The probability of occurrence of asthma increased markedly with increased frequency of episode of common cold [$\beta = 0.069$, SE (β) = 0.027; $P = 0.010$] (Table 2). There were no significant differences in BMI status ($P = 0.060$) and age of children ($P = 0.560$). Detailed information of variables based on univariate regression logistic is observable in table 2.

In the multiple regression model in the presence of variables with $P \leq 0.200$, the variables of frequency of common cold [$\beta = 0.094$, SE (β) = 0.031; $P < 0.001$], birth order (adjusted odds ratio (AOR) = 2.54, 95% CI = 1.18-5.46; $P = 0.010$) and maternal collegiate education level (AOR = 6.12, 95% CI = 1.43-26.20; $P = 0.010$) remained significant (Table 3). In the multiple regressions model, the variables of intra-family marriage and maternal diploma (12 years education) education level were observed to be significant while in the univariate regression logistic test, they were not significant

statistically. Odds of having asthma was higher in children whose parents have an intra-family marriage (AOR = 2.89, 95% CI = 1.21-6.89; P = 0.010) and children whose mothers had a diploma education level were more likely to have asthma than children

whose mothers had elementary or less than elementary education level (AOR = 3.76, 95% CI = 1.10-12.88; P = 0.030) (Table 3). There was no significant difference between asthma and mode of delivery (P = 0.320) in the multiple logistic regression model (Table 3).

Table 1. The frequency distribution of case and control groups based various variables in children aged 5-14 years

| Variable | Asthma | Control |
|--|-------------|------------|
| Delivery mode [n (%)] | | |
| Vaginal section | 32 (39.5) | 74 (48.7) |
| Caesarian section | 49 (60.5) | 78 (51.3) |
| Age (month) (mean ± SD) | 92.9 ± 29.2 | 95 ± 24.9 |
| Sex [n (%)] | | |
| Male | 44 (54.3) | 81 (53.3) |
| Female | 37 (45.7) | 71 (46.7) |
| Residence [n (%)] | | |
| City | 72 (88.9) | 138 (90.8) |
| Village | 9 (11.1) | 14 (9.2) |
| Birth weight (kg) (mean ± SD) | 3.2 ± 0.54 | 3.2 ± 0.54 |
| Duration of pregnancy [n (%)] | | |
| Full-term | 66 (83.5) | 128 (84.8) |
| Pre-term | 13 (16.5) | 23 (15.2) |
| Newborn hospitalization [n (%)] | | |
| Yes | 14 (17.5) | 29 (19.1) |
| No | 66 (82.5) | 123 (80.9) |
| Cause of hospitalization [n (%)] | | |
| Icterus | 10 (71.4) | 22 (71.0) |
| Low blood sugar | 0 (0.0) | 2 (6.4) |
| Premature and TTN | 2 (14.4) | 6 (19.4) |
| Congenital heart malformations | 1 (7.1) | 0 (0.0) |
| Infection | 1 (7.1) | 1 (3.2) |
| Infancy feeding kind [n (%)] | | |
| Breastfeeding | 79 (81.4) | 150 (77.4) |
| Powdered milk | 14 (14.4) | 29 (14.9) |
| Cow and Pasteurized cow's milk | 4 (4.2) | 15 (7.7) |
| Duration of breastfeeding (month) (mean ± SD) | 20.5 (6.7) | 19.9 (7.0) |
| Duration of powder milk feeding (month) (mean ± SD) | 19.6 (7.9) | 14.7 (6.9) |
| Duration of cow and pasteurized cow's milk feeding; in children less than 1 year age (month) (mean ± SD) | 9.8 (7.8) | 4.8 (1.5) |
| Eating snacks [n (%)] | | |
| Yes | 70 (86.4) | 138 (91.4) |
| No | 11 (13.6) | 13 (8.6) |
| Snack type [n (%)] | | |
| Potato chips-Pastilles-corn snacks | 65 (55.6) | 124 (37.5) |
| Chocolates-ice creams | 3 (2.6) | 98 (29.6) |
| Fruit leathers | 11 (9.4) | 92 (27.8) |
| Cakes-Biscuits | 38 (32.4) | 17 (5.1) |
| Quantity of snacks (per day) (mean ± SD) | 0.68 (1.0) | 0.87 (0.9) |
| Having pet [n (%)] | | |
| Yes | 4 (4.9) | 9 (5.9) |
| No | 77 (95.1) | 143 (94.1) |
| Pet type | | |
| Birds | 2 (50.0) | 6 (75.0) |
| Furry animals | 2 (50.0) | 2 (25.0) |
| Duration of pet keeping (years) (mean ± SD) | 5 ± 3.6 | 4.4 ± 3.6 |
| Having a severely negative event [n (%)] | | |
| No | 34 (38.6) | 86 (50.0) |

Table 1. The frequency distribution of case and control groups based various variables in children aged 5-14 years (Continue)

| Variable | Asthma | Control |
|----------------------------------|-------------|--------------|
| A chronic disease | 16 (18.2) | 34 (19.8) |
| A family member death | 2 (2.3) | 3 (1.7) |
| Hospitalization and surgery | 36 (40.9) | 49 (28.5) |
| Family history of asthma [n (%)] | | |
| Yes | 9 (11.1) | 11 (7.2) |
| No | 72 (88.9) | 141 (92.8) |
| Asthmatic family member* [n (%)] | | |
| Father | 5 (50.0) | 5 (41.7) |
| Mother | 3 (30.0) | 5 (41.7) |
| Brother | 2 (20.0) | 2 (16.6) |
| Current weight (kg) (mean ± SD) | 29.5 ± 14.8 | 26.9 ± 7.97 |
| Current height (cm) (mean ± SD) | 129 ± 15.4 | 128.8 ± 12.4 |
| BMI status [n (%)] | | |
| Sever thinness | 1 (1.2) | 1 (0.7) |
| Thinness | 20 (24.7) | 31 (20.8) |
| Normal | 41 (50.6) | 92 (61.7) |
| Overweight | 11 (13.6) | 21 (14.1) |
| Obesity 1 | 5 (6.2) | 3 (2.0) |
| Obesity 2 | 3 (3.7) | 1 (0.7) |
| Paternal occupation [n (%)] | | |
| Staff | 25 (32.1) | 40 (27.0) |
| Skilled worker | 43 (55.1) | 80 (54.1) |
| Unskilled worker | 10 (12.8) | 28 (18.9) |
| Maternal occupation [n (%)] | | |
| Staff | 5 (6.2) | 12 (8.1) |
| Skilled worker | 4 (4.9) | 2 (1.4) |
| Unskilled worker | 0 (0.0) | 1 (0.7) |
| Housekeeper | 72 (88.9) | 133 (89.9) |
| Paternal age (mean ±SD) | 39.6 (6.3) | 38.4 (6.67) |
| Maternal age (mean ± SD) | 33.6 (4.96) | 33.5 (5.54) |
| Paternal education level [n (%)] | | |
| Illiterate | 2 (2.6) | 7 (4.7) |
| Elementary | 14 (18.0) | 27 (18.2) |
| Middle and high school | 11 (14.1) | 43 (29.1) |
| Diploma (12 years) | 29 (37.2) | 45 (30.4) |
| Colligate | 22 (28.1) | 26 (17.6) |
| Maternal education level [n (%)] | | |
| Illiterate | 0 (0.0) | 8 (5.3) |
| Elementary education | 15 (18.5) | 38 (25.3) |
| Middle and high school | 15 (18.5) | 33 (22.0) |
| Diploma education | 32 (39.5) | 51 (34.0) |
| Colligate education | 19 (23.5) | 20 (13.4) |
| Birth order [n (%)] | | |
| First | 47 (58.0) | 108 (71.0) |
| Second | 28 (34.6) | 30 (19.7) |
| Third | 5 (6.2) | 10 (6.6) |
| Fourth | 1 (1.2) | 3 (2.0) |
| ≥ Fifth | 0 (0.0) | 1 (0.7) |
| Having sister [n (%)] | | |
| Don't have | 46 (56.8) | 85 (55.9) |
| One | 32 (39.5) | 59 (38.8) |
| Two | 3 (3.7) | 7 (4.6) |
| ≥ Three | 0 (0.0) | 1 (0.7) |
| Having brother [n (%)] | | |
| Don't have | 50 (61.7) | 85 (55.9) |
| One | 26 (32.1) | 54 (35.5) |
| Two | 5 (6.2) | 10 (6.6) |

Table 1. The frequency distribution of case and control groups based various variables in children aged 5-14 years (Continue)

| Variable | Asthma | Control |
|--|------------|-------------|
| Two | 0 (0.0) | 3 (2.0) |
| ≥ Three | 0 (0.0) | 0 (0.0) |
| Living with family members [n (%)] | | |
| Father and mother | 78 (96.3) | 143 (94.1) |
| Father | 2 (2.5) | 7 (4.6) |
| Mother | 1 (1.2) | 2 (1.3) |
| Intra-family marriage [n (%)] | | |
| Yes | 18 (22.2) | 20 (13.2) |
| No | 63 (77.8) | 131 (86.8) |
| Paternal current smoking [n (%)] | | |
| Yes | 23 (28.4) | 44 (28.9) |
| No | 58 (71.6) | 108 (71.1) |
| Cigarettes frequency of parent (per day) (mean ± SD) | 10.9 ± 7.3 | 13.6 ± 8.4 |
| Maternal current smoking [n (%)] | | |
| Yes | 1 (1.2) | 0 (0.0) |
| No | 80 (98.8) | 152 (100.0) |
| Frequency of common cold (per year) (mean ± SD) | 7.2 ± 5.6 | 5.2 ± 5.1 |
| Family history of Allergy [n (%)] | | |
| Yes | 35 (43.2) | 42 (27.6) |
| No | 46 (56.8) | 110 (72.4) |
| Allergic family member* [n (%)] | | |
| Father | 13 (31.7) | 14 (29.8) |
| Mother | 24 (58.6) | 32 (68.1) |
| Brother | 1 (2.4) | 1 (2.1) |
| Sister | 3 (7.3) | 0 (0.0) |

TTN: Transient tachypnea of newborn; BMI: Body mass index; SD: Standard deviation

*Cases may have more than one asthmatic or allergic family member

Table 2. Relationship between asthma and mode of delivery beside various variables based univariate regression logistic in children 5-14 years old

| Variables | Unadjusted OR | Unadjusted 95% CI (OR) | | β | SE (β) | P |
|-------------------------|---------------|------------------------|-------|-------|--------|-------|
| | | Lower | Upper | | | |
| Delivery mode | | | | | | |
| Vaginal | 1 | | | | | |
| Cesarean | 1.41 | 0.84 | 2.49 | - | - | 0.180 |
| Age (month) | - | - | - | 0.003 | 0.005 | 0.560 |
| Sex | | | | | | |
| Male | 1 | | | | | |
| Female | 0.96 | 0.56 | 1.61 | - | - | 0.880 |
| Residence | | | | | | |
| City | 1 | | | | | |
| Village | 1.21 | 0.52 | 2.98 | - | - | 0.640 |
| Duration of pregnancy | | | | | | |
| Full-term | 1 | | | | | |
| Pre-term | 1.09 | 0.52 | 2.32 | - | - | 0.810 |
| Newborn hospitalization | | | | | | |
| Yes | | | | | | |
| No | 1.10 | 0.55 | 2.19 | - | - | 0.770 |
| Paternal occupation | | | | | | |
| Staff | 1 | | | | | |
| Skilled worker | 0.86 | 0.24 | 1.42 | - | - | 0.210 |
| Unskilled worker | 0.57 | | | | | |
| Maternal occupation | | | | | | |
| Staff | 1 | | | | | |
| Worker | 3.21 | 0.52 | 19.92 | - | - | 0.630 |
| Housekeeper | 1.32 | 0.44 | 3.81 | - | - | 0.630 |

Table 2. Relationship between asthma and mode of delivery beside various variables based univariate regression logistic in children 5-14 years old (Continue)

| Variables | Unadjusted OR | Unadjusted 95% CI (OR) | | β | SE (β) | P |
|----------------------------------|---------------|------------------------|-------|---------|----------------|-------|
| | | Lower | Upper | | | |
| Paternal age | - | - | - | 0.027 | 0.021 | 0.190 |
| Maternal age | - | - | - | 0.000 | 0.026 | 0.990 |
| Paternal education level | | | | | | |
| ≤ Elementary | 1 | 0.22 | 1.32 | | | 0.180 |
| Middle and high school | 0.54 | 0.64 | 2.89 | | | 0.410 |
| Diploma (12 years) | 1.37 | 0.79 | 4.00 | - | - | 0.160 |
| Collegiate | 1.79 | | | | | |
| Maternal education level | | | | | | |
| ≤ Elementary | 1 | 0.63 | 3.22 | | | 0.440 |
| Middle and high school | 1.39 | 0.92 | 3.89 | | | 0.080 |
| Diploma (12 years) | 1.89 | 1.21 | 6.86 | | | 0.010 |
| Collegiate | 2.91 | | | - | - | |
| Infancy feeding kind | | | | | | |
| Breastfeeding | 1 | | | | | |
| Other | 0.72 | 0.38 | 1.37 | - | - | 0.310 |
| Eating snacks | | | | | | |
| Yes | 1 | | | | | |
| No | 1.71 | 0.71 | 3.92 | - | - | 0.240 |
| Birth order | | | | | | |
| First | 1 | 1.15 | 3.89 | | | 0.010 |
| Second | 2.12 | 0.36 | 2.71 | - | - | 0.970 |
| ≥ Third | 0.98 | | | | | |
| Having sister | | | | | | |
| No | 1 | | | | | |
| Yes | 0.96 | 0.56 | 1.71 | - | - | 0.890 |
| Having brother | | | | | | |
| No | 1 | | | | | |
| Yes | 0.71 | 0.45 | 1.36 | - | - | 0.390 |
| Living with family member | | | | | | |
| Father and mother | 1 | | | | | |
| Else other | 0.54 | 0.15 | 2.01 | - | - | 0.370 |
| Intra-family marriage | | | | | | |
| No | 1 | | | | | |
| Yes | 1.87 | 0.92 | 3.78 | - | - | 0.080 |
| Having pet | | | | | | |
| Yes | 1 | | | | | |
| No | 1.21 | 0.36 | 4.06 | - | - | 0.760 |
| Paternal current smoking | | | | | | |
| Yes | 1 | | | | | |
| No | 1.02 | 0.57 | 1.91 | - | - | 0.930 |
| Having a severely negative event | | | | | | |
| No | 1 | | | | | |
| Yes | 1.81 | 1.04 | 3.12 | - | - | 0.030 |
| Family history of asthma | | | | | | |
| Yes | 1 | | | | | |
| No | 0.61 | 0.25 | 1.62 | - | - | 0.320 |
| Family history of allergy | | | | | | |
| Yes | 1 | | | | | |
| No | 0.52 | 0.28 | 0.88 | - | - | 0.010 |
| Frequency of common cold | - | - | - | 0.069 | 0.027 | 0.010 |
| BMI | - | - | - | 0.081 | 0.043 | 0.060 |

CI: Confidence interval; BMI: Body mass index; OR: Odds ratio; SE: Standard error

Table 3. Relationship between asthma and mode of delivery beside various variables based multiple logistic regressions in children 5-14 years old

| Variables | Adjusted OR | Adjusted 95% CI (OR) | | β | SE (β) | P |
|----------------------------------|-------------|----------------------|-------|---------|----------------|---------|
| | | Lower | Upper | | | |
| Delivery mode | | | | | | |
| Vaginal | 1 | | | | | |
| Cesarean | 0.69 | 0.34 | 1.42 | - | - | 0.320 |
| Frequency of common cold | - | - | - | 0.094 | 0.031 | < 0.001 |
| Having a severely negative event | | | | | | |
| No | 1 | | | | | |
| Yes | 1.90 | 0.99 | 3.63 | - | - | 0.050 |
| Birth order | | 1.18 | 5.46 | - | - | 0.010 |
| First | 1 | | | | | |
| Second | 2.54 | 0.77 | 9.82 | | | 0.110 |
| ≥ Third | 2.76 | | | | | |
| BMI | - | - | - | 0.096 | 0.050 | 0.050 |
| Intra-family marriage | | | | | | |
| No | 1 | 1.21 | 6.89 | - | - | 0.010 |
| Yes | 2.89 | | | | | |
| Family history of allergy | | | | | | |
| Yes | 1 | 0.40 | 1.50 | - | - | 0.450 |
| No | 0.77 | | | | | |
| Maternal education level | | | | | | |
| ≤ Elementary | 1 | | | | | |
| Middle and high school | 1.87 | 0.63 | 5.48 | - | - | 0.250 |
| Diploma (12 years) | 3.76 | 1.10 | 12.88 | | | 0.030 |
| Collegiate | 6.12 | 1.43 | 26.20 | | | 0.010 |
| Paternal education level | | | | | | |
| ≤ Elementary | 1 | 0.15 | 1.28 | | | 0.130 |
| Middle and high school | 0.44 | 0.27 | 2.73 | - | - | 0.810 |
| Diploma (12 years) | 0.87 | 0.33 | 4.03 | | | 0.810 |
| Collegiate | 1.16 | - | - | | | - |

OR: Odds ratio; CI: Confidence interval; SE: Standard error; BMI: Body mass index

Discussion

The present study investigated the relationship between the mode of delivery and asthma in the presence of potential confounding variables, and no relationship was observed. Previous studies reported conflicting results; similar to ours; some studies found no relationship between the mode of delivery and asthma,¹³⁻¹⁸ while some others reported a significant statistical relationship.⁵⁻¹²

It should be noted that the majority of these studies did not state cesarean delivery as a definite risk factor for asthma and suggested the possible influence of some factors such as confounding variables or effect modifiers. For example, Roduit et al.¹⁰ showed that there is strong interaction between genetic factors such as the history of parental allergy and mode of delivery and

development of asthma. He pointed out that the complex interaction between gene-environment factors can justify incompatible results. In spite of finding a relationship between the mode of delivery and asthma, since Baizhuang did not find any relationship between the mode of delivery and atopic diseases and other allergic diseases, he proposed a potential relationship between cesarean section and other unknown factors.⁵

Debley et al.²³ also discovered a strong relationship between the mode of delivery and asthma in premature infants while there was no correlation in full-term infants. He stated that genetics and intrauterine influences related to maternal asthma or reduced lung function in premature infants can justify contradicting results of relationship between the mode of delivery and childhood asthma in previous studies.

Some other studies have suggested prematurity as a strong confounding factor which should have been considered in previous studies.^{5,9,24} Some other studies have shown that the correlation of asthma with emergency cesarean section compared to planned cesarean section is suggestive of other causal mechanisms, which should be investigated.^{5,9,12}

In Iran, due to mothers' fear of natural childbirth and the encouragement of gynecology and obstetrics specialists for financial reasons, the cesarean section has become more planned than an emergency. This eliminates the possibility of bias in our study. On the basis of our findings, odds of asthma were a higher in children with well-educated mothers. However, this relationship was far from expectation and inconsistent with some studies such as the one by Juhn et al.¹⁵ On the other hand, consistency with a similar study on atopic diseases³ indicates the need for further investigation in this region. According to the study by Roduit et al.,¹⁰ parental allergy is a strong factor for childhood asthma. Although univariate analysis showed increased odds of childhood asthma in this study due to history of parental allergy no relationship was observed in the model. The inconsistency between our study and other studies can be due to environmental and geographical diversity. In the present study, second born children had a greater odds of asthma compared to firstborns, which is consistent with the results of the study by Matricardi et al.²⁵

Moreover, the risk of asthma increased with increased frequency of catching infectious respiratory diseases which are shown as the common cold in the present study. Studies on the relationship between respiratory diseases and asthma indicate that there is a relationship between viral respiratory diseases and asthma, but regarding the relationship between bacterial respiratory diseases and asthma, it is not clear if bacterial infections are an epiphenomenon or a pathogenic event in asthma.^{26,27}

Cohort study in this area seems extremely necessary because if respiratory infectious

diseases are casual, asthma can be prevented to a considerable extent. In this study, the lack of intra-family marriage in the model was shown as a preventive factor of asthma, which can suggest the dominance and phenotypic expression of the disease's gene due to intra-family marriage. Furthermore, no relationship was observed between paternal smoking and asthma. Not having smoking mothers during pregnancy or afterward (only one case of post-pregnancy maternal smoking) and paternal smoking outside the house according to their own report can be good justification for the lack of relationship. Strengths of this study were diagnosing of the disease by a pediatric pulmonary specialist and did not depend on the self-report information obtained via questionnaire, considering potential confounding factors (obtained by previous study) in the development of asthma, lack of measurement errors because of diagnosis of the disease by just one specialist and filling out questionnaires just by one interviewer. Limitations of the study were its small sample size and the possibility of being recall bias because of reliance on self-reporting of some of the information such as gestational age, birth weight, and duration of breastfeeding. Exception the present study, a case-control study was conducted in Babol, Iran,¹⁶ between risk of asthma and mode of delivery and there was not seen a statistical relationship between risk of asthma and mode of delivery and because no cohort study was performed in Iran, Due to the importance of childhood asthma in the region and because the prevalence of cesarean section in Iran is much higher (33.1%-Iran, 45.6%-Tabriz)^{19,20} than WHO'S recommendation that is 10-15%;²⁸ it is seem conducting a cohort study in the region can be useful for examination of real relationship between risk of asthma and mode of delivery.

Conclusion

There was no relationship between the mode of delivery and the risk of developing childhood asthma. Intra-family marriage increased the risk of childhood asthma. A

cohort study on the relationship between maternal education and the risk of childhood asthma is suggested.

Conflict of Interests

Authors have no conflict of interest.

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Acknowledgments

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