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ARBRES-3705; No. of Pages 3
ARTICLE IN PRESS
Archivos de Bronconeumología xxx (xxxx) xxx–xxx
Sociedad Española de Neumología y Cirugía Torácica SEPAR
ARCHIVOS DE Bronconeumología
www.archbronconeumol.org

Scientific Letter

The Importance of ZIP Code-related Average Household Income on the Severity of Respiratory Syncytial Virus Infection in Infants

To the Director,

Respiratory syncytial virus (RSV) bronchiolitis is the leading cause of hospitalization in infants, is responsible for more than 3 million of hospital admissions in infants worldwide and is the second leading cause of death in infants under 12 months of age, especially in countries with low socioeconomic resources.[1,2]

Some factors, including age less than three months old, premature birth, chronic illnesses, or malnourishment, have been associated with an increased risk of RSV infection.[2,3] It is uncertain, nevertheless, how social determinants of health play a role in the severity of RSV bronchiolitis.

There are some studies suggesting an association between lower socioeconomic status and the incidence of RSV infection, emergency department attendance and hospital admissions.[4,5] However, there are very few studies linking socioeconomic status to the severity of RSV bronchiolitis.[6–8] Addressing health inequity is crucial, especially now, with the availability of RSV prevention strategies with long half-life monoclonal antibodies for all infants and maternal RSV vaccine.[9,10]

The main objective of this exploratory study was to determine whether mean household income, related to zip code, could affect the severity of RSV infection in infants admitted to a hospital.

We conducted a retrospective observational study in a single center including all infants under 2 years of age hospitalized with a diagnosis of RSV infection over a period of 7 calendar years from January 1, 2015 to December 31, 2021. Patients were identified using ICD-10 discharge diagnosis codes, including codes J21.0, acute RSV bronchiolitis; J12.1, RSV pneumonia; and J21.9, unspecified bronchiolitis.

Demographic, epidemiologic, clinical, laboratory, radiologic data, and medical interventions during hospitalization were collected from the electronic health care records (EHR). Disease severity was assessed using length of stay (LOS), need for high flow nasal cannula (HFNC), non-mechanical ventilation (NMV), mechanical ventilation (MV), need for admission to the pediatric intensive care unit (PICU) and the Wood-Downes severity score.[11] Microbiological diagnosis was done by rapid antigen test (2015–2019) or by PCR (2020–2021).

Socioeconomic data comes from Geoportal datos del Ayuntamiento de Madrid, Portal de datos abiertos del Ayuntamiento de Madrid IGUALA: https://iguala.madrid.es/pages/presentacion, Ranking de vulnerabilidad según distritos en Madrid en 2020-2021, Instituto Nacional de Estadística, Ministerio de Hacienda, and Comunidad Autónoma de Madrid.

The average household income in Madrid's districts was 35,510 euros. Each patient was assigned the average household income corresponding to his or her zip code and the database was divided into four groups:

- Group 1: 20,000–29,999 euros.
- Group 2: 30,000–39,999 euros.
- Group 3: 40,000–49,999 euros.
- Group 4: >50,000 euros.

A sensitivity analysis was conducted using the economic vulnerability index, which takes into account three factors: households with incomes below 23,076 euros, adults working less than 20%, and households unable to afford basic items. We considered a economic vulnerability test high when the value is above the median (>5.32).

Statistical analysis was performed using R statistical software, version 3.5.3.[12] The association between qualitative variables was analyzed using Fisher or Chi-square test and quantitative variables with Kruskal–Wallis or Mann–Whitney test and most appropriate post-hoc analyses. To assess the severity of infection, logistic regression models were built and included biologically important variables or those that were significant in bivariate analyses. Associations of risk factors with qualitative variables (PICU admissions) were displayed as odds ratios (ORs) and 95% CI. A p value <0.05 was considered significant.

From 2015 to 2021 a total of 1080 infants under 2 years of age were hospitalized with a laboratory-confirmed diagnosis of RSV bronchiolitis, and 1058 (98%) were successful geocoded in Comunidad Autonoma de Madrid and therefore included in the analysis. Eight hundred and sixty-fourth children (81.6%) lived in the metropolitan area of Madrid and the rest outside of the city. Median age was 3 (1.5–7) months, 53.4% were male, LOS was 5 (3–7) days and 21.7% required admission to the PICU (Table 1).

Three hundred and two children (28.5%) lived in households with a mean income between 20,000 and 29,999 euros (Group 1), 37.5% (n = 397) had a mean income between 30,000 and 39,999 euros (Group 2), 11.3% between 40,000 and 49,999 euros (Group 3) and 22.3% had an income above 50,000 euros (Group 4).

Lower household incomes were associated with lower proportions of breastfeeding higher exposure to tobacco smoke and lower day care attendance (p < 0.01) (Table 1).

Severity of RSV bronchiolitis was analyzed according to average household income and we found that infants with lower family income, had a higher proportion of severe scores [Group 1: 129/302 (42.7%) vs Group 2: 139/397 (35%) vs Group 3: 35/120 (29.2%) vs Group 4: 68/235 (28.9%); p < 0.01], need for HFNC [Group 1: 45.7% vs Group 2: 37.8% vs Group 3: 33.3% vs Group 4: 31.1%; p < 0.01], PICU admission [Group 1: 29.5% vs Group 2: 19.4% vs Group 3: 20%

https://doi.org/10.1016/j.arbres.2024.12.002
0300-2896/

Please cite this article as: R. Rodríguez-Fernández, J. Pérez-Moreno, F. González-Martínez et al., The Importance of ZIP Code-related Average Household Income on the Severity of Respiratory Syncytial Virus Infection in Infants, Archivos de Bronconeumología, https://doi.org/10.1016/j.arbres.2024.12.002

Table 1
Differences According to Socioeconomic Status and Economic Vulnerability Index in Hospitalized RSV Infections in Infants.

Variable	Average Household Income					Economic Vulnerability Index		
	20–29.999 euros (Group 1)	30–39.999 euros (Group 2)	40–49.999 euros (Group 3)	>50,000 euros (Group 4)	p[a]	High Index (>5.32)	Low Index (≤5.32)	p[b]
Age (months)	3 (1.7–7)	2.8 (1.3–7)	3 (1.5–7)	3.5 (1.5–8)	0.40	3.5 (1.5–6.5)	3 (1.5–7)	0.47
Sex (male)	176/302 (58.3%)	206/397 (51.9%)	70/120 (58.3%)	112/235 (47.7%)	0.06	231/391 (59.1%)	226/465 (48.6%)	0.04
Breastfeeding	168/264 (63.6%)[#]	260/361 (72%)	89/114 (78.1%)[#]	167/216 (77.3%)[#]	**<0.01**	244/355 (68.7%)	322/431 (74.7%)	0.06
Second hand smoke	90/248 (36.3%)[#]	120/324 (37%)[#]	27/97 (27.8%)	37/197 (18.8%)[#]	**<0.01**	113/319 (35.4%)	107/393 (27.2%)	**0.02**
Day care attendance	17/254 (6.7%)[#]	31/344 (9%)	14/107 (13.1%)	30/212 (14.2%)[#]	**0.03**	32/342 (9.4%)	46/412 (11.2%)	0.47
Preterm birth	59/302 (19.5%)	55/397 (13.9%)	18/120 (15%)	43/235 (18.3%)	0.18	59/391 (15.1%)	68/465 (14.6%)	0.84
Underlying condition	64/302 (21.2%)	61/397 (15.4%)	28/120 (23.3%)	46/235 (19.6%)	0.11	73/391 (18.7%)	74/465 (19.1%)	0.31
Severity score								
Mild	20/302 (6.6%)	35/397 (8.8%)	7/120 (5.8%)	13/235 (5.5%)		27/391 (6.9%)	38/465 (8.2%)	
Moderate	153/302 (50.7%)	223/397 (56.2%)	78/120 (65%)	154/235 (65.5%)	**0.01**	221/391 (56.5%)	299/465 (64.3%)	**0.01**
Severe	129/302 (42.7%)[#]	139/397 (35%)	35/120 (29.2%)	68/235 (28.9%)[#]		143/391 (36.6%)	128/465 (27.5%)	
Respiratory rate	50 (41–60)	50 (44–60)	50 (42–60)	50 (42–60)	0.20	50 (42–60)	50 (42–60)	0.15
Heart rate	156 (140–170)	156 (140–170)	154.5 (140–170)	154 (138–170)	0.82	156 (140–170)	155 (139–170)	0.34
LOS (days)	5 (3–7)	5 (3–8)	5 (3–7)	5 (3–7)	0.29	5 (3–8)	5 (3–7)	0.16
Enteral feeding	99/302 (32.8%)[#]	82/397 (20.7%)[#]	23/120 (19.2%)[#]	45/235 (19.1%)[#]	**<0.01**	105/391 (26.9%)	71/465 (15.3%)	**<0.01**
Apnea	32/302 (10.6%)	55/397 (13.9%)	18/120 (15%)	24/235 (10.2%)	0.32	45/391 (11.5%)	49/465 (10.5%)	0.66
Pneumonia in X-ray	57/302 (18.9%)	70/397 (17.6%)	16/120 (13.3%)	39/235 (21.4%)	0.45	59/457 (15.1%)	78/391 (16.8%)	0.10
HFNC	138/302 (45.7%)[#]	150/397 (37.8%)	40/120 (33.3%)	73/235 (31.1%)[#]	**<0.01**	153/391 (39.1%)	143/465 (30.8%)	**0.01**
PICU	89/302 (29.5%)[#]	77/397 (19.4%)[#]	24/120 (20%)	39/235 (16.6%)[#]	**<0.01**	96/391 (24.6%)	58/465 (12.5%)	**<0.01**
NMV	82/302 (27.2%)[#]	75/397 (18.9%)	19/120 (15.8%)	37/235 (15.7%)[#]	**<0.01**	87/391 (22.3%)	56/465 (12%)	**<0.01**
MV	10/302 (3.3%)	10/397 (2.5%)	2/120 (1.7%)	4/235 (1.7%)	0.67	11/391 (2.8%)	5/465 (1.2%)	0.07

Abbreviations: LOS: length of stay; HFNC: high flow nasal cannula; PICU: pediatric intensive care unit; NMV: non-mechanical ventilation; MV: mechanical ventilation.
Continuous variables were analyzed using the *U*-Mann–Whitney or Kruskal–Wallis tests and categorical variables using Fisher's exact or Chi-square test. Data are reported as medians, 25–75% interquartile range.
Bold highlights the significant.

[a] Comparison according average household income.
[b] Comparison according economic vulnerability index.
[#] Indicates significance in analysis post hoc after Chi-square test with Bonferroni correction (specifically, there are differences between groups 1–3 and 1–4 in terms of breastfeeding, there are differences between groups 1–4 and 2–4 in terms of passive exposure to tobacco smoke, and there are differences between groups 1 and 4 in daycare attendance. Regarding the severity score, there are differences between groups 1 and 4 in the % of severe bronchiolitis. Regarding PICU there are differences between groups 1–2 and 1–4, in HFNC between groups 1 and 4, in NMV between groups 1 and 4 and in enteral feeding between groups 1–2, 1–3 and 1–4).

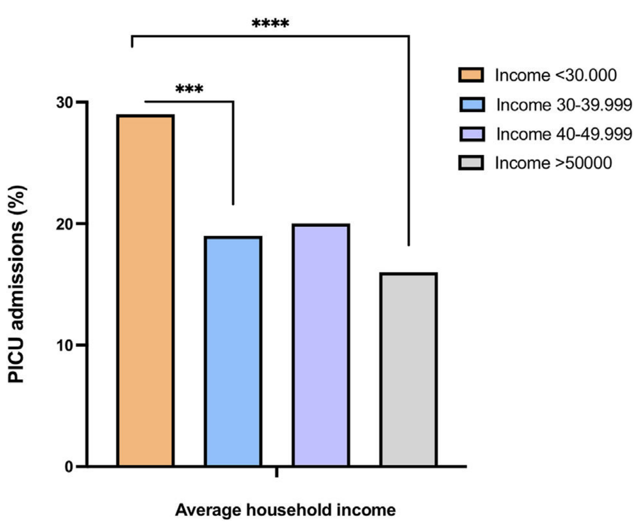

Fig. 1. The figure shows four groups of infants admitted for RSV bronchiolitis according to their family income by zip code and their differences in PICU hospitalizations. Asterisks indicate statistical significance.

vs Group 4:16.6%; $p<0.01$] and NMV [Group 1: 27.2% vs Group 2: 18.9% vs Group 3: 15.8% vs Group 4: 15.7%; $p<0.01$], Fig. 1. These results were consistent in sensitivity analyses using the economic vulnerability index (Table 1). There were no deaths during the study period.

In logistic regression analysis, infants with lower household income had higher risk of admission to the PICU [OR = 1.90 (1.13–3.16), $p=0.01$], HFNC [OR: 1.59 (1.04–2.42); $p=0.02$] and NMV [OR: 1.81 (1.08–3.09); $p=0.02$].

This study provides data associating lower household income with higher severity of RSV bronchiolitis in terms of PICU admission, need of HNFC, NMV and Wood-Downes score severity. More vulnerable infants living in lower income areas were at higher risk of admission to the PICU. This association is probably multifactorial, since infants living in more disadvantaged areas with lower income are associated with higher exposure to tobacco smoke and lower breastfeeding rates, both risk factors for severe RSV infection.[13,14]

It is widely reported that poverty can impede access to medical care and hinder the prevention of certain diseases, affecting life expectancy in adulthood.[15–17] Recently, it has been published in the United Kingdom that children living in low socioeconomic communities are at greater risk of developing severe persistent asthma, and are more likely to be admitted to hospital.[18] In 2020, Esteban et al., published that some health issues in the City of Madrid are intimately related to social and economic attributes, such as obesity, smoking, or sedentary lifestyles. They suggest implementing targeted policies for prevention and health promotion in vulnerable populations.[19]

In contrast to our study, Zheng et al. published in 2020 in children admitted for bronchiolitis that a higher mean family income was associated with a higher risk of admission to the PICU.[7] In this multicenter study, unlike our study, data were collected through a survey that up to 29% of the participants refused to answer. In addition, the socioeconomic context and health care in the United States and Spain are very different, which may at least partly explain these differences. Recently, a study conducted in Tennessee using data collected by the RSV Hospitalization Surveillance Network from 2016 to 2023 demonstrated that RSV hospitalization was linked to socially vulnerable census tracts.[6]

Therefore, it is essential to have a good understanding of the social characteristics of infants with RSV bronchiolitis in order to ensure that new preventive interventions with long half-life monoclonal antibodies (nirsevimab) or bivalent pre-Fusion maternal RSV vaccine reach the most vulnerable and low-income infants.[9,10,20]

This study has some limitations; it is a retrospective and single-center study. Family income has been estimated according to the zip code, which can sometimes give an inaccurate income. Our hospital is a referral center and receives patients with severe RSV bronchiolitis from other hospitals, which may bias the results.

In conclusion, the social determinants of health and specifically the mean income associated with the zip code may have an important influence on the clinical course of RSV bronchiolitis.

Funding

This study has been partially funded by FIS grant PI21/00840.

Conflict of Interests

RRF reports having given talks related to RSV bronchiolitis funded by Pfizer, Sanofi, Astra Zeneca, and MSD. He has participated in Advisory boards funded by Pfizer, Merck, Moderna and Sanofi. He has received scholarships to attend conferences and congresses financed by Pfizer and Sanofi.

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