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Incidence of other respiratory viruses in Brazil during SARS-CoV2 Pandemic

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ABSTRACT

OBJECTIVE

Viruses are commonly associated with respiratory infections. Pandemics caused by respiratory viruses have affected humans considerably throughout history. We are currently facing a pandemic caused by SARS-CoV-2. Control measures the aimed to slow the virus spread may have interfered with the spread of other season respiratory viruses. Understanding the incidence of viral respiratory cases is necessary to corroborate this hypothesis. The aim of this study was to compare the incidences of the respiratory viruses that were reported in the weekly report of respiratory viruses between 2019 and 2020.

METHODS

Epidemiological bulletins of 2019 and 2020 for cases of severe acute respiratory syndrome available at the Ministry of Health were consulted in order to determine the incidences of cases of viral respiratory infection, bulletins were considered for up to week 32.

RESULTS

A substantial decrease was observed in cases of Severe Acute Respiratory Syndrome related to respiratory viruses other than SARS-CoV-2, suggesting that pandemic-related control in progress can affect the circulation of other respiratory viruses, since transmission of these viruses is very similar and protected measures such as social distance and an increase in the level of personal hygiene can be effective in reducing the spread of most of them. In addition, the closure of school units during the period of greatest incidence of respiratory viruses may have contributed to the decrease in cases among children.

CONCLUSIONS

The measures adopted may have influenced considerably in the spread of other respiratory viruses.

DESCRIPTORS

SARS-CoV2. Respiratory viruses. Epidemiology.

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INTRODUCTION

In December 2019, a series of hospitalizations of pneumonia from unknown etiology was reported in Wuhan province in China. After intense efforts to identify the origin of cases, the possibility that the pathogen could be one of the respiratory viruses already known, such as Influenza, adenovirus, SARS-CoV, MERS-CoV, among others, was ruled out. The extraction of RNA and the use of modern methods of sequencing and assembly of genomes, enabled the identification of a new virus, never previously described, associating recent cases of pneumonia with a coronavirus, a member of the *Coronaviridae* family, genus *Betacoronavirus*, later called SARS- CoV-2[1].

Respiratory infections have been among the top ten causes of death worldwide[2]. Interestingly, respiratory viruses are frequently found as responsible for these respiratory infections, there are several antigenic distinct viruses were responsible for causing these infections[3]. The easy transmission of these viruses associated to factors related to population growth, environmental fragmentation and great human mobility worldwide are the main reasons for the emergence of epidemics and pandemics over the years[4]. Historically, Influenza virus has been responsible for the main pandemics, as in the "Spanish Flu" in 1918-1919, caused by Influenza H1N1, causing the death of more than 50 million people worldwide. The pandemic viruses H2N2 of 1957, H3N2 of 1968, the resurgence of pandemic H1N1 in 1977 and the swine flu H1N1 in 2009. The easy adaptation of these viruses to a new host combined with high genetic recombination capacity, has produced several types of Influenza with potential to be pandemic[5].

Until 2002, coronaviruses were not considered to cause serious diseases, however, in November of the same year, cases of severe respiratory disease reported in China, and quickly spread through the population through accelerated transmission, mainly in hospital environments where patients were treated. The disease was called Severe Acute Respiratory Syndrome (SARS), and its etiological agent was only identified in late March 2003, as a new coronavirus called SARS-CoV of the genus *Betacoronavirus*. The virus spread quickly to 25 countries on 5 continents, causing more than 8,000 infections and approximately 800 deaths. Fortunately, characteristics related to the viral load present in the host at the beginning of the infection, allowing or effective control of the viral transmission from person to person and in July 2003 this transmission was controlled. Later, in 2012 cases of severe pneumonia, with high lethality rates, originated in the Middle East, the disease was named Middle East Respiratory Syndrome (MERS), the it was identified to be caused by a new coronavirus entitled MERS-CoV. This virus had a different spread pattern than SARS-CoV, with the elderly and / or people with underlying diseases tending to be the most affected by the disease6. In all, there were 2494 confirmed cases and 858 related deaths, with a lethality rate of 34.4%[7].

The impact of viral respiratory infections on the public health

When dealing with respiratory viruses, one of the major concerns is the possibility of the emergence of new viruses, which may spread easily for reasons well known related to the lack of immunity of the population, ways of transmission, cause pandemics. Among the viruses commonly related to seasonal infections, the following are highlighted.

Influenza is a segmented single-stranded RNA virus of. It is subdivided into three genus that may infect humans *Alphainfluenzavirus*, *Betainfluenzavirus* and *Gammainfluenzavirus*, (influenza A, B and C, respectively), and type A is the one with the greatest variability and can be further divided into subtypes, separated according to the characteristics present in the glycoproteins on its surface[8]. Influenza is the main agent of viral infections, responsible for epidemics of seasonal flu. Transmission can occur through the air, through the inhalation of particles that can be carried over 1 meter further, in addition, transmission can also occur indirectly, through particles left on fomites, which can be easily transferred to hands and later can be directly transmitted to the oral, nasal and ocular mucous membranes. This transmission may also be facilitated in places such as daycare centers, where there is a cluster of children, who, in addition to having a very close contact, still share materials that could easily be infected if any child contracted the virus, and later transmit to other close contact individuals such as family. Children under 5 years old are among the risk groups for Influenza[9]. Prevention, control and identification of circulating strains are mandatory to prevent further infections, as well as to understand their route of transmission, given the high rates of recombination that may occur when different types of the Influenza virus infect the same host, the so called antigenic shifts may contribute for pandemic to emerge[10].

Respiratory Syncytial Virus (RSV), is a single-stranded RNA virus, which belongs to the *Paramyxoviridae* family. It has two subtypes, A and B, which are antigenically distinct[11]. RSV is among the most frequent causes of acute respiratory infections in children and its primary infection is associated with the development of bronchiolitis and severe pneumonia[12]. By the age of three virtually all children have come into contact with the virus, with episodes occurring up to two years of age tending to be the most severe due to low age-related immunity, and the fact that airways are still small, presenting characteristics of a developing respiratory tract[11]. The clinical manifestations of the disease caused by the virus can vary, from asymptomatic cases to the evolution to death. Studies indicate that RSV is among the viruses most frequently found in respiratory tract infections in children under five years of age in Brazil[11,13]. Studies with children hospitalized for respiratory infections have pointed out RSV as the cause of many infections, leading to a high number of hospitalizations and generating large consumption of resources[14].

Parainfluenza is a single-stranded, negative, non-segmented RNA virus that belongs to the *Paramyxoviridae* and its genome is around of 15 kbp[15]. A previous study indicates that Parainfluenza can be detected in 9 to 30% of pediatric patients admitted with acute respiratory disorders[16]. This virus is commonly associated with the development of pneumonia in adults, and is also a more common viral cause for hospitalizations of children under five years of age. In addition, factors associated with host immunity may be fundamental to the development of the virus in order to generate fatal cases. Parainfluenza is divided into 4 types, which differ in their genetic and antigenic characteristics. Interestingly type 3 is more frequently found in Parainfluenza respiratory infections[17].

Adenoviruses (AdV) are double-stranded DNA viruses that belong to the *Adenoviridae* family. Fifty one serotypes and more than 70 genotypes have been described. About a third of the serotypes are associated with diseases in humans. Respiratory infections caused by AdV are generally mild and affect children more often due to lack of immunity[18]. Dissemination is easier in closed environments. Complications caused by AdV are more frequent in immunocompromised individuals. Infected patients usually experience symptoms such as fever, pharyngitis, tonsillitis, cough and sore throat. In patients who do not have any immune compromise, symptoms usually resolve spontaneously and immunity is generated for the specific type to which the individual has been exposed. Children under two years of age can develop pneumonia related to AdV infection, which if left untreated can be fatal. In addition, frequent infections can generate long-term respiratory sequelae in children[18].

Coronaviruses are single-stranded, positive-sense, enveloped, non-segmented RNA viruses. They belong to the *Coronaviridae* family[19]. These viruses are responsible for mild to severe respiratory infections, such as bronchitis, pneumonia and the Severe Acute Respiratory Syndrome[20]. They are divided into four genera: *Alphacoronavirus, Betacoronavirus, Gammacoronavirus* and *Deltacoronavirus*. The alpha and beta genera are responsible for causing infections in mammals[21]. Within the *Alphacoronavirus* is the human coronavirus NL63 (HCoV-NL63), whereas *Betacoronavirus* includes the Severe Acute Respiratory Syndrome (SARS-CoV) and the Middle East Respiratory Syndrome (MERS-CoV)[22]. Also two others human coronaviruses, OC43 (HCoV-OC43) and 229E (HCoV-229E), belongs to Betacoronavirus and Alphacoronavirus genus, respectively, they were identified in the 1960s and in humans they are related to cause the common cold. From the SARS-CoV outbreak, there was an increase in research for these viruses, which led to the discovery of other types, such as HCoV-NL63 and HCoV-HKU123. Today, the world is experiencing a pandemic caused by a *Betacoronavirus*, SARS-CoV-2. Coronavirus disease or COVID-19, from its first report in December 2019 to September 2020, the virus has affected almost 40 million people and caused more than 1 million deaths worldwide. Throughout this period, several countries have come together to raise funds and apply guidelines to guide the population to prevent the virus spread. The World Health Organization (WHO) has been mediating the exchange of information on possible forms of treatment and preventive measures that can slow the spread of this virus. Since March, when a pandemic state was determined by WHO, countries have adopted measures aimed at social distancing, such as the closure of schools and non-essential commercial establishments. In addition, the population has been oriented to avoid mass gatherings and intensify measures hygiene, such as the correct washing of hands and the use of alcohol in the hands frequently[24].

The follow up of the respiratory infections in Brazil

Brazil has a sentinel Influenza surveillance system, which aims to identify influenza and the main circulating respiratory viruses, in order to monitor care demands and deaths, to assist in better decision-making in emergency situations. The Sentinel Units are spread out geographically and record the information on any cases of Influenza Syndrome (IS) and Severe Acute Respiratory Syndrome (SARS). The viral isolation of the collected samples is done using the real-time reverse transcription polymerase chain reaction (RT-PCR) assay to identify Influenza, Respiratory Syncytial Virus, Parainfluenza 1,2 and 3 and Adenovirus. This identification contributes to the composition of the annual influenza vaccine. In addition, there is the dissemination of information on cases of monitoring and investigation of specific seasonal diseases through Epidemiological Bulletins, which are open access publications, on a monthly and weekly basis. These bulletins aim to disseminate relevant information that can contribute to the information that guides the actions in Public Health[25,26].

Every year the world population deals with several viral types that affect the respiratory tract. The seasonality of already known viruses is the cause of the increase in the demand for medical care, especially in winter periods. In Brazil, the Health Surveillance Secretariat is responsible for receiving, analyzing and disseminating epidemiological data regarding the monitoring and investigation of specific seasonal diseases, in order to assist with the guidance of public health actions in the country, in the presence of possible outbreaks. Data related to the incidence of respiratory viruses are made available through epidemiological bulletins, making it possible to monitor the number of cases and deaths by region in the country. In the face of the current pandemic, in which little is known about the influence of SARS-CoV-2 and the preventive measures used on other respiratory viruses that commonly circulate among the population, the aim of this study is to analyze the incidence of respiratory viruses that occurred in Brazil during the years 2019 and 2020.

METHODS

The study was carried out with the public data available in the Ministry of Health website. Weekly Epidemiological bulletins were assessed for the epidemiological situation of IS and SARS during the period of 2019 and 2020 until week 32. Only cases related to respiratory viruses were considered in this study. The data were tabulated and the incidences of one-year viral respiratory infections were compared to the same period in the previous year, incidence of each respiratory infections, and frequency of hospitalizations were also considered in this study.

RESULTS

In 2019, two main epidemiological bulletins were issued by the Ministry of Health to monitor Influenza cases, one covering the epidemiological week 01 to 32, which covers the period from January to August 2019 and the other covering the weeks 01 to 49 , which covers the period from January to December 2019. On January 22, 2020, the Emergency Operations Center for the new Coronavirus started to issue epidemiological bulletins weekly, bringing information about the cases of COVID-19 and SRAG in Brazil and worldwide. To compare the incidence, we used the epidemiological bulletins that cover weeks 01 to 32, both in 2019 and 2020. Until August 2019, there were 22,870 samples of SARS with results inserted in the system, of which 47.6% (10,889 / 22,870) were positive for respiratory viruses. Due to the COVID-19 pandemic, the number of reported cases increased substantially, with 548,353 notifications in the same period in 2020, with 51.7% (283,566 / 548,353) positive samples for respiratory viruses. Among the SARS cases positive for respiratory viruses in 2020, 50.8% (278,714 / 548,353) were positive for SARS-CoV-2, 0.9% (4,852 / 548,353) were positive for other non-SARS-CoV-2 respiratory viruses . In our analysis we excluded the data related to COVID-19, obtaining a total of 269,639 notified cases of SARS in the period of 2020, thus obtaining 1.8% (4,852 / 269,639) of cases related to respiratory viruses (Influenza, RSV, Parainfluenza and/or Adenovirus). This result suggests a 45.8% reduction in the incidence of seasonal respiratory viruses during the COVID-19 pandemic compared to the same period last year (table 1).

Table 1. Cases of SARS up to epidemiological week 32, in 2019 and 2020.

Data	2019		2020		2020 (without SARS-CoV-2)	
	N	%	N	%	N	%
Notified cases	29.978		548.353		269.639	
Samples with results in the system	22.870	77,9	*		*	
Unidentified/Non viral etiology	11.981	52,4	264.787	48,3	264.787	98,2
Respiratory viruses positive cases	10.889	47,6	283.566	51,7	4.852	1,8
Influenza	4.911	21,5	2.251	0,4	2.251	0,8
influenza A(H1N1) pdm09	2.610	53,1	*	-	*	-
Influenza B	394	8,0	*	-	*	-
Influenza A not subtyped	1.296	26,4	*	-	*	-
influenza A(H3N2)	611	12,4	*	-	*	-
RSV/parainfluenza/adenovirus	5.978	26,1	2.601	0,5	2.601	1,0
RSV	4.827	80,8	*	-	*	-
Covid-19			278.714	50,8		

(*) Data not available.

Regarding deaths, 11.7% (3,514 / 29,978) of the reported cases died, 35.9% (1,261 / 3,514) were caused by respiratory viruses. In the same period in 2020, deaths represented 26.4% (144,663 / 548,353) of the total cases of SARS, 68.2% (98,709 / 144,663) were caused by respiratory viruses, of these 67.9% (98,195 / 144,663) were positive for SARS-CoV-2, 0.4% (514 / 144,663) were positive for other non-SARS-CoV-2 respiratory viruses. In our analysis we excluded the data related to COVID-19, obtaining a total of 8.5% (46,468 / 264,787) deaths due to SARS in the period of 2020. Also, in this analysis 1.1% (514 / 46,468) of the deaths are related to a respiratory viruses (Influenza / RSV / Parainfluenza / Adenovirus). This result represent a reduction of 34.8% in deaths from SARS caused by seasonal viruses during a COVID-19 pandemic compared to the same period last year (table 2).

Table 2. Notified Deaths by SARS up to the epidemiological week 32, in 2019 and 2020.

Data	2019		2020		2020 (excluído SARS-CoV-2)	
	N	%	N	%	N	%
Deaths (absolute numbers by SARS)	3.514	11,7	144.663	26,4	46.468	8,5
Unidentified/Non viral etiology	2.253	64,1	45.954	31,8	45.954	98,9
Respiratory viruses positive cases	1.261	35,9	98.709	68,2	514	1,1
Influenza	917	26,1	310	0,2	310	0,7
influenza A(H1N1) pdm09	589	64,2	*	-	*	-
Influenza B	53	5,8	*	-	*	-
Influenza A not subtyped	188	20,5	*	-	*	-
influenza A(H3N2)	87	9,5	*	-	*	-
Deaths by RSV/parainfluenza/adenovirus	344	9,8	204	0,1	204	0,4
RSV	242	70,4		-		

(*) Data not available

The analyses of frequency of viral infection by age group revealed that in 2019 most of the cases of SARS occurred among children under 2 years of age (41.62%), while in 2020 the highest percentage of cases is among adults aged 60 years or older (50.51%). In addition, in 2019 more than half of the cases (60.31%) are concentrated among children and young individuals under 19 years-old, whereas in 2020 we observed that this age group is represented by a much smaller number, representing only 7.37% cases (table 3). The analysis by age group was performed by analyzing all cases of SARS by any etiology.

Table 3. Percentage of SARS cases up to epidemiological week 32, in 2019 and 2020, distributed by age group.

Faixa etária	2019	2020
<2	41,62	2,07
2-4	9,52	1,06
5-9	5,21	0,85
10-19	3,96	1,20
20-29	4,97	4,24
30-39	5,99	10,52
40-49	5,77	15,21
50-59	6,79	18,27
60+	16,16	46,58

DISCUSSION

In this study, we analyzed the incidence of non SARS-CoV2 respiratory viruses in the years 2019 and 2020, with the aim of identifying whether the circulation of seasonal viruses could be affected by measures to combat the pandemic caused by SARS-CoV-2. Studies carried out during the Influenza A (H1N) 1 pdm09 pandemic, demonstrated that there was a change in the spread pattern of the other seasonal respiratory viruses, suggesting the influence of the circulation of a new respiratory virus on the existing ones, the circulation pattern was normalized after H1N1 pdm09 becomes seasonal[27,28].

Our results suggest a decrease in the incidence of seasonal respiratory viruses in Brazil during the COVID-19 pandemic. Olsen et al analyzed the incidence of Influenza during the current pandemic in the United States, Australia, Chile and South Africa and the results were similar to ours, showing lower rates of Influenza circulation during the period of 2020 compared to the same period of the previous year[29]. Since the beginning of this pandemic, government authorities have worked with health agencies and proposed to the population the adoption of control measures aimed at reducing the spread of SARS-CoV-2, such as correct hand hygiene, social distance and the use of masks, the use of these measures may have had an impact on the incidence of other respiratory viruses that circulate seasonally in the country.

Interestingly, we observed an inversion in the relationship between the age group and the percentage of cases of SARS between 2019 and 2020. The role of children in the transmission of respiratory viruses has been discussed over the years, at high rates of incidence of these viruses, has associated with school-age children who play an important role in dissemination, since the school environment provides a close relation-

ship between children and young people, facilitating the circulation of viruses and consequently transmitting them to their adult relatives[30]. In addition, children under two years of age have higher rates of hospitalizations for respiratory viruses, this effect has been suggested by the lack of immunity and maturity of the developing respiratory system[31,32]. These data elucidate the highest percentage of children with SARS found in our analysis in 2019. In contrast, in 2020 the situation has changed, where adults from the age of 30 and the elderly were the most affected. Finally, we believe that the measures adopted to control the pandemic may have considerably contributed to the reduction of non-SARS-CoV2 viral respiratory infections in Brazil and also the low incidence in young people may be related to the closure of school units and kindergarten for a prolonged period of time.

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