Early Impact of social distancing in response to COVID-19 on hospitalizations for acute bronchiolitis in infants in Brazil

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Summary

Social distancing as public health measure to control the COVID-19 pandemic had a significant impact on the incidence of hospitalizations for acute bronchiolitis. In Brazil, children have been out of school and daycare centers have been closed since March 2020.

ABSTRACT

Background: Interventions to tackle the COVID-19 pandemic may affect the burden of other respiratory diseases. Considering the repercussion of these unique social experiences in infant's health, this study aims to assess the early impact of social distancing due to the COVID-19 pandemic in hospital admissions for acute bronchiolitis.

Methods: Data from hospitalizations of acute bronchiolitis in infants under one year were obtained from the Department of Informatics of the Brazilian Public Health database (DATASUS) for the period between 2016 and 2020. These data were also analyzed by macro-regions of Brazil (North, Northeast, Southeast, South and Midwest). To evaluate the effect of social distancing strategy on the incidence of acute bronchiolitis, the absolute and relative reduction was calculated by analyzing the yearly subsets of 2016vs2020, 2017vs2020, 2018vs2020, and 2019vs2020.

Results: There was a significant reduction in all comparisons, ranging from -78% [IRR 0.22 (0.20 to 0.24)] in 2016vs2020 at -85% [IRR 0.15 (0.13 to 0.16)] in 2019vs2020, for the data from Brazil. For analyzes by macro-regions, the reduction varied from -58% [IRR 0.41 (0.37 to 0.45)] in the Midwest in 2016vs2020 to -93% [IRR 0.07 (0.06 to 0.08)] in the South in 2019vs2020.

Conclusions: There was a significant reduction in hospitalization for acute bronchiolitis in children under one year old, in Brazil, of the order of more than 70% for most analysis. Our data suggest an important impact of social distance on reducing the transmission of viruses related to acute bronchiolitis. Such knowledge may guide strategies for prevention of viruses spread".

Key words: COVID-19, bronchiolitis, lockdown, infants, hospitalization.

INTRODUCTION

According to the World Health Organization's "COVID-19 strategy update", health authorities should adopt and adapt measures of distance and movement restrictions at the population level, besides other public health measures to reduce exposure and suppress virus transmission.[1] Such measures may impact on the epidemiology of a variety of other diseases.

Acute bronchiolitis (AB) is among the main communicable diseases of childhood and is the most frequent cause of hospitalization in infants worldwide.[2] In Brazil, AB represented around 6% of total hospitalizations in the age group under one year old between the 2008-2015 period.[3]

Respiratory Syncytial Virus (RSV) is the main etiologic agent and has high transmissibility, especially in autumn-winter months.[2] Due to the seasonal epidemiology of bronchiolitis and regional differences, the peak incidence of hospitalizations is different throughout Brazil, between the months of February and August. [3] The COVID-19 pandemic hit Brazil in February 2020, just before autumn-winter in the southern hemisphere (March to September) with the first case officially registered in São Paulo. Collective measures to contain the pandemic were implemented in the middle of March: social distancing, restriction of commerce activities and non-essential services. Suspension of teaching activities at all educational levels throughout the country started by mid-March. Additionally, besides overall hygiene measures and mask protection strategies[4] (with variable degrees of adherence by the population), children have stayed out of schools and daycare centers, since all has been closed since then.

Considering the repercussion of these unique social experiences in infants' health, this study aims to assess the early impact of social distancing due to the COVID-19 pandemic on bronchiolitis hospitalizations in infants under one year old, in a large country as Brazil.

METHODS

Data from hospitalizations of acute bronchiolitis were obtained from the Department of Informatics of Brazilian Public Health System (DATASUS) database (http://datasus.saude.gov.br/)which provides the diagnosis at hospital admission [5] for the period of 2016–2020. To assess data the links "Informações de Saúde" (Health Information), (TABNET) – "Epidemiológicas e Morbidade" (Epidemiological and Morbidity) – "Morbidade Hospitalar" (Hospital Morbidity), "Lista de Morbidade" (Morbidity List) - International Classification of Diseases (ICD) version 10 (acute bronchiolitis - AB—ICDJ21) were used, for the age group of < 1 year old. These data were also analyzed by macro-regions of Brazil (North, Northeast, Southeast, South and Midwest) and in the months of January, February, March, April, May and June of each year, since this covers the typical season of high AB hospitalizations. In order to assess the reliability of the report, ICDP96 - other conditions originating in the perinatal period (congenital renal failure, neonatal withdrawal symptoms, wide cranial sutures of newborn, termination of pregnancy e.g.) was used as comparisson, since social distancing measures are not expected to have a major impact on these conditions.

To calculate the incidence of hospitalizations in the public heath system, we used the following formula: total number of hospitalizations / population number by age (per year and place [Brazil-IBGE]) x 100,000 inhabitants).[6] The Brazilian National Health Agency provides the percentage of population that has health insurance per year and the same percentage was excluded from the denominator, as this population use another hospital

structures, and admissions data are not included in DATASUS. These percentages means 25.3% in 2016, 23.1% in 2017, 24.4% in 2018, 24.1% in 2019 and 21.2% in 2020 for the population of children under one year old. [7] In addition to the closing date of schools, we used as parameter of social distance the technological information system for tracking urban mobility by apps of INLOCO. This index exists to assist authorities in targeting public security, communication and health resources and shows the percentage of the population that is respecting the isolation recommendation. [8] To evaluate the effect of social distancing strategy on the incidence of AB, the absolute reduction (without social distancing - with social distancing) and relative reduction (without social distancing - with social distancing / without social distancing) was calculated by analyzing the subsets 2016vs2020, 2017vs2020, 2018vs2020 and 2019vs2020. For this analysis, the months of March to June were used because March is the period of implementation of the social distancing strategy in Brazil in the year of 2020, including the law to determine the closing of schools and daycare centers for infants. [9] Data analysis has been truncated at the end of June for the purpose of this article since there is a delay in data entry.

To calculate the difference in incidence rates between the without and with social distancing periods, incidence rate ratio (IRR) was used to assess statistical significance, considering a 95% confidence interval (CI). This data analysis methodology is already well documented in the literature.[10–12]

To ensure quality, two independent authors reviewed all data. This study does not contain personal or individual data, so it was considered exempt from evaluation by the Research Ethics Committee.

RESULTS

From January 2016 to June 2020, there were 595,482 hospitalizations for respiratory diseases (all hospitalizations registered for diseases related to the respiratory system) registered in DATASUS, in children under 1 year of age in Brazil; AB represented 28.2% (167,870) of these cases. In the Brazilian public heath system, the monthly distribution of the incidence of hospitalizations in the months from January to March was similar, with a trend of increasing cases throughout the studied period (2016-2020). The lowest incidence was observed in January 2016 with 489.4 / 100,000 and the highest in March 2019 with 2491.5 / 100,000 hospitalizations. In the period from April to May, the years 2016 to 2019 kept the increase trend in the incidence of hospitalizations. In June of the years 2017, 2018 and 2019 there was a slight reduction in incidence. In that same period, in the year 2020, there is an observable drop in incidence, with numbers ranging from 379.4 / 100,000 in April to 106.6 / 100,000 in June. In the period from January-June of the years 2016 to 2020 the incidence was 1689.8 / 100,000 (2016), 2207.1 / 100,000 (2017), 2171.1 / 100,000 (2018), 2599.7 / 100,000 (2019) and 574.2 / 100,000 (2020), respectively (Figure 1A).

When comparing the subsets of March / June 2016, March / June 2017, March / June 2018 and March / June 2019 with March / June 2020, there was an expressive reduction in all comparisons, with reductions ranging from -78 % [IRR 0.22 (0.20 to 0.24)] in 2016vs2020 to -85% [IRR 0.15 (0.13 to 0.16)] in 2019vs2020 (Figure 1B and Table 1). Conversely, hospitalizations for other conditions originating in the perinatal period varied little in the same periods (Figure 1B). The data obtained by the INLOCO application show that, in the period from March to June 2020, the average social distance in Brazil remained at 47.3%. When comparing the subsets by macro-regions of Brazil (2016vs2020, 2017vs2020, 2018vs2020 and 2019vs2020), there was also an expressive reduction in all comparisons. In the North region, there was a decrease in the incidence of hospitalizations that varied from -

78% [IRR 0.22 (0.19 to 0.24)] in 2016vs2020 to -87% [IRR 0.13 (0.11 to 0.15)] in 2017vs2020. In the Northeast, the reduction ranged from -80% [IRR 0.19 (0.17 to 0.22)] in 2016vs2020 to -88% [IRR 0.11 (0.10 to 0.13)] in 2019vs2020. For the Southeastern region, a reduction was observed that fluctuated from -75% [IRR 0.24 (0.23 to 0.26)] in 2016vs2020 to -81% [IRR 0.18 (0.17 to 0.19)] in 2019vs2020. The Southern region had the greatest impact, with a drop in incidence ranging from -90% [IRR 0.10 (0.09 to 0.11)] in 2016vs2020 to -93% [IRR 0.07 (0.06 to 0.08)] in 2019vs2020. In the Midwest region, the variation was of -58% [IRR 0.41 (0.37 to 0.45)] in 2016vs2020 to -86% [IRR 0.14 (0.13 to 0.15)] in 2019vs2020 in the incidence of hospitalizations.

The total absolute number of hospitalizations, the incidence of hospitalizations per 100,000 inhabitants (> 1 year old) and the comparisons between hospitalizations in the period, between 2016 and 2020, are shown in Table 1.

DISCUSSION

To the best of our knowledge, this study is the first to assess the impact of social distancing interventions in reducing hospitalizations due to AB in Brazil, using a temporal trend analysis. Also noteworthy is the fact that interventions to control the COVID-19 pandemic in schools (extended to daycare centers) [13] were implemented by Educational Ministry of Brazil at March 17, few days before the beginning of autumn season on southern hemisphere, a period of historical significant increases in hospitalizations for bronchiolitis. In addition, probably no other country in the Southern hemisphere has such robust national and regional epidemiological data, considering the population size, the viral seasonality and the higher incidence than in developed contries. [14]

Our results show a annual increase in the incidence of hospitalizations for AB in the past few years, similar to studies carried out in developing countries.[2] Since 2016, the peak of

incidence begins in March and April, and goes on until July. In 2020, however, there was an abrupt decline in the monthly incidence of hospitalization due to AB that coincides with the implementation of the social distancing measures. Our analysis of the DATASUS dataset detected a reduction of more than 70% in hospital admissions coded for AB in infants younger than one year in all regions of the country and the April- June incidence of AB admissions in 2020 was the lowest for the past 5 years.

Even when annual and geographical variations [15,16] were considered, in 2020 there was an impressive decline in admissions. The absolute number of bronchiolitis admissions in Brazil in April range from 3,391 (2016) to 7,356 (2019) and at June from 6,214 (2016) to 5,836 (2019). In 2020 those absolute numbers fell to 733 in April and 206 in June.[5] In addition, less than 1,000 registered bronchiolitis hospitalizations is a rare event in Brazil, even during summer season in Brazil (December or January).

The impact of social distancing interventions has been reported in some studies (some still in the pre-publication stages). Studies conducted in pediatric emergence department settings in Italy [17–19] reveal a marked change in the pattern of care and hospitalizations, with a significant reduction, especially in respiratory infections, of up to more than 90%. [18] In France, a time series analysis of more than 871,000 pediatric emergency visits found a significant decrease over 70% in infectious diseases spread by air or fecal-oral route: common cold, gastroenteritis, bronchiolitis, acute otitis, associated with school closure and lockdown due to COVID-19. [20] So, our results could be considered in line with these studies, including the high percentage of reduction of cases.

Before the COVID 19 pandemics, studies that addressed changes in the pattern of social contact and school closures in diseases such as measles, influenza and H1N1 pointed out to the effect of such measures in slowing the transmission of diseases and mitigating the impact

of the epidemic.[21–23] Our data suggest that the measures applied to the control of COVID-19 also have a critical impact on the spread of AB.

The impact of each preventive action is very difficult to acsses. Social distancing was accompanied by many measures, as the widespread use of masks,[24] recommendations for hand washing and the use of gel alcohol before and after contact with other people and inanimate objects, which are in line with guidelines to controlling the transmission of infection by RSV and other etiologic agents related to AB, at the population level. [25]

Some other behavioral changes in a pandemic context may also influence our results, such as avoidance of looking for health care in a hospital or clinic. Nonetheless, it could be an reason for reduction only in mild AB episodes and our study addresses only AB requiring hospitalization, sometimes with serious signs and symptoms. [26] As the dynamics of SARS-CoV-2 interaction with others respiratory viruses is not fully understood, other factors as an decreased susceptibility to other viruses due to the colonization of the nasopharynx for SARS-CoV-2 could be an issue. However, as respiratory coinfection or codetection rates with SARS-CoV-2 up to 26.1% are reported, this rationale does not explain our findings completely.[27]

Further, it could be questioned why the social distancing had a higher impact in reducing transmission of RSV and other AB-related viruses than in SARS-CoV-2, considering that the basic reproductive number (R0) of RSV, which is the most frequent cause of bronchiolitis, is around 3.0,[28,29] and the R0 estimated of SARS-CoV-2 between 2.0 to 3.5. [30] However, the actual of SARS-CoV-2 R0 could be higher (5.7 (95% CI 3.8–8.9) [31] which could explain impact of social distancing in the incidence of AB compared to COVID-19, as respiratory viruses share similar routes of transmission.

Conducting a retrospective study has some limitations, especially in the context of a pandemic. The biggest one refers to the fact that we use a database that is filled by third parties. To minimize this impact and ensure that the data is treated reliably, we captured data after two months of the month of hospitalization. According to our previous experiences,[10–

12] this period is sufficient for the base to present the final numbers or very approximate values, since the data are included based on the Hospitalization Authorizations forms, in Brazil AIH (hospital admission authorization).In addition, we used ICDP96 - other conditions originating in the perinatal period, as comparison.

In summary, the incidence of hospitalizations related to AB was importantly reduced after the implementation of the social distancing measures. To our knowledge, such epidemiology changes in AB-related hospitalizations during South hemisphere autumn-winter season in Brazil have not been previously reported. .

CONCLUSIONS

Our data provide novel and significant evidence of huge impact of social distancing measures in reducing of spread of AB-related viruses. Further, we hope that our results can help in the planning preventive strategies in the post-COVID-19 era. Data presented here is probably useful in the planning of further studies and may help clarify how distancing measures or environmental protection of viral dissemination may affect the burden of AB.

NOTES

Contributions of each author: Frederico Friedrich participated in the conception and design of the study, acquisition, analysis and interpretation of data; elaborating the article and reviewing it critically. Talitha Comaru participated in the conception and design of the study, analysis and interpretation of data, elaborating the article and reviewing it critically and Leonardo A. Pinto participated in the design of study, analysis and interpretation of data; writing the article and reviewing it critically. Renata Ongaratto, Tiago N. Veras, Marcelo C. Scotta, Renato T. Stein, Magali Santos Lumertz and Marcus Herbert Jones participated in the acquisition, analysis and interpretation of data; article writing and critical review. All the authors approved the final version for publication.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interests.

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Figure Caption

Figure I. Monthly distribution of incidence of hospitalizations for acute bronchiolitis in children under one year of age in Brazil (2016–2020).

Table Caption

Table I. Total absolute number and incidence of hospitalizations for acute bronchiolitis from 2016 to 2020 in children under 1 year of age in Brazil and Brazilian macro-regions.

Figure legends1B

ICDP96 Other conditions originating in the perinatal period

	Total absolute number of hospitalizations (number of hospitalizations per 100,000/children/subset of month)[a]					Relative difference in rate (without social distancing versus with social distancing)			
< 1 year old	**March-June 2016**	**March-June 2017**	**March-June 2018**	**March-June 2019**	**March-June 2020**	**change 2016 vs 2020 % [IRR (95% CI)]***	**change 2017 vs 2020 % [IRR (95% CI)]***	**change 2018 vs 2020 % [IRR (95% CI)]***	**change 2019 vs 2020 % [IRR (95% CI)]***
Brazil	16,743 (3048.1)[a]	21,782 (3872.3)[a]	22,006 (3909.5)[a]	25,434 (4526.9)[a]	3,953 (682.0)[a]	- 78% [0.22 (0.20-0.24)]*	- 82% [0.17 (0.16-0.19)]*	- 83% [0.17 (0.16-0.18)]*	- 85% [0.15 (0.13-0.16)]*
North	1,035 (1439.5)[a]	1,716 (2367.9)[a]	1,648 (2223.9)[a]	1,631 (2212.3)[a]	237 (318.3)[a]	- 78% [0.22 (0.19-0.24)]*	- 87% [0.13 (0.11-0.15)]*	- 86% [0.14 (0.12-0.16)]*	- 86% [0.14 (0.12-0.16)]*
Northeast	2,790 (1553.0)[a]	3,946 (2177.8)[a]	3,505 (1922.0)[a]	4,674 (2595.2)[a]	555 (304.3)[a]	- 80% [0.19 (0.17-0.22)]*	- 86% [0.13 (0.12-0.15)]*	- 84% [0.15 (0.14-0.17)]*	- 88% [0.11 (0.10-0.13)]*
Southeast	9,112 (5166.4)[a]	11,059 (5945.7)[a]	12,145 (6616.0)[a]	12,641 (6842.8)[a]	2,508 (1286.6)[a]	- 75% [0.24 (0.23-0.26)]*	- 78% [0.21 (0.20-0.22)]*	- 81% [0.19 (0.18-0.20)]*	- 81% [0.18 (0.17-0.19)]*
South	3,096 (4305.4)[a]	3,614 (4957.7)[a]	3,180 (4404.4)[a]	4,367 (5992.9)[a]	338 (445.1)[a]	- 90% [0.10 (0.09-0.11)]*	- 91% [0.08 (0.08-0.09)]*	- 90% [0.10 (0.09-0.11)]*	- 93% [0.07 (0.06-0.08)]*
Midwest	710 (1553.4)[a]	1,447 (3082.4)[a]	1,528 (3217.7)[a]	2,121 (4496.0)[a]	315 (645.4)[a]	- 58% [0.41 (0.37-0.45)]*	- 79% [0.20 (0.19-0.22)]*	- 80% [0.20 (0.18-0.21)]*	- 86% [0.14 (0.13-0.15)]*

Table I. Total absolute number and incidence of hospitalizations for acute bronchiolitis from 2016 to 2020 in children under 1 year of age in Brazil and Brazilian macro-regions.

IRR: Incidence rate ratio. CI: Confidence interval. [a] Incidence number. *p<0.05.

Figure 1