

Disability-adjusted Life Years for Acute Bronchiolitis

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Abstract

BACKGROUND: The burden of disease generated by acute bronchiolitis (AB) in infants is unknown in developing countries. Evidence on the disease burden is important for decision-making processes within the health sector. The objective of the present study is to determine the Disability-Adjusted Life Years in a middle-income country **METHODS:** DALYs were calculated, using the methodology of Global Burden of Disease Study, for the following health outcomes of AB: AB uncomplicated, AB with complications, AB with severe complications, with long term complications. To estimate the DALY of each outcome, we performed a systematic review of evidence and complemented with information from the national epidemiological surveillance system. Sensibility analysis was made using a bootstrapped method with 10000 iterations in package DALY calculator of R program. **RESULTS:** In 2019, we estimated that 482 993 years of life (IC 95% 366 565- 690 294) were lost due to AB in infants. The rate of DALYs estimated for AB with mild complications were 19 DALYs / 1000 person-year, 6 DALYs / 1000 person-year for AB with severe complications, 6 DALYs / 1000 person-year for AB uncomplicated **CONCLUSION:** The burden of AB is a serious problem in Colombia, with a considerable social impact in terms of disability and mortality. It is necessary novel pharmacological strategies to minimize the impact of this serious problem in Colombia.

Background

Bronchiolitis is the most common cause of hospitalization in pediatric patients worldwide (1). Approximately a quarter of patients develop severe bronchiolitis (2, 3). The high medical cost associates with severe bronchiolitis impose a relevant economic burden, especially in middle-income countries (4, 5). Middle-income countries are home to 75% of the world's population, and approximately 96% of severe cases occur in these countries (1, 6).

Although the seasonality, risk factors, and clinical presentation of bronchiolitis in Colombia, a middle-income country, have been well characterized; the burden of disease generated by this disease in infants is unknown. The Global Burden of Disease study quantified the health effects of morbidity and mortality attributable to more than 100 diseases around the world. In this study, a new more-complex metric was used to estimate incidence, prevalence, and mortality, to characterize the real burden of disease by measuring both years of life lost as well as premature death and disability (7). The burden of disease of acute lower respiratory infections has been reported in the global and local burden of disease studies, but these reports do not differentiate between different types of lower respiratory infections. A valid and consistent description of the burden of disease is necessary to generate better health-policies and planning processes. This study aimed to estimate the DALYs of BA in infants less than 2 years in Colombia.

Methods

To estimate the burden of disease of acute bronchiolitis (AB), we calculated the Disability Adjusted Life Years (7) (7) for AB using methods described by Murray and Lopez (8); which summed the years of potential life lost due to premature mortality and the years of productive life lost due to disability (YLD) (9). DALYs were calculated for the most important health outcomes of AB: AB, uncomplicated, AB with complications (hypoxemia, atelectasis, and pneumonia), AB with severe complications (PICO admission, pneumothorax,

pleural effusions, sepsis) and AB with long term complications (recurrent wheezing). The study was approved by the Institutional Review Board of the University of Antioquia (2015-4690).

Sources of information:

To estimate the incidence and mortality of each outcome needed to estimated YLD and YLL, we performed a systematic review of evidence. This search was performed in February 2020 and was limited to the published primary literature in the English or Spanish language, human subjects, and infant (birth to 5 years). The following engines were searched for the periods specified: MEDLINE from 1950 on, EMBASE from 1974 on, BIREME from 1980 on. To avoid missing any articles published we performed a search using Google search engine and we reviewed the first 100 results returned. The search terms used were: Colombia, infants, acute bronchiolitis, incidence, or mortality. All potentially relevant references were reviewed independently and selected relevant publications. This information was complemented with information on lower tract respiratory diseases (LTRI) in infants younger than 2 years of age, reported to the national epidemiological surveillance system (SIVIGILA) (10). The mortality data was validated with the data reported by the National Department of Statistics - DANE during the same period. Informed consent was not required because we used surveillance data without personal identifiers(11).

We estimated YLL by multiplying the number of AB deaths in infants under 2 years by the number of years of expected remaining life at the age of death according to reference life tables of the global burden of disease study (12). Next, the YLD was obtained by multiplying the number of AB cases in an infant under 2 years by both the average duration of AB obtained from the literature (7, 13-17), and a disability weight that reflected the severity of AB on a scale from 0 (perfect health) to 1 (death) derived from the 2015 Global Burden of Disease study, **table 1**.

Sensitivity analysis

The final estimations, with their confidence intervals, of YLD and YLL, were made by performing 10 000 iterations in a Monte Carlo simulation of each parameter using the bootstrapped technique of DALYs calculator package in R program (18). All estimates are performed using a discount rate of 3% and weighting by age ($C = 0.1658$, $\beta = 0.04$). Subgroup analyzes were performed according to age group and sex. The probabilistic sensitivity analysis was performed using the entire range of initial values of each of the parameters used to calculate the DALYs using the standardized regression coefficient method. The simulated overall DALY estimates were regressed against the simulated values for the stochastic input parameters. To facilitate comparison, the independent terms are standardized such that they were normally distributed with mean zero and standard deviation one. The resulting regression coefficients were therefore referred to as standardized regression coefficients. The regression coefficients correspond to the number of standard deviations change in overall DALY given one standard deviation change in the corresponding input parameter. The internal consistency of each parameter was evaluated using the DISMOD II program (19) following the recommendations and methodology described in the manual for national studies of the WHO disease burden (8).

Results

In 2019, we estimated that 482 993 years of life (IC 95% 366 565- 690 294) were lost due to AB in infants under the age of 2 in Colombia; 99% due to YLL (481 038 CI 95% 364 635 - 688 359). The estimated rate was 37.51 DALYs / 1000 person-year (95% CI 28.47 – 53.61). 51.14% (246 614 DALYs) occurred in male infants, and 61.9 % (298 914) of DALYs affected infants between 1 to 2 years of age (**Table 2**).

Around 55% of DALYs were generated by AB with mild complications, 18% AB with severe complications, 17% AB uncomplicated, and 12% AB with long term complications, **figure 1**. The rate of DALYs estimated for AB with mild complications were 19 DALYs / 1000 person-year, 6 DALYs / 1000 person-year for AB with severe complications, 6 DALYs / 1000 person-year for AB uncomplicated and 3 DALYs / 1000 person-year for AB with long term complications

The results were robust in the sensitivity analysis. The percentage of change in the total estimate of DALYS

did not exceed 25% with the variables analyzed; being the probability of death in infants between 1-2 under the variable associated with the highest percentage of change in the DALYs (between 5-25%, of the final estimate). There were no significant variations in the discount rate, between 0 to 5% (**Figure 2**).

Discussion

This study aimed to estimate the DALYs of BA in infants less than 2 years in Colombia. The burden of disease method analyzes the impact of disease upon populations through a combination of mortality and morbidity measures into a single summary statistic of population health. A global burden of disease study estimated that lower tract respiratory infections account for around 14.1% of DALYs in infants less than 4 years worldwide (7). In our study, more than 400 000 years of life were lost due to AB in Colombia during 2019. This is, to our knowledge, the first estimate of the burden of bronchiolitis in infants under age two years and remarks the weight in relative and absolute terms of this disease in our society. This disease is potentially preventable pathology since it is mostly caused by common respiratory viruses that are preventable with hygiene, or immunization.

Our study obtained a higher rate of DALYs due to BA compared to the rate by all lower respiratory tract infections in Colombia. The national burden of disease study in 2015 estimated by lower respiratory tract infections 9.9 DALYs per 1000 in infants less than 4 years and 3.98 DALYs per 1000 in infants less than 2 years (20). We estimated only for BA 37.51 DALYs / 1000 person-year (95% CI 28.47 – 53.61). These differences are due to different sources of information, as the national burden of disease study used data from national health surveys while we directly examined the records of epidemiological surveillance. The surveillance records have a greater degree of completeness and less probability of information biases since they are mandatory records in Colombia and completed directly by physicians treating the infant. Also, higher estimates of DALYs based on epidemiological surveillance have been seen in paraquat poisoning (21, 22).

Most of DALYs (62 %) were generated by an infant between 1-2 years. This can be explained by a considerable delay in medical consultation in severe cases, respect for younger infants. A similar result was found in a meta-analysis of six studies of RSV-bronchiolitis in Latin America (23). The pooled of case fatality were higher in infant between 0 to 23 month than 0-11 months (1.74 [CI 95%1.20–2.43] vs 0.51 [CI 95% 0.06–2.76]). This evidence could suggest that an infant older than one year there is a considerable delay in medical consultation in severe cases, respect to the younger infant. This hypothesis must be confirmed by prospective studies comparing if there is any difference in time to medical consultation and their outcomes in morbidity and mortality.

Respect to other diseases, AB generates more DALYs than other diseases "more publicized" like cervical cancer between 45-59 years (1.6 DALYs per 1000 inhabitants), epilepsy between 30-44 years (1 DALYs per 1000 inhabitants) and leukemia in an infant between 5-14 years (1 DALYs per 1000 inhabitants)(20). This differences are important for decision-making processes within the health sector. An accurate estimate of the population's health status can be used for determining the expected health care use and is vital for prioritizing effective interventions and evaluating their impact (24).

This study has limitations. First, we may have some degree of information bias and underestimation due to the use of data from the national surveillance and notification system (25). However, since 2008, an increase in the reporting of cases to SIVIGILA has been noted (10). To adjust for underestimation, a sensitivity analysis was performed for each of these parameters taking a range of possible values and their distribution. Importantly, the final result of DALYs was not sensitive to the change in values of these probabilities, guaranteeing the robustness of the model. There are no specific "disability weights" for Bronchiolitis. In this case, we used data reported for lower respiratory infection because in terms of mortality it does not differ from data presented by patients with other viruses in Colombia (13). In the sensitivity analysis, the percentage of change in the total estimate of DALYS did not exceed 25% within the variables analyzed.

Conclusions

The burden of AB is a serious problem in Colombia, with a considerable social impact in terms of disability and mortality. It is necessary novel pharmacological strategies to minimize the impact of this serious problem in Colombia.

Declarations

Ethics approval and consent to participate : This study was approved by the Institutional Review Board of University of Antioquia (2015-4690)

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References

1. Nair H, Nokes DJ, Gessner BD, Dherani M, Madhi SA, Singleton RJ, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. *Lancet*. 2010;375(9725):1545-55.
2. Rodriguez DA, Rodriguez-Martinez CE, Cardenas AC, Quilaguy IE, Mayorga LY, Falla LM, et al. Predictors of severity and mortality in children hospitalized with respiratory syncytial virus infection in a tropical region. *Pediatr Pulmonol*. 2014;49(3):269-76.
3. Flores-Gonzalez JC, Mayordomo-Colunga J, Jordan I, Miras-Veiga A, Montero-Valladares C, Olmedilla-Jodar M, et al. Prospective Multicentre Study on the Epidemiology and Current Therapeutic Management of Severe Bronchiolitis in Spain. *Biomed Res Int*. 2017;2017:2565397.
4. Buendia JA, Patino DG. Costs of Respiratory Syncytial Virus Hospitalizations in Colombia. *Pharmacoecon Open*. 2020.
5. Rodriguez-Martinez CE, Sossa-Briceno MP, Castro-Rodriguez JA. Direct medical costs of RSV-related bronchiolitis hospitalizations in a middle-income tropical country. *Allergol Immunopathol (Madr)*. 2019.
6. The World Bank Group. The World Bank in Middle Income Countries 2020 [29/06/2020]. Available from:<https://www.worldbank.org/en/country/mic/overview#:~:text=They%20are%20defined%20as%20lower,62%25%20of%20>
7. DALYs GBD, Collaborators H, Murray CJ, Barber RM, Foreman KJ, Abbasoglu Ozgoren A, et al. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990-2013: quantifying the epidemiological transition. *Lancet*. 2015;386(10009):2145-91.
8. Mathers CD VT, Lopez AD, Salomon J, Ezzati M. National Burden of Disease Studies: A Practical Guide: Global Program on Evidence for Health Policy. Geneva: World Health Organization.; 2001 [Available from:<http://www.who.int/healthinfo/nationalburdenofdiseasemanual.pdf>].
9. Shi T, McAllister DA, O'Brien KL, Simoes EAF, Madhi SA, Gessner BD, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. *Lancet*. 2017;390(10098):946-58.
10. Instituto, Nacional, Salud d. Infeccion respiratoria aguda en Colombia 2017 [05/07/2019]. Available from:<https://www.ins.gov.co/busador-eventos/Informesdeevento/Informe%20IRA%20Final%202017.pdf>.
11. Estadísticas DAN. Proyecciones de poblacion 2018 [03/07/2019]. Available from:<https://www.dane.gov.co/index.php/estadisticas-por-tema/demografia-y-poblacion/proyecciones-de-poblacion>.
12. Murray CJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years. *Bull World Health Organ*. 1994;72(3):429-45.

13. Barbosa Ramirez J, Pulido Dominguez P, Rey Benito G, Mendez Rico J, Castellanos J, Paez Martinez A. Human respiratory syncytial virus and metapneumovirus in patients with acute respiratory infection in Colombia, 2000 - 2011. *Rev Panam Salud Publica*. 2014;36(2):101-9.
14. Hernando Puente M, Lopez-Herce Cid J, Bellon Cano JM, Villaescusa JU, Santiago Lozano MJ, Sanchez Galindo A. [Prognostic factors for bronchiolitis complications in a pediatric intensive care unit]. *An Pediatr (Barc)*. 2009;70(1):27-33.
15. Bueno FU, Piva JP, Garcia PC, Lago PM, Einloft PR. Outcome and characteristics of infants with acute viral bronchiolitis submitted to mechanical ventilation in a Brazilian pediatric intensive care. *Rev Bras Ter Intensiva*. 2009;21(2):174-82.
16. Arraut PB, Lesmes, A.C. Caracterización de la población con bronquiolitis en la Clínica Infantil Colsubsidio en el año 2013 Universidad del Rosario 2013 [Available from: <http://repository.urosario.edu.co/bitstream/handle/10336/10515/53106146-2015.pdf?sequence=1>].
17. Dumas O, Hasegawa K, Mansbach JM, Sullivan AF, Piedra PA, Camargo CA, Jr. Severe bronchiolitis profiles and risk of recurrent wheeze by age 3 years. *J Allergy Clin Immunol*. 2019;143(4):1371-9 e7.
18. Brecht Devleeschauwer, Scott McDonald, Juanita Haagsma, Nicolas Praet, Havelaar A, Speybroeck N. DALY: The DALY Calculator - A GUI for stochastic DALY calculation in R. 2014 Available from: <http://cran.rproject.org/package=DALY>.
19. Barendregt JJ, Van Oortmarssen GJ, Vos T, Murray CJ. A generic model for the assessment of disease epidemiology: the computational basis of DisMod II. *Popul Health Metr*. 2003;1(1):4.
20. Peñaloza R, Salamanca B, Rodriguez J, Beltran A. Estimación de la carga de enfermedad para Colombia, 2010. 2014(Editorial Pontificia Universidad Javeriana).
21. Buendia JA, Chavarriaga GJR, Zuluaga AF. Burden of paraquat poisoning in the department of Antioquia, Colombia. *BMC Pharmacol Toxicol*. 2019;20(1):11.
22. Buendia JA, GJ R. Cost Illness of paraquat poisoning in Colombia. *Value Health Reg Issues*. 2018;In Edition.
23. Bardach A, Rey-Ares L, Cafferata ML, Cormick G, Romano M, Ruvinsky S, et al. Systematic review and meta-analysis of respiratory syncytial virus infection epidemiology in Latin America. *Rev Med Virol*. 2014;24(2):76-89.
24. Pichon-Riviere A, Augustovski F, Garcia Marti S, Alfie V, Sampietro-Colom L. The link between health technology assessment and decision making for the allocation of health resources in Latin America. *Int J Technol Assess Health Care*. 2020:1-6.
25. Gibbons CL, Mangan MJ, Plass D, Havelaar AH, Brooke RJ, Kramarz P, et al. Measuring underreporting and under-ascertainment in infectious disease datasets: a comparison of methods. *BMC Public Health*. 2014;14:147.

Figure Legends

Figure 1. DALYs by outcome and age.

Figure 2 . Results of sensitivity analysis: Mapped standardized regression coefficients

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