

ORIGINAL ARTICLE: ASTHMA

Asthma mortality among Mexican children: Rural and urban comparison and trends, 1999-2016

Eduardo Hernández-Garduño MD, MHSc 

Dirección de Administración y Desarrollo de Personal, Instituto de Seguridad Social del Estado de México y Municipios (ISSEMyM), Toluca de Lerdo, Mexico

Correspondence

Eduardo Hernández-Garduño, Dirección de Administración y Desarrollo de Personal, Constituyentes # 703, Colonia Barrio de la Merced, Toluca de Lerdo 50080, México.
Email: epidemiologist.researcher@gmail.com

Abstract

Objective: Although there are more studies showing higher asthma prevalence in urban rather than rural zones, few assessed asthma mortality by zone in children. The objective of this study is to compare asthma mortality rates (AMR) by zone of residence of Mexican children.

Design: Using national death certificate and population projections data, AMR were compared in children aged 0 to 14 years by gender, age group, and zone of residence from 1999 to 2016. AMR trends were calculated using Joinpoint regression.

Results: Of the 680 823 deaths, 2464 (0.36%) were due to asthma. Asthma mortality was higher in rural (0.65%) than urban (0.26%) zones, $P < .0001$. Whole period AMR median was also higher in rural vs urban zones (0.6 vs 0.3, respectively), $P < .05$. The average annual percent change (AAPC) of AMR for the whole period was -5.1 in all children with a higher percent decrease in rural vs urban zones (girls' AAPC = -6.3 vs -4.1 , respectively and boys' AAPC = -4.8 vs -4.2 , respectively). AMR decreased in children aged 0 to 4 from both zones (rural's AAPC: girls = -7.9 , boys = -5.2 ; urban's AAPC: girls = -5.1 , boys = -5.4), $P < .05$. No trend was found in children aged 5 to 14.

Conclusions: Asthma mortality in Mexican children is higher in rural than urban zones. The decrease of mortality over time in early childhood is reassuring. More research is needed to determine reasons for higher mortality in rural Mexico and for the lack of a favorable decreasing trend in children aged 5 to 14 from both zones.

KEYWORDS

cause of death, epidemiology, mortality trends, zone of residence

1 | INTRODUCTION

Approximately 339 million people worldwide suffer from asthma and nearly 1000 patients die daily from the disease.¹ Asthma is the most common chronic condition among children, currently affecting an estimated 6.1 million children under 18 years and more than half of these suffered an asthma attack in 2016 in the United States.² Though adults are four times more likely to die from asthma than children, mortality is avoidable with proper treatment and care.

Higher asthma prevalence in urban compared with rural settings,³⁻⁵ have been shown in studies in children and adolescents. Other studies found higher prevalence in rural zones⁶ and still others

showed no difference between farm and nonfarm rural dwellers⁷ or between farm and small-town zones.⁸ While the majority of data show higher asthma prevalence in urban settings, studies in asthmatic children showed that rural children develop more symptoms than urban children.³

Asthma mortality rate (AMR) trends can determine not only the burden of asthma but evaluate the impact of changes to asthma care/treatment and control of environmental triggers. Asthma mortality studies by zone report conflicting results whether populations of all ages,⁹ children, adults or combinations of both. While one study showed increased asthma mortality with urbanization¹⁰ others found higher mortality in rural zones.^{11,12} Some of these studies, including

an old Mexican study,¹³ reported a favorable decreasing trend of asthma mortality overtime. Contrary to this, a recent US study found no significant changes from 1999 to 2015 and low mortality rate in children aged 1 to 14.¹⁴ However, analysis by zone of residence was not performed neither the Mexican nor US studies.

Due to the lack of a national asthma registry the prevalence and incidence of asthma in Mexico is unknown with prevalence estimates determined only by specific cities/hospitals. However, national mortality data has been kept up to date for decades and is publicly available online at the "Dirección General de Información en Salud" website.¹⁵

While prevalence estimates for various health conditions and associated outcomes have been reported for rural children in the aggregate, information stratified by gender and geographic location is limited. Health research studies by zone of residence remain scarce in Mexico.

No previous studies have compared asthma mortality by zone of residence in Mexican children. To bridge this knowledge gap this countrywide study attempts to determine and assess differences and trends in AMR by gender, age groups, and zone of residence (rural and urban) among Mexican children.

2 | METHODS

2.1 | Study population

Databases of death certificates of all children younger than 15 years of age in the whole country of Mexico from 1999 to 2016 are available to the public through the "Dirección General de Información en Salud" webpage¹⁵ which is under the responsibility of the "Instituto Nacional de Geografía y Estadística or INEGI" and the Mexican Ministry of Health. Database information includes age at the time of death, gender, the zone of residence, based on community size, defined in Mexico as rural, less than 2500 inhabitants and urban 2500 or more. The database also includes place of death (home, others) and the cause of death which is coded with the International Classification of Diseases 10th edition (ICD-10th) codes for asthma (J45 and J46).

2.2 | Analysis

The annual number of asthma deaths (ANAD) was divided by total causes of death (after excluding external causes of death, codes: S00-Y98 such as accidents) to determine the percentage of asthma as cause of death by gender and zone of residence. The AMR was calculated annually by gender, age group (0-4, 5-9, and 10-14 years), and zone of residence and expressed per 100 000 population. The annual population projections data set was available from "Consejo Nacional de Población o CONAPO".¹⁶

ANAD and AMRs were calculated by year to obtain whole period medians of both zones of residence. The Kruskal-Wallis test was used

to determine differences in ANAD and AMR medians of the 18-year period by gender and zone. The percent change of the whole period was calculated as follows: 2016 estimates (ANAD or AMR) time 100 divided by 1999 estimate minus 100. These analyses were performed with SAS version 9.4 (Statistical Analysis System, Cary, NC).

To determine mortality trends, the average annual percent change (AAPC) and 95% confidence intervals of AMR were calculated by gender, age group, and zone of residence using Joinpoint trend analysis software.¹⁷ The AAPC is derived by first estimating the underlying Joinpoint model that best fits the data. The AAPC over any fixed interval is calculated using a weighted average of the slope coefficients of the underlying Joinpoint regression line with the weights equal to the length of each segment over the interval. The final step of the calculation transforms the weighted average of slope coefficients to an annual percent change. If we denote b_i as the slope coefficients for each segment in the desired range of years, and the w_i as the length of each segment in the range of years, then:

$$APC_i = \{ \text{Exp}(b_i) - 1 \} \times 100.$$

and

$$AAPC = \left\{ \exp \left(\frac{\sum w_i b_i}{\sum w_i} \right) - 1 \right\} \times 100.$$

Asthma diagnosis is difficult to ascertain in children under 2 years of age since several other important causes of mortality could be erroneously ascribed to asthma. For instance, children hospitalized with rhinovirus bronchiolitis have asthma-like characteristics¹⁸ so it would be desirable to analyze AMR in children age <2 years, however, the annual population projection estimates are usually available in 5-year groups, that is, 0 to 4, 5 to 9, and 10 to 14 and, therefore, it was not possible to determine AMR. Instead, the option was to run a separated joinpoint regression analysis of ANAD for each year of life starting with those <1 (0 years) by zone.

Ethics approval was not required as the study was based on deidentified data available online.

3 | RESULTS

A total of 680 823 deaths in children age <15 years were recorded during the study period and 2464 of these (0.36%) were due to asthma. Asthma deaths were more likely in rural rather than urban zones in all children (0.65% vs 0.26%, respectively), boys (0.60% vs 0.26%), and girls (0.72% vs 0.27%), $P < .0001$. Rural girls aged 0 to 4 or 5 to 9 were more likely to die from asthma compared with urban girls. Rural boys age 0 to 4 were more likely to die from asthma than their counterpart urban boys. No statistically significant difference between zones was found in girls aged 10 to 14 or boys age 5 to 9 or 10 to 14. Girls aged 0 to 4 from both zones were more likely to die from asthma compared with boys of the same age group, ($P < .02$) but no significant difference was found in the other age groups (Table 1).

TABLE 1 Number of asthma deaths and percentage (of all deaths) by zone of residence, gender, and age groups

	Zone of residence				Total		P value ^a	P value ^b
	Rural		Urban					
	N =	%	N =	%	N =	%		
Both sexes								
All ages	1137	0.65	1327	0.26	2464	0.36	<.0001	
All other causes ^c	173 800	99.35	504 559	99.74	678 359	99.64		
Total	174 937		505 886		680 823			
Age 0-4	916	0.60	894	0.20	1810	0.30	<.0001	
Age 5-9	109	0.98	192	0.77	301	0.83	.04	
Age 10-14	112	0.99	241	0.91	353	0.93	.45	
Girls								
All ages	561	0.72	604	0.27	1165	0.39	<.0001	.003
Age 0-4	449	0.66	399	0.20	848	0.32	<.0001	.02
Age 5-9	57	1.09	83	0.71	140	0.83	.01	.91
Age 10-14	55	1.04	122	0.98	177	1.00	.72	.21
Boys								
All ages	576	0.60	723	0.26	1299	0.34	<.0001	
Age 0-4	467	0.55	495	0.19	962	0.28	<.0001	
Age 5-9	52	0.88	109	0.82	161	0.84	.65	
Age 10-14	57	0.95	119	0.84	176	0.88	.48	

Note: Analysis includes all deaths in children aged 0 to 14 y, Mexico 1999-2016.

^aP value between zones.

^bP value between boys and girls including both zones together by the χ^2 test.

^cExternal causes of death were excluded.

Asthma deaths in rural zones represented 46.1% of all asthma deaths (1137 out of 2464), 48.1% in girls and 44.3% in boys. The 18-year period ANAD medians were higher in urban rather than rural zones but the difference was not statistically significant. However, AMR medians were significantly higher in rural vs urban zones (respectively, 0.6 vs 0.3 in all children, 0.7 vs 0.3 in boys, and 0.6 vs 0.3 in girls), $P < .05$, Table 2. The analysis by zone showed no difference in AMRs medians between boys and girls.

From 1999 to 2016 the ANAD and AMR decreased between 43.9% and 76.8% in the analysis of the whole sample. The highest decline was found in rural girls (ANAD, 76.8%; AMR, 73%; Table 2). The Joinpoint regression analysis of the whole period (zero Joinpoints) showed a favorable decreasing trend of AMR including all children and both zones together (AAPC = -5.1).

The stratified analysis by zone showed a higher percent decrease in rural compared with urban children (AAPC = -5.6 vs -4.1, respectively; Figure 1). The same trend was found in the analysis by gender with higher percent of decrease in rural girls (AAPC = -6.3) than rural boys (AAPC = -4.8). About the same AAPC was found in both genders from urban zones (Figure 2). The joinpoint regression analysis by age group showed that children age 0 to 4 years was the only group that showed a statistically significant decreasing trend in both, rural (AAPC = -7.9 in girls and -5.2 in boys) and urban zones (-5.1 and -5.4 respectively), all P values less than .05 (Figure 3). Again, a higher percent change was found in rural girls. The separated joinpoint analysis of each year of life showed that ANAD statistically decreased in urban children age 0, 1, 2, 3, and 4 years and rural children age 0, 1, and 2 years (Figure 4). No statistically significant AMR trends were found in children aged 5 to 9 or 10 to 14 nor in the

separated analysis of the ANAD for each year of life in children aged 5 to 14 (data not shown).

4 | DISCUSSION

This is the first Mexican study analyzing the association of asthma mortality by gender, age group, and zone of residence. Disparities in AMR emerged across rural and urban areas. A statistically significant zone of residence differences was found with higher asthma mortality in rural vs urban zones which was consistent in the whole sample, in boys and girls. The whole period's AMR medians were twice as high in rural compared with urban zones.

Contrary to gender differences in asthma prevalence reported in the literature, there was no statistically significant difference in ANAD or AMR medians between girls and boys in all children and each age group in the analysis by zone indicating that the degree of exposure to risk factors including environmental factors leading to death are similar for both sexes from both zones. The higher overall mortality in girls compared with boys aged 0 to 4 years should be further investigated.

Among the potential reasons for the higher asthma mortality in rural Mexico include differences in access to specialized health services suggested by the separate analysis of the place of death by zone which found that rural children were more likely to die at home compared with urban children ($P < .05$, data not shown). This agrees with the findings of another study that included patients from Chile, Argentina, and Paraguay¹⁹ suggesting less healthcare use by rural patients or lack of access to medical care or monitoring. This has yet to be conclusively proven in rural Mexican children.

TABLE 2 Asthma deaths and mortality rates by year of death, gender and zone of residence among children aged 0 to 14 y

Year of death	Boys				Girls				All					
	Rural		Urban		Rural		Urban		Rural		Urban		Total	
	N =	R	N =	R	N =	R	N =	R	N =	R	N =	R	N =	R
1999	54	1.06	61	0.51	69	1.37	41	0.35	123	1.22	102	0.43	225	0.66
2000	46	0.91	48	0.40	50	1.0	47	0.40	96	0.96	95	0.40	191	0.56
2001	40	0.80	50	0.41	41	0.83	46	0.39	81	0.82	96	0.40	177	0.52
2002	51	1.03	55	0.45	46	0.95	32	0.27	97	0.99	87	0.36	184	0.54
2003	44	0.90	51	0.41	37	0.77	36	0.30	81	0.84	87	0.36	168	0.49
2004	30	0.62	40	0.32	40	0.85	42	0.35	70	0.73	82	0.33	152	0.45
2005	34	0.71	45	0.36	38	0.82	37	0.30	72	0.76	82	0.33	154	0.45
2006	23	0.49	30	0.24	30	0.65	33	0.27	53	0.57	63	0.26	116	0.34
2007	32	0.68	30	0.24	18	0.40	30	0.25	50	0.54	60	0.24	110	0.32
2008	32	0.69	45	0.36	26	0.58	45	0.37	58	0.63	90	0.36	148	0.44
2009	23	0.50	44	0.35	25	0.56	38	0.31	48	0.53	82	0.33	130	0.38
2010	41	0.89	34	0.27	24	0.54	30	0.25	65	0.72	64	0.26	129	0.38
2011	21	0.46	53	0.42	17	0.39	35	0.29	38	0.42	88	0.35	126	0.37
2012	22	0.48	27	0.21	20	0.46	26	0.21	42	0.47	53	0.21	95	0.28
2013	21	0.46	31	0.25	21	0.48	25	0.21	42	0.47	56	0.23	98	0.29
2014	20	0.44	33	0.26	26	0.60	22	0.18	46	0.52	55	0.22	101	0.30
2015	21	0.46	18	0.14	17	0.39	16	0.13	38	0.43	34	0.14	72	0.22
2016	21	0.46	28	0.22	16	0.37	23	0.19	37	0.42	51	0.21	88	0.26
Total	576		723		561		604		1137	0.68	1327	0.30	2464	0.40
Median	31.0	0.7 ^a	42.0	0.3	26.0	0.6 ^a	34.0	0.3	55.5	0.6 ^a	82.0	0.3	129.5	0.4
1999-2016 % change	-61.1	-56.6	-54.1	-56.9	-76.8	-73.0	-43.9	-45.7	-69.9	-65.6	-50.0	-51.2	-60.9	-60.6

Note: Whole country of Mexico, 1999-2016. No statistically significant differences between boys and girls in the analysis by zone.

Abbreviations: N, number of asthma deaths; R, asthma mortality rate per 100 000 population.

^aStatistically significant difference between rural vs urban rates (all P s < .0001) within the same gender.

Other potential reasons include delays in seeking care until the condition is severe, travel time to healthcare facilities (which is considered a risk for poor health outcomes and increased asthma mortality²⁰), level of asthma control, availability of appropriate medications, appropriate use of inhalers including corticosteroids, medication adherence, education about the disease and recognition of risks of complications, socioeconomic status/poverty level, parental employment and education,²¹ environmental exposures or triggers including wood or cigarette smoke. All these warrant further investigations.

Another important finding is that estimated asthma mortality has reduced markedly from 0.66 deaths per 100 000 children in 1999 to 0.26 deaths per 100 000 in 2016 (61% decrease). A previous Mexican study published more than two decades ago, for the period from 1960 to 1988 and including asthmatics of all ages also showed a favorable decreasing trend.¹³ However, this is the first Mexican study that compared mortality rates by zone of residence, gender, and age group and the findings indicate that the decrease in asthma mortality is occurring specifically in children 0 to 4 years from both zones with a higher percent decrease in rural girls.

The separated joinpoint analysis of ANAD for each year of life confirmed our findings indicating that the favorable trend is taking place in early childhood with no changes in children 5 years of age or older. This is consistent with the findings of a Brazilian study covering the period 1980 to 2014 where asthma mortality decreased in children aged 0 to 4 and in a combined group of children and adults (5-35 years). Although the reduction in asthma mortality was more prominent in the 0 to 4 group.²²

Analysis of AMR by each year of life is needed to confirm findings once population estimates of each year of life by zone of residence become available. Differences in the diagnosis of asthma or bronchiolitis in children less than 2 years of age might also explain the results and deserves further investigation.

Improvements in socioeconomic status, asthma education, and management with more access to asthma medications are among the likely contributors for the favorable decreasing asthma mortality over time. Other potential factors include improvements of the health insurance system and decrease in wood smoke or cigarette exposure overtime. In 2004 when half of Mexicans had no health insurance^{23,24} the "Seguro Popular" was implemented extending health insurance nationwide mainly for the poor. In the same year, pneumococcal vaccine

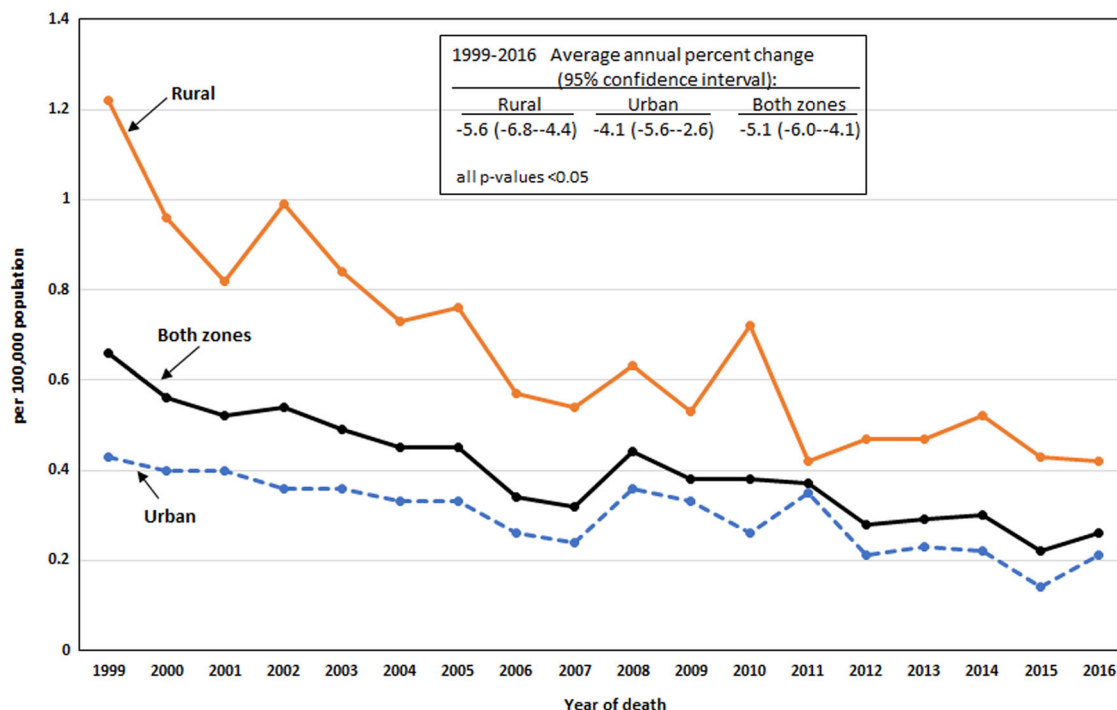


FIGURE 1 Asthma mortality rates and average annual percent change for children aged 0 to 14 years by zone of residence, whole country of Mexico 1999-2016 [Color figure can be viewed at wileyonlinelibrary.com]

was introduced, and it is currently administered in Mexico to children at 2, 4, and 12 months of age. The “Seguro Popular” provides secondary care for asthma and access to sodium cromoglycate, ipratropium bromide, salbutamol and beclomethasone. Budesonide and montelukast were added later. It is likely that the main reason for the favorable decreasing trend relates to changes in drug treatment and the reduction

of asthma hospitalizations and mortality attributed in part to the widespread use of inhaled corticosteroids,²⁵ but more detailed in-depth Mexican studies are needed to determine their impact on mortality. Differences in type of health insurance and/or accessibility to asthma medications by age group and zone of residence should also be investigated to determine inequalities.

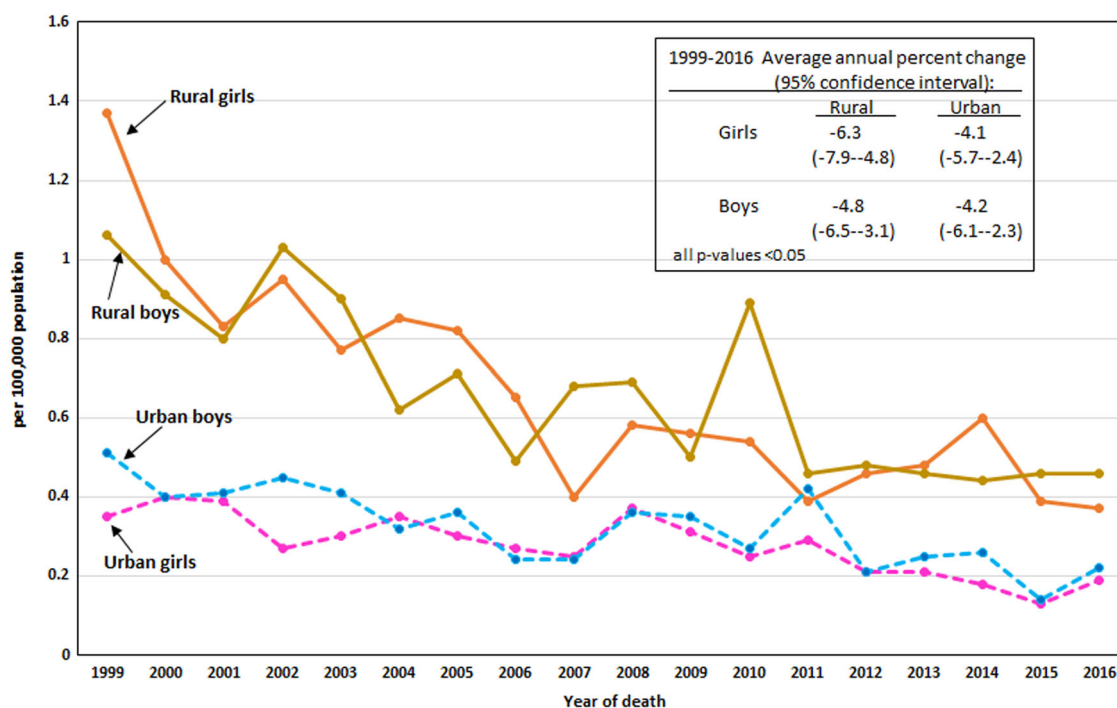


FIGURE 2 Asthma mortality rates for children aged 0 to 14 years by gender and zone of residence, whole country of Mexico 1999-2016 [Color figure can be viewed at wileyonlinelibrary.com]

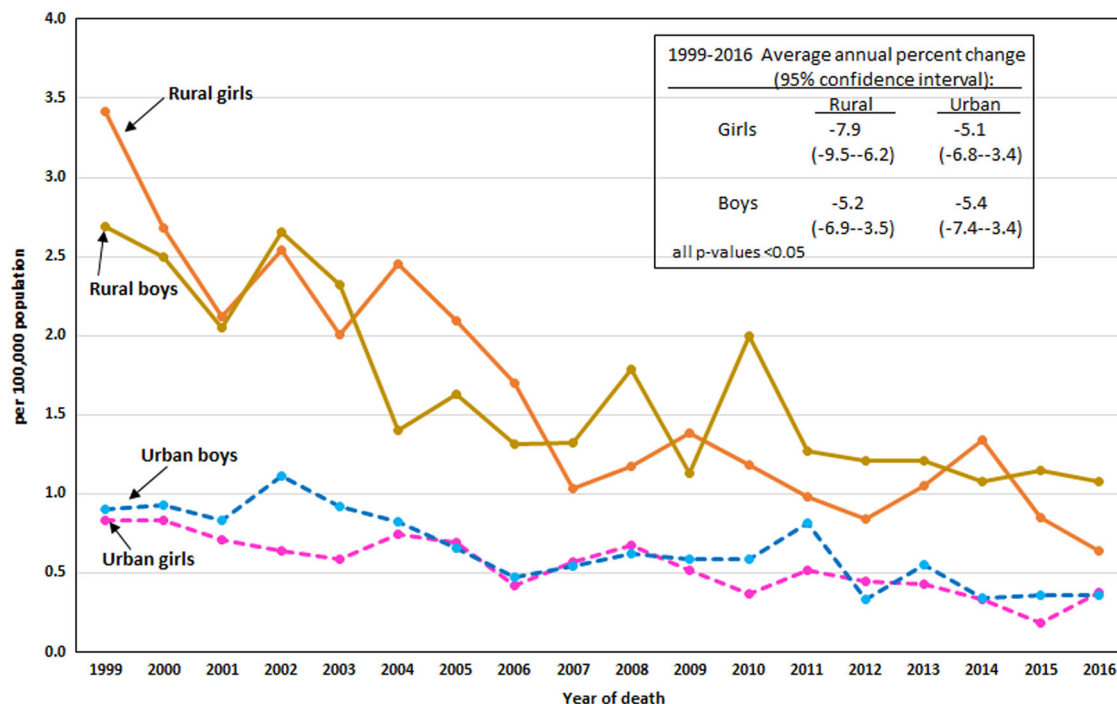


FIGURE 3 Asthma mortality rates for children aged 0 to 4 years by gender and zone of residence, whole country of Mexico 1999-2016 [Color figure can be viewed at wileyonlinelibrary.com]

Indoor pollution resulting from solid fuel combustion has also been considered a risk factor for asthma in rural zones²⁶ with higher prevalence of asthma symptoms in children in households that use open fires compared to those with stoves with chimneys²⁷ which is an important problem in Mexico. Even though wood use as the main

cooking fuel in rural zones has decreased, it remains high (62.3% in 1990, 58.7% in 2000, and 44.5% in 2012-2013).²⁸ With an inverse correlation between zone/community size and households' prevalence of wood use for cooking in Mexico (1.5%, 9.8%, and 40.5% for urban, suburban, and rural zones, respectively).²⁸ The still higher prevalence of

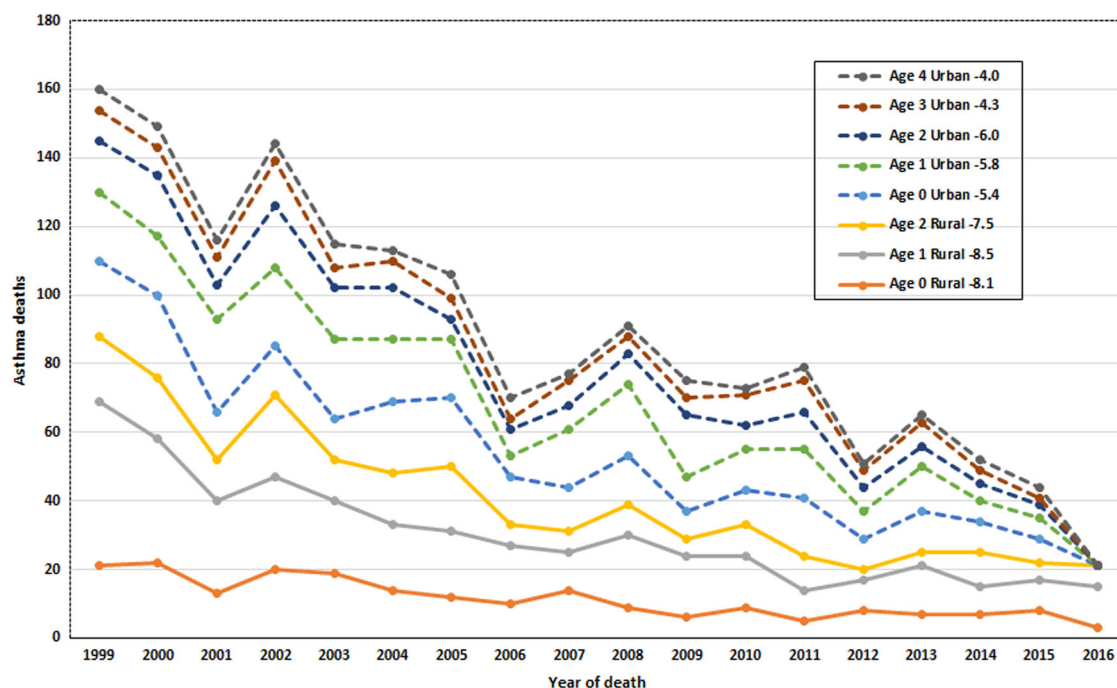


FIGURE 4 Asthma deaths by each year of life. Only statistically significant trends ($P < .05$) are shown. Numbers in the legend with the negative sign are the average annual percent changes for each year of life from 1999 to 2016 for both sexes grouped together [Color figure can be viewed at wileyonlinelibrary.com]

wood use as the main cooking fuel in rural vs urban zones may explain in part the results of a higher mortality in rural vs urban zones.

Following implementation of smoke-free legislation, a 9.8% reduction in childhood hospital admissions for asthma was found in a recent systematic review and meta-analysis.²⁹ Antitobacco policies implemented in Mexico in 2007, increasing cigarette taxes³⁰ and new legislation protecting nonsmokers from second-hand smoke in 2008³¹ translated to a reduction of smoking prevalence over time (estimated 26.2% in 1998-2002 and 21.7% in 2011).³² The prevalence of smoking in Mexico has been found to be lower in rural rather than urban areas (14.3% vs 26.4%, respectively).³³ The lower exposure to environmental tobacco smoke resulting from antitobacco policies in Mexico has likely contributed in part to the decrease of asthma mortality in early childhood but this must be further investigated.

The decrease of smoking prevalence and of wood smoke exposure over time and the awareness of the adverse health effects of cigarette smoking and wood smoke exposure are likely contributing factors to the decrease of AMR overtime in early childhood. This population represents one of the most susceptible to environmental factors. Further Mexican studies are needed to determine the association between asthma mortality and exposure to air pollution, improvements in asthma diagnosis, treatment and compliance and to determine the impact of the introduction of pneumococcal vaccine in 2004 on asthma mortality which likely have played an important role on the favorable decreasing asthma mortality in early childhood.

Figures 1 to 3 show a peak in AMR in 2010 in rural children probably due to the 2009 flu pandemic. This peak may have, to some degree, underestimated the AAPC of the whole period however, the consistently negative AAPC estimates in both zones confirm that AMR is decreasing over time in early childhood.

The lack of mortality trend in age groups 5 to 9 or 10 to 14 years is consistent with the findings of a recent multi country study that found no significant changes in mortality from 2006 to 2012³⁴ in the group that included a combination of asthmatic children and adults (age 5-34 years). The recent US study¹⁴ from 1999 to 2015 did not show changes in asthma mortality either with low mortality rates in children aged 1 to 14.

Some potential limitations of population-based studies on asthma mortality should be mentioned. One is the possibility that asthma deaths may be reported incorrectly on death certificates. This was suggested by studies re-examining death certificates in patients who died outside hospital³⁵ or upon review of all death certificates coded as asthma death in Danish children and young adults³⁶ where 4% coded as asthma were false positives and 12% were false negative asthma deaths wrongly coded as due to other causes. Only 62% of all true positive deaths caused by asthma were appropriately coded. Validity problems make comparisons between countries difficult when even interpretation of national trends requires caution.³⁶ This evidence suggest that mortality rates may have been overestimated to some degree.

The difficulty to define/diagnose asthma in children due to comorbidities complicates the determination of asthma as the cause of death. Diagnosis overlap with other respiratory conditions or chronic obstructive pulmonary disease (COPD) represents another limitation in this or any other asthma mortality study. Findings in the 0 to 4 age

group should be interpreted with caution because the diagnosis of asthma is difficult to ascertain in children under 2 years of age as other important causes of mortality could be erroneously ascribed as asthma (eg, bronchiolitis obliterans). The focus of the study was to present a snapshot of asthma mortality in Mexican children.

Unfortunately, asthma prevalence estimates in children are not available for all of Mexico, particularly the prevalence of severe asthma symptoms in pediatric populations which is associated with higher risk of death. Without asthma prevalence it is not possible to calculate case-fatality rates which would be a better indicator of inequalities in asthma care and management between both zones. Comparison of case-fatality rates is desirable in future studies when asthma prevalence estimates become available.

Asthma represents the most frequent chronic respiratory disease of children with more than 80% of asthma deaths worldwide occurring in low-income countries. This impressive estimate justifies more urgently needed asthma studies to identify risk factors for death in populations at the highest risk of death, rural Mexican children. About half of asthma deaths can be potentially preventable if recommended guidelines are followed.³⁷

In summary, this is a nuanced picture of rural-urban disparities in asthma mortality among Mexican children. Rural children have higher asthma mortality (about twice urban children) with the consequent loss of many potential years of life. Asthma-related mortality decreased in children age 0 to 4 years in Mexico from 1999 to 2016 which is reassuring. This study illustrates the health authorities' implementation of appropriate and accessible asthma programs in these communities with the goal of decreasing asthma mortality in older children. Further research is needed to determine factors that prevent the decrease in mortality in all children. The still higher mortality in rural zones is alarming and call for action from health authorities. Most importantly, solutions must be multisectoral, engaging asthma education, economic development, and other community perspectives. This will provide some guidance for asthma health policy prioritizations for rural Mexico.

ACKNOWLEDGMENT

The author thanks the staff of the Instituto Nacional de Estadística y Geografía, Aguascalientes, Mexico, for their hard work that made this study possible

ORCID

Eduardo Hernández-Garduño  <http://orcid.org/0000-0001-5725-8078>

REFERENCES

1. Global Asthma Network. *The Global Asthma Report 2018*. Auckland, New Zealand: Global Asthma Network, 2018. <http://www.globalasthmaareport.org/Global%20Asthma%20Report%202018%20EMBARGOED.pdf> Accessed November 28, 2019.

2. Centers for Disease Control and Prevention. National Center for Health Statistics. National Health Interview Survey, 2016. Analysis by the American Lung Association Epidemiology and Statistics Unit.
3. Lawson JA, Rennie DC, Cockcroft DW, et al. Childhood asthma, asthma severity indicators, and related conditions along an urban-rural gradient: a cross-sectional study. *BMC Pulm Med*. 2017;17:4.
4. Zhu WJ, Ma HX, Cui HY, et al. Prevalence and treatment of children's asthma in rural areas compared with urban areas in Beijing. *Chin Med J*. 2015;128:2273-2277.
5. Lawson JA, Janssen I, Bruner MW, Madani K, Pickett W. Urban-rural differences in asthma prevalence among young people in Canada: the roles of health behaviors and obesity. *Ann Allergy Asthma Immunol*. 2011;107:220-228.
6. Valet RS, Gebretsadik T, Carroll KN, et al. High asthma prevalence and increased morbidity among rural children in a Medicaid cohort. *Ann Allergy Asthma Immunol*. 2011;106:467-473.
7. Barry RJ, Pickett W, Rennie DC, et al. The role of farm operational and rural environments as potential risk factors for pediatric asthma in rural Saskatchewan. *Pediatr Pulmonol*. 2014;49:842-851.
8. Barry RJ, Pickett W, Rennie DC, Senthilselvan A, Cockcroft DW, Lawson JA. Factors contributing to risks for pediatric asthma in rural Saskatchewan. *Ann Allergy Asthma Immunol*. 2012;109:255-259.
9. Tong S, Drake P. Hospital admission and mortality differentials of asthma between urban and rural populations in New South Wales. *Aust J Rural Health*. 1999;7:18-22.
10. Ponte EV, Cruz AA, Athanazio R, et al. Urbanization is associated with increased asthma morbidity and mortality in Brazil. *Clin Respir J*. 2018;12:410-417.
11. Kearney GD, Wooten W, Mohan A, et al. Asthma deaths in North Carolina: 1999-2016. *J Asthma*. 2019;1-9. <https://doi.org/10.1080/02770903.2019.1579830>
12. Brito TS, Luiz RR, Silva JRL, Campos HdS. Asthma mortality in Brazil, 1980-2012: a regional perspective. *J Bras Pneumol*. 2018;44:354-360.
13. Salas Ramírez M, Segura Méndez NH, Martínez-Cairo Cueto S. [Asthma mortality trends in Mexico]. *Bol Oficina Sanit Panam*. 1994;116:298-306.
14. Pennington E, Yaqoob ZJ, Al-Kindi SG, Zein J. Trends in asthma mortality in the United States: 1999 to 2015. *Am J Respir Crit Care Med*. 2019;199:1575-1577.
15. Secretaría de Salud. Defunciones Datos abiertos. http://www.dgis.salud.gob.mx/contenidos/basesdedatos/da_defunciones_gobmx.html. Accessed November 28, 2019.
16. Consejo Nacional de Población. *Proyecciones de la población de México, 1990-2010, 2010-2050*. Mexico: Consejo Nacional de Población; 2018.
17. Surveillance Research Program. *Joinpoint trend analysis software*. National Cancer Institute, Division of Cancer Control and Population Sciences; 2018. <https://surveillance.cancer.gov/joinpoint/> Accessed November 28, 2019
18. Mansbach JM, Clark S, Teach SJ, et al. Children hospitalized with rhinovirus bronchiolitis have asthma-like characteristics. *J Pediatr*. 2016;172:202-204.
19. Solé D, Aranda CS, Wandalsen GF. Asthma: epidemiology of disease control in Latin America - short review. *Asthma Res Pract*. 2017;3:4.
20. Jones AP, Benthall G, Horwell C. Health service accessibility and deaths from asthma. *Int J Epidemiol*. 1999;28:101-105.
21. Valet RS, Perry T, Hartert TV. Rural health disparities in asthma care and outcomes. *J Allergy Clin Immunol*. 2009;123:1220-1225.
22. Graudenz GS, Carneiro DP, Vieira RP. Trends in asthma mortality in the 0- to 4-year and 5- to 34-year age groups in Brazil. *J Bras Pneumol*. 2017;43:24-31.
23. King G, Gakidou E, Imai K, et al. Public policy for the poor? A randomised assessment of the Mexican universal health insurance programme. *Lancet*. 2009;373:1447-1454.
24. Sistema de Protección Social en Salud. *Elementos financieros conceptuales y operativos*. <http://www.salud.gob.mx/unidades/cdi/documentos/DOCSAL7723.pdf>. Accessed November 28, 2019.
25. Suissa S, Ernst P. Inhaled corticosteroids: impact on asthma morbidity and mortality. *J Allergy Clin Immunol*. 2001;107:937-944.
26. Agrawal S. Effect of indoor air pollution from biomass and solid fuel combustion on prevalence of self-reported asthma among adult men and women in India: findings from a nationwide large-scale cross-sectional survey. *J Asthma*. 2012;49:355-365.
27. Schei MA, Hessen JO, Smith KR, Bruce N, McCracken J, Lopez V. Childhood asthma and indoor woodsmoke from cooking in Guatemala. *J Expo Anal Environ Epidemiol*. 2004;14(suppl 1):S110-S117.
28. Hernández-Garduño E, Gómez-García E, Campos-Gómez S. Prevalence trends of wood use as the main cooking fuel in Mexico, 1990-2013. *Salud Publica Mex*. 2017;59:68-75.
29. Faber T, Kumar A, Mackenbach JP, et al. Effect of tobacco control policies on perinatal and child health: a systematic review and meta-analysis. *Lancet Public Health*. 2017;2:e420-e437.
30. Impuesto Ley del Especial sobre Producción y Servicios Diario Oficial de la Federación, miércoles 27 de diciembre de 2006. Cuarta sección (México City, México: Gobierno de México, 2006), p 80.
31. Protección Ley de a la Salud de los No Fumadores en el Distrito Federal Aprobada por la Asamblea Legislativa del Distrito Federal el 26 de febrero y publicada en la Gaceta Oficial del Distrito Federal el 4 de marzo de 2008 (México City, México: Gobierno de México, 2008) <http://www.ordenjuridico.gob.mx/Documentos/Estatad/Distrito%20Federal/wo27594.pdf>. Accessed November 28, 2019.
32. Reynales-Shigematsu LM, Guerrero-López CM, Lazcano-Ponce E, et al. Encuesta Nacional de Adicciones 2011: Reporte de Tabaco. Ciudad de México: Secretaría de Salud, 2012. http://www.conadic.salud.gob.mx/pdfs/ENA_2011_TABACO.pdf. Accessed November 28, 2019
33. Kuri-Morales PA, González-Roldán JF, Hoy MJ, Cortés-Ramírez M. [Epidemiology of tobacco use in Mexico]. *Salud Publica Mex*. 2006;48(suppl 1):S91-S98.
34. Ebmeier S, Thayabaran D, Braithwaite I, Bénomara C, Weatherall M, Beasley R. Trends in international asthma mortality: analysis of data from the WHO Mortality Database from 46 countries (1993-2012). *Lancet*. 2017;390:935-945.
35. Kamei T, Kanaji N, Nakamura H, et al. Asthma mortality based on death certificates: a demographic survey in Kagawa, Japan. *Respir Investig*. 2019;57:268-273.
36. Jørgensen IM, Jensen VB, Bülow S, Dahm TL, Prah P, Juel K. Asthma mortality in the Danish child population: risk factors and causes of asthma death. *Pediatr Pulmonol*. 2003;36:142-147.
37. Royal College of Physicians. Why asthma still kills. The National Review of Asthma Deaths (NRAD). 2015. <https://www.rcplondon.ac.uk/projects/outputs/why-asthma-still-kills>. Accessed November 28, 2019.

How to cite this article: Hernández-Garduño E. Asthma mortality among Mexican children: Rural and urban comparison and trends, 1999-2016. *Pediatric Pulmonology*. 2020;1-8. <https://doi.org/10.1002/ppul.24658>