INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

ENGLISH VERSION of Article

https://doi.org/10.31005/iajmh.v4i.173

Analysis of hospitalizations and mortality from febrile diseases, infectious and parasitic, during the COVID-19 pandemic in Brazil

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INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

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https://doi.org/10.31005/iajmh.v4i.173
Conflicts of interest: The authors declare no conflict of interest.

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ABSTRACT

Introduction: During the COVID-19 pandemic, undifferentiated febrile illnesses are being less detected and / or confused in clinical diagnoses, which implies in late treatments and a worse prognosis. **Objective**: Evaluate hospitalizations and the mortality rate of undifferentiated febrile illnesses that occurred simultaneously with COVID-19 in Brazil. **Method**: A descriptive and quantitative analysis of the number of hospitalizations, mortality rates, expenses, and average length of hospitalizations for visceral leishmaniasis, leptospirosis, malaria and dengue were performed. The information was obtained from the Sistema de Informações Hospitalares do Sistema Único de Saúde (SIH / SUS), during the first eight months of 2020 and compared with average values from the same period from the years 2017 to 2019. **Results**: The number of hospitalizations for visceral leishmaniasis, leptospirosis and malaria in 2020 showed a decrease of 32.87%, 43.59%, 29.31%, respectively, while dengue showed an increase of 29.51% compared to the averages from 2017 to 2019. The mortality rate (2020) increased by 32.64%, 38.98%, 82.55% and 14.26% for the respective illnesses. Expenses and average length of stay fluctuated proportionally according to hospitalizations, with no important variations detected. **Discussion**: The possibility of underreporting, misunderstanding and late diagnoses was discussed, with a consequent increase in the mortality rate in undifferentiated febrile illnesses.

https://doi.org/10.31005/iajmh.v4i.173

It is necessary for the health system to pay attention and not to neglect the undifferentiated febrile illnesses already endemic to the country because of the pandemic moment.

Keywords: Coronavirus infections; Visceral leishmaniasis; Leptospirosis; Malaria; Dengue.

INTRODUCTION

In December 2019, the Coronavirus disease (COVID-19), caused by Severe Acute Syndrome Coronavirus 2 (SARS-CoV-2), was detected in patients with pneumonia in Wuhan, a Chinese city located in Hubei Province [1]. Since the first cases in China to October 18, 2020, the World Health Organization (WHO) recorded approximately 40 million cases and 1,1 million deaths by COVID-19 [2].

Due to the absence of vaccines and drugs to contain the disease, non-pharmaceutical interventions were recommended, such as to maintain physical distancing, hand hygiene and the use of masks [3,4]. In Brazil, to face the pandemic, the Ministry of Health has promoted the strengthening of hospital care provided by the Unified Health System (SUS), through the training and hiring of health professionals, production and distribution of protective equipment and mechanical ventilators, setting up field hospitals and expanding the capacity of existing hospital units [3]. The Brazilian government has allocated more than R$ 5 billion (Brazilian reais) to promoted measures to intensify surveillance and to carry out viral identification tests, in order to detect more cases and control transmission [5].

The occurrence of COVID-19 at the same time as seasonal diseases can overburden the health system, if mitigation measures to face this disease are not

https://doi.org/10.31005/iajmh.v4i.173

carried out. These aspects can generate an excess of critically ill patients in relation to the number of hospital beds available and collapse the health system [5-7].

It has also been argued that the reduction of care for other diseases during the pandemic can cause great damage to health systems, this happens as a secondary consequence of the prioritization of medical care for COVID-19 [8, 9].

The existence of disparities between the real number of deaths by COVID-19 and the number reported in registry offices and the Sistema de Informação de Agravo de Notificações (SINAN) indicates the probable occurrence of underreporting of deaths [10].

These uncertainties imply, not only deaths, but also in the differential diagnosis of COVID-19 and undifferentiated febrile illnesses, which have similar clinical characteristics [11]. In the USA, for example, a patient, hospitalized for developing heart block, was diagnosed with Lyme Disease with delay, because the diagnoses for COVID-19 were made first and the failure to identify erythema migrans skin lesion in the telemedicine service [12].

As opposed to the previous case, in Thailand, a patient was initially diagnosed with dengue, because he had a skin rash with petechiae and low platelet count, but later on, this individual was diagnosed with COVID-19 through the RT-PCR test [13]. In Singapore, patients, who manifested fever, thrombocytopenia and lymphopenia, were considered false-positive for dengue, after serological tests, but were later confirmed with severe acute respiratory syndrome by SARS-CoV-2 [14].

Considering the context of possible underreporting, difficulties in clinical and epidemiological diagnoses and the reduction of prevention and control measures for endemic diseases, the purpose of the present study is to evaluated hospitalizations and the mortality rate due to febrile illnesses that occurred simultaneously with COVID-19 in Brazil.

INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

ENGLISH VERSION of Article

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METHOD

A descriptive and quantitative analysis of secondary data on hospitalizations caused by undifferentiated febrile illnesses that occurred in all Brazilian states was performed. The data were analyzed in Microsoft Excel spreadsheets and obtained from information on Hospital Morbidity in the Sistema de Informações Hospitalares do Sistema Único de Saúde (SIH/SUS), which is available at the SUS Department of Informatics (DATASUS) [15].

The diseases were classified by the International Classification of Diseases (ICD 10) and adapted to the need of the Brazilian reality [16], were Dengue fever (classical dengue), hemorrhagic Dengue fever, Visceral leishmaniasis, Leptospirosis icterohemorrhagica, unspecified Leptospirosis and Other forms of leptospirosis, Unspecified malaria and malaria caused by *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae* and other forms of malaria confirmed by parasitological examinations. In the present study, these diseases were organized in the groups of dengue, visceral leishmaniasis, leptospirosis and malaria. For each group, the number of monthly hospitalizations, by place of residence, from January to August 2017 to 2020 was evaluated.

The data show the average series of monthly hospitalizations and mortality rates during the years 2017 to 2019 and hospitalizations and the mortality rate for these diseases in 2020, during the first eight months of the pandemic. Additionally, the values total spending in the Unified Health System (SUS) were also estimated and the average monthly hospitalization values and the average length of hospital stay times during the years surveyed were calculated.

RESULTS

INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

ENGLISH VERSION of Article

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For hospitalizations from January to August 2017 to 2019, averages of 222,25 hospitalizations for visceral leishmaniasis, 220,5 for leptospirosis and 160,67 for malaria were calculated. The number of hospitalizations in the first eight months of 2020 was 125,38 hospitalizations for visceral leishmaniasis, 155,87 for leptospirosis and 113,25 for malaria, which represent decreases in hospitalizations in the order of 43,59%, 29,31% and 29,51%, respectively, compared to the averages of the three years prior to the pandemic (figures 1A, 1B and 1C - table 1). Different of this standard, dengue (between the years 2017 to 2019) had an average of 3297,5 hospitalizations, while in 2020, 4071,3 hospitalizations were recorded, which represents a 23.47% increase in the number of hospitalizations (figure 1D - table 1).

According to figures 1A, 1B, 1C and 1D, it is observed that the hospitalizations for these four groups of diseases in 2020 remained below the average hospitalizations that occurred between 2017-2019 from the month of May.

The average values spent on hospitalizations (between 2017 and 2019) for visceral leishmaniasis, leptospirosis, malaria and dengue were R$ 127.217,59, R$ 264.613,28, R$ 52.310,27 and R$ 1.201.043,81, respectively. In the year 2020, we observed a reduction of 39.36%, 11.27% and 15.44% for visceral leishmaniasis, leptospirosis and malaria, respectively and an increase of 27.92% for dengue (table 1).

For mortality rates from January to August 2017, 2018 and 2019, the average of deaths due to visceral leishmaniasis was 3.58, 5.66 due to leptospirosis, 0.80 due to malaria and 0.85 due to dengue. Mortality rates, calculated for the first eight months of 2020, were 4.75 for visceral leishmaniasis, 7.87 for leptospirosis, 1.46 for malaria and 0.97 for dengue, and represent increases of 32.64%, 38.98%, 82.55% and 14.26%, respectively, compared to the averages of the three years prior to the pandemic (figures 1 and table 1). According to figures 1A, 1B, 1C and 1D, in comparison to the average series of mortality rates (2017-2019), it was shown

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that, in several months of the year 2020, the mortality rates of the four diseases remained higher.

For the average length of hospital stay times, from January to August 2017, 2018 and 2019, averages of 13.08 days of hospitalization for visceral leishmaniasis, 7.22 for leptospirosis, 4.28 for malaria and 3.18 for dengue were calculated. The averages of these times, calculated for the first eight months of 2020, were 7.96 for leptospirosis, 4.69 for malaria and 3.24 for dengue and represent increases of 10.33%, 9.54% and 1.83%, however, visceral leishmaniasis represented a decrease of 10.59% (table 1).

In total, from January to August 2017 until 2020, there were 129.347 hospitalizations and 1560 deaths from visceral leishmaniasis, leptospirosis, malaria and dengue in Brazil. The total spending on these hospitalizations in 2020 was R$ 15.140.794,34, which represents an increase of R$ 1.979.314;68 (15.03%) for the Unified Health System in comparison to the average total spend of R$ 13.161.479.66 in the three years prior to the pandemic.

INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

ENGLISH VERSION of Article

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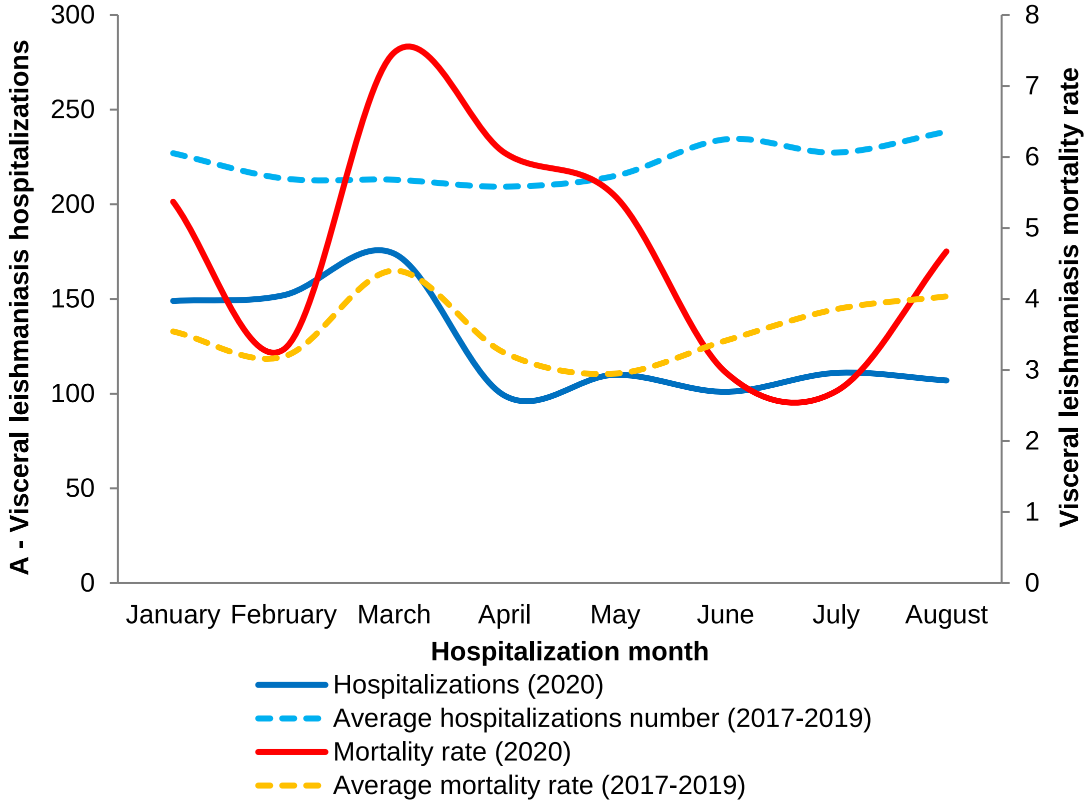

INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

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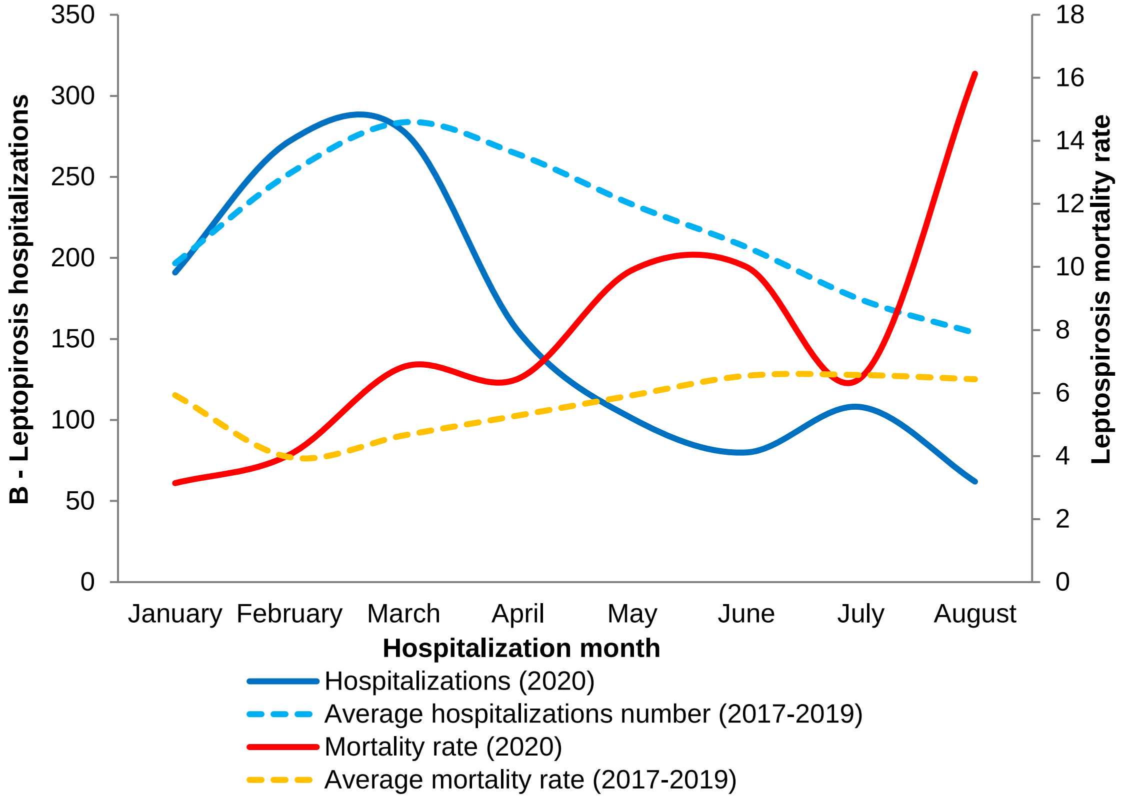

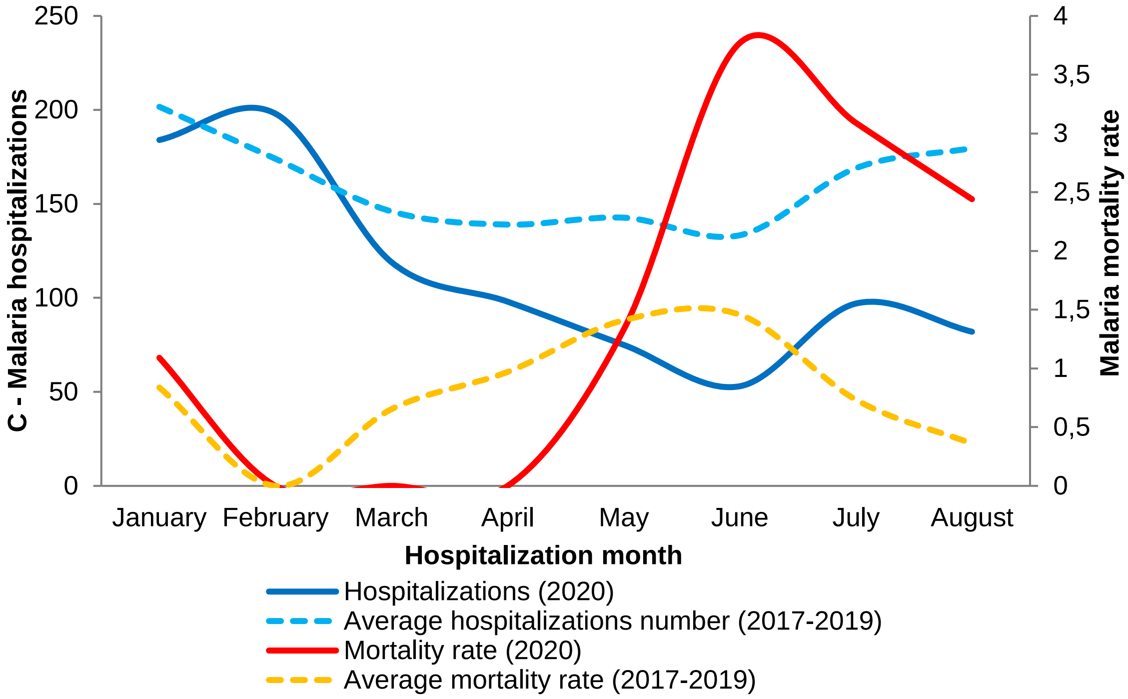

INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

ENGLISH VERSION of Article

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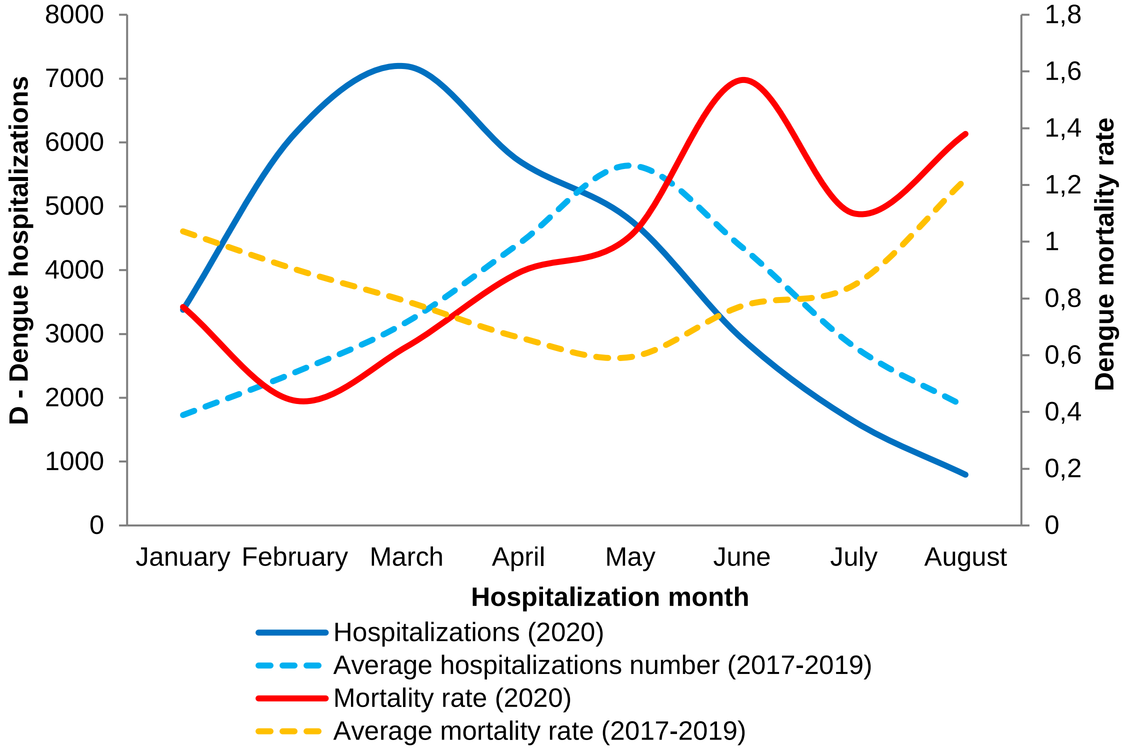

Figure 1: A - Average hospitalizations number and average mortality rate due to visceral leishmaniasis between the years 2017 to 2019 and the number of hospitalizations and mortality rate due to visceral leishmaniasis in 2020, Brazil. B - Average number of hospitalizations and mortality rate due to leptospirosis between the years 2017 to 2019 and number of hospitalizations and mortality rate due leptospirosis in 2020, Brazil. C - Average number of hospitalizations and the mortality rate due malaria between the years 2017 to 2019 and number of hospitalizations and mortality rate due malaria in 2020, Brazil. D - Average number of hospitalizations and mortality rate due dengue between the years 2017 to 2019 and number of hospitalizations and mortality rate due dengue in 2020, Brazil.

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INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

ENGLISH VERSION of Article

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Table 1: Number of hospitalizations, hospitalization values, mortality rates and average length of stay in hospitalizations from January to August from the years 2017 to 2020. Averages, variations in numbers and percentages of the number of hospitalizations, values of hospitalizations, rates of mortality and average length of stay in hospitalizations between the years 2017 to 2019 and the year 2020.

Diseases	Visceral leishmaniasis				Leptospirosis				Malaria				Dengue			
	Hospitalization number															
Year/Month	2017	2018	2019	2020	2017	2018	2019	2020	2017	2018	2019	2020	2017	2018	2019	2020
January	222	226	233	149	178	180	232	191	163	239	203	184	2203	1111	1875	3378
February	205	250	186	152	240	236	280	272	154	215	153	198	2507	1493	3191	6136
March	214	240	185	174	277	256	318	278	122	171	145	119	2750	1899	4907	7192
April	183	253	192	99	180	294	318	155	117	160	140	98	2489	2490	8243	5720
May	238	227	180	110	166	242	291	101	129	155	144	75	2519	2656	11736	4786
June	263	263	177	101	202	188	230	80	124	128	148	53	2048	2004	9028	2929
July	255	246	181	111	186	121	216	108	162	139	206	97	1280	1441	5700	1634
August	252	268	195	107	139	132	190	62	193	179	167	82	971	1035	3563	795
Total	1832	1973	1529	1003	1568	1649	2075	1247	1164	1386	1306	906	16767	14129	48243	32570
Average		222,25		125,38		220,5		155,88		160,67		113,25		3297,46		4071,25
Variation 2017-2019 and 2020 (number / percentage)		96,88		43,59%		64,63		29,31%		47,42		29,51%		-773,79		-23,47%
	Spent Total Value (R$)															
January	122.687,69	98.308,94	133.112,52	104887,19	121.065,51	157.016,29	204.882,02	216.950,85	44.339,72	82.640,13	94.404,34	59.600,82	709.019,54	389.531,82	700.854,83	1.233.147,25
February	124.903,57	176.291,11	88.808,57	94980,54	243.363,48	292.880,75	217.999,95	315.995,65	39.020,87	65.875,73	42.243,99	61.046,23	816.775,31	498.360,54	1.171.571,84	2.150.785,72
March	124.878,33	97.431,51	95.906,82	94346,34	357.942,83	316.446,30	384.772,61	445.329,68	35.941,25	44.760,26	52.307,67	43.837,44	939.882,33	646.809,78	1.892.156,74	2.644.652,21

INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

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April	136.989,26	157.291,38	100.316,77	58335,56	265.764,93	323.624,89	321.779,51	220.410,83	27.812,39	52.382,31	43.876,19	31.989,59	844.634,09	845.874,16	3.107.489,80	2.160.491,75
May	119.044,80	145.869,02	109.272,21	68856,5	182.820,36	358.105,82	438.245,67	163.774,70	44.072,07	46.536,80	57.599,04	37.120,84	828.622,65	941.652,36	4.277.534,08	1.843.512,62
June	176.644,14	154.447,40	79.734,58	83157,17	228.997,83	259.599,42	282.089,68	195.052,28	50.182,34	62.216,77	58.531,25	38.060,10	741.016,31	720.880,02	3.496.275,64	1.209.667,06
July	173.874,99	126.374,72	107.063,38	65919,6	193.157,39	110.978,36	354.817,04	157.082,35	45.750,74	37.573,37	73.127,36	34.702,83	438.185,74	513.419,33	2.230.424,87	650.973,95
August	150.938,91	157.671,75	95.359,90	46655,33	274.694,82	189.550,78	270.122,58	163.835,76	55.300,09	48.719,50	50.232,37	47.507,29	341.605,02	386.101,77	1.346.372,77	398.128,31
Total	1.129.961,69	1.113.685,83	809.574,75	617.138,23	1.867.807,15	2.008.202,61	2.474.709,06	1.878.432,10	342.419,47	440.704,87	472.322,21	353.865,14	5.659.740,99	4.942.629,78	18.222.680,57	12.291.358,87
Average		127.217,59		77.142,28		264.613,28		234.804,01		52.310,27		44.233,14		1.201.043,81		1.536.419,86
Variation 2017-2019 and 2020 (number / percentage)		50075,32		39,36%		29809,27		11,27%		8077,13		15,44%		-335376,05		-27,92%
Mortality rate (deaths / hospitalization)																
January	3,6	5,31	1,72	5,37	6,74	8,89	2,16	3,14	0,61	0,42	1,48	1,09	0,73	1,53	0,85	0,77
February	4,88	2	2,69	3,29	4,17	5,93	1,79	4,04	0	0	0	0	0,72	1,14	0,85	0,44
March	4,67	5,83	2,7	7,47	3,61	4,69	5,66	6,83	0	0,58	1,38	0	0,8	0,84	0,73	0,63
April	3,83	2,77	3,13	6,06	5,56	3,06	7,23	6,45	0,85	0,63	1,43	0	0,76	0,48	0,75	0,89
May	3,78	3,96	1,11	5,45	3,61	6,61	7,56	9,9	1,55	1,29	1,39	1,33	0,67	0,45	0,66	1,02
June	5,32	2,66	2,26	2,97	8,42	4,26	6,96	10	0	2,34	2,03	3,77	0,88	0,6	0,84	1,57
July	3,53	5,28	2,76	2,7	6,45	9,09	4,17	6,48	1,23	0	0,97	3,09	0,78	0,83	0,93	1,1
August	5,16	3,36	3,59	4,67	6,47	7,58	5,26	16,13	0,52	0,56	0	2,44	1,03	1,45	1,18	1,38
Average	4,35	3,9	2,5	4,75	5,63	6,26	5,1	7,87	0,6	0,73	1,09	1,47	0,8	0,92	0,85	0,98
Average		3,58		4,75		5,66		7,87		0,8		1,47		0,85		0,98
Variation 2017-2019 and 2020 (number / percentage)		1,17		32,64%		2,21		38,98%		0,66		82,55%		0,12		14,26%
Average length of hospitalization stay time																
January	14,3	13,1	13,4	12,5	5,7	5,8	6,7	6,3	3,8	4,1	5	4,5	3	3,2	3	3,1
February	13,9	14,3	13,2	11	6,7	6,6	5,8	6,5	3,9	4,5	4,2	4,1	2,9	3,2	3	3
March	13,3	12,1	12,8	12,6	7,1	7,2	6,5	7,6	4,1	4,4	4,8	4,7	2,9	3	3,1	3,1

INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

ENGLISH VERSION of Article

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April	14,1	13,5	13,1	11,4	7,7	6,9	6,3	7,4	3,7	4,8	4,4	4,2	3	3,1	3,1	3,1
May	12,4	13,1	13	11,7	7,4	8,5	8,2	8,1	4,1	4,3	4,6	4,6	3,1	3,3	3,1	3,1
June	12,8	13,6	12,1	12	6,6	8,4	7,6	9,5	3,6	4,5	4,3	5,5	3,1	3,4	3,3	3,3
July	13,1	13	12,3	11,1	7,1	7,3	8,5	9,1	4,2	4,6	4,6	4,8	3,2	3,6	3,4	3,4
August	11,8	12,3	12,1	10,9	8,7	7,3	8,6	9,2	3,5	3,9	4,8	5,1	3,4	3,5	3,4	3,8
Average		13,03		11,65		7,22		7,96		4,28		4,69		3,18		3,24
Variation 2017-2019 and 2020 (number / percentage)		1,38		10,59%		-0,75		-10,33%		-0,41		-9,54%		-0,058		-1,83%

INTERAMERICAN JOURNAL OF MEDICINE AND HEALTH

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DISCUSSION

Due to the prioritization of COVID-19, it can be said that there are fewer clinical suspicions that may be related to dengue, visceral leishmaniasis, leptospirosis and malaria in Brazil, similarly to other countries, such as Colombia, in which a reduction was evidenced nationally in the number of dengue fever cases reported in 2020 compared to previous years and the number of notifications epidemiological week [17]. In addition, there was a reduction in notifications of dengue cases in São Paulo, after the tenth epidemiological week in March 2020 [18].

On the other hand, in Colombia, comparatively high numbers of dengue and COVID-19 notifications were noted in Valle del Cauca and a higher number of dengue notifications compared to COVID-19 in Huila and Tolima [17]. In countries such as Bolivia, Honduras, Mexico and Paraguay, increases in dengue cases have been noted in the first four weeks of 2020 compared to those same weeks in 2019 [19]. In Zimbabwe there have been increases in malaria deaths and a 44.7% increase in cases of malaria in 2020 [20]. Considering the forecast of increases in cases of several diseases [7], including dengue in 2020 in Brazil [5], it may suggest that the reduction of notifications resulted in decreases of hospitalizations for visceral leishmaniasis, leptospirosis, and malaria in 2020 compared to the average of admissions of the three previous years (Figures 1A, 1B and 1C and Table 1), with the exception of dengue, in which hospitalizations decreased during the pandemic (figure 1D and table 1).

Reductions in hospitalizations and increases in mortality rates may result from difficulties in clinically differentiating COVID-19 from other diseases [13,14], since, for example, some symptoms are shared with malaria [20] and can be confused with the initial symptoms of dengue [5,21]. Incorrectly diagnosing COVID-19 as dengue and failing to isolate patients can lead to disease outbreaks in healthcare settings, as well as not recognizing dengue as a diagnosis and failing to hydrate patients results in preventable deaths [21]. In Germany, a patient with flu-like symptoms, was confirmed with leptospirosis by the late

https://doi.org/10.31005/iajmh.v4i.173

differential diagnosis, tested negative for SARS-CoV-2 five days after performing a throat swab [22].

There are also situations in which undifferentiated febrile illnesses and COVID-19 affect, at the same time, the same patient. A case of infection by COVID-19 and visceral leishmaniasis was observed [23], in which the different pathogens increased the immunological vulnerability against antiviral responses, causing a worsening of the clinical picture that led the patient to death [24]. Co-infection with dengue and COVID-19 was confirmed in a young man with persistent fever, dry cough, scarlatiniform-like rash, headache and retro-orbital eye pain [25], and another adult patient who had a flu-like syndrome during his trips to France and Switzerland [26]. The possibility of co-infection of dengue and COVID-19 may lead to a delayed diagnosis leading to greater spread of SARS-CoV-2 and clinical progression to death in endemic areas [27]. Finally, a co-infection was noted in Qatar, in which an adult man manifested fever, myalgia, vomiting and abdominal pain with absence of cough and shortness of breath and tested positive for *Plasmodium vivax* malaria and for SARS-CoV-2 by PCR nasopharyngeal swab [28]. Therefore, since many of these diseases can be ignored due to the pandemic, it is important that physicians consider the possibilities of occurrence of simultaneous secondary infection with SARS-CoV-2 and co-infection [28].

Then, due to the possibility of co-infection increases the risk of only one of the diseases that affected the patient to be reported, if not detected in the diagnosis, which may also explain the reduction in hospitalizations. Consequence for the lack of treatment of the disease not recognized may result in death implying an increase in the mortality rate. In addition, patients who have symptoms similar to respiratory syndrome related to SARS-CoV-2 or similar diseases, may hesitate to seek testing and treatment in health services or may not seek medical attention for fear of performing exam associated with the diagnosis of COVID-19 [29].

The social distancing helps reduce the transmission of disease from

https://doi.org/10.31005/iajmh.v4i.173

respiratory droplets, because it helps to reduce the interactions between people in a community in which there may be infected individuals [30]. In addition, the reduction in urban mobility resulting from social isolation may be related to the decrease in dengue cases in São Paulo, because the transmission of this disease depends on the mobility of infected people to more distant areas, since mosquito vectors only travel short distances during life [18].

However, measures that encourage social distancing, can influence the reduction of interventions required to address transmissions by undifferentiated febrile illness. In Singapore the implementation of social distancing is associated with increased cases of dengue [31], and in French Guiana, dengue transmission grew during the rainy season at the same time as the implantation of social distance, because vector control measures were interrupted, such as home interventions to eliminate larvae, inspect breeding grounds and spray homes and the maintenance services for public spaces, gardens and the collection of potential water containers were reduced [32]. Many of the essential interventions to control dengue are at odds with the COVID-19 prevention and blocking guidelines, because they require or imply proximity between vector control teams and the resident population [33].

Sherrad-Smith et al., [34], based on the simulation of a scenario of the impacts on malaria cases in Sub-Saharan Africa caused by the implementation of measures to mitigate COVID-19, estimated a significant increase in cases and deaths from malaria if the distribution of long-lasting insecticidal nets (LLINs) is canceled in 2020 and the reduction in half of the treatment of clinical cases, if the seasonal malaria chemoprevention and the indoor residual spraying of insecticide are stopped. Already modeled results indicated that, during the peak of malaria transmission in Mali, a portion of those infected with SARS-CoV-2, who are over fifteen years old, have malarial parasites, so they cannot be isolated if they have fever caused by this disease [20]. Already modeled results indicated that, during the peak of malaria transmission in Mali, a portion of those infected with SARS-CoV-2, who are over fifteen years old, have malarial parasites, so

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they cannot be isolated if they have fever caused by this disease [20]. In addition, it is noteworthy that indicators like sewage in the surroundings, waste in environment and poverty ratios increase the chance of municipalities exhibit more critical for infectious and parasitic diseases [35], thus, as the absence of running water, wooden housing and unpaved street, it favors the establishment of leptospirosis [36].

In comparison to the increase in deaths during the pandemic, estimated by projections [20,34], the results of the present study showed increases in mortality rates, not only for hospitalizations for malaria, but also for dengue, visceral leishmaniasis and leptospirosis in Brazil. These increases suggest that the existence of susceptibility indicators [35,36] and the decrease in measures to control the reservoirs and vectors of these diseases can lead to increased transmission, leading to more severe hospitalizations that result in deaths of the patients.

In relation to the preparation of health professionals, it is proposed the management of the place, protection and training, with a focus on helping to relieve the fear of contagion and proposes measures for the prevention and control of infection at the hospital and peripheral level, such as the separation of hospital waste and the use of personal protective equipment [37]. Clinical care protocols and guidelines should be established to address patients with co-infection [27], diagnosis for dengue and COVID-19 should be allowed without delay, beds for severe dengue should be planned, and patients should remain under mosquito nets [32]. Health promotion should encourage communities to seek out potential vector breeding sites and protect themselves from mosquito bites [32].

Secondary data were limiting for the development of this study, because not all hospitalizations and deaths that occur in the Brazilian reality are included in the SIH-SUS, due to underreporting or late notification, the latter being noted by the increase in hospitalizations and deaths, when the information was updated monthly, therefore, the data analyzed in this study will probably be changed in

https://doi.org/10.31005/iajmh.v4i.173

the coming months at the collection source. The results could be better discussed, if there were information about the dates of care, death, initial and differential diagnoses, and about the diseases recorded in these diagnoses of hospitalizations, in order to obtain more reliable data to confirm delays, co-infections and diagnostic confusions.

Finally, this article fulfills its objective of presenting the reductions in hospitalizations and the increase in deaths from dengue, visceral leishmaniasis, leptospirosis and malaria in the months from January to August 2020, arguing that the causes of these changes may be reductions in notifications or delays in notifications, which can be caused by difficulties in differentiating between these undifferentiated febrile diseases and COVID-19, as they have a similar clinical picture, and in the identification of co-infections.

In addition, it is inferred that reductions in the control of reservoirs and vectors may increase transmission rates, which may imply an increase in the number of deaths. Therefore, this study contributes to avoid neglect of endemic undifferentiated febrile illnesses that affect the population of Brazil and other countries and to encourage measures to reduce the impacts of such diseases.

Authors' Contribution: NLCD, AAFM and SVO participated in all stages of the article, approved the final version of the manuscript and assumed public responsibility for its content.

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