Original Article

Analysis of the spatio-temporal dynamics of incidence, mortality and test rates (rapid and RT-PCR) of COVID-19 in the state of Minas Gerais, Brazil

Análise da dinâmica espaço-temporal da incidência, mortalidade e taxas de testes (rápidos e moleculares) da COVID-19 no estado de Minas Gerais, Brasil

Análisis de la dinámica espacio-temporal de la incidencia, mortalidad y tasas de prueba (rápida e RT-PCR) de COVID-19 en el estado de Minas Gerais, Brasil

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ABSTRACT

Background and Objectives: A novel type of coronavirus, SARS-CoV-2, is responsible for an unprecedented pandemic with profound socioeconomic consequences. Owing to its recent discovery still represents a great unknown to researchers. Thus, this study aims to establish the spatio-temporal associations of the incidence, mortality, and the rate of both rapid and RT-PCR tests in Minas Gerais. **Methods**: This is a quantitative analysis of secondary data based on a cross-sectional research design. Incidence, mortality, date of the first notification of COVID-19 and number of rapid and RT-PCR tests were obtained from the sources: "GAL", "e-SUS VE" and "SES-MG". Pearson coefficient for correlation was calculated to establish the level of association between the relevant data. Descriptive statistical procedures were used to provide a comprehensive understanding of the distribution of incidence, mortality and test rates in the territory. **Results**: Positive correlations were found between the rate of rapid tests and incidence; rate of RT-PCR tests and incidence/mortality. At the municipal level, incidence, mortality, rate of rapid tests and RT-PCR revealed a negative correlation with days elapsed since the First Notified Case. The same effect occurs at the level of health macro-regions. **Conclusion**: The heterogeneity of the incidence and mortality of COVID-19 in the territory of Minas Gerais, as well as the rate of tests may be caused, in part, due to the different dates of introduction of the virus in the municipalities/macro-regions. It is speculated that this phenomenon occurs due to the dynamics of regional and inter-regional flows of people.

RESUMO

Justificativa e Objetivos: Um novo tipo de coronavírus, SARS-CoV-2, é responsável por uma pandemia sem precedentes com profundas consequências socioeconômicas. Devido à sua recente descoberta, o vírus surgido na cidade chinesa de Wuhan, em dezembro de 2019, ainda lança grandes incógnitas. Este estudo objetiva estabelecer as associações espaço-temporais da incidência; mortalidade; e taxas de testes rápidos e RT-PCR em Minas Gerais. **Métodos**: Trata-se de uma análise quantitativa de dados secundários a partir de um desenho de pesquisa transversal. Incidência, mortalidade, data da(s) primeira(s) notificações da doença, número de testes rápidos e de RT-PCR foram obtidos nas fontes: "Gerenciador de Ambiente Laboratorial", "e-sus VE" e SES-MG. O coeficiente de Pearson para correlação foi calculado para estabelecer o nível de associação entre os dados relevantes. Técnicas estatísticas descritivas foram empregadas para compreender a distribuição da incidência, mortalidade e taxas de testes no território. **Resultados**: Correlações positivas foram encontradas entre taxa de testes rápidos e incidência; taxa de testes RT-PCR e incidência/mortalidade. A nível municipal, incidência, mortalidade, taxa de testes rápidos e de RT-PCR têm correlação negativa com dias transcorridos desde o Primeiro Caso Notificado. O mesmo efeito ocorre, em diferentes intensidades, a nível das macrorregiões de saúde. **Conclusão**: A heterogeneidade da incidência e mortalidade da COVID-19 no território mineiro, assim como, das taxas de testes (rápidos e RT-PCR) pode ser causada, em parte, devido às diferentes datas de introdução do vírus nos municípios/macrorregiões de saúde. Especula-se que esse fenômeno se deve às dinâmicas dos fluxos regionais e inter-regionais de pessoas.

Descritores: COVID-19. Epidemiologia. SARS-CoV-2. Pandemias. Testes Imunológicos. Análise Espaço-Temporal.

RESUMEN

Justificación y Objetivos: El SARS-CoV-2 es responsable por una pandemia sin precedentes con profundas consecuencias socioeconómicas. Debido a su reciente descubrimiento, este vírus representa una gran incógnita para los investigadores. Así, este estudio tiene como objetivo establecer las asociaciones espacio-temporales de la incidencia, la mortalidad y la tasa de pruebas rápidas y RT-PCR en Minas Gerais. **Métodos**: Trata-se de un análisis cuantitativo de datos secundarios basado en un diseño de investigación transversal. Incidencia, mortalidad, fecha de la primera notificación de COVID-19 y número de pruebas rápidas y RT-PCR se obtuvieron de las fuentes: "GAL", "e-SUS VE" y "SES-MG". Se calculó el coeficiente de correlación de Pearson para establecer el nivel de asociación entre los datos relevantes. Se utilizaron procedimientos estadísticos descriptivos para proporcionar una comprensión integral de la distribución de la incidencia, la mortalidad y las tasas de prueba en el territorio. **Resultados**: Se encontraron correlaciones positivas entre la tasa de pruebas rápidas y la incidencia; tasa de pruebas de RT-PCR y incidencia/mortalidad. A nivel municipal, la incidencia, mortalidad, tasa de pruebas rápidas y RT-PCR revelaron una correlación negativa con los días transcurridos desde el Primer Caso Notificado. El mismo efecto ocurre a nivel de

macrorregiones de salud. **Conclusiones**: La heterogeneidad de la incidencia y mortalidad de COVID-19 en el territorio de Minas Gerais, así como la tasa de pruebas puede deberse, en parte, a las diferentes fechas de introducción de la virus en los territorios. Se especula que este fenómeno ocurre debido a la dinámica de los flujos regionales e interregionales de personas.

Palabras-clave: *SARS-CoV-2. Epidemiología. COVID-19. Pruebas inmunológicas. Pandemias. Análisis Espacio-Temporal.*

INTRODUCTION

For 50 years, different types of coronaviruses have been listed as a cause of respiratory infections[1]. However, in December 2019, several cases of pneumonia with unknown etiology were documented in the city of Wuhan, China. Afterwards, Chinese authorities isolated and identified a novel type of coronavirus, named SARS-CoV-2, which has a phylogenetic similarity with other beta-coronaviruses, including SARS-CoV, coronavirus of the severe acute respiratory syndrome, and MERS-CoV, responsible for the Middle East respiratory syndrome[2]. COVID-19 was declared a pandemic by the World Health Organization on March 11, 2020[1-3].

The virus is transmitted by inhalation through expelled droplets and aerosols, but also by fomites, through contaminated objects and surfaces that provide contact with an infected carrier with the hands and, later, with the face, eyes and nose[1, 3]. In order to contain the rampant spread of the novel coronavirus, countries have adopted measures of social isolation[3]. These measures, which include closing international borders, have caused devastating and long-lasting economic consequences around the world[2, 3].

Up to 11 April, 2021, 134.957.021 cases were confirmed worldwide, and 2.918.752 thousand deaths[4]. In most countries, the confirmation of cases increases exponentially, especially during the initial stages of the outbreak[3]. Although it is difficult to compare fatal case rates between the countries, as they are at different stages of the outbreak, the variations are probably related to the scope of population tests, age structure, health status of population and health systems of each country[3]. In Brazil, the first confirmed case was reported in the state of São Paulo on February 26, 2020[2]. To the current date, April 11, 2021, 13,449,940 cases and 351,591 deaths are attributed to COVID-19 in the country[5].

Minas Gerais (MG) has a pivotal role at the national level as it is the second largest Brazilian state in population size, estimated at 21 million people, located in a strategic

region, close to states with high incidence rates, such as São Paulo and Rio de Janeiro, hence making it highly conducive to the transmittal of COVID-19[2].

According to the Government of the State of Minas Gerais, in its last update of the human infection protocol for SARS-CoV-2 of July 20, both the reverse transcription assays followed by the polymerase chain reaction (RT-PCR) and the immunological techniques, which include rapid tests, can be used as a diagnostic criterion. It is noteworthy that negative results in rapid tests are not able to discard suspicious cases[6].

In this sense, the importance of prevention, correct care and treatment of infection, as well as the need of establishing epidemiological correlations between tests and the temporal and geographical behavior of the disease in Minas Gerais is justified by the high rate of viral transmissibility, hospitalization and mortality[1], which undoubtedly overburden the health system and harm the local economy.

Thus, this study aims to establish the spatio-temporal associations of the incidence, mortality, and the rate of both rapid and RT-PCR tests in Minas Gerais. The comprehension of these epidemiological phenomena according to the proposed prism can elucidate questions on which regions are most vulnerable and prepare health institutions to deal with the logistics of tests and health equipment, hence improving the management of the COVID-19 pandemic.

METHODS

Quantitative assessment of secondary data was performed from a cross-sectional epidemiological research design, and descriptive and inferential statistical methods were used for statistical analysis. In short, the descriptive statistical methods were aimed at detailing the relationship between two pandemic variables (i.e. the distribution of tests and the incidence of COVID-19) – in a given city and in a given health-macro-region (figure 1) – and core statistical estimators of the population demographic characteristics (e.g. population size); the statistical inferential method was aimed at trying to establish correlations between pandemic variables (e.g. incidence, mortality, rate of rapid and molecular tests and the date of the first notification).

The results were obtained through the use of the libraries Matplotlib (version 3.2.1), Pandas (version 1.0.5) and Statistics in the Python™ programming language (version 3.7.7). The programming environment used was Project Jupyter©.

The data obtained through the COVID-19 database available on the website of the Minas Gerais State Health Secretariat (SES-MG)[7] are as follows: Incidence and Mortality for COVID-19 per 1000 inhabitants among March 4, 2020 and June 22, 2020; date of the

first notification of the disease in regard to the municipalities that reported cases of COVID-19 until the date of July 10, 2020.

Through the Datasus system, by accessing the e-SUS Epidemiological Surveillance platform (e-SUS VE), the number of rapid tests per 1000 inhabitants carried out between March 4 and June 22, 2020 was extracted. Similarly, by accessing the Laboratory Environment Manager (GAL) platform, the number of RT-PCR tests performed between March 4, 2020 and June 21, 2020 was extracted.

Initially, we merged the data according to the Brazilian Institute of Geography and Statistics (IBGE) code for the municipalities and prepared the descriptive statistical analyzes as follows: cities that exhibited more than two standard deviations from the mean in the distribution of rapid tests (>12.58) and RT-PCR tests (>4.84) were excluded due to the noise of these outliers in the general data, thus resulting in the exclusion of 23 cities for rapid tests and 28 for molecular tests. Then, mean, median and quartiles for city distributions according to the type of test were generated.

The quartiles for the two distributions obtained were assessed according to the macro-regions that were part of their composition. After, the number of tests, both rapid and molecular, was extracted according to the health macro-region.

The inferential analysis consisted of calculating Pearson's coefficients[8] for correlation between the data obtained in the systems previously mentioned. The data used for this analysis refer to the period from March 4 to June 22, 2020. Only cities in which there was at least one notification of the disease until June 22 were considered. Therefore, it was necessary to exclude cities that did not present notifications of COVID-19 until that date, resulting in the exclusion of 215 cities. The variables incidence, mortality, rate of rapid and molecular tests and the date of the first notification were used to establish Pearson's coefficients, both at the municipal level and at the level of the health macro-regions.

Figure 1. Health macro-regions of Minas Gerais State as of 2020 according to SES-MG.
Source: https://www.saude.mg.gov.br/parceiro/regionalizacao-pdr2

RESULTS

Until June 22, 2020, 638 cities had reported at least one positive case for COVID-19, while 215 cities had not reported any cases of the disease. Among the cities of the first group, 72 days (early May) have passed since the date of the first notification in the state - March 4 - for 319 cities (less than half of the 853 cities in Minas Gerais, all of which were included in the current study) to register at least one notification of the disease.

Notwithstanding that, the most populous municipalities have reported positive cases since at least mid-March 2020 (Figure 2). Remarkably, the two most populous cities in the state (Belo Horizonte and Uberlandia) totaled 7815 cases of COVID-19 (26.12% of the total cases) until the analyzed date (June 22), and revealed the first notifications of the disease in early March.
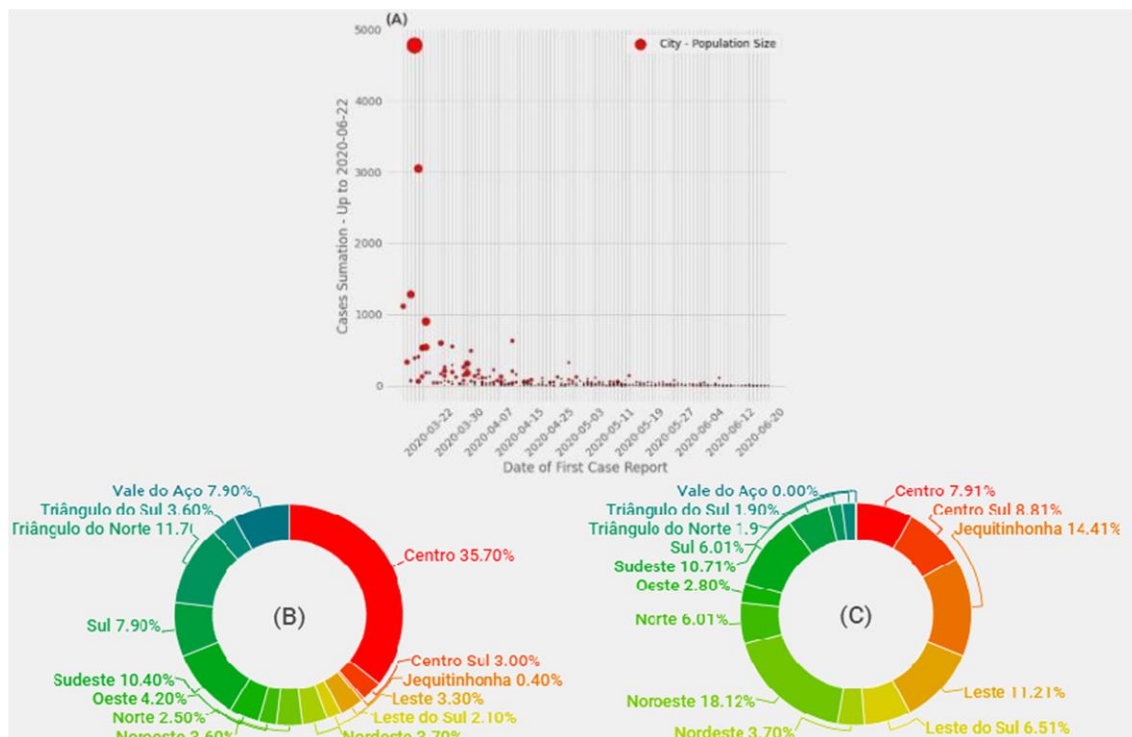
Figure 2. (A) Sum of notified cases in a specific city according to the date of the first notified case (March 4, 2020). (B) Cases notified according to the health macro-region by the date of June 22, 2020. (C) Health macro-regions to which cities belong without cases notified by the date of June 22, 2020.

Cities in which there was no notification of COVID-19 until the date of analysis were less populous and exhibited lower rates of tests, both rapid and molecular (Table 1), in comparison to the cities in the other group. Accordingly, there was a notorious predominance of disease notifications in the health macro-regions (Figure 1) Central, Northern Triangle and Southeast. In turn, the macro-regions Northeast, Jequitinhonha and East concentrated more than 40% of the 215 cities without records of the disease until the date of analysis.

Table 1. Comparison between cities with reported cases and cities without reported cases. Mean and standard deviation for the variables population size, rate of rapid tests and rate of molecular tests. *Until June 22, 2020.

	Population Size (2019)		ABtests performed (per 1000)		RT-PCR tests performed (per 1000)	
	Mean	SD	Mean	SD	Mean	SD
Cities with reported cases* (n=638)	31175.97	115698.24	3.51	5.29	0.94	1.1

Cities with no reported cases* (n=215)	5946.6	3789.18	1.26	2.32	0.47	0.56

The cities of the health macro-regions Central, South Central, South and Northern Triangle accounted for 59% of the cities above the third quartile of the RT-PCR test rate (between 1.1 and 2.8). In turn, the analysis of the same quartile for rapid tests (between 3.4 and 12.58) showed a more homogeneous representation of other regions. However, the cities in the Central and Northern Triangle regions still represented the majority of cities in this category. In fact, the Central, Central South and Northern Triangle regions revealed the highest test rates (both rapid and molecular).

Both rapid and RT-PCR tests performed for the detection of COVID-19 are in accordance with the incidence and mortality rates (Figure 3). The Pearson coefficients for correlation, at the municipal level, were: +0.39, between the rapid tests and the incidence rate; and +0.21 between the RT-PCR tests and the incidence rate. Regarding to the mortality rate, the same coefficients were 0 and +0.12 for rapid and RT-PCR tests, respectively.

Despite this, the temporal correlation was even more pronounced (Figure 4). At the municipal level, the analysis of the association between the elapsed time of the First Notified Case in the state of Minas Gerais and rapid tests produced a coefficient of -0.11; between the first notified case and RT-PCR tests, the coefficient was -0.22; between the first notified case and incidence rate, it was -0.25; and between the first notified case and mortality rate, -0.19.
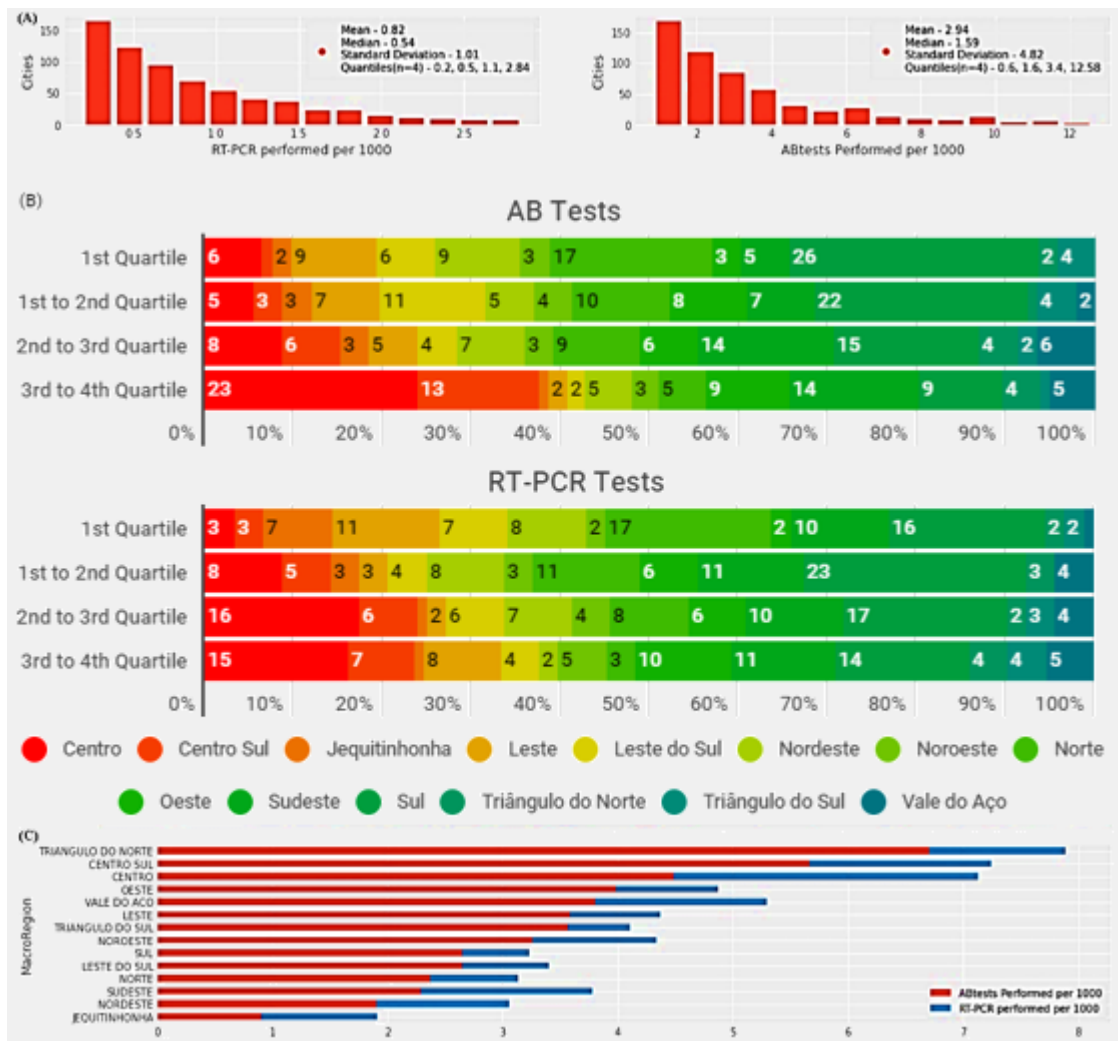
Figure 3. (A) Distribution of cities according to the tests performed; (left) rapid tests; (right) RT-PCR tests. (B) Composition of the quartiles of the distributions (A) according to the health macro-region; for rapid tests and RT-PCR tests, respectively. (C) Distribution of tests performed according to the health macro-region.

The same analysis used for the health macro-regions makes the association more evident. In fact, by aggregating cities in large regions, the outlier cities - whose tests per thousand exceed more than two standard deviations from the average and are small-sized - have their effect on the total overall reduced. Pearson's coefficient for correlation between the elapsed time of the first notified case in the state of Minas Gerais and rapid tests was -0.59; between the first notified case and RT-PCR tests, it was -0.25; between the first notified case and incidence rate, -0.70; and between the first notified case and mortality rate, -0.71.
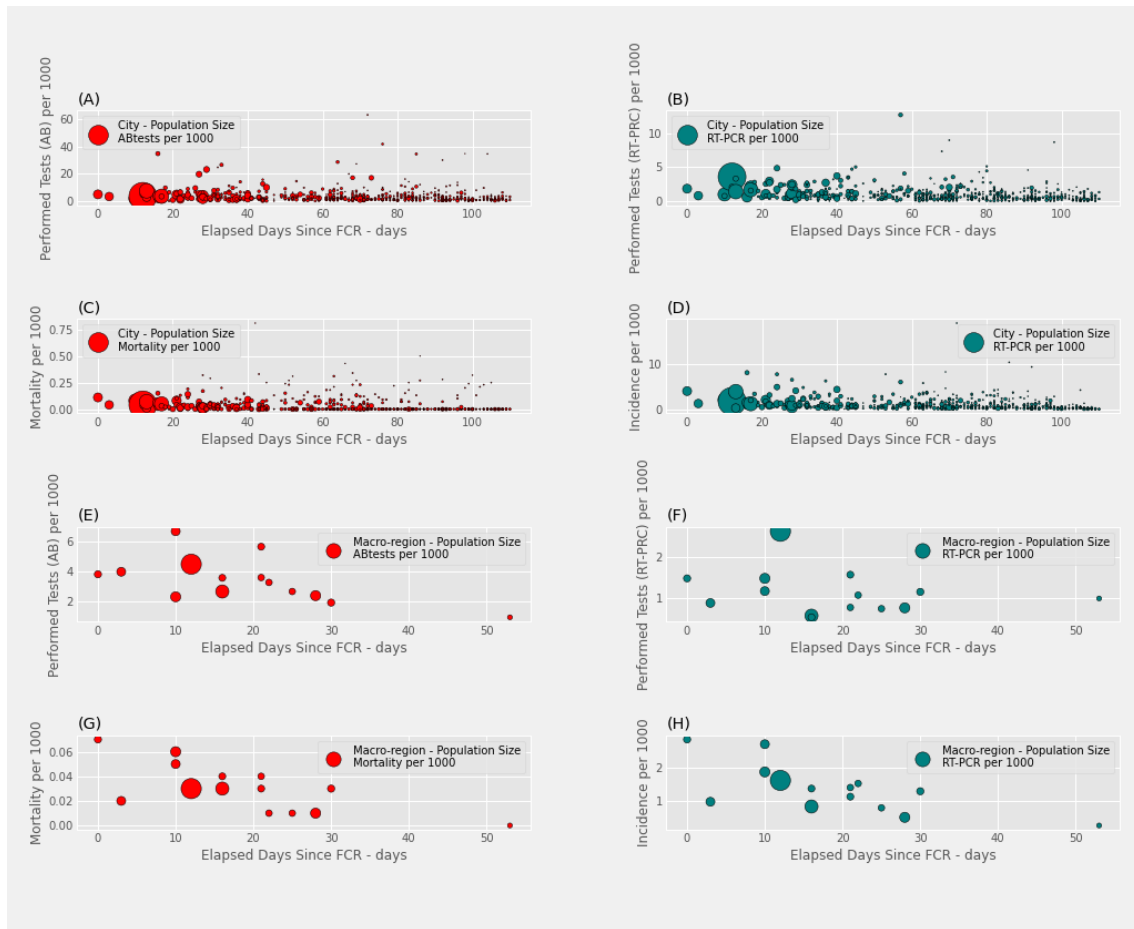
Figure 4. [Cities] Association between days elapsed since the first notified case and (A) Rapid tests per 1000 inhabitants; (B) RT-PCR tests per 1000 inhabitants; (C) Mortality per 1000 inhabitants; (D) Incidence per 1000 inhabitants. [Health macro-region] Association between days elapsed from the first notified case and (E) Rapid tests performed by 1000 inhabitants; (F) RT-PCR Tests per 1000 inhabitants; (G) Mortality per 1000 inhabitants; (H) Incidence per 1000 inhabitants.

DISCUSSION

The highest concentrations of COVID-19 cases accumulate in the hierarchically most influential regions of the state of Minas Gerais[9, 10]. The health macro-regions Central, Southeast, Northern Triangle, Vale do Aço and South were responsible for just over 73% of all cases of the infectious disease in the state until the date of analysis. All of these five regions contain at least one city of great relevance, being the metropolis or strong regional and sub-regional centers [9], with the exception of Vale do Aço, which is adjacent to the Central region and where it was notified the first case of COVID-19 in the state.

Case prevalence follows a pattern of regional distribution. The present study revealed that the Vale do Aço, Northern Triangle, Southeast and Central regions had the

highest share of cases as shown in figure 2B. Based on the literature, it can be inferred that the causes of this pattern of territorial distribution are due to anthropogenic and environmental factors that can contribute to the spread of the virus[11-13], including climatic factors[14], transport flows[13, 15], economic activity[13, 14] and air pollution[12].

In a study[13], the author finds that the spread of influenza viruses in the twentieth century is accompanied with human flows, since there was a strong association between the spread of COVID-19 in the territory and different factors, such as economic activity and availability of transport, especially those from long distance. This phenomenon was corroborated in a study that confirmed a greater spread of the disease associated with the increase in distances traveled by air[16]. Due to the similarity in transmission, it is expected that the spread of SARS-CoV-2 virus occurs in the same way. In fact, for the Chinese territory, the close association related to the flows of people between the territories and the disease incidence rates[15]. Furthermore, the authors established a relationship between gross domestic product (GDP) and the population size, which loses predictive value over time, hence suggesting migration of the virus to economically diverse and less affluent regions.

Therefore, the population size, economic activity and transport flow are essential factors to understand the spread of SARS-CoV-2 throughout the territory[12, 17, 18]. The mortality rate, in turn, follows a similar pattern of territorial distribution in Brazil[19]. Hence, there is multitude of parameters capable of explaining the distribution of tests, incidence and mortality.

In order to determine the effect size of each parameter on the phenomena at hand a multivariate analysis is imperative. But such an analysis has proved to be burdensome and complex due to the necessity to measure beforehand the relevant parameters (e.g. economic and political importance of a territory and human flow).

Therefore, we opted to investigate the relation between what we deemed probable parameters capable of explaining the tests (rapid and molecular) application throughout the Minas Gerais State territory. The reasoning behind this decision is as follows, the governmental officials would be motivated to test its population based on the perception of incidence and mortality of COVID-19, which would imply that more tests would be performed according to the rising of incidence and mortality of the disease.

The analysis has yielded a small correlation effect indicating that there is a significant relation between incidence and distribution of tests and mortality and distribution of tests. Which could indicate, but not prove, that the aforementioned

reasoning is true, but, nonetheless, insufficient to explain all factors driving the tests distribution.

Another analysis of correlation has also proven to be of small, but significant, effect size. Time elapsed since first notification of COVID-19 in a given territory seems to play a role in the rates of the pandemic variables (e.g. incidence, mortality and tests performed). The effect size is greater at the health macro-regions level, which could be due to a filter effect, small cities play small roles on the aggregate of statistical data. Accordingly, the authors posit that territories in which the disease appeared early would perform more tests, and would be more prone to higher rates of incidence and mortality.

The negative correlations observed when analyzing the time elapsed between the first notified case in the city and the first notified case in the state may indicate that there is heterogeneity in the date of introduction of the virus in the territory, especially when considering the incidence and mortality rates that tend to be lower the later the first case is reported. In a study, the spatio-temporal flow of COVID-19 in the Brazilian territory was established and the authors described that the health macro-regions of the Northern Triangle, Central, Central South, South and Southeast are those in which the virus first entered the territory of Minas Gerais[16]. This is in agreement with the findings of studies in Brazil[19] and China[15], which demonstrated that the most affluent regions receive the virus before other regions.

The same negative correlation - with different coefficients and of greater intensity - was observed when the geographic level used was the health macro-region. This more pronounced effect seems to indicate that SARS-CoV-2 tends to be concentrated for a longer time in the sub-region where it was first inserted, that is, interregional spread is subsequent to the spread in the locality itself. In fact, in Brazil, the virus seems to spread through the territory in two ways: spatial, when the virus leaves the metropolitan region for the rest of the territory; and hierarchical, located in sub-regions in which cities of regional importance allow the spread of COVID-19 to other locations at a lower hierarchical level[19].

Across the state, at the municipal level, there was a positive correlation between the rate of rapid tests and incidence and the rate of RT-PCR tests and incidence. Also, the rates of RT-PCR tests and mortality remained positively correlated and more concentrated in three health macro-regions (Central, Central South and Northern Triangle). Besides that, there was a notable negative correlation between time and test rates, at the municipal and regional level.

The incidence rate, as a function of time, reflects biological factors, including the microorganism-host interaction, susceptible population size, contagiousness of the infection and the rate of tests. Moreover, the incidence rate reflects the organizational capacity and infrastructure of the health sector of a territory. Therefore, richer regions would have more available testing resources[20], which was confirmed in this study.

Although the findings of the present research, this study has limitations. The methods applied, notably the Pearson coefficient for correlation, without other studies regarding the flow of people or even the flow of disease spread through the state of Minas Gerais are less sensitive tools to point the cause of the explored phenomena. The univariate analysis also limits our comprehension of the role that each variable has in the overall effect. Notwithstanding that, the procedures used, together with the literature, are capable of directing new paths to clarify the nature of the evidenced associations.

It is worthwhile noting that the test rate must influence the incidence and mortality rates, as the diagnostic criterion for the disease is based on diagnostic tests. In this context, it is expected that the higher the rate of tests in a given territory, the greater the reported number of incidence and mortality. Thus, territories that are not suitable for testing can suffer from severe underreporting[21]. The present methodological design would be more appropriate in a homogeneous situation of the rate of tests, which is not possible.

The heterogeneous distribution of COVID-19 across the territory overlaps the areas with the highest affluence in the state. This may indicate that the most interconnected regions are those with a greater increase in incidence and mortality in the first moments of the pandemic, which would cause the testing rate to increase in parallel, with privilege for rapid tests in all regions and RT-PCR tests where there is a higher mortality rate.

Undoubtedly, this study reported a phenomenon underlying the spatio-temporal dynamics of the rates of tests, incidence and mortality in Minas Gerais, notably the influence of the hierarchy levels of urban centers and the demographic aspects of the territory. Thus, these findings contribute to a greater understanding of the association between parameters of territorial dynamics and epidemiological parameters of COVID-19, which may imply in the preparation of health systems and competent institutional authorities in order to develop potential strategies to combat the life-threatening disease based on prior knowledge of the demographic and hierarchical aspects of the territory.

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