THE BURDEN OF DISEASE ATTRIBUTABLE TO COVID-19 IN MARANHÃO

ORIGINAL ARTICLE

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ABSTRACT

The objective of this study was to estimate the burden of morbidity and mortality of Covid-19 in Maranhão over a 24-month period, between the years 2020 and 2022. For this purpose, the data used were obtained from the bulletins of the State Department of Health of Maranhão, the IBGE portal, and the 2019 Global Burden of Disease Study. Using this information (confirmed cases and deaths, life expectancy, and disability weights), the average fatality rate and DALYs for the period were estimated. In the calculation of YLLs, two age distributions were used: 10-year age groups and individual ages. An average fatality rate of 2.58% (3.51% for men and 1.86% for women) and a mortality rate of 0.15% (151.73 deaths per 100,000 inhabitants) were observed. According to IBGE, life expectancy in Maranhão in 2021 was 68 years for men and 76 for women. Based on this, an estimate of 95,206 YLLs and 938.377539 YLDs was obtained, totaling 96,144.377 DALYs for the period or 1,344 DALYs per 100,000 inhabitants. Thus, it can be concluded that these results place Covid-19 at a very high level of morbidity and mortality, surpassing the DALYs recorded for all lower respiratory diseases in Maranhão in 2018 and 2019. These values make studies on the burden of Covid-19 in the region important efforts in understanding the damage caused by this disease.

Keywords: Pandemic, Disease burden, Sars-Cov-2.

INTRODUCTION

The SARS-CoV-2 virus has caused significant loss of life and human health globally since the beginning of 2020, resulting from the ongoing pandemic, named Covid-19.

Following its first notification on December 31, 2019, this disease quickly spread worldwide and was declared a pandemic on March 11, 2020, leading to the death of approximately 7.727 million individuals by April 1, 2023, as projected at the beginning of the same year (WHO, 2020; IHME, 2023). Brazil, having reported its first case on February 26, 2020, soon became a major global hotspot for Covid-19, with 363,211 confirmed cases and 22,666 deaths by May 25, 2020 (3 SIMÕES and SILVA *et al.*, 2020).

Maranhão had its first confirmed case on March 20 and the first death by March 29 of the same month. During the first wave of infections (first half of 2020), the state reached 1,396 cases by April 20 and exceeded 30,000 by the end of May, according to data from the State Department of Health of Maranhão (4 SES-MA, 2020). By March 16, 2022, already in the observed third wave of infections, Maranhão had accumulated 420,183 confirmed cases and 10,854 deaths (SES-MA, 2020).

In this context, it is useful to apply a disease burden study to Covid-19. Such studies are systematic efforts to quantify the comparative magnitude of health loss due to diseases, injuries, and risk factors by age, sex, and geography at a specific moment. The units used to measure human health are Years of Life Lost (YLL), Years Lived with Disability (YLD), and Disability-Adjusted Life Years (DALY), the sum of the two previous factors (CAMPOS *et al.*, 2020).

In general, for an appropriate response to epidemiological emergencies, it is necessary to know the costs of the disease to human health, as well as the burden of such disease on healthcare systems and their clinical protocols. Such measures can assist in the management of medical resources, such as preventive materials, beds, and medicines. Furthermore, for Covid-19, the scientific literature emphasizes the importance of diagnosing and treating the disease as well as preventive measures and post-discharge patient surveillance to prevent lasting sequelae. In summary, these efforts contribute to maximizing the number of total recoveries, as well as organizing health actions in the face of similar diseases in the future.

In addition to the diagnostic costs, in the recent past and currently, Covid-19 has been consuming various human and financial resources, making it particularly useful to identify its debilitating potential, an ongoing process. In this context, the aim here is to estimate the burden of Covid-19 for the state of Maranhão, gather epidemiological and demographic information about the disease, and conduct a comparative analysis of the burden of this infection on public health compared to other diseases.

MATERIALS AND METHODS

DATA COLLECTION

Records of Covid-19 cases between 16/02/2020 and 16/03/2022 were included, including the number of confirmed cases, deaths due to Covid-19, and their age group. The literature search involved general terms: life expectancy in Maranhão, population of Maranhão, convalescence period of Covid-19, infection weights, and Covid-19-related sequelae. Information regarding the progression of the disease in Maranhão was extracted from the available epidemiological bulletins of the State Department of Health of Maranhão (SES-MA). Life expectancies for men and women in the Maranhão population were obtained from IBGE.

The values of the weights for the disease and its sequelae were derived from the 2019 Global Burden of Disease study (GBD 2019), whose weight spreadsheet is available on the Global Health Data Exchange (GHDx) portal of IHME. The variables of interest were input into the calculation model to estimate years of life lost due to mortality and morbidity. In total, the disease prevalence, Years of Life Lost (YLL), and Years Lived with Disability (YLD) were estimated. The sum of these last two values allowed the estimation of Disability-Adjusted Life Years (DALY).

CALCULATION OF YLLs

Careful monitoring of Covid-19-related deaths yielded specific values for the number of deaths at each identified age. This monitoring allows for the verification of deaths by specific ages for both men and women. Thus, the calculation of YLLs in this study

could account for individual years of life, using the formula below, where "$M_{i,g}$" it represents the number of deaths for each death at a specific age (*"i"*) in the analyzed gender (*"g"*) (for both men and women), "*LE*" indicates life expectancy for each analyzed gender, and "I" indicates the age in question, measured in years).

$$\sum_{i=<1}^{LE} M_{i,g} \cdot (LE - I)$$

The presented expression is based on an adaptation of the age group formula used by two authors, Vieira *et al.*, (2021) and Mitra *et al.*, (2020). Both in studies of measurement and analysis, respectively, of YLLs in the context of Covid-19, both following the methodological contributions recommended by WHO. The measurement of YLLs in this study was based on the methodology used for GBD 2010 onwards, thus it does not involve the use of age weights or time discounting.

Life expectancy values were, for practical purposes, approximated to the nearest whole numbers in both calculations.

YLDs CALCULATION

For the calculation of YLDs, a numerical estimate of the severity of Covid-19 and its short- and long-term symptoms (based on incidence) was necessary. This estimate involves applying disability weights (ranging from 0 to 1), where "*0*" indicates perfect health and "*1*" indicates death. In essence, the inclusion of weights involves fractionalization of the years lost to account for the loss of quality of life during the specific period. Therefore, the formula for calculating this value is as follows:

$$\sum_{s=1}^{5} C_{f,s} \cdot D \cdot p_s$$

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In the formula above, used under different terms by Rommel *et al.* (2021), the years lost due to disability (YLD) result from a summation of the products obtained by directly multiplying the incident cases $(C_{f,s})$ by the average duration of symptoms in years (*"D"*) and the disability weight for the condition (p_s) regarding the average duration of the symptomatic phase of the disease for each type of manifestation, an average of 14 days was used for mild and moderate cases, 21 days for severe cases, and 32 days for critical cases, with a frequency of 42%, 25%, 27%, 5%, and 1% for asymptomatic, mild, moderate, severe, and critical cases, respectively. These values were extracted from the Covid-19 burden study conducted by Rommel *et al.* (2021) in Germany, based on data extracted from 1.7 million cases detected throughout 2020. Additionally, the duration values were reinforced based on Ferreira *et al*. (2022), which determined an average of 15.9 days (or approximately 2 weeks) for the total duration of symptoms in most home cases, as well as the recommendation of a 14-day isolation period issued by the WHO, since the symptomatology of Covid-19 presents a high variability in duration (13 GRENDENE *et al.*, 2021).

As for the long-term effects of Covid-19, a disability weight of 0.006 was determined for cases of post-acute sequelae. This value corresponds to the weight assigned to mild infections, as the symptoms observed in long Covid-19 are similar in terms of severity (MORENO-PÉREZ *et al.*, 2021). The average duration of the post-acute syndrome varies widely, with several studies reporting between 3 to 24 weeks after the acute phase, with an incidence between 4.7% to 80% (CABRERA MARTIMBIANCO *et al*., 2021). In our study, an average duration of 12 weeks was assumed, with a frequency of 50% of affected cases, values that approximate those used by Petersen *et al.* (2021) and Moreno-Pérez (2021) in Denmark and Spain, respectively. A more accurate determination of the nature of the post-acute phase should be an immediate objective of future studies analyzing the clinical and symptomatic characteristics of Covid-19.

ETHICAL CONSIDERATIONS

This research, involving consultation of publicly available secondary databases where identification of any subjects is not possible, is exempt from submission to the Research Ethics Committee.

RESULTS

According to the epidemiological bulletin of March 16, 2022, from the State Department of Health of Maranhão, there were 420,183 confirmed cases of Covid-19 in the state since the beginning of the count (03/16/2020). During this same period, 10,854 deaths due to the disease were recorded in a territory with 7,153,262 inhabitants (IBGE, 2021). Furthermore, an average fatality rate of 2.58% (3.52% for men and 1.86% for women) and an average mortality rate of 0.152% (151.73 deaths per 100,000 inhabitants) were recorded in the same interval.

The calculation of YLLs resulted in a total of 95,206 years of life lost for all age groups considered, summing the totals for men and women (with an average of 1,236.441 per specific year) (Table 1 and Graph 1).

Table 1 – YLLs by specific age in men and women in Maranhão between 3/2020 and 3/2022

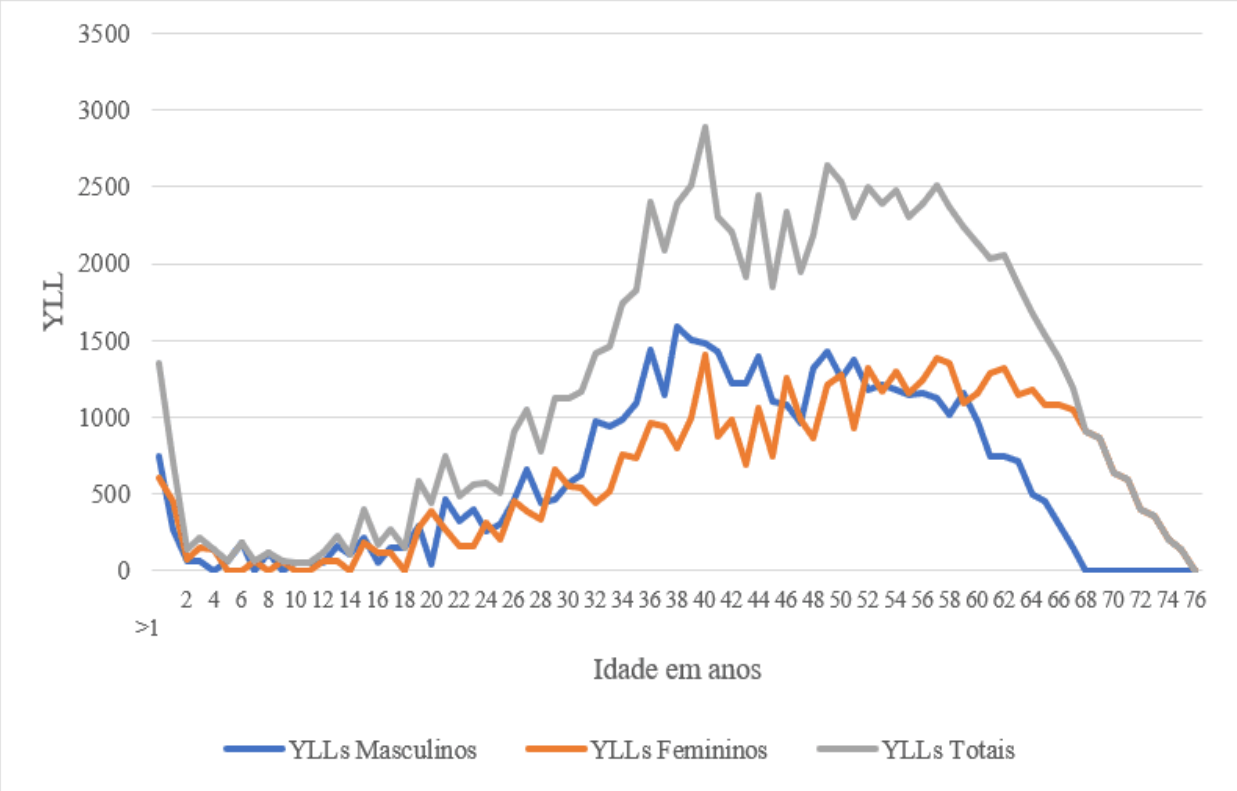
Ages	Male Deaths	Female Deaths	Male YLLs	Female YLLs	Total YLLs
>1	11	8	748	608	**1356**
1	4	6	268	450	**718**
2	1	1	66	74	**140**
3	1	2	65	146	**211**
4	0	2	0	144	**144**
5	1	0	63	0	**63**
6	3	0	186	0	**186**
7	0	1	0	69	**69**
8	2	0	120	0	**120**
9	0	1	0	67	**67**
10	1	0	58	0	**58**

11	1	0	57	0	**57**
12	1	1	56	64	**120**
13	3	1	165	63	**228**
14	2	0	108	0	**108**
15	4	3	212	183	**395**
16	1	2	52	120	**172**
17	3	2	153	118	**271**
18	3	0	150	0	**150**
19	6	5	294	285	**579**
20	1	7	48	392	**440**
21	10	5	470	275	**745**
22	7	3	322	162	**484**
23	9	3	405	159	**564**
24	6	6	264	312	**576**
25	7	4	301	204	**505**
26	11	9	462	450	**912**
27	16	8	656	392	**1048**
28	11	7	440	336	**776**
29	12	14	468	658	**1126**
30	15	12	570	552	**1122**
31	17	12	629	540	**1169**
32	27	10	972	440	**1412**
33	27	12	945	516	**1461**
34	29	18	986	756	**1742**
35	33	18	1089	738	**1827**
36	45	24	1440	960	**2400**
37	37	24	1147	936	**2083**
38	53	21	1590	798	**2388**
39	52	27	1508	999	**2507**
40	53	39	1484	1404	**2888**
41	53	25	1431	875	**2306**
42	47	29	1222	986	**2208**
43	49	21	1225	693	**1918**

44	58	33	1392	1056	**2448**
45	48	24	1104	744	**1848**
46	49	42	1078	1260	**2338**
47	46	34	966	986	**1952**
48	66	31	1320	868	**2188**
49	75	45	1425	1215	**2640**
50	70	49	1260	1274	**2534**
51	81	37	1377	925	**2302**
52	74	55	1184	1320	**2504**
53	81	51	1215	1173	**2388**
54	84	59	1176	1298	**2474**
55	88	55	1144	1155	**2299**
56	96	62	1152	1240	**2392**
57	102	73	1122	1387	**2509**
58	102	75	1020	1350	**2370**
59	128	64	1152	1088	**2240**
60	122	72	976	1152	**2128**
61	107	86	749	1290	**2039**
62	124	94	744	1316	**2060**
63	143	88	715	1144	**1859**
64	125	98	500	1176	**1676**
65	151	98	453	1078	**1531**
66	150	108	300	1080	**1380**
67	150	116	150	1044	**1194**
68	156	113	0	904	**904**
69	177	123	0	861	**861**
70	174	107	0	642	**642**
71	161	118	0	590	**590**
72	164	100	0	400	**400**
73	194	118	0	354	**354**
74	148	104	0	208	**208**
75	159	135	0	135	**135**
76	118	119	0	0	**0**

Source: Authors, 2023.

Graph 1 - Comparison of YLLs by specific age and by gender, due to Covid-19 in the State of Maranhão, from 2020 to 2022



Source: Authors, 2023.

Table 2 shows the preliminary values used and the total amount of Years Lived with Disability - YLDs.

Table 2 - YLDs Estimate due to Covid-19 in Maranhão from 2020 to 2022

Severity	Frequency	Weight	Duration (in years)	YLDs
Asymptomatic	42%	0.000	0.03833	**0,00**
Mild	25%	0.006	0.03833	**24,158421**
Moderate	27%	0.051	0.03833	**221,77431**
Severe	5%	0.133	0.05749	**160,639532**
Critical	1%	0.655	0.08761	**241,120124**
Post-Acute Syndrome (Long Covid)	50%	0.006	0.23061	**290,695205**

Total	100%	**		**	**938,377539**

Source: Authors, 2023.

In Maranhão during the study period, the number of YLLs was 95,206, YLDs were 938.377, and DALYs* were 96,144.377 (The value of Disability-Adjusted Life Years - DALYs, is equivalent to the simple arithmetic sum of YLLs and YLDs).

DISCUSSION

This study aimed to provide an initial estimate of the disease burden of Covid-19 in Maranhão for a broad period of 2 years. To do so, epidemiological and demographic data from the state were aggregated, a comparison was made between the morbidity and mortality of Covid-19 and other diseases, and the current state of research on the global burden of diseases at the national level was assessed.

The average YLLs per 10-year age group was 11,900.75 (with 1,236.44 being the average for each individual year). Additionally, the average years lost for each of the 6,130 deaths considered was 15,531.1. This result is similar to the average of 16 years obtained by Pifaré I Arolas *et al.* (2021) in a compilation of 81 studies seeking a universal sum of YLLs due to Covid-19 in 2020 and is significantly higher than the 9.6 YLLs per death obtained by Rommel *et al.* (2021).

The age group with the highest YLLs was 50 to 59 years, with 24,230 YLLs in the period (sum of individual years), followed by the age groups 40 to 49 years (22,801 YLLs), 60 to 69 years (18,477 YLLs), and 30 to 39 years (15,118 YLLs). These results partially reflect international estimates that classify the 50 to 70 age group as the largest contributors to the total YLLs, accounting for approximately 44.85% of representation (PIFARÉ I AROLAS *et al*., 2021). The age strata with the lowest number of YLLs were 10 to 19 (1,596 YLLs), 0 to 9 years (3,074 YLLs), and 20 to 29 years (6,003 YLLs).

The age group with the lowest number of years of life lost per confirmed case was 10 to 19 years (also with the lowest number of deaths), with 0.0506 YLLs per case, while the ages with the highest number were between 60 and 69 years, with 0.5820 YLLs per case.

In the calculation of individual years, it was observed that the specific age most affected was 42 years, with 2,888 YLLs added per 92 registered deaths. It is suggested that such variations in years may be related to the conjunction of random events of contagion in populations of certain ages and the balance between their vulnerability to severe clinical manifestations of Covid-19 and the high number of years of life remaining in the face of average life expectancy. Studies that have explored Covid-19 burden elements by individual years have not been located at this time, so comparisons at this level cannot be made.

Regarding mortality by gender, a total of 46,569 YLLs were observed in men and 48,637 YLLs in women. However, the average years lost per specific age were 674.913 and 631.649 in men and women, respectively. These two comparisons express the higher number of YLLs in women due to their higher life expectancy and the higher average of YLLs in men due to their greater vulnerability to the lethal manifestations of the disease, producing higher lethality.

The population of Maranhão is estimated at 7.15 million in 2021 (IBGE), which yields an average of 0.01331 YLLs per person (or 4.86 days lost), or 1,331 YLLs for every 100,000 inhabitants of the state. This value is considerably below that of other socioeconomically similar regions, such as the 1,998 YLLs per 100,000 inhabitants in Malaysia, according to another study covering 2 years of the pandemic (TAN *et al.*, 2022). It also falls below the DALYs measured in severely affected regions at the beginning of the pandemic and with a high proportion of elderly people in the population, such as Italy, which obtained an average of 2010 DALYs per 100,000 inhabitants (NURCHIS *et al.*, 2020).

Regarding the averages of DALYs, 0.01344 per person (4.91 days lost) or 13.44 DALYs for every 100,000 inhabitants were obtained. As for the YLDs, the values were

0.0001311 per person (1.14 hours lost) or 13.11 YLDs for every 100,000 inhabitants. The total YLDs obtained constitute 0.0976% of the total DALYs

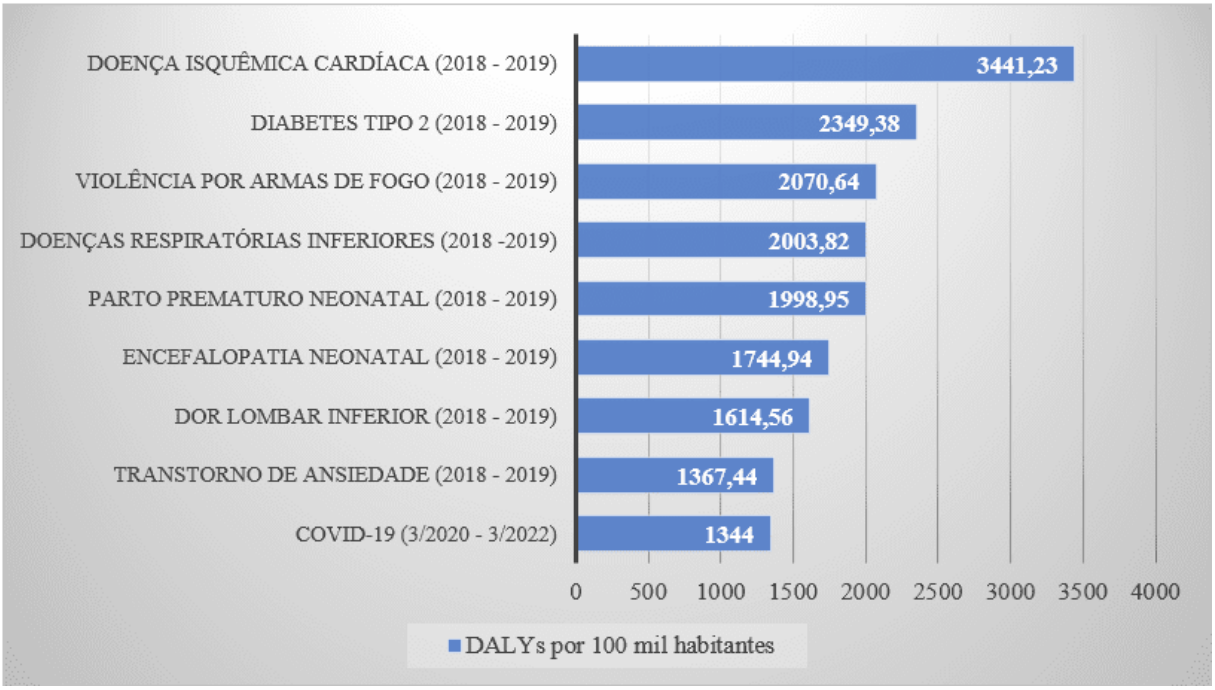
(99.9024% YLLs), and 69% (647.69238 YLDs) are represented by the acute phase of Covid-19, within which critical manifestations of the disease were the largest contributors, with 241.1201 YLDs, followed by moderate (221.7743 YLDs) and severe (160.6395 YLDs) phases, respectively. The largest individual contributor to the disability component was the post-acute phase, with 290.695205 YLDs in the period (cases that exceeded the end date were considered, provided they originated within the period of interest).

Similar proportions between YLLs and YLDs in this context are seen in various studies, such as Tan *et al.* (2022), with 99.5% YLLs, and Jo *et al.* (2020), with 98.2%, respectively. It is worth mentioning that, with the differences in lethality by age group, such proportions vary according to age, as evidenced by Jo *et al.* (2020) in a study in South Korea at the beginning of the pandemic, in which a variation of 1.8% was observed between YLLs and YLDs between ages 0 and 30 years, and those ages above 80 years (high regional life expectancy).

COMPARISON WITH OTHER DISEASES

For a better understanding of the burden of this disease on public health, the final result was compared to the DALYs per 100,000 inhabitants related to the seven major general causes of morbidity and mortality in Maranhão in 2018 and 2019 (according to GBD 2019 data). These causes were: Ischemic heart diseases, type 2 diabetes mellitus, physical violence by firearms, lower respiratory infections, complications from premature birth, neonatal encephalopathies due to trauma or asphyxia, lower back pain, and anxiety disorders (IHME, 2019).

Figure 6 - DALYs resulting from the major aggregated causes of morbidity and mortality in Maranhão between 2018 and 2019, and Covid-19 from 3/2020 to 3/2022

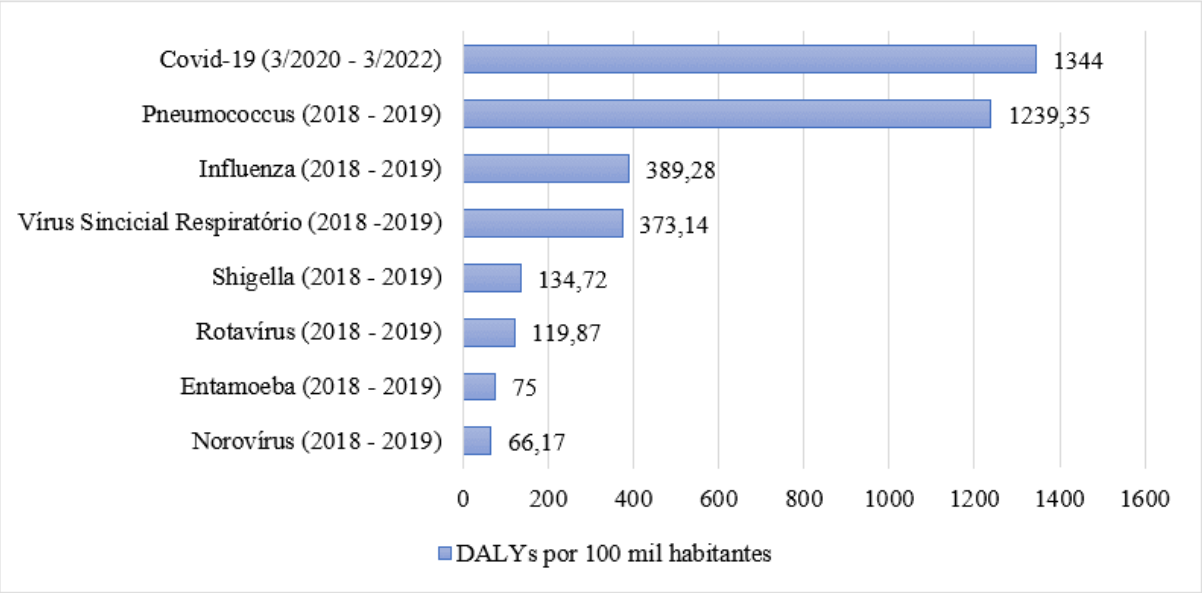


Source: Author's elaboration.

It is possible to observe that Covid-19, from March 2020 to March 2022, ranks ninth among the major causes of morbidity and mortality in the state (ICD-10 elements) for the years 2018 and 2019. It is also noted that Covid-19 accounted for 67.07% of the total DALYs per population share compared to the aggregate of lower respiratory infections from the two years preceding the pandemic.

Furthermore, Covid-19 as a communicable disease (lower respiratory tract) surpassed all seven communicable diseases with the highest morbidity and mortality in Maranhão in 2018 and 2019 in terms of DALYs per 100,000 inhabitants. These are, by etiology: Pneumococcus, Influenza, Respiratory Syncytial Virus, Shigella, Rotavirus, Entamoeba, and Norovirus. These data also stem from GBD Compare for 2018 and 2019 (IHME, 2019).

Figure 7 - Comparison between the morbidity and mortality of the most influential communicable diseases in Maranhão between 2018 and 2019, and Covid-19 (by etiological agent), from 3/2020 to 3/2022



Source: Author's elaboration.

It is observed that Covid-19 obtained 8.44% more DALYs per 100,000 inhabitants than pneumococcal diseases (etiologic agent Streptococcus pneumoniae or Pneumococcus) and 345.25% more DALYs per 100,000 inhabitants than influenza infections (etiologic agent Influenza viruses). Thus, the Sars-Cov-2 virus and its various variants of concern stand out for their high capacity to inflict damage on public health. It is worth noting that during the course of the Covid-19 pandemic, infection mitigation strategies such as hygiene and social distancing led to a global reduction in the transmissibility of various communicable diseases, which may result in a more pronounced discrepancy in morbidity and mortality between the years 2020 and 2022 (KITANO, 2021).

CURRENT RESEARCH CONTEXT ANALYSIS

Currently, there are few studies measuring the burden of Covid-19 on the general population over long periods of time. Studies in the Brazilian context mostly pertain to the early stages of the pandemic, such as Silva *et al.* (2021), used as methodological reference for this work, which observed 498.1 DALYs (216.02 DALYs per 100,000

inhabitants) among nursing professionals in Brazil from March 20 to May 5, 2020. Other national studies on this topic are primarily literature reviews and discussion articles, like Campos *et al.* (2020), which proposes the use of Covid-19 disease burden studies to aid health actions during the pandemic.

No disease burden studies of Covid-19 in Maranhão were found. The available publications focus on epidemiological characterization in the state or municipalities, such as Dos Santos Almeida *et al.* (2020), which identified a rapid increase in confirmed cases between March and April 2020. Therefore, this work is the first study on the disease burden of Covid-19 to be conducted in Maranhão and the region, and is among the first at the national level.

The perspective of studying Covid-19 and its sequelae as a risk factor for future diseases, as well as the psychological burden during the pandemic, is difficult to ascertain at this time. This perspective can be observed in certain national studies such as Ferreira da Mata *et al.* (2021) and Pereira *et al.* (2021), in literature reviews that highlighted significant impacts of the pandemic on the mental health of young individuals and healthcare professionals, respectively.

The scarcity of Covid-19 disease burden studies (especially in Brazil) posed certain challenges in conducting this project. Notably, the weights used here for calculating YLDs are based on methodological foundations from the last decade and the body of research on this topic since the beginning of the pandemic. Therefore, several assumptions about the behavior of the disease on a large scale had to be made, such as the use of disability weights related to lower respiratory diseases from the latest editions of the GBD for a disease that, in many cases, has a systemic reach. These uncertainties are shared with all available literature at the moment, making the determination of the exact nature of Covid-19 and the magnitude of its long-term sequelae a topic of fundamental importance for future studies in the field.

CONCLUSION

The observed data attest, in fine detail, to the extremely high clinical significance of Covid-19 for public health in Maranhão during the analyzed period, being the second major general cause of morbidity and mortality, and the most influential communicable disease in the state within the 2020s. Inside and outside the context of the Covid-19 pandemic that shook the world in recent years, the impact of this disease will have long-term repercussions, as its wide range of direct and indirect sequelae will continue to affect the public to some extent, even after the control of the disease and its variants, necessitating proper healthcare preparedness.

It is hoped that this work contributes to the expansion of the available knowledge base regarding the impact of Covid-19 and the behavior of the Sars-Cov-2 virus on a large scale in the state of Maranhão and similar regions. Information useful in the design of future disease burden studies, as well as other epidemiological monitoring actions involving the history of the disease in the North and Northeast regions of Brazil during the early 2020s, was consolidated here.

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