

FACTORS ASSOCIATED WITH CONTROLLED ASTHMA IN CHILDREN AND ADOLESCENTS IN THE MUNICIPALITY OF PRIMAVERA DO LESTE MATO GROSSO IN 2016

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Abstract: Introduction: Asthma is a very prevalent disease in childhood and is usually associated with various environmental and household exposure factors, personal history and family history. It is a condition that affects the quality of life of individuals.

Goal: It is to analyze the influence of sociodemographic and economic factors, birth and childhood conditions, paternal and maternal pathological history, intra-household exposure and, mainly, exposure to pesticides on controlled asthma in children and adolescents. **Methodology:** Case-control study with primary data collected through the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire in children and adolescents in the city of Primavera do Leste - MT. The sample obtained by randomization is 452 individuals, 226 cases and 226 controls. **Results:** In logistic regression, low birth weight (OR = 2.04), attendance at daycare (OR = 1.78), household activity that uses pesticides (OR = 2.74) remained factors favorable to the development of controlled asthma. Breastfeeding (OR = 0.04) as a protective factor against asthma. **Conclusion:** The association of several sociodemographic factors, the child's physiological history, household exposure and exposure to pesticides with controlled asthma was observed. Therefore, prevention and health promotion actions must start from primary health care, with education of the population about the need for the correct use of Personal Protective Equipment, as well as the cautious use of pesticides in or near the home.

Keywords: Asthma; Pesticides; Risk factors; Protective factors

INTRODUCTION

Asthma is a chronic inflammatory disease of the lower airways characterized by bronchial hyperresponsiveness and, consequently, airflow obstruction¹. Regarding the level of control, asthma can be classified as controlled, partially controlled or uncontrolled. The criteria that define controlled asthma are: having a low frequency of daytime symptoms, not having sleep interrupted by the disease, not needing to use rescue medication and not having limitations in daily activities¹.

It is estimated that asthma affects 10% of the Brazilian population and, being a condition that even under control, can evolve into exacerbations, causing social, emotional and financial impacts^{2,3}. It is the cause of school and work absenteeism, as well as the inability or fear of practicing physical activities^{2,3}. Furthermore, when severe or uncontrolled, it generates costs that impact health systems and the family budget^{2,3}.

Numerous factors are related to asthma in the literature, which may be individual or environmental. Among them we have exposure to pets in the first year of life and in the present^{4,5}, family history of asthma⁵, breastfeeding⁶, attendance at daycare centers and kindergartens^{10,11}, exposure to tobacco²³ and household dust²⁸.

A very important environmental factor that has been discussed in the context of respiratory diseases is the increased use of pesticides. Such substances can generate persistent inflammation of the airways and bronchial hyperreactivity, the underlying pathophysiology of asthma⁸. This inflammation causes bronchial spasms, mucus hypersecretion and epithelial cell dysfunction, conditions that reflect as a reduction in forced expiratory volume in one second (FEV1) in spirometry. Some studies correlate exposure to pesticides and the obstructive spirometric pattern, indicating an association with

asthmatic disease¹².

In Brazil, the state of Mato Grosso is among those that consume the most pesticides, and the municipality of Primavera do Leste, having an economy based on agribusiness, shares this high consumption rate. It is estimated that the main producing municipalities use more than 5 million liters of pesticides per year and that the state of Mato Grosso as a whole use around 140 million liters of herbicides, pesticides and fungicides per year⁴⁰. It is believed that constant exposure to these products is associated with the development of controlled asthma in the region.

Since research on respiratory diseases, such as asthma, in regions where pesticides are used on a large scale is scarce, but relevant to contribute to the discussion on regulating the use of these products, as well as possible damage reduction methods, this study has the objective of analyzing the influence of sociodemographic and economic factors, birth and childhood conditions, paternal and maternal pathological antecedents, household exposure and, mainly, exposure to pesticides on controlled asthma in children and adolescents in the municipality of Primavera do Leste.

METHODS

This is a case-control study with the purpose of analyzing the factors associated with controlled asthma in children and adolescents in the community. The primary study collected data in the municipality of interest, using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire to determine the prevalence of asthma and the severity of symptoms in children aged 6 to 7 years and adolescents aged 13 and 14 years.

In addition to phase I of the ISAAC, 2 other questionnaires were applied, with phase II of the ISAAC responsible for investigating factors

associated with asthma, and a complementary questionnaire to evaluate the variables of exposure to pesticides. This questionnaire addressed the proximity of family members to agricultural areas, the use of pesticides near the home, care related to the use of pesticides and maternal exposure during pregnancy.

Following the ISAAC criteria, cases were defined as those who responded positively to the following questions: "In the last 12 (twelve) months, how many attacks of wheezing (wheezing) has your child had? Less than 4 attacks in the last year or no attacks." and/or "In the last twelve (12) months, how often has your child had his sleep disturbed by wheezing? Less than one night per week of sleep disturbed by wheezing or never." and/or "In the last 12 (twelve) months, has your child's wheezing been so severe that it prevented him from being able to say more than two words between each breath? No", configuring controlled asthma. Those classified as having uncontrolled asthma were excluded from the study.

The control group was defined as non-asthmatics, that is, those who responded negatively to the following question "In the last 12 (twelve) months, has your child had wheezing?". After excluding uncontrolled asthmatics, the group of non-asthmatics remaining in the database was randomized, then estimating a 1:1 ratio between cases and controls.

The dependent variable is the controlled asthma present in children and adolescents.

The independent variables analyzed were sociodemographic and economic variables (gender, age group, family income, mother's education and marital status and household situation), the pathological history of the parents (father with rhinitis or asthma, mother with rhinitis), personal history of the child (breastfeeding, attending daycare and kindergarten), exposure within the home

(presence of a cat at home in the present and in the first year of life, presence of a dog in the house in the present and in the first year of life, smoking habit indoors), exposure to pesticides (presence of people in the household who work in agriculture, household activity that uses pesticides, proximity of the household to the agricultural activity, spraying of pesticides near the home, place of work of the mother during pregnancy).

In the statistical analysis, bivariate analyzes were performed using the Mantel-Haenszel chi-square method and obtaining odds ratio measurements with their respective confidence intervals.

To obtain the multiple model, the logistic regression method was used, including variables that in the crude analyzes presented a p-value lower than 0.20. The removal of variables that did not show significance in the regression model was done through an iterative process (step-by-step) "Backward Stepwise Selection" method. The variables were gradually removed according to their loss of statistical significance in the regression stages. Those with a p-value lower than 0.05 remained in the final model. Statistical analyzes were performed using the SPSS (Statistical Package for the Social Science) program, version 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

As this was primary data collection, before carrying out the interviews, the Free and Informed Consent Form was presented to parents and/or guardians so that, after reading, they could sign it. This study was approved by the Research Ethics Committee of Hospital Júlio Muller (CAAE: 3998.4114.0.0000.5541, opinion no. 209 981471, dated March 11, 2015), in compliance with Resolution number: 196/1996 and Resolution number: 347 /2005, from the National Health Council.

RESULTS

The number of study participants was 452 children and adolescents, 226 cases and 226 controls. In the bivariate analysis, the sociodemographic variables associated with controlled asthma were maternal marital status without a partner (OR = 7.13; 95%CI: 4.48-11.35), mother with incomplete secondary education (OR = 2.17; 95%CI: 1.44-3.27), rural household situation (OR = 1.84; 95% CI: 1.04-3.28) and family income with more than 4 minimum wages (OR = 4.9; 95% CI: 3.24-7.52).

When assessing the child's personal history, attending daycare (OR = 1.51; 95% CI: 1.04-2.20) and being born by cesarean section (OR = 4.64; 95% CI: 3.08-6.99) were associated with controlled asthma. Low birth weight (OR = 0.37; 95% CI: 0.20-0.68) and breastfeeding (OR = 0.06; 95% CI: 0.03 0.10) were inversely associated with the outcome. Prematurity, father with rhinitis and asthma, mother with rhinitis and attending kindergarten were not statistically significant.

Sharing the environment with a dog in the first year of life (OR = 0.29; 95% CI: 0.19-0.43), as well as with a cat in the present (OR = 0.42; 95% CI: 0.28-0.62) and in the first year of life (OR = 0.40; 95% CI: 0.27-0.60) it acted as a protective factor against controlled asthma. The presence of dogs at present was not statistically significant.

Regarding intra-household exposure, the presence of people who smoke indoors (OR = 2.44; 95% CI: 1.64-3.62), the use of pesticides in household activities (OR = 6.82; 95% CI: 4.05-11.49) and the presence of people in the household who work in agriculture (OR = 7.33; 95% CI: 4.82-11.15) were associated with the group of cases. In terms of exposure to pesticides, the mother's work while pregnant in a rural area (OR = 6.32; 95% CI: 3.84-10.41) acted as a risk factor for asthma.

The proximity of the home to agricultural

areas and the spraying of pesticides near the home were not statistically relevant.

In the final logistic regression model, household activity that uses pesticides (OR = 2.74; 95% CI: 1.33-5.64), low birth weight (OR = 2.04; 95% CI: 1.01- 4.14) and daycare attendance (OR = 1.78; 95% CI: 1.01-3.15) were associated with controlled asthma. The variable breastfeeding (OR = 0.04; 95% CI: 0.019-0.070) acted as a protective factor against controlled asthma.

Variables	OR adjusted	CI 95%	p-value
Birth weight (Up to 2,499g */≥ 2.500g)	2,04	1,01-4,14	0,049
Breastfeeding (Yes*/No)	0,04	0,019-0,070	<0,001
Attendance at daycare (Yes*/No)	1,78	1,01-3,15	0,047
Home activity that uses pesticides (Yes*/No)	2,74	1,33-5,64	0,006

Table 4: Final logistic regression model

95%CI: 95% confidence interval; OR: odds ratio

* Reference category

DISCUSSION

The main results found in the present study through multivariate analysis were the association between household activity that uses pesticides, low birth weight and attendance at daycare with the development of controlled asthma. In addition, this study also identified that breastfeeding acted as an important factor protective against the development of asthma.

The association between household activity and the use of pesticides remained in the logistic regression, corroborating several studies that address this topic^{8, 29, 30}.

Currently, pyrethroid insecticides are the most used pesticides in domestic environments, replacing organophosphates that were previously used for the same function. Both are low volatile, therefore, capable of depositing with dust and remaining

on surfaces for long periods, prolonging the exposure of residents²⁸. Chronic exposure to pyrethroids was associated with spirometric changes in children and adolescents³². Other studies demonstrate that even acute cutaneous exposure to pesticides such as organophosphates, paraquat and methylcarbamates is capable of having an impact on the respiratory system, leading to bronchoconstriction and wheezing⁸.

The presence of people in the household who work in agriculture and the mother living in a rural area while pregnant were associated in the bivariate analysis. It is known that rural workers tend to carry pesticide residues in their boots and vehicles^{27,34}, that accumulate in dust and are deposited in the home environment. This way, the presence of rural workers increases exposure not only for children and adolescents but also for pregnant women in the household. Studies show that children of pregnant women exposed to pesticides were more likely to present respiratory symptoms in childhood^{32,33}. These factors also justify living in rural areas being associated with controlled asthma.

Daycare attendance remained associated with asthma in the final logistic regression model, in line with previous studies^{11,15}. The association becomes even more evident the earlier these children are exposed to the daycare environment, as early contact with viruses responsible for upper respiratory tract infections is responsible for the risk of developing asthma¹¹. In addition to the age of exposure, the number of children in the same daycare center, air circulation and the length of time the child spends in that environment must also be considered¹¹.

Breastfeeding has been shown to be a protective factor against controlled asthma. It is known that breastfeeding is essential for the development of the child's immune system, but in addition to immunological action, it

Variables	Case:		Control		Brute OR	CI 95%		p-value
	n	%	n	%				
Gender								
Male	115	50,88	120	53,10	0,91	0,63	1,32	0,6
Female	111	49,12	106	46,90	1,00	-	-	-
Age (years)								
6-7	131	57,96	128	56,64	1,05	0,72	1,53	0,77
13-14	95	42,04	98	43,36	1,00	-	-	-
Family income								
Over 4	123	54,42	44	19,47	4,9	3,24	7,52	<0,01
Up to 4	103	45,58	182	80,53	1,00	-	-	-
Mother's Education								
Incomplete high school	89	39,38	52	23,01	2,17	1,44	3,27	<0,01
High school concluded	137	60,62	174	76,99	1,00	-	-	-
Mother's marital status								
Without partner	118	52,21	30	13,27	7,13	4,48	11,35	<0,01
With partner	108	47,79	196	86,73	1,00	-	-	-
Home situation								
Countryside	36	15,93	21	9,29	1,84	1,04	3,28	0,03
Urban	190	84,07	205	90,71	1,00	-	-	-

Table 1: Odds ratio (OR) and 95% confidence interval (95% CI) of sociodemographic and economic variables associated with controlled asthma in children and adolescents

Variables	Case:		Control		Brute OR	CI 95%		p-value
	n	%	n	%				
Did the person attend daycare?								
Yes	141	62,39	118	52,21	1,51	1,04	2,20	0,02
No	85	37,61	108	47,79	1,00	-	-	-
Is the mother breastfeeding?								
Yes	80	35,40	203	89,82	0,06	0,03	0,10	<0,01
No	146	64,60	23	10,18	1,00	-	-	-
Did the person attend kindergarten?								
Yes	168	74,34	178	78,76	0,78	0,50	1,20	0,26
No	58	25,66	48	21,24	1,00	-	-	-
Does the mother have asthma?								
Yes	23	10,18	50	22,12	0,33	0,23	0,67	<0,01
No	203	89,82	176	77,88	1,00	-	-	-
Does the mother have rhinitis?								
Yes	107	47,35	117	51,77	0,83	0,57	1,21	0,34
No	119	52,65	109	48,23	1,00	-	-	-
Does the father have asthma?								
Yes	32	14,16	31	13,72	1,03	0,60	1,76	0,89
No	194	85,84	195	86,28	1,00	-	-	-
Does the father have rhinitis?								
Yes	93	41,15	95	42,04	0,96	0,66	1,40	0,84
No	133	58,85	131	57,96	1,00	-	-	-
Birth weight (grams)								
Up to 2.499	17	7,52	40	17,70	0,37	0,20	0,68	<0,01
> 2.500	209	92,48	186	82,30	1,00	-	-	-

Prematurity								
Pre-term	41	18,14	47	20,80	0,84	0,52	1,34	0,47
Term or post-term	185	81,86	179	79,20	1,00	-	-	-
Type of birth								
Cesarean	130	57,52	51	22,57	4,64	3,08	6,99	<0,01
Normal	96	42,48	175	77,43	1,00	-	-	-

Table 2: Odds ratio (OR) and 95% confidence interval (95% CI) of paternal pathological history and child physiological history associated with controlled asthma in children and adolescents

Variables	Case:		Control:		Brute OR	CI 95%		p-value
	n	%	n	%				
Dogs at home in the present								
Yes	135	59,73	139	61,50	0,92	0,63	1,35	0,70
No	91	40,27	87	38,50	1,00	-	-	-
Dogs at home in the first year of life								
Yes	93	41,15	159	70,35	0,29	0,19	0,43	<0,01
No	133	58,85	67	29,65	1,00	-	-	-
Cats at home in the present								
Yes	63	27,88	108	47,79	0,42	0,28	0,62	<0,01
No	163	72,12	118	52,21	1,00	-	-	-
Cats at home in the first year of life								
Yes	60	26,55	106	46,90	0,40	0,27	0,60	<0,01
No	166	73,45	120	53,10	1,00	-	-	-
People who Smoke indoors								
Yes	106	46,99	60	26,55	2,44	1,64	3,62	<0,01
No	120	53,10	166	73,45	1,00	-	-	-
Home activity with pesticides								
Yes	93	41,15	21	9,29	6,82	4,05	11,49	<0,01
No	133	58,85	205	90,71	1,00	-	-	-
Home close to agricultural activity								
Yes	51	22,57	55	24,34	0,90	0,58	1,40	0,65
No	175	77,43	171	75,66	1,00	-	-	-
Presence of people in the household who work in agriculture								
Yes	154	68,14	51	22,57	7,33	4,82	11,15	<0,01
No	72	31,86	175	77,43	1,00	-	-	-
Pesticide spraying close to home								
Yes	51	22,57	55	24,23	0,90	0,58	1,40	0,65
No	175	77,43	171	75,66	1,00	-	-	-
Location of mother's work while pregnant								
Countryside	97	42,92	24	10,62	6,32	3,84	10,41	<0,01
Urban	129	57,08	202	89,38	1,00	-	-	-

Table 3: Odds ratio (OR) and 95% confidence interval (95%CI) of household exposure and exposure to pesticides associated with controlled asthma in children and adolescents.

is clear that breastfeeding prevents the early introduction of potentially immunogenic foods such as cow's milk^{5,6,7}. Studies prove the contamination of breast milk by pesticides, especially in mothers who live in rural areas and work directly exposed to them¹⁴.

Although this is not strong enough evidence to discourage breastfeeding, it is another means of exposure for children living in rural areas and municipalities with intense agricultural activity.

In the bivariate analysis, we found an association between high family income and controlled asthma. It is worth highlighting that people with high socioeconomic status, literate, tend to have greater knowledge about the pathology, access to specialist doctors and quality medicines, so it is possible that higher incomes reflect the presence of asthma. From this perspective, individuals with lower income may be excluded from statistics as they have less access to doctors and may have a delay in diagnosing asthma⁴.

On the other hand, mothers with incomplete secondary education represented a risk for asthma, with a possible explanation being the intersection between a lower level of education, lower social class, absence of a steady partner and worse housing conditions¹⁵.

Cesarean delivery is considered a risk factor for the development of asthma in children of different ages, as demonstrated in the bivariate analysis. One of the hypotheses indicates that the initial colonization of the intestinal microbiota in children born via cesarean section with *clostridium difficile* is associated with the risk of asthma^{36,37}. Another possibility already reported is the EPIC (Epigenetic Impact of Childbirth) hypothesis, which suggests that the fetal genome undergoes chromatin remodeling and that DNA methylation occurs during the intrapartum period³⁸. Children born by cesarean section have higher DNA methylation than children

born vaginally, possibly leading to greater susceptibility to disease³⁸.

Furthermore, cesarean section births are often associated with premature children and low birth weight, leading to the question of possible bias in the analysis, given that low birth weight itself is associated with asthma²⁰.

Despite the controversy over the association between low birth weight and asthma, it remained in the logistic regression of this study⁵. It is believed that children born weighing less than 2500g, in addition to specifically neonatal respiratory complications¹⁹, suffer from changes in lung development and have reduced airway caliber⁵, as well as histamine hyperreactivity¹⁹. Studies show that children with low birth weight are predisposed to lower respiratory tract infections, which can act as triggers for bronchial hyperreactivity, thus increasing the risk of asthma. Despite these data, the association tends to be questioned since there is difficulty in separating low birth weight from other perinatal factors such as intrauterine growth restriction, intrauterine nutritional deficiency and prematurity¹⁹.

Exposure to pets is a controversial issue related to atopic diseases such as asthma, and may act as a beneficial factor for asthmatic patients or as a decompensating factor^{4, 35}, varying according to the age at which contact began, contact time and number of animals⁵. In this study, exposure to animals, especially in the first year of life, was shown to be a protective factor against asthma, corroborating the theory that early exposure may predispose tolerance and immunomodulation⁵.

The presence of smokers at home was associated with controlled asthma in the bivariate analysis, in line with the literature. Studies estimate that children who live with smoking parents are passively exposed to around 30-150 cigarettes a year, thus being at greater risk of wheezing and even asthma exacerbations⁵. In addition to the association

between exposure to smoke and worsening bronchial hyperresponsiveness, tobacco is also associated with changes in the action of anti-asthmatic medications²³.

This study has some limitations, such as not matching gender and age. Despite this, the ISAAC tool stratifies individuals into just 2 age groups, meaning that, even without pairing, the ages are sufficiently similar to allow for a good analysis. Furthermore, the randomization of cases and controls allowed for the even division of these variables. Another limiting point is the difficulty of specifically determining which pesticides are associated with controlled asthma, since individuals are exposed to several of them.

A favorable point of this analysis is the derivation of a previous study³⁹ focused on uncontrolled asthma, allowing controlled asthma to be evaluated in the present study in a complementary manner to the other analysis. Furthermore, the research site represents an important agricultural hub in which there is abundant use of pesticides and, consequently, intense exposure of the population, making it necessary to investigate and debate the possible harm of such a practice.

CONCLUSION

Associations were found between low birth weight, daycare attendance and household activities that use pesticides with the development of controlled asthma, as well as the association of breastfeeding as a protective factor against the development of controlled asthma.

These results point to the importance of actions aimed at educating the population about the need for the correct use of PPE, as well as the cautious use of pesticides in or near the home. It is also necessary to debate the control of pesticides used in large productions, as they are responsible for the dispersion of chemicals. The integral view of individuals is discussed, remembering that the mother-child binomial is usually exposed together, thus making it necessary to provide guidance on ways to reduce maternal exposure and ways to protect the child, such as breastfeeding.

Furthermore, in the case of controlled asthma, prevention and health promotion actions must come mainly from primary health care, aiming to control and reduce possible exacerbations.

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