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Prevalence and associated factors for asthma in Brazilian and Japanese schoolchildren living in the city of São Paulo, Brazil

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Summary
Objectives. *Ethnic background interferes on the prevalence of asthma among schoolchildren (4 to 9 years old, SC) born and living in São Paulo, Brazil.* ***Methods.*** *International Study of Asthma and Allergy in Childhood (ISAAC)'s written standard and complementary questionnaires were applied to SC (similar socioeconomic status) living in the city of São Paulo: no-Japanese Brazilian (NJB, N = 306) and Japanese Brazilian (third generation, born in Brazil, from Japanese families with no miscegenation, JB, N = 258).* ***Results.*** *The prevalence of current asthma was significantly higher among NJB in comparison to JB (22.2% vs 14.7%, respectively). To have rhinitis and to exercise less than once/week were risk factors for both groups of children.* ***Conclusion.*** *Although both groups were apparently exposed to the same environment, other cultural differences do not allow us to conclude about the ethnic component having greater influence than the environment in the development of asthma in these individuals.*

Introduction

Despite overall improvements in health, there is renewed concern that racial and ethnic disparities in health persist and in some cases may have expanded. Ethnic health disparities are inherently linked to immigration because ethnic identities are traced to the country of origin of an immigrant or their ancestors. A body of international literature suggests that there is an increased prevalence of atopy and asthma in immigrants following migration (1-16).
Migration studies examining children of the same ethnic background living in different environments for part or all of their lives may help to identify relevant factors to the development of diseases and may explain some of the observed geographic variations in prevalence.
Leung et al. evaluated the prevalence of asthma and allergic diseases among Asian immigrants (Chinese) in Australia compared to non-Asian Australians and Asians born in Australia (1,2). They observed an increased prevalence of asthma among immigrants depending on time of immigration to Australia, regardless of age when immigrated, gender and atopic status, suggesting that the environment plays an important role in the pathogenesis of asthma and allergy (1,2). Similar results were observed by Wang et al.

in studying the prevalence of asthma among Canadian-born Chinese teenagers, young Chinese immigrants to Canada and young Chinese living in China, using data from the International Study of Asthma and Allergies in Childhood (ISAAC) phase 3. The prevalence of asthma among Chinese teenagers was lower than that of immigrants or those born in Canada, strengthening the influence of environmental factors on the prevalence of asthma (3). Other studies evaluated populations immigrated to Sweden (4), Italy (5-10), Israel (11), and United States of America (12-16).

In the last century, many people immigrated to Brazil, including the Japanese and nowadays they constitute the largest colony of Japanese individuals outside of Japan. The prevalence of current asthma in Brazil is 24.2% for children aged 6-7 years (17,18) while in Japan, it is 18.2% (18). This difference in prevalence opens the opportunity to evaluate the influence of environmental factors on ethnic factors, in relation to asthma.

Brazilian children of Japanese ancestry (i.e. no mixed marriages and whose grandparents were born in Japan), despite sharing genetic polymorphisms with those Japanese children, were born and live in a different environment: Brazil.

Migrating populations with no miscegenation provide an opportunity to observe changes in disease with changes in environment, just as genetically different groups living in the same region allow study of the effects of genetic diversity.

The aim of this study was to examine prevalence and risk factors for asthma manifestation among Brazilian children of Japanese ancestry and Brazilian children of non-Japanese ancestry period.

Materials and Methods

Children - children (aged 4 to 9) from three private schools - located in the southern part of the city of São Paulo, Brazil, and intended primarily for Japanese descendants (Japanese Brazilian, JB) - were invited to participate in this study. All schools were informed and acreddited by the Japanese Consulate in São Paulo. After an initial agreement by telephone, an interview was scheduled with the school's principal. Detailed explanation of the purpose of the study and the steps necessary to complete it correctly were provided (i.e. response to ISAAC written questionnaires (WQ) and informed consent signed by the parents or guardians). According to their origin children were divided into two ethnic groups, those born of marriages between Japanese only (third generation, born in Brazil, from Japanese families with no miscegenation; JB group) and those of non-Japanese Brazilian group (NJB). All students were from same socioeconomic level.

Sample size was calculated considering a α error of 5%, power of the test equal to 80% and 10% of difference in the prevalence of asthma (groups JB and NJB). So, the sample was estimated in 256 students in each group.

Questionnaires - ISAAC, standard (prevalence, phase 1, WQ) and complementary (risk factors - phase 2; CQ) written questionnaires, translated and validated for Brazilian culture (19,20) were applied according to the ISAAC protocol and answered by parents. The CQ was applied in order to evaluate the association between possible risk factors and asthma development and was answered by the parents at classroom.

The answers to the questions were transcribed to a database used by the ISAAC (Epi-Info 6.0), with double entry.

Statistical analysis - results were presented as percentage of affirmative responses among those applying. The comparative analysis between the two ethnic groups (JB and NJB) was performed by Chi-square test.

An affirmative answer to the question about wheeze in the last year and wheeze severe enough to limit speech in the last year defined SC with current asthma, and severe asthma respectively (18).

The groups of children with asthma symptoms and without asthma symptoms, in each ethinicity, were compared with respect to exposure to several factors identified by the CQ, and risk factors were identified by logistic regression. All variables from CQ were included in the univariate analysis and those with a $p < 0.20$ were included in the multivariate analysis and complemented with Forward stepwise regression. Variables with significant value were identified ($p < 0.05$).

Study was approved by the Ethics Committee of Federal University of São Paulo - Hospital São Paulo and all parents signed an informed consent.

Results

Table 1 shows the prevalence of asthma and related symptoms among NJB and JB children according to their progeny. The prevalence rates were in overal higher among NJB children. The prevalence of current asthma (22.2% *vs* 14.7%) and of wheezing with exercise (5.6% *vs* 1.9%) was significantly higher among NJB.

Table 2 shows the prevalence of asthmatic children exposed to some factors, during the first year of life and nowadays, and the comparison of the two progenies. NJB children were significantly more like to: be born by cesarean section, have dog and birds in the house nowadays, have dog and birds in the house during the first year of life, doing exercise less than once a week, eating fish once a week, have fruits and crude vegetables twice a week. The JB were significantly exposed to: being breastfeed equal or more than 6 months, attending day care/nursery, having father with rhinitis, sharing bedroom nowadays, and taking soft drinks twice a week (**table 2**).

All these factors were submitted to a multivariate analysis and to logistic regression (**tables 3**). To have rhinitis and to do exercise less than once a week remained as independent risk factors for current asthma among JB and NJB. To be a boy and to have shared the bedroom in the first year of life increased the risk for asthma manifestation only among JBs (**table 3**). To have eczema and have lived in an urban area during the first year of life was significantly associated with asthma only in NJB children.

Table 1 *- Prevalence of asthma and related symptoms among schoolchildren living in São Paulo, according to their progeny: Japanese Brazillian (JB) or non-Japanese Brazilian (NJB).*

Question	JB N = 258 (%)	NJB N = 306 (%)	OR (95% CI)
Wheezy ever	121 (46.9)	150 (49.0)	0.96 (0.80-1.14)
Wheezy last 12 months	38 (14.7)	68 (22.2)[1]	0.66 (0.42-0.95)[1]
More than 4 attacks last 12 months	6 (2.3)	5 (1.6)	1.42 (0.44-4.61)
Sleep disturbance last 12 months	22 (8.5)	41 (13.4)	0.64 (0.39-1.04)
Speech problem last 12 months	1 (0.4)	1 (0.3)	1.29 (0.81-2.05)
Asthma ever	20 (7.8)	21 (6.9)	1.22 (0.68-2.20)
Wheeze with exercise last 12m	5 (1.9)	17 (5.6)*	0.35 (0.13-0.93)[1]
Cough at night last 12 months	90 (34.9)	128 (41.8)	0.83 (0.67-1.03)

Chi-square/Fisher - [1]$p < 0.05$

Finally, owning a dog and live in an urban area was identified as protective factors for NJB (**table 3**).

Discussion

This study was performed to examine the prevalence of asthma and related symptoms, as well as to identify risk factors for asthma manifestation among Brazilian children of Japanese ancestry (JB) and Brazilian children of non-Japanese ancestry (NJB).

We observed lower prevalence of current asthma and related symptoms among JB born in Brazil, from non miscigenated marriages, in comparison to NJB students. However, our rates were close to those previously observed in Japan and obtained as part of the ISAAC phase III (18). Similar tendency was observed by other authors evaluating different immigrant populations (1,2,14,15,21). Indeed there are studies showing that the prevalence of asthma is lower among individuals who were not born in the country where the study was carried out. However, there are also evidences that the prevalence among immigrants, tends to match to that of the local population when enough time elapses (22).

So, regarding our findings, some questions remain with no answer: Would be the sample of JB schoolchildren evaluated by the ISAAC phase III in Japan representative of the country? Would be the ancestors of Japanese born in Brazil from the same locality of those Japanese who were evaluated in Japan? The lowest rate of interracial marriages would guarantee lower mixing of the JB population?

In fact, interactions among genetic, environmental and social factors seem to be crucial in determining the prevalence of asthma and asthma-related symptoms. Predictive factors for asthma vary among racial/ethnic groups (1-4,12). Identifying race/ethnicity-specific modifiable environmental and host-related factors can be important in developing targeted interventions to reduce the health and economic impact of asthma.

Given that the mixture of environment and genetic background may vary across racial/ethnic populations, in many instances it may be difficult to identify the causal genetic effect separately from the environmental one.

As already pointed out, migrating populations with stable genetics provide an opportunity to observe changes in disease due to changes in environment. The environment has unequivocally undergone changes over the past decades and it has been shown as an important risk factor associated mainly with westernized lifestyle (urbanization, lack of exercise, dietary patterns, air pollution, and indoor pollution by passive smoking and aeroallergens, improved hygiene and health care etc. (23,24).

To be born and to live in the same locality give us the wrong idea that our children, JB and NJB, would be exposed to the same environmental factors. However, we must take into account the importance of cultural factors that may significantly influence lifestyle. This fact becomes clear when evaluating the differences on exposures observed between JB and NJB. Significant differences ocurred with respect to: type of delivery, duration of exclusive breastfeeding, type of feeding, having pets personal and family history of allergic diseases. We believed that some of these differences could be explained mainly by the maintenance of very ingrained habits in Japanese culture.

However, after logistic regression we observed some of our findings were unexpected. First of all we found that it remained as independent risk factors for current asthma, among JB and NJB, to have rhinitis and lack of exercise (less than once a week). Recent meta-analysis evaluated the prevalence and interrelationships between asthma, allergic rhinitis and eczema in children using data obtained from ISAAC questionnaires. The analisys has shown that the prevalence of children with a co-occurrence of asthma, eczema and allergic rhinitis was low, but significantly higher than could be expected by chance (25).

Table 2 *- Factors associated to asthma manifestation identified by univariate analysis among children aged from 4 to 9 years according their progeny - comparisons between Japanese Brazilian (JB) and No-Japanese Brazilian (NJB).*

Associated factors	NJB			JB		
	N total	N +ve	%	N total	N+ve	%
Birth weight < 2500g	302	33	10.9	258	38	14.7
Cesarean section	290	247	*85.2*[1]	246	170	69.0
Be twin	298	8	2.7	254	4	1.6
Breast feeding	304	282	92.8	258	244	94.6
Breastfeeding ≥ 6 months	282	167	59.2	246	188	*76.4*[1]
Breastfeeding ≥ 4 months	282	98	34.8	246	116	*47.2*[1]
To have older brothers	304	157	51.6	258	145	56.2
To have younger brothers	303	87	28.7	254	99	39.0
Day care / nursery	303	53	17.5	254	88	*34.6*[1]
Day care / nursery ≤ 1st year	53	31	58.5	88	63	71.6
Kind garden	284	284	100	241	240	99.6
Kind garden ≤ 1st year	283	14	4.9	250	21	8.4
Mother with asthma	306	15	4.9	258	5	1.9
Mother with rhinitis	306	110	35.9	258	88	34.1
Mother with eczema	306	19	6.2	258	25	9.7
Father with asthma	306	26	8.5	258	11	4.3
Father with rhinitis	306	84	27.5	258	78	*30.2*[1]
Father with eczema	306	13	4.3	258	19	7.4
Share bedroom today	293	163	55.6	252	176	*69.8*[1]
Share bedroom 1st year	244	139	57.0	231	147	63.6
Dog in the home today	306	96	*31.4*[1]	258	44	17.1
Cat in the home today	306	16	5.2	258	8	3.1
Birds in home today	306	53	*17.3*[1]	258	20	7.8
Dog in home 1st year	306	43	*14.1*[1]	258	18	7.0
Cat in home 1st year	306	9	2.9	258	3	1.2
Birds in home 1st year	306	26	*8.5*[1]	258	1	0.4
Smoking mother	294	31	10.5	253	17	67.2
Smoking mother 1st year	253	24	9.5	236	17	64.6
Smoking during pregnancy	253	21	8.3	224	10	4.5
Smoking in the house	303	41	13.5	256	32	12.5
Damp in home today	302	36	11.9	257	43	16.7
Damp in home 1st year	302	35	11.6	235	29	12.3
Mold today	300	27	9.0	257	22	8.6
Mold 1st year	259	25	9.7	239	17	7.1
Rural neighborhood today	278	57	20.5	248	41	16.5
Rural neighborhood 1st yr	236	46	19.5	232	58	25.0
Exercise less than once / week	298	241	*80.9*[1]	256	185	72.3
Eat meat twice a week	300	88	29.3	253	67	26.5
Eat fish once / week	286	258	*90.2*[1]	254	178	70.0
Fruits twice / week	294	103	*35.0*[1]	257	66	25.7
Crude vegetables twice / week	294	182	*61.9*[1]	254	89	35.0
Soft drink twice / week	299	195	65.2	255	208	*81.6*[1]

[1]Chi-square - Values in italic bold were $p < 0.05$; +ve = positive

Table 3 *- Factors associated with symptoms of asthma among children aged from 4 to 9 years, according to their progeny: Japanese Brazilian (JB) or No-Japanese Brazilian (NJB) identified by Logistic regression.*

Associated factors	JB	NJB
	OR (95% CI)	OR (95% CI)
Have cat nowadays	5.60 (0.89-35.33)	-
Urban neighborhood 1st year	-	5.32 (1.51-18.78)[1]
Have rhinitis	3.71 (1.69-8.14)[1]	2.85 (1.53-5.32)[1]
Male gender	2.96 (1.34-6.57)[1]	-
Have eczema	-	2.39 (1.06-5.40)[1]
Father with asthma	-	2.39 (0.95-6.06)
Exercise less than once / week	2.36 (1.04-5.34)[1]	2.01(1.00-4.03)[1]
Share bedroom 1st year	2.20 (1.00-4.87)[1]	-
Have dog nowadays	-	0.47 (0.23-0.93)[1]
Urban neighborhood nowadays	-	0.16 (0.05-0.49)[1]
Father with eczema	0.16 (0.02-1.32)	-

[1]$p < 0.05$; - = not included in the analysis

There is no doubt that a sthma and rhinitis should be viewed as a single disease, considering the high frequency of association between them. The presence of allergic rhinitis was significantly associated with current asthma in both groups. This fact, amply reported by other authors (26,27) had been previously documented by our group in schoolchildren assessed by the ISAAC phase III when we observe that to have active rhinitis increased significantly the risk of active asthma, and severe asthma in those schoolchildren (28).

We found that JB and NJB children who exercised less than once a week had a risk 2.36 and 2.01 times higher, respectively, to manifest asthma. In this regard, several studies suggest that nutrients (e.g. omega-3 fatty acids, vitamin D) and consumption of fruits and vegetables protect against asthma, while obesity and lack of exercise could have the opposite effect (29-31). The links that exist between asthma and obesity suggest that obesity probably leads to asthma in many cases and could be in part responsible for the "asthma epidemic". Moreover, there are two other very important factors - diet and exercise - which can favour both asthma and obesity in parallel. There is a growing body of literature that implicates specifically decreased physical activity, as a contributor to the increase in asthma prevalence and severity. Although the prevalence of asthma and related symptoms in our study has been lower among the JB, there were no differences regarding severity which remained intense in both groups (32,33).

To live in an urban area in the first year of life was significantly associated with asthma in NJB children. Intriguingly, among JB this effect was not observed, while the exposure to urban environment - nowadays - indeed protected NJB from asthma. Asthma prevalence and morbidity use to be greater in urban areas. Despite the number of studies looking for information about the relationship between early life exposures and asthma in this "high-risk environment" this association remain not completely clear and the doubts persist.

The urban environment has a number of features that could have adverse effects on children's respiratory health, especially during the first few years of life when the lung and immune system are rapidly developing (34).

However, there are limitations in ecological studies due to the difficulty in accurately estimating specific exposure - individual or combined - to infer a cause-effect (35-37). So the specific factors or combinations of factors that lead to asthma and/or protect against asthma when analising the indoor and outdoor environment, remains not completely elucidated.

It is quite possible that the differences between the indoor environment of JB and NJB can explain our observations (i.e. no association between urban neighborhood over the 1st year and asthma manifestation, among JB). In other words, perhaps differences in customs and habits - between JB and NJB - account for differences in indoor environment and consequently in exposures.

On the other hand although, there is evidence suggesting that exacerbations of asthma may be triggered by different air pollutants, the association between air pollution and increased prevalence of asthma is still controversial (38). Maybe this association would be clearer during the first year of life for the NJB children and not detectable nowadays. We found that to have eczema

increased in almost 2.4 fold the risk of asthma among NJB children. Intriguingly, we did not observe this association among JB. Whether eczema is a true risk factor for asthma has been debated, and the relationship between the different allergy-related disorders is unclear. There are evidences from cross-sectional and also from large prospective studies, indicating a strong association between eczema and asthma (28) period.

However, it is noteworthy that in addition to the early manifestation of eczema, it is commonly believed that the severity of eczema, male sex, early wheezing, heredity and allergic sensitisation are possible risk factors for the development of childhood asthma (39).

To be a boy and to have shared the bedroom in the first year of life increased the risk for asthma manifestation only among JBs. We can not explain why the classical association "male gender and increased risk for asthma" did not occur among NJB. Gender seems to be an important determinant for asthma and allergies and its impact varies considerably from childhood into adolescence and adulthood. In childhood, boys are consistently found to be at increased risk of asthma, which has been explained by differential growth of lung/airway size, and immunological differences (40,41).

The hygiene hypothesis suggests a protective effect of large families, with many children living in the same environment and often sharing the same bed. This kind of environmente favours viral infecctions and may increase the exposure to endotoxins, and these factors may protect the child from sensitization to aeroallergens, asthma and rhinitis.

A number of epidemiological studies, using different measures of crowding such as total number of residents in the home, number of siblings, number of persons sharing the bed, room occupancy, and population density, have reported an association between crowding and respiratory diseases (42).

There are studies demonstrating an inverse relationship between the number of people in the bedroom and the frequency of asthma (protection) (42) and others an association between sharing a bedroom during the first year of life and asthma (risk) (43).

Unlike one of the proposals of the hygiene hypothesis, we found that sharing a bedroom during the first year of life was a risk factor, not a protective factor for current asthma among JB.

In this study, the association between exposures to pets at home was different depending on ethnicity. Among JB, to have been exposed to a cat or a dog during the first year of life or nowadays did not exert any significant effect on asthma manifestation. On the other hand to be exposed nowadays to dogs protects NJB from the disease. The role of pet exposure, mainly cat and dog, inside the house as either a risk or a protection factor for childhood asthma manifestation is still controversial. Exposure to cats and dogs at home was evaluated in children aged 6-7 years and adolescents (13-14 years) participating in the ISAAC phase 3. Early-life exposure to cats was identified as a risk factor for symptoms of asthma, rhinoconjunctivitis, and eczema in 6-7-year-old children, especially in less-affluent countries. Current exposure to cats and dogs combined, and only to dogs, is a risk factor for symptom reporting by 13-14-year-old adolescents worldwide (44) period.

There are lots of evidence about the strong genetic component on allergic diseases and asthma manifestation. In this respect, maternal and paternal history of asthma and allergic diseases has been consistently implicated on a higher risk of childhood asthma, on the great majority of studies. Maternal history of asthma seems to has greater impact on the subsequent development of asthma in children, than paternal history of asthma.

Surprisingly, we did not observe a significant relationship between family history of allergic diseases and asthma manifestation neither among JB nor NJB. We can not explain this finding. Even knowing that this type of study could have led to memory bias, we didn't believe that these items could explain the "absence of the role of maternal and paternal history on the risk of asthma development".

In conclusion, we observed lower prevalence of current asthma and related symptoms among JB born in Brazil, from non miscigenated marriages, in comparison to NJB students.

Different factors were implicated on the risk of asthma depending on ethnicity/race, except "to have rhinitis" and "lack of exercise" that were independent risk factors for current asthma among JB and NJB. "Owning a dog" and "living in an urban area" were the only protective factors identified just among NJB children.

It is known that genetically similar populations exposed to different environmental conditions display different temporal trends in the prevalence of allergic symptoms. However, because of the interaction and of the multiple causal pathways between the factors studied, the exact contribution or the exact influence that each one it would have exerted on differences and similarities observed - according to race/etinicity - is very difficult to establish and to validate.

Further studies in Brazil and Japan, including objective measures such as allergen skin prick test, bronchial hyperresponsiveness and environmental measurements (e.g., endotoxins and diesel exhaust particles) are necessary to identify the risk factors or protective factors associated with asthma.

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