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Multiple causations of hospitalizations due to mycoses in a Brazilian region: from anthropogenic to climate factors

Múltiplas causas de hospitalizações por micoses em uma região brasileira: dos fatores antrópicos aos climáticos

Múltiples causas de internaciones por micosis en una región brasileña: de factores antropogénicos a climáticos

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Abstract

Fungal infections are a public health problem. Mycoses are neglected, some are related to regions with low human development and under the influence of climatic conditions. The study aimed to analyze a series of hospitalizations due to mycoses (HM) that occurred in Minas Gerais, Brazil, from 1998 to 2018, as outcomes of anthropic and climate variability. We performed predictive analyses using Spearman's rank correlation and logistic regression modeling to determine the correlation between HM and social, demographic, economic, epidemiological, and climate factors in Minas Gerais, Brazil. Data were obtained from national databases from 1998 to 2018. We found significant correlations between HM and population size, demographic density, health facilities (negative correlations), rural population, and coffee area harvested or cultivated (positive correlations), indicating that living in small urban centers is a strong predictor. We find weak but statistically significant associations between HM and meteorological conditions. Interestingly, the outbreak of hospitalizations matched La Niña events in the municipality with the highest frequency of hospitalization due to mycoses in Minas Gerais. Complex interactions among social, demographic,

economic, and climatic factors drive mycoses dynamics. This work provides evidence that climatic and human activities influences hospitalizations due to mycoses in a Brazilian region.
Keywords: Environment and public health; Mycoses; Socioeconomic factors; Climate.

Resumo
As infecções fúngicas são um problema de saúde pública. Algumas micoses são consideradas como doenças negligenciadas, onde a prevalência pode ser influenciada pelas condições em que as pessoas vivem e trabalham. No entanto, é relatado que algumas infecções fúngicas acontecem com maior frequência em determinadas condições climáticas. Assim, o objetivo desse estudo foi analisar se as hospitalizações causadas por micoses (HM) ocorridas em Minas Gerais, Brasil, no período de 1998 a 2018, sofreram interferência antrópica e/ou climática. Os dados foram obtidos a partir bancos de dados públicos nacionais. Para tal, foram realizadas análises estatísticas usando correlação de *Spearman* e regressão logística para determinar a correlação entre HM e fatores sociais, demográficos, econômicos, epidemiológicos e climáticos. Foram encontradas correlações significativas entre a HM e o tamanho da população da cidade, a densidade demográfica, unidades de saúde presentes no município (correlações negativas), tamanho da população rural e a área de café colhida ou cultivada (correlações positivas), indicando que viver em pequenas centros urbanos é um forte preditor para HM. Foram encontradas correlações fracas, mas estatisticamente significativas entre HM e condições meteorológicas. Importante ressaltar que o surto de HM no município com maior frequência de internação por micoses em Minas Gerais coincidiu com os eventos de La Niña. Este trabalho fornece evidências de que as atividades climáticas e humanas influenciam nas HM em uma região brasileira.
Palavras-chave: Saúde única; Micoses; Fatores socioeconômicos; Clima.

Resumen
Las infecciones fúngicas son un problema de salud pública. Algunas micosis son consideradas enfermedades desatendidas, cuya prevalencia puede verse influida por las condiciones en las que vive y trabaja la gente. Sin embargo, se sabe que algunas infecciones por hongos ocurren con mayor frecuencia en ciertas condiciones climáticas. Así, el objetivo de este estudio fue analizar si las hospitalizaciones por micosis (HM) ocurridas en el estado de Minas Gerais, Brasil, entre 1998 y 2018, sufrieron interferencias antrópicas y/o climáticas. Los datos fueron obtenidos de bases de datos públicas nacionales. Para esto, se realizaron análisis estadísticos mediante correlación de Spearman y regresión logística para determinar la correlación entre HN=M y factores sociales, demográficos, económicos, epidemiológicos y climáticos. Se encontraron correlaciones significativas entre HM y el tamaño de la población de la ciudad, la densidad demográfica, los establecimientos de salud presentes en la ciudad (correlaciones negativas), el tamaño de la población rural y el área de café cosechado o cultivado (correlaciones positivas), indicando que vivir en pequeños centros urbanos es un fuerte predictor de HM. Se encontraron correlaciones débiles pero estadísticamente significativas entre HM y las condiciones meteorológicas. Es importante destacar que el brote de HM en el municipio con mayor frecuencia de hospitalización por micosis en Minas Gerais coincidió con los eventos de La Niña. Este trabajo proporciona evidencia de que el clima y las actividades humanas influyen en HM en una región brasileña.
Palabras clave: Medio ambiente y salud pública; Micosis; Factores socioeconómicos; Clima.

1. Introduction

Mycoses threaten the life of approximately one billion people around the world (Bongomin et al., 2017). More than 150 million may be suffering from serious fungal infections (Bongomin et al., 2017). The Global Action Fund for Fungal Infections (GAFFI) estimates that 150 people die every hour due to mycoses, and 80% of these deaths could be avoidable. Public health authorities have failed to provide appropriate diagnoses and treatment for all (Bongomin et al., 2017).

World Health Organization (WHO) recognizes mycetoma, chromoblastomycosis, and some deep mycoses as Tropical Neglected Diseases (TND). Other mycoses (e.g., paracoccidioidomycosis) fulfill the criteria for a TND, but they are ignored by the researchers, press, and funding bodies ("Stop neglecting fungi," 2017). Although poverty drives the dynamic of several neglected mycoses, fungal pathogens are influenced by environmental factors (Polgreen & Polgreen, 2018). Climatic elements, such as rainfall, temperature, and humidity, have documented effects on fungi (Barrozo et al., 2010; Panackal et al., 2010; Silva et al., 2019) The air minimum temperature was associated with a high frequency of hospitalizations due to mycoses (HM) in the 10 Brazilian capitals, a period that coincided with La Niña events (Silva et al., 2019).

Brazil is a developing country that faces social inequality, megadiverse dimensions, and infectious diseases. In this way, poor living conditions and environmental factors can enhance the incidence of mycoses (Bueno et al., 2016). Minas Gerais corresponds a 7% of the total area of Brazil (similar to Spain) and has three predominant biomes: Savanna, Atlantic

Forest, and Semi-arid woodland (Scolforo et al., 2015). Minas Gerais is also marked by severe socioeconomic distortions. As a result, Human Development Index's (HDI) municipalities range from 0.529 (medium HDI) to 0.813 (very high HDI). (IBGE, 2010; United Nations Development Programme, 2020). Minas Gerais is afflicted by mycoses, with high mortality index for paracoccidioidomycosis, as well as Brazil (Prado et al., 2009).

In this way, we asked ourselves: do anthropogenic and/or climatic elements influence the incidence of mycoses in Minas? This study aimed to answer these questions through the evaluation of the association between social, demographic, economic, and climate factors in Minas Gerais during 1998 – 2018.

2. Methodology

This study is a descriptive epidemiological work, as described previously (Silva et al., 2019; da Silva et al., 2020). It is based on secondary data from 1998 to 2018, covering a historical series of 21 years

Study area

The State of Minas Gerais (Figure 1) has 853 municipalities located in the southeast region of Brazil. This state covers an area of 586,521.1 km2 (IBGE, 2010). This state has a population of 21,040,662 inhabitants and a population density of 33.41 inhabitants/km2. Approximately 79.4% of the population lives in urban areas. The HDI is 0.731 (IBGE, 2010).

Minas Gerais presents a pronounced climate variability, with rainfall and temperature gradients from north to south. The altitudes vary from 76 to 2,891.9 m above sea level. Predominant biomes are Savanna, Atlantic Forest, and Semi-arid woodland, representing 57%, 41%, and 2%, respectively (Scolforo et al., 2015).

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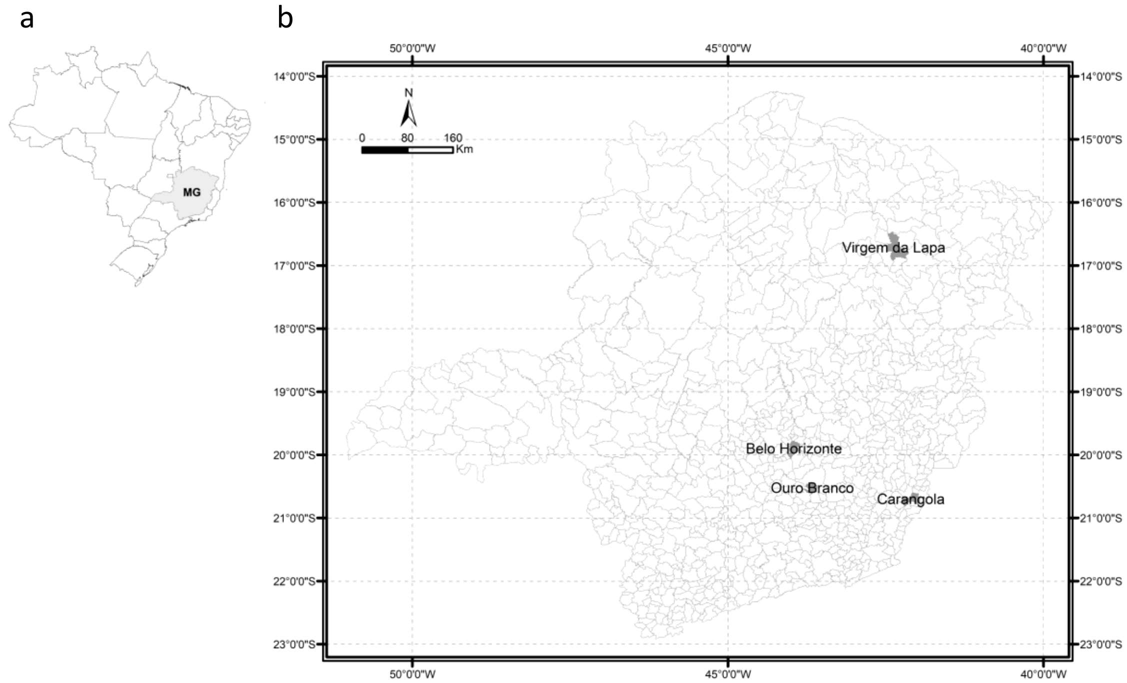
Figure 1 - Location of the study area. The state of Minas Gerais, Brazil.



Minas Gerais state (a, light grey) and the Belo Horizonte (capital of the state), Carangola, Ouro Branco and Virgem da Lapa municipalities (b, dark grey) are displayed in the maps. Carangola, Ouro Branco and Virgem da Lapa were the municipalities with a higher frequency of HM (more than 1 / 10,000 inhab). MG is the acronym of Minas Gerais. Source: IBGE's cartographic bases and ESRI ArcGIS Desktop version 10.5.F. Source: Authors.

Collection of Health, Demographic, Socioeconomic, and Climate Data

This research used secondary data available in the Department of Informatics at SUS (DATASUS) public domain. DATASUS is the official database of government health record from the Ministry of Health in Brazil. This database used the rules and the tabulation list for morbidity from the International Classification of Diseases (ICD) 10th revision codes to classify the cause of hospitalization. The list for morbidity uses code 042 to refer to all cases of hospitalizations due to mycoses (the database does not inform the etiologic agent of the mycoses). The instruction manual ICD-10 explains that the condition to be used for single-condition disease investigation is the main assisted illness during the episode of health care.

The hospitalization due to mycoses (HM) gathered monthly by DATASUS were tabulated from 853 municipalities according to the place of residence. We selected fifty municipalities that together have approximately 50% of total cases of HM in Minas Gerais (criteria of inclusion) for subsequent analyses (Figure 2).

To calculate the average annual relative frequency of HM, we used the following formula, as described previously (da Silva et al., 2020):

Frequency of HM/10,000 inhabitants = average annual number of HM / population * 10,000

where HM is the number of hospitalizations for mycoses accounted for between 1998 and 2018 and population is the population of the municipality.

The municipal demographic and socioeconomic variables obtained from Instituto Brasileiro de Geografia e Estatística (IBGE) database were population (2010), demographic density (inhabitants/Km²), HDI (2010), number of health facilities (2009), % of adequate sanitary sewage (2010), percentage of the rural population (2010), coffee and sugarcane area harvested or cultivated in hectares (HA) from 1998 to 2018. This cutoff points on the HDI for grouping municipalities were: low > 0.550, medium 0.550 – 0.699, high 0.700 – 0.799, and very high > 0.800 (United Nations Development Programme, 2020). The latest Brazilian census was in 2010. It is important to note that data collected from IBGE are the most recent available.

Climate data were obtained from 26 conventional meteorological stations operated by the National Institute of Meteorology (INMET). The following criteria were used to select a station: 1) conventional stations closest to each municipality in a straight line, and 2) have at least ten years of data between 1998 and 2018. The monthly meteorological data used in this study were: total precipitation (mm), wind speed (m/s), maximum temperature (•C), and minimum temperature (•C).

We analyzed the effect of El Niño/Southern Oscillation (ENSO), a climate oscillation pattern that is the primary predictor for global climate disruptions, as impacting the hospitalizations due to mycoses (Wolter & Timlin, 2011). We use the Multivariate ENSO Index (MEI) to proceed with the ENSO dynamics because it integrates the largest number of data and combines both oceanic and atmospheric variables. The highest MEI values represent the El Niño (warm ENSO phase), while the lowest values represent the La Niña (cold ENSO phase). (Wolter & Timlin, 2011). This time series was obtained from National Oceanic and Atmospheric Administration (NOAA). MEI was provided as a bimonthly index (e.g. Dec–Jan, Jan–Feb, …, Nov–Dec), which we summarized in months (e.g. Dec–Jan = Jan, Jan–Feb = Feb, …, Nov-Dec = Dec) as the index hospitalizations due to mycoses (obtained monthly) for posterior analyses (de Beurs et al., 2018).

Since only secondary data available on public domain virtual were used, ethical committee approval was not required, as stipulated in resolutions 466/2012 and 510/2016 of the Brazilian National Health Council and letter Nº 004 - 2019 / CEP / UFJF.

Data Analysis

We used GraphPad Prism Software 9.0 (San Diego, California, USA).

Analyses of climatic, demographic, socioeconomic, and health data were performed by Spearman's rank correlations. A P value of < 0.05 was considered significant. Spearman coefficients were interpreted as describing the strength of correlation: negligible (0.00 – ± 0.10), weak (± 0.11 - ± 0.39), moderate (± 0.40 - ± 0.69), strong (± 0.70 - ± 0.89), and very strong (± 0.90 - ± 1) (Akoglu, 2018).

To identify if climate oscillation measured by MEI could change the risk of HM in municipalities with a frequency higher than 1 / 10,000 inhabitants (Ouro Branco, Virgem da Lapa, and Carangola), we used logistic regression analyses. Logistic regression models are largely used in medical journals to study the effects of predictor variables (in this case, MEI) on categorical binary (Nick & Campbell, 2007). In this way, we classified the 252 months (total months between 1998 and 2018) into two measures of outcomes: (1) positive or negative MEI values (binary) and (2) presence or absence of HM records (binary). Then P values, OR, and 95%CI were calculated. We considered positive values related to the warm ENSO phase and negative values related to the cold phase.

By visually analyzing the MH data for these three cities, we observed that Ouro Branco had an outbreak between 2011 and 2014. In this way, we analyzed the data of climatic variables and HM from 2011 to 2014 by Spearman's rank correlations.

3. Results

Rural environment impacts on hospitalization due to mycoses

From 1998 to 2018, a total of 8,148 HM was recorded in Minas Gerais. Of the 853 municipalities in the state, 50 accounted for approximately 50% (4,464) of the cumulative total number of HM (Figure 2). The socio-economic data of these

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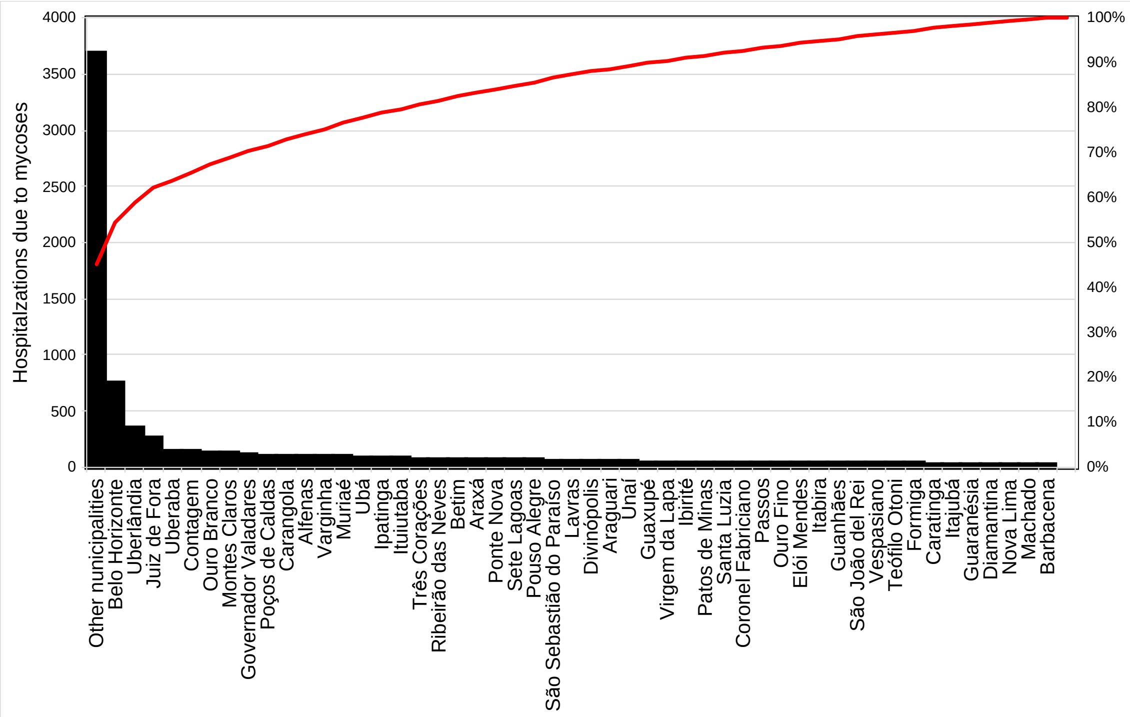
50 municipalities and Spearman's correlation analysis are shown in Table 1.

Figure 2 - Cumulative percentage of hospitalization due to mycoses by Minas Gerais municipalities between 2008 and 2018. The fifty municipalities included in this study corresponds to 54% of total records.



Source: Authors.

Table 1 – Sanitary, demographic and socioeconomic data of the municipalities with the highest incidence of hospitalizations for mycoses (HM) in the state of Minas Gerais, Brazil. The association between HM and variables is demonstrated through Sperman's rank correlation.

Municipalities	Frequency HM (10,000 inhab)	Population (2010)	DD (Inhab./km2) (2010)	HDI (2010)	HF/SUS (2009)	% of Sanitary (2010)	Rural population (%) (2010)	Coffee area (HA) (1998-2018)
Alfenas	0.65	73774	86.75	0.761	33	94.80	6.23	243333
Araguari	0.24	109801	40.23	0.773	48	84.50	6.57	251719
Araxá	0.34	93672	80.45	0.772	24	96.90	1.48	52290
Barbacena	0.11	126284	166.34	0.769	57	87.30	0.34	5
Belo Horizonte	0.15	2375151	7167.02	0.81	328	96.20	0.00	0
Betim	0.09	378089	1102.80	0.749	73	86.00	0.73	36
Carangola	1.53	32296	91.39	0.695	24	70.10	19.31	89259
Caratinga	0.20	85239	67.72	0.706	50	71.40	17.32	158715
Contagem	0.11	603442	3090.33	0.756	170	92.20	8.49	0
Coronel Fabriciano	0.20	103694	468.67	0.755	31	87.50	1.25	563
Diamantina	0.34	45880	11.79	0.716	33	76.50	12.68	7121
Divinópolis	0.13	213016	300.82	0.764	47	90.10	2.58	3025
Elói Mendes	0.77	25220	50.49	0.685	10	87.60	19.21	198830
Formiga	0.26	65128	43.36	0.755	36	90.00	8.66	69434
Governador Valadares	0.21	263689	112.58	0.727	127	92.80	3.94	20
Guanhães	0.62	31262	29.08	0.686	22	72.80	18.68	1231
Guaranésia	0.84	18714	63.47	0.701	10	96.60	10.04	85474
Guaxupé	0.48	49430	172.59	0.751	15	94.00	5.97	119756
Ibirité	0.14	158954	2190.26	0.704	28	83.60	0.23	4
Ipatinga	0.17	239468	1452.34	0.771	57	97.70	4.83	566
Itabira	0.18	109783	87.57	0.756	44	92.00	6.80	717
Itajubá	0.18	90658	307.49	0.787	37	90.50	8.71	983
Ituiutaba	0.40	97171	37.40	0.739	53	94.30	4.16	93
Juiz de Fora	0.25	516247	359.59	0.778	165	94.10	1.14	4310
Lavras	0.32	92200	163.26	0.782	32	94.60	4.71	82540
Machado	0.37	38688	66.03	0.715	18	81.80	17.11	306473
Montes Claros	0.17	361915	101.41	0.77	116	93.40	1.04	655
Muriaé	0.48	100765	119.72	0.734	66	88.90	7.48	34124
Nova Lima	0.19	80998	188.78	0.813	33	94.00	2.18	2
Ouro Branco	1.82	35268	136.31	0.764	18	90.50	10.38	568
Ouro Fino	0.63	31568	59.15	0.722	18	74.50	24.72	132485
Passos	0.19	106290	79.44	0.756	47	96.70	5.13	59608
Patos de Minas	0.16	138710	43.49	0.765	50	91.60	7.92	118812
Poços de Caldas	0.33	152435	278.54	0.779	82	98.00	2.44	96425
Ponte Nova	0.56	57390	121.94	0.717	36	85.60	10.81	25162
Pouso Alegre	0.24	130615	240.51	0.774	45	92.00	8.44	2100
Ribeirão das Neves	0.12	296317	1917.90	0.684	76	74.30	0.73	100
Santa Luzia	0.11	202942	862.38	0.715	45	84.00	0.28	16
São João del Rei	0.23	84469	57.68	0.758	39	85.80	5.46	3861
São Sebastião do Paraíso	0.48	64980	79.74	0.722	33	97.40	7.74	242270
Sete Lagoas	0.15	214152	398.32	0.76	72	93.90	2.43	11
Teófilo Otoni	0.13	134745	41.56	0.701	49	77.10	18.31	6409
Três Corações	0.49	72765	87.88	0.744	32	91.40	9.54	186980
Ubá	0.43	101519	249.16	0.724	50	87.80	3.82	1354
Uberaba	0.23	295988	65.43	0.772	71	97.20	2.23	16110
Uberlândia	0.28	604013	146.78	0.789	108	98.20	2.77	9994
Unaí	0.31	77565	9.18	0.736	19	79.00	19.64	48403
Varginha	0.39	123081	311.29	0.778	47	97.60	17.06	148390
Vespasiano	0.17	104527	1468.49	0.688	24	91.00	0.00	0
Virgem da Lapa	1.68	13619	15.67	0.61	10	40.10	49.78	47
Spearman R value		**-0.778**	**-0.504**	**-0.191**	**-0.597**	**-0.010**	**0.612**	**0.577**
P value		**< 0.001**	**< 0.001**	**0.184**	**< 0.001**	**0.943**	**< 0.001**	**< 0.001**

Abbreviations: HM – hospitalizations due to mycoses; DD - demographic density (inhabitants/km^2); HDI - human development index.
Source: Authors.

There was no significant (P < 0.05) correlation between the relative frequency of HM and HDI or sanitary sewage (Table 1). Ninety percent (45 of 50) of the selected municipalities in this study have high or very high HDI (< 0.700) (Table 1). However, two of five municipalities with medium HDI (0.550 – 0.699) have a frequency of HM higher than 1 case / 10,000 inhabitant. Just as important of this, only three municipalities reached this high frequency of HM: Ouro Branco (1.86 / 10,000 inhab – HDI 0.764), Virgem da Lapa (1.68 / 10,000 inhab – HDI 0.610), and Carangola (1.53 / 10,000 inhab – HDI 0.695) (Table 1).

On the other hand, we found strong correlation between HM and population size (P < 0.001, r = - 0.778), and moderate correlations between HM and demographic density (P < 0.001, r = - 0.504), health establishments (P < 0.05, r = - 0.597), rural population (P < 0.001, r = - 0.612), and coffee area harvested or cultivated (P < 0.001, r = - 0.577) (Table 1).

Climatic factors could contribute to rise in HM

The results of significant Spearman's rank correlation analysis (P < .05) between climate variables (total precipitation, wind speed, maximum temperature, and minimum temperature) and HM are showed in Table 2. They were weak correlations because no one R value exceeded ± 0.39. However, HM data from 22% (11 of 50) of the municipalities have a positive association with wind speed, and only 4% (2 of 50) have a negative correlation.

Table 2 – Significant Spearman's rank correlations between hospitalizations due to mycoses and climatic variables in the state of Minas Gerais, Brazil, from 1998 to 2018.

Climatic variables	Significative Sperman Correlation	
	Mucipalities - Positive	Municipalities - Negative
Total precipitation	Poços de Caldas (r = 0.14) Ubá (r = 0.18)	None
Medium wind speed	Carangola (r = 0.15) Contagem (r = 0.12) Diamantina (r = 0.14) Passos (r = 0.15) Poços de Caldas (r = 0.35) Ponte Nova (r = 0.16) Pouso Alegre (r = 0.25) São Sebastião do Paraíso (r = 0.26) Ubá (r = 0.17) Uberlândia (r = 0.16) Virgem da Lapa (r = 0.25)	Ouro Branco (r = -0.31) Unaí (r = -0.21)
Maximum temperature	None	Guaranésia (r = -0.25) Juiz de Fora (r = -0.14) Unaí (r = -0.13)
Minimum temperature	None	Guaranésia (r = -0.21) Ipatinga (r = -0.16) Nova Lima (r = -0.13)

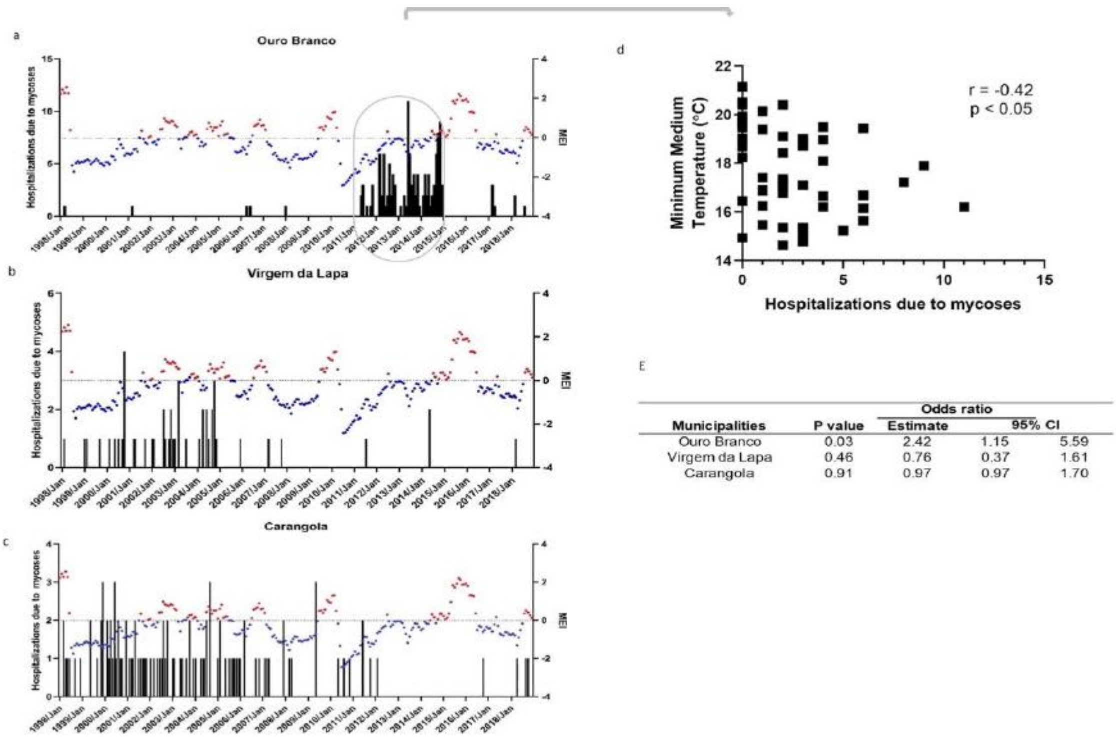
*Statistically significant values (P < 0.05). Source: Authors.

We also found weak negative correlations for maximum (3 of 50 municipalities) and minimum (3 of 50 municipalities) temperature and weak positive correlations for total precipitation (2 of 50 municipalities).

It is our knowledge, ENSO can produce severe effects on regional weather (Wolter & Timlin, 2011). In this way, we ask ourselves if the climate oscillation measured by MEI will impact environmental factors and raise the risk of HM. For these analyses, we chose Ouro Branco (Figure 3a), Virgem da Lapa (Fig. 3b) and, Carangola (Fig. 3c) because they were the municipalities with a higher frequency of HM (more than 1 / 10,000 inhab). MEI was significantly associated with occurrence of HM for Ouro Branco (OR 2.42, 95% CI = 1.15 to 5.59; P < 0.05), but not for Virgem da Lapa (OR 0.76, 95% CI = 0.37 to 1.61; P = 0.46) or Carangola (OR 0.97, 95% CI = 0.56 to 1.70; P = 0.91) (Figure 3e).

Interestingly, we observed an HM outbreak in Ouro Branco from 2011 to 2014, with 89.55% (120 of 134 HM) of the cases during the 21 years studied (Figure 3a). When we analyzed the data of climatic variables and HM from 2011 to 2014, we found a moderately significant correlation between minimum temperature (r = -0.42) and HM (others variables no presented significant correlation) (Figure 3d).

Figure 3 - Effects of El Niño/Southern oscillation on hospitalization due to mycoses (HM).



Municipalities	P value	Odds ratio Estimate	95% CI	
Ouro Branco	0.03	2.42	1.15	5.59
Virgem da Lapa	0.46	0.76	0.37	1.61
Carangola	0.91	0.97	0.97	1.70

The relationships between Multivariate ENSO Index (MEI) predictor variable and monthly HM were analyzed for Ouro Branco (a), Virgem da Lapa (b) and, Carangola (c), since these three municipalities have registered frequency higher than 1 / 10,000 inhabitants of HM. Logistic regression demonstrated a significant association between MEI and HM for Ouro Branco ($P < 0.05$), but not for Carangola and Virgem da Lapa (e). We observed an outbreak of HM in Ouro Branco between 2011 and 2014 (A), and in this period, we found a significant ($P < 0.05$) Spearman's rank correlation between minimum temperature and monthly HM (d). CI – Confidence interval. Blue dot plots – negative MEI values. Red dot plots – positive MEI values. Source: Authors.

4. Discussion

There are an estimated 300 fungal species pathogenic to humans ("Stop neglecting fungi," 2017). Environmental exposure to spores of pathogenic fungi could cause a range of outcomes, ranging from subclinical infection to severe diseases (Nargesi et al., 2021). However, some fungi belong to normal microbiota and can cause diseases in susceptible hosts. It is known that social and environmental factors can influence the incidence of mycoses, like exposure to etiological agents due to poverty, the difficulty of accessing health services, and climatic variations (Costa et al., 2019).

Our results statistically demonstrated a negative correlation between municipalities with a high frequency of HM and the population size, demographic density, and the number of health care establishments. It is known that systemic mycoses are frequently misdiagnosed as bacterial infections (e.g. tuberculosis) (Queiroz-Telles et al., 2017). This situation can result in a lag time between the symptoms and the start of treatment (Queiroz-Telles et al., 2017). Because of this, diagnosis of mycoses requires exams performed by trained health care professionals. In Brazil, diagnostic and therapeutic equipment of medium and high complexity is concentrated in large urban centers (Costa et al., 2019). Although Brazil's health system has to ensure access to health care for Brazilian citizens, the country has to address lingering geographical inequalities (Silva et al., 2017). In this way, Minas Gerais is not different since it has a large territory and its municipalities are located far away from regional poles.

Soil and plants can be the source of some pathogenic fungi, and the infection can occur during agricultural activities. Because of this, people living in rural areas are at risk for mycoses like mycetoma, chromoblastomycosis, sporotrichosis, histoplasmosis, and paracoccidioidomycosis (Queiroz-Telles et al., 2017). Paracoccidioidomycosis is endemic to many parts of Latin America, especially southeastern Brazil (Barrozo et al., 2009; Costa et al., 2019; Silva-Vergara et al., 1998). Interestingly, several endemic regions for paracoccidioidomycosis are located in areas where coffee is grown in Brazil and Colombia (Bittencourt et al., 2005; Calle et al., 2001). *Paracoccidioides brasiliensis* have been previously isolated from soil at a coffee plantation in Minas Gerais (Silva-Vergara et al., 1998). Our results support this evidence since the municipalities with a higher frequency of HM have a moderate positive correlation with the percentage of the rural population and coffee cultivated area.

The variations in the incidence of infectious diseases have been linked to climatic factors in many studies (Waits et al., 2018; Xiao et al., 2013). For systemic mycoses, the scenario is not different. Researchers provide evidence that paracoccidioidomycosis (Barrozo et al., 2010) and aspergillosis (Panackal et al., 2010) responds to climatic factors. But depending on the fungi studied, these associations can be more evidence for some fungi than others. We found weak associations between the frequency of HM and total precipitation, wind speed, maximum temperature, and minimum temperature for some municipalities during 1998-2018. However, caught our attention as 11 of 50 municipalities (22%) included in this study showed a positive correlation between wind speed and HM.

The wind appears to be a climatic variable important to the dispersion of fungal propagules that permits acquisition by a susceptible host (Baumgardner, 2009). It is important to note that we found two municipalities with a negative correlation between HM and wind speed. We suspect that the negative association with HM may be a confounding factor, such as air pollution or the influence of another climactic event that impacts wind speed.

The municipalities with a frequency of HM higher than 1 / 10,000 inhabitants were Ouro Branco, Virgem da Lapa, and Carangola. Interestingly these municipalities differ considerably in several aspects. Geographically, the highway distance of Ouro Branco from Belo Horizonte (capital of the state) is 100 km, while the other municipalities are far away from Belo Horizonte (more than 300 km). Demographically, Virgem da Lapa and, Carangola have four times and twice, respectively, a percentage of rural population compared to Ouro Branco. Finally, Ouro Branco has better social indicators than Virgem da Lapa and Carangola. Considering that a higher incidence of mycoses is usually related to socio-environmental vulnerability, Virgem da Lapa and Carangola showed expected results, but not Ouro Branco. Interestingly, MEI was only significantly associated with the occurrence of HM for Ouro Branco (the probability that an HM will happen during negative MEI events was 0.7).

The effect of El Niño/Southern Oscillation on the enhancement of disease transmission is largely described in the literature (Chretien et al., 2015). The influence of La Niña and minimum temperature on the prevalence of HM in Brazil was previously demonstrated by researchers from our group (da Silva et al., 2020; Silva et al., 2019). On the other hand, other researchers observed the greatest number of acute/subacute paracoccidioidomycosis cases coincided with previous El Niño events in southeastern Brazil (Barrozo et al., 2010; Barrozo et al., 2009). The paracoccidioidomycosis outbreak in 1985 was claimed to be a consequence of the ecological effects generated by this climate phenomenon, such as higher soil water storage levels that enhanced fungal growth in the soil and conidia liberation (Barrozo et al., 2010). Interestingly, the analyses of the temporal series of HM records from Ouro Branco demonstrated an outbreak of HM during 2011 - 2014 that was preceded by positive MEI events during 2009 - 2010. Maybe a similar phenomenon happened in Ouro Branco, contributing to pathogenic fungal transmission and enhancement of HM.

We found a moderate correlation between the minimum medium temperature and HM during the outbreak in the municipality with the highest frequency of HM. Annual variations in physiological functions are common in nature. Changes in day length (Onishi et al., 2020), among other factors, are sufficient to enhance or suppress the immune system. Based on the premise that immune function can be compromised by winter stressors (Nelson, 2004), we can hypothesize that low temperatures could have contributed to increasing the host's susceptibility to fungal infections. Interestingly, although the tropical climate is predominant in Minas Gerais, many of the municipalities studied are located in the south-central portion of the state, a region of Minas Gerais with a temperate climate prevailing.

5. Conclusion

In literature, researchers postulated that climate drivers the incidence of some mycoses, but others claimed that anthropic factors are more crucial to predict fungal infections. Our data suggest that the causes of HM in Minas Gerais are complex and multifactorial. Living in small municipalities is a strong predictor of hospitalization due to mycoses, either because of the reduced number of health care facilities and/or rural labor. But climatic changes also influence the frequency of mycoses recorded from the municipalities. In this way, we suggest more studies in this field of knowledge management for public health officials should make decisions about preventive socio-environmental measures based on an accurate understanding of local reality to mitigate the incidence of mycoses.

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