**Asthma in Latin America**

**Online Supplementary Material**

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**Supplemental Table – Summary of selected studies on Asthma in Latin America**

| Reference | Study Design | Main Findings / Comments |
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| Prevalence, morbidity, and mortality | | |
| Mallol *et al*.[5] | Multicenter study on the prevalence of asthma in 165,917 schoolchildren from 56 centers in 17 Latin American countries, as part of the International Study of Asthma and Allergies in Childhood (ISAAC). | 55% of centers reported a prevalence of asthma over 15%. There was no significant correlation between asthma symptom prevalence and latitude, altitude, tropical setting, or gross national income (GNI). |
| Rodriguez *et al*.[16] | Study assessing differences in asthma prevalence in 59 transitional communities in northeastern Ecuador, based on indicators of urbanisation grouped into socioeconomic, lifestyle and urban infrastructure factors. | Three of the four indices presented significant associations with community asthma prevalence: socioeconomic ($r = 0.295$, $p = 0.023$), lifestyle ($r = 0.342$, $p = 0.008$) and summary urbanisation index ($r = 0.355$, $p = 0.006$). In summary, the prevalence of asthma increased with higher levels of urbanisation in these communities. |
| Ancestry, genetics, and epigenetics | | |
| Brehm *et al*.[18] | Cross-sectional case-control study of 943 Puerto Rican children aged 6 to 14 years with (n= 520) and without (n= 423) asthma living in Hartford, CT, and San Juan, PR. | Each 20% increment in African ancestry was associated with lower prebronchodilator FEV1 (–105 mL; 95% CI, –159 to –51 mL) and FVC (–133 mL; 95% CI, –197 to –69 mL), and postbronchodilator FEV1 (–152 mL; 95% CI, –210 to –94 mL) and FVC (–145 mL; 95% CI, –211 to –79 mL) in children with asthma. |
| Hunninghake *et al*.[29] | Candidate-gene study of the association between TSLP polymorphisms and asthma in Costa Rican children, with replication in two cohorts of African-American participants and two cohorts of non-Hispanic white participants. | Two SNPs in TSLP were significantly associated with a reduced risk of asthma in combined analyses of all cohorts. In a sex-stratified analysis, the T allele of rs1837253 was significantly associated with a reduced risk of asthma in males only, while the T allele of rs2289276 was significant in females only. |
| Torgerson *et al*.[31] | Meta-analysis of North American genome-wide association studies of asthma in 5,416 individuals with asthma (cases) including individuals of European American, African American or African Caribbean, and Latino ancestry, with replication in an additional 12,649 individuals. | Identified five susceptibility loci, and reported for the first time that these loci are associated with asthma risk in three ethnic groups. In addition, identified a new asthma susceptibility locus at PYHIN1, with the association being specific to individuals of African descent. |
| Moreno-Macías *et al*.[40] | Study on the effect of ozone on lung function in 257 asthmatic children in Mexico City. | Higher ozone exposure was associated with lower lung function in children with low vitamin C, only among those with more (4-6) risk alleles in putative anti-oxidant genes, compared to those with fewer (1-3) risk alleles. Genetic susceptibility may interact with the environment (high oxidant stress and low intake of antioxidants) and lead to lower lung function in children with asthma. |
| Early-life risk factors | | |
| García-Marcos *et al*.[41] | Population-based study of 28,687 children in centers in Latin America (LA) and Europe (EU). | Both in LA and EU, having a cold during the first 3 months of life and attending a nursery were the most significant risk factors for recurrent wheezing. Breastfeeding for 3 or more months reduced the risk of recurrent wheezing (aOR 0.8; 95%CI 0.71-0.89 in LA, and aOR 0.77; 95%CI 0.63-0.93 in EU). |

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| Rosas-Salazar *et al*.[42] | Case-control study of 1,127 Puerto Rican children (6-14 years) living in Hartford, Connecticut (n = 449) and San Juan, Puerto Rico (n = 678). | Breastfeeding for up to 6 months reduced the odds of asthma by 30% compared to no breastfeeding. Breastfeeding for longer than 6 months did not significantly change the odds of asthma. |
| Diet and obesity | | |
| Brehm *et al*.[44] | Cross-sectional, case-control study of 616 children ages 6-14 years in the Central Valley of Costa Rica. | Up to 28% of children had insufficient vitamin D levels (<30ng/mL). Vitamin D was associated with lower total IgE, eosinophil count, reduced odds of asthma-related hospitalizations, and reduced used of anti-inflammatory medications in the previous year. This was the first study to demonstrate an inverse association between vitamin D levels and markers of atopy and asthma severity. |
| Checkley *et al*.[46] | Population-based study of 1,441 children in two communities in Peru with different latitudes and degrees of urbanization. | Both asthma and vit.D deficiency were higher in Lima (latitude 12ºS) than in Tumbes (3.6ºS). Low vit.D was associated with asthma in both populations, but only among atopic children. |
| Psychosocial stress | | |
| Lange *et al*.[61] | Parents of 339 pairs of Puerto Rican twins were interviewed (separately) about their own psychosocial stress. Asthma-related outcomes in the children included asthma status, recent symptoms, oral steroid use, and hospitalizations. | In the adjusted analyses, paternal PTSD symptoms, depression, and antisocial behavior were each associated with increased asthma symptoms at age 1 year; and maternal depression symptoms were associated with increased odds of hospitalizations at ages 1 and 3 years. This was the first report of an independent association of both maternal depression and paternal stress with asthma outcomes in childhood. |
| Alves Gda *et al*.[63] | Cross-sectional study of 1,232 parents in 24 peripheral neighborhoods in Salvador, Brazil, looking at acts of violence in the community and asthma symptoms in children. | Children exposed to violence showed higher asthma prevalence (28.4%) as compared to non-exposed children (16.4%). Children exposed to maximum levels of violence were nearly twice as likely to present asthma symptoms (aOR = 1.94; 95%CI: 1.12-3.36). |
| Infections | | |
| Cooper *et al*.[65] | Cross-sectional study of the effects of farming and poor hygiene exposures on atopic symptoms in 2,526 urban and 4,295 rural school children in Ecuador. | Urban children had a similar prevalence of atopy, eczema and wheeze but a higher prevalence of rhinitis compared with rural children. Some farming and poor hygiene exposures were associated with an increase in the prevalence of wheeze or rhinitis, while birth order was inversely associated with these symptoms. |
| Alcantara-Neves *et al*.[66] | To investigate the effect of single or multiple infections on atopy and wheeze, infections by 8 pathogens, specific IgE levels, and skin prick testing were measured in 1128 urban children (ages 4-11). | Negative results for *A.lumbricoides*, *T.gondii*, herpes simplex virus, and EBV were associated with a higher prevalence of skin test reactivity. Children with 3 or fewer infection markers had a higher prevalence of IgE and skin reactivity compared with those with 4 or more infection markers. However, isolated infections or pathogens were not associated with the prevalence of wheeze. |
| Allergens and pollutants | | |
| Forno *et al*.[85] | Indoor dust allergen levels were measured in Puerto Rican | Higher mouse allergen levels were associated with higher $FEV_1$ |

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| | children with and without asthma living in Hartford, CT (n=449) and San Juan, PR (n=678). | among children with asthma, and with lower odds of skin test reactivity among controls, who were not sensitized to mouse. |
| Gómez *et al*.[88] | Cross-sectional survey of 3000 adolescents aged 13-14 years in northern Argentina as part of ISAAC. | Active smoking and passive smoke exposure from a parent were both associated with asthma and with rhinitis, after adjusting for parental smoking, sex, and maternal educational level. |
| Escamilla-Núñez *et al*.[90] | Longitudinal study of 147 children with asthma and 50 controls, followed for an average of 22 weeks. Exposure was estimated from outdoor $PM_{2.5}$, $NO_2$ and $O_3$ concentrations, as recorded by the Mexico City government at four fixed sites for central monitoring. | Wheezing was significantly associated to all three traffic-related air pollutants. Diesel-fueled motor vehicle traffic was also associated with increased bronchodilator use. |
| Rosser *et al*.[93] | Cross-sectional study of 351 children in Puerto Rico, based on distance to major roadways and asthma-related outcomes. | Each 100-meters closer to a major roadway was associated with 15% increased odds of severe asthma exacerbations; children living within <172 meters had 3-fold higher risk than those >440 meters. Children living closer to a roadway who were also vit.D insufficient had 4.8 times higher risk. This was the first report of a joint effect of traffic-related air pollution and low vit.D levels. |
| Diagnosis, management, and economic impact | | |
| Soto-Martinez *et al*. [96] | Ecological study examining trends in asthma hospitalizations and mortality in Costa Rica before and after implementation of a National Asthma Program (NAP). | After implementation of NAP, there was a marked reduction in asthma hospitalizations and mortality (from 25 deaths in 2000 to 5 deaths in 2011). During this same time, prescriptions for inhaled beclomethasone increased by ~130%. |
| Neffen *et al*.[97] | Ecological study of asthma mortality and asthma drug sales in Argentina, 1990-1999. | Compared to the previous decade, sales if inhaled corticosteroids (ICS) increased ~4-fold, and this increase in ICS correlated with a decrement in age-adjusted asthma mortality. |
| Neffen *et al*.[105] | Cross-sectional study of cost and level of health care for 2,074 asthmatic patients from 10 Latin American countries. | Over 57% of patients required unscheduled visits for asthma, with 45% reporting at least one emergency room visit. On average 73% of annual costs of asthma-related care in the 10 countries was due to unscheduled visits. |
| Cruz *et al*.[109] | The Program for Control of Asthma (ProAR) with 2,385 patients in Salvador, Brazil, included education, free medications, and regular follow-up. | The ProAR markedly reduced health resources utilization, and decreased asthma-related hospitalizations by 74%. It also reduced asthma-related costs to both the family and the health system. |