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ORIGINAL ARTICLE

Hospitalizations for pulmonary embolism in Brazil (2008-2019): an ecological and time series study

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ABSTRACT

Objective: To assess the temporal trends of hospitalizations for pulmonary embolism (PE) in Brazil, its regions, and states between 2008 and 2019. **Methods:** An ecological and time series study was conducted. Data were obtained from the Hospital Information System (SIH) of the Brazilian Ministry of Health. The inflection point regression model was applied for temporal trend analyses. Trends were classified as increasing, decreasing, or stationary according to the slope of the regression line. The Annual Percent Charge (APC) and the Average Annual Percent Change (AAPC) were calculated considering a confidence interval of 95% and *p*-value <0.05. Furthermore, spatial distribution maps of epidemiological indicators related to PE in Brazil were elaborated. **Results:** There was an increasing trend in the hospitalization rate for PE in Brazil, ranging from 2.57 in 2008 to 4.44/100,000 in 2019 (AAPC=5.6%; p<0.001). Total and average hospitalizations costs also showed increasing trend in the country (AAPC=9.2% and 3.0%, respectively). Still, there was a decrease in the in-hospital mortality rate (from 21.21% to 17.11%; AAPC=-1.9%; p<0.001). Similar trends were observed in most regions. The average hospitalization time in Brazil showed a stationary trend. The hospitalization rate has also increased in 18 states (66.67%). Seven states showed a decrease in the mortality rate (25.93%), except for Roraima, which showed an increasing trend. **Conclusion:** Hospitalizations for PE represent a serious public health problem in Brazil and the temporal patterns observed herein demonstrate an increasing trend in all regions and states of the country.

Keywords: Pulmonary embolism; Epidemiology; Ecological studies; Time series.

INTRODUCTION

Pulmonary Embolism (PE) is considered a severe clinical condition, characterized by obstruction, usually by a thrombus, in the pulmonary artery or in one of its branches,[1] causing hypoxemia, release of potent vasoconstrictors, increased pulmonary vascular resistance and ventricular afterload.[2,3]

Currently, PE is considered one of the leading causes of death in hospitalized patients.[4] After a first episode of embolism, there is a 39.9% greater chance of recurrence in the following ten years, with the risk of death being higher during the first two years.[5] Additionally, the mortality rate is around 15.3% in three months, and it ranges from 25% to 30% in five years if left untreated.[6]

Ageing is one of the main factors associated with increased risk of developing thromboembolism.[7] In Brazil, it is estimated that in 2050, the elderly population will reach 30.3 million, approximately 14.6% of the total number of Brazilians. Also, the increase in life expectancy has been accompanied by epidemiological changes and an increase in chronic diseases and risk factors, such as obesity and cardiovascular diseases (hypertension, myocardial infarction and heart failure), which increase the risk of pulmonary embolism.[7] In 2020, for example, data from Vigitel survey (*Surveillance of risk factors and protection for chronic diseases by telephone survey*) showed a prevalence of obesity in 21.5% of respondents, and hypertension in 25.5% of them in Brazilian capitals.[8]

In the period between 2003 and 2013, the annual number of inpatient episodes for patients diagnosed with pulmonary embolism showed an increase in incidence rate from 20.6 to 35.0.[1] On the other hand, the availability and use of risk stratification and diagnosis tools in the hospital environment has supported the early

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identification of patients at low risk of complications, who are discharged early, impacting the reduction of hospital costs.[9]

In Brazil, previous studies on PE epidemiology are scarce. In addition, those available in the scientific literature may not reflect the current reality, as the time periods of the analyzes are already outdated. In this sense, Brazil lacks new evaluations on the temporal trend of PE at national level, which are quite important for the design and implementation of public health strategies. Thus, this study aimed to assess the temporal trend of hospitalizations for PE in Brazil, its regions, and states between 2008 and 2019.

METHODS

An ecological and time-series study was conducted using data from PE hospital admissions from January 2008 to December 2019 in Brazil, its regions, and states. A 10-year time series was used as it allows identifying changes in the occurrence of the studied phenomenon. Furthermore, 2020 was not included due to the COVID-19 pandemic. During this period, the Brazilian population increased from 191 million inhabitants to about 210 million, being the Southeast (88 million) and Northeast (56 million) regions the most populous.[10]

In this study, the following variables were assessed: i) number of hospitalizations; ii) hospitalization rate per 100,000 inhabitants; iii) total and average cost (BLR) of the Hospital Admission Authorization (AIH); iv) hospitalization time (in days); v) average of hospitalization time (in days); and vi) number of deaths and in-hospital mortality rate (%). Data were extracted from the Hospital Information System (SIH), through the Department of Informatics of the Brazilian Unified Health System.[11]

Importantly, SIH gathers information from about 70% of public hospital admissions in the country.[11] Its data collection instrument is AIH, currently issued by the states and based on a single numerical series annually defined by decree of the Brazilian Ministry of Health.[11] Data related to the ICD-1/I26 were collected. Moreover, the population data used in the study were obtained from the Brazilian Institute of Geography and Statistics (IBGE),[10] considering 2010 census and inter-census projections for the other years.

Time trend analyzes were performed using the inflection point regression model (Joinpoint Regression Model). This method consists of a regression model that tests whether a line with multiple segments is statistically more adequate to describe the temporal evolution of a set when compared to a straight line or fewer segments.[12] In addition, the Annual Percent Change (APC) and the Average Annual Percent Change (AAPC) were calculated considering a confidence interval of 95% (95% CI) and significance of 5% (p-value<0.05). The trend can be classified either as increasing (APC/AAPC+ and p-value<0.05), decreasing (APC/AAPC- and p-value<0.05), or stationary (p-value>0.05). The model automatically identifies at which point in time an inflection occurred. In this sense, each analyzed location may present different trends at different points in time. Time trend analyzes were performed using the Joinpoint regression software program (version 4.5.0.1, National Center Institute, Bethesda, MD, USA).

To map the spatial distribution of the epidemiological indicators related to hospital admissions for PE, firstly was obtained the digital cartographic mesh (in shapefile format) of Brazil, segmented by regions and states, in the Geographic Projection System latitude/longitude. Mesh was also obtained from IBGE database.[10] Subsequently, maps were constructed, considering data on all epidemiological indicators assessed herein. Results were represented on choroplethic maps. We used QGis software, version 3.4.11 (QGIS Development Team; OpenSource Geospatial Foundation Project) to create the maps.

Considering the use of secondary data, in which it is not possible to identify any subject, this study did not require the approval by an ethics committee.

RESULTS

Spatial distribution of the epidemiological indicators on pulmonary embolism in Brazil (2008-2019)

In the analyzed period (2008-2019), a total of 81,152 cases of PE were recorded in Brazil, which corresponds to a hospitalization rate of 3.38 per 100,000 inhabitants. These hospitalizations have cost a total of BRL 138 million and an average of BRL 1,676.30 per hospitalization. The sum of the total hospitalization time was 774,427 days and the average was 9.5 days per hospitalization. Among them, 16,332 evolved to death (in-hospital mortality rate =20.1%; Figure 1 A-H).

The Southeast region ranked first in five indicators: number of hospitalizations (n=44,945), total cost of hospitalizations (BRL 79,291,311.70), total time of hospitalization (450,176 days), number of deaths (9,277), and average cost per hospitalization (BRL 1,744). Neverheless, the South region had the highest hospitalization rate (5.7/100,000) and the Northeast had the highest average of hospitalization time (10.3 days) and in-hospital mortality rate (25.1%).

Regarding Brazilian states, São Paulo had the highest number of hospitalizations (n=23,540), total cost of hospitalization (BRL 42,959,761.00), total time of hospitalization (n=273,280), and number of deaths (n=5,203). Nevertheless, the longest average time of hospitalization was observed in the Federal District (14 days); the state of Sergipe had the highest average cost per hospitalization (BRL 2,219.90); the highest rate of hospitalization was recorded in Minas Gerais (6.75/100,000); and the highest in-hospital mortality rate was registered in Paraiba state (45.3/100,000).

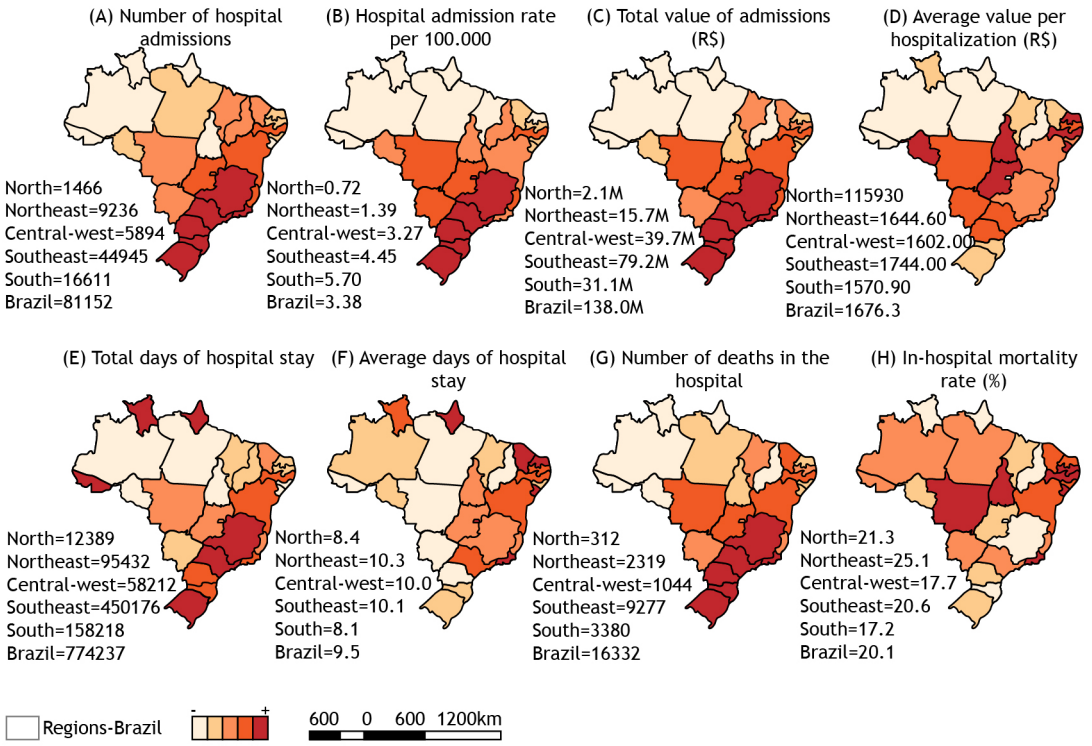

Figure 1. Spatial distribution maps of epidemiological indicators related to hospital admissions for Pulmonary Embolism (PE) in the states and regions of Brazil between 2008 and 2019.

Time trend analysis of national, regional, and state indicators

An increasing time trend in the hospitalization rate was observed in Brazil (from 2.57 in 2008 to 4.44/100,000 in 2019; AAPC=5.6%; p<0.001). Likewise, the Northeast, Central-West, Southeast, and South regions showed increasing trends in hospitalization rates. Importantly, the Northeast region showed the greatest increase in the period studied (AAPC=11,7%; p<0,001), while the North region had a stationary trend. Regarding the data by state, 66.67% (n=18) had an increasing trend, while in 33.33% the trend was stationary. The state of Roraima (in the North region) had the highest growth in hospitalization rate (AAPC=42.7%; p<0.001; Figure 2; Table S1).

Likewise, the total cost of hospitalizations also showed an increasing trend in Brazil (from BRL 6.3 million to 16.5 million; AAPC=9.2%; p<0.001). This temporal pattern was observed in all Brazilian regions, especially in the Northeast (AAPC=15.9%; p<0.001). Additionally, 20 states (74.07%) showed an increasing trend in the total costs, while 7 states (25.93%) presented a stationary trend. The state of Roraima showed the highest increasing rate during the period studied (AAPC=113%; p<0.001; Figure 3; Table S2).

Furthermore, the average cost per hospitalization also showed an increasing trend in Brazil (from BRL 1,298.24 to 1,775.4; AAPC=3%; p<0.001) and in all its regions. The North and Central-West regions showed the greatest increase in the period (AAPC=5.1%; p<0.001 in both), and the Northeast region showed the smallest increase (AAPC=2% p<0.001). Similarly, increasing temporal patterns were observed in 12 states (44.44%; Figure 4; Table S3).

On the other hand, the average time of hospitalization showed a stationary trend in Brazil (from 9.1 to 8.7 days; AAPC=-0.4%; p=0.4) and in all regions. Notwithstanding, the Southeast region showed a decreasing trend from 2010 to 2019 (APC=-1.6%; p<0.001). Similar patterns were observed in three other regions: Central-West (2012-2018; APC=-3.2%; p<0.001), South (2013-2018; APC=-2.5%; p<0.001) and Northeast (2013-2018; APC=-1.7%; p<0.001). As to the analyses per state, six (22.22%) showed an increasing trend, while three (11.11%) showed a decreasing trend (Figure 5; Table S4).

Finally, the in-hospital mortality rate due to PE showed a decreasing trend (from 21.21% to 17.11%; AAPC=-1.9%; p<0.001) in Brazil and in the Southeast region (AAPC=-2.7%; p<0.001). Conversely, other regions showed a stationary pattern. Interestingly, region South showed an inflection point, showing a decreasing trend from 2011 onwards (APC=-4.8%; p<0.001). In the analysis by states, only Roraima

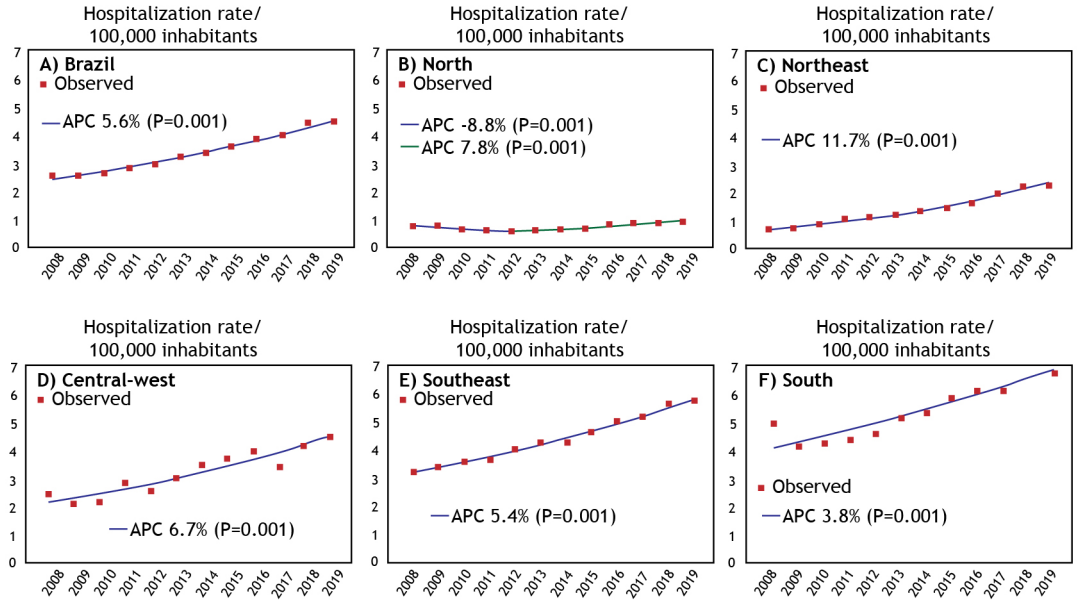

Figure 2. Temporal trend of the hospitalization rate due to pulmonary embolism (PE) in Brazil, its regions, between 2008 and 2019.

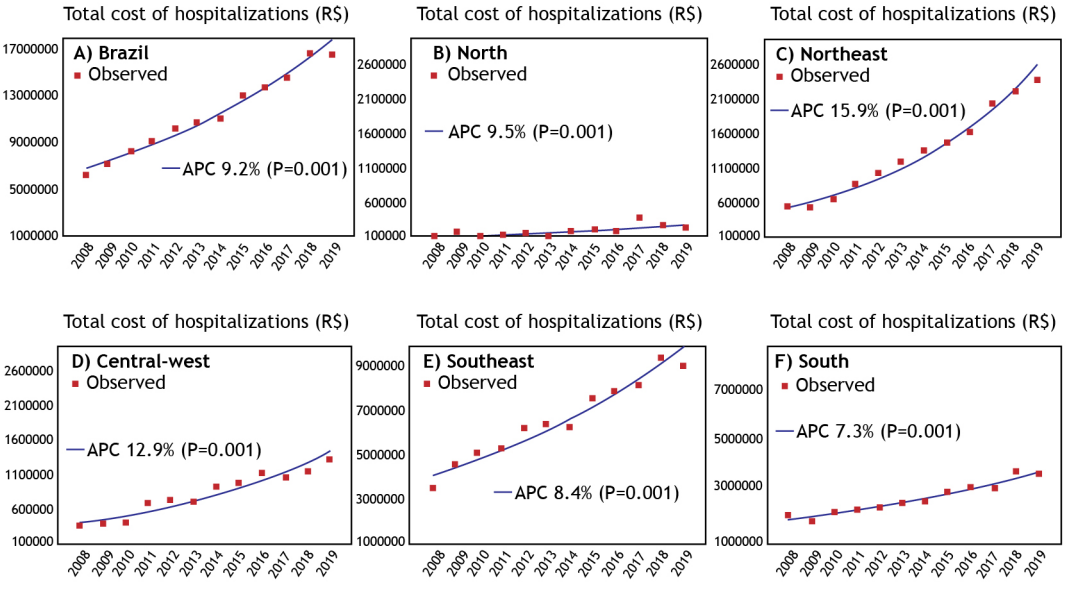

Figure 3. Temporal trend of the total cost of hospitalizations due to pulmonary embolism (PE) in Brazil, its regions, between 2008 and 2019.

showed an increasing trend of in-hospital mortality rate (APC=85.7%; p<0.001), while 7 states (25.93%) had a stationary trend (Figure 6; Table S5).

The specific analyzes of each of the regions of Brazil or its states are presented in the Supplementary Tables.

DISCUSSION

An ecological and population-based study was carried out to assess the temporal trends of hospital admissions caused by PE in Brazil between 2008 and 2019. Our data showed an increasing trend in the rate and in the

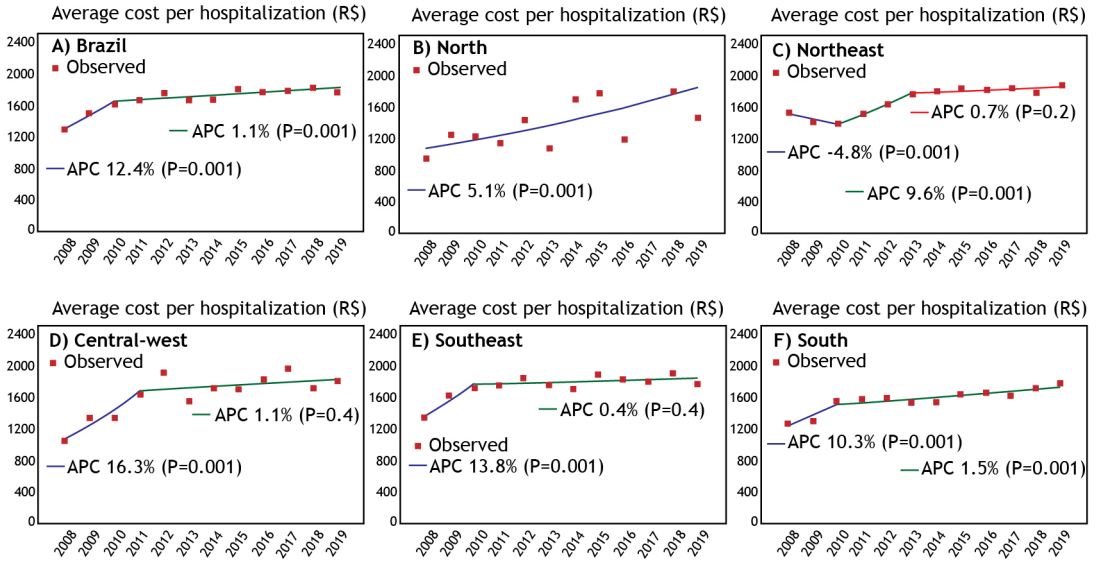

Figure 4. Temporal trend of the average cost per hospitalizations due to pulmonary embolism (PE) in Brazil, its regions, between 2008 and 2019.

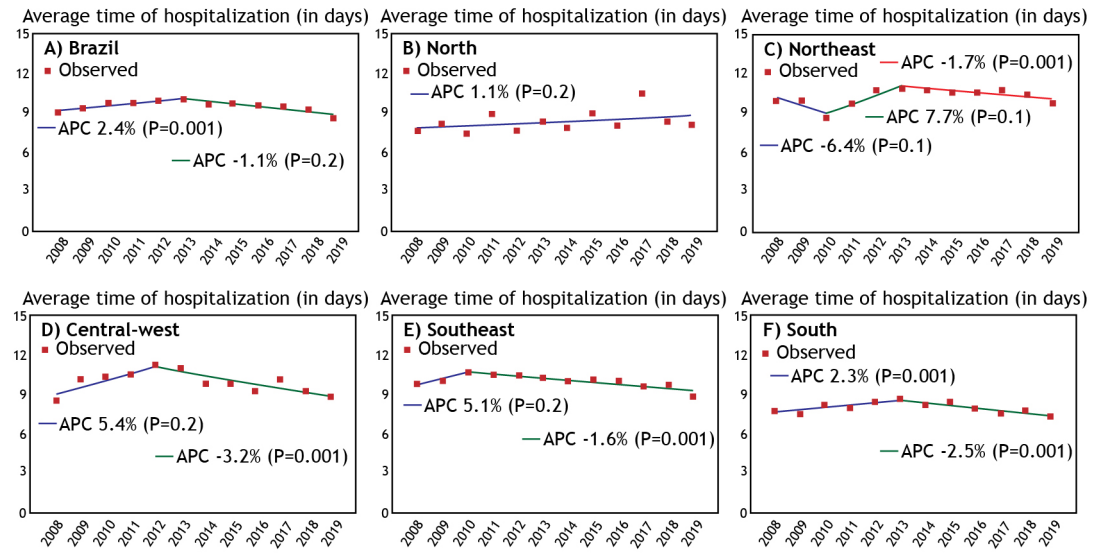

Figure 5. Temporal trend of average time of hospitalization (in days) due to pulmonary embolism (PE) in Brazil, its regions, between 2008 and 2019.

total cost of hospitalizations for PE in Brazil. However, a decreasing trend in the in-hospital mortality rate due to PE was observed. Besides, important spatial variations in the epidemiological indicators associated with PE, as well as in temporal trends among Brazilian regions and states were demonstrated.

Notably, the increase in the hospitalization rate due to PE observed in this study may be related to the context of demographic and epidemiological transition that Brazil has been going through in recent decades, with a decline in birth and mortality rates, and a significant increase in the population's life expectancy.[13,14] The aging of the population also leads to an increase in the occurrence of cardiovascular diseases such as PE, which corresponds to one of the most prevalent diseases in the elderly, especially in those over 65 years old.[7]

It is estimated that in 2050, the number of elderly in Brazil will exceed that of children under 15 years old.[10]

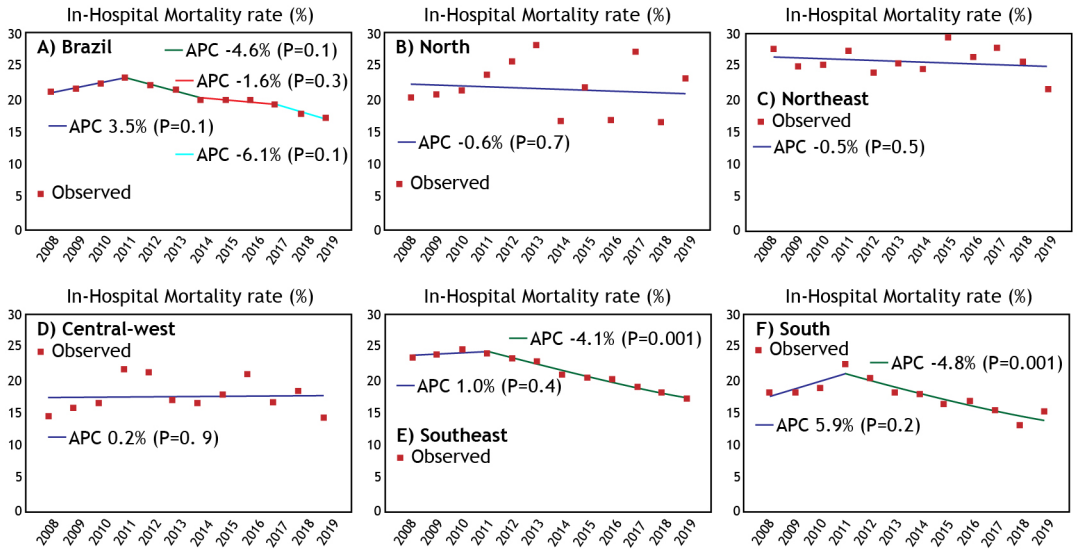

Figure 6. Temporal trend of in-hospital mortality rate (%) due to pulmonary embolism (PE) in Brazil, its regions, between 2008 and 2019.

In 2040, it is expected that there will be about 153 elderly people for every 100 young people under 15 years of age.[15] Furthermore, the proportion of those over 65 years old will increase from 9.6% in 2020 to 31.3% in 2075. In 2100, this proportion is expected to be 34.1%.[16] As a result, an increase in the prevalence of many non-communicable chronic diseases (NCDs) is also expected, such as cardiovascular diseases, cancer, and respiratory diseases, which represent risk or aggravating factors for the occurrence of PE.[17,18]

In Brazil, the South region has the highest rate of aging (54.94%).[19] This may explain the higher rate of hospitalization for PE observed (5.7/100,000) in this study, when compared to other regions. Also, the Southeast and South regions have better hospital infrastructure and availability of technological resources in the country.[14] Consequently, the population has a greater access to diagnostic tools, such as computed tomography angiography (CT-angiography), which allows for an early diagnosis and the identification of cases that would not be captured by other methods. In addition, scores, diagnostic flowcharts, and risk stratification can be used, which allows for more adequate management and better patient outcome.[9,20-22]

Additionally, the use of oral anticoagulant drugs, such as rivaroxaban, dabigatrana and apixabana, has been shown to be an effective measure for the clinical improvement of patients.[23,24] These drugs have reduced the monitoring and hospital stay time of the patient and has led to an increase in early discharge. However, access to these drugs is still not adequate, especially for patients in the public system, which may explain the stationary trend in the average length of stay for PE.

The stable trends observed in the average time of hospitalization, at national and regional levels, may be associated with the availability of technological and pharmaceutical resources. For example, despite the stationary trend observed in Brazil, hospital stay days in the Northeast region are longer than in the South (24.5% higher). Regardless of the social, economic, and health advances achieved in recent decades in Brazil, access to the health system is still unequal.[25,26] Patients from the South and Southeast regions are more likely to have access to better health services when compared to those in the North and Northeast regions.[25] These findings reinforce the importance and need to adopt strategies to mitigate existing socioeconomic and technological inequalities in Brazil and improve access to early diagnosis and adequate treatment for PE.

In the USA, the average PE hospitalization time was 4 days, with a progressive reduction between 2000 (4) and 2015 (2 days).[27] In another study carried out in Portugal, the average time of hospitalization was 12.3 days, with a slight reduction between 2003 (12.3) and 2013 (11.5 days).[1] In our study, this average was 9.5 days between 2008 and 2019. Despite the reduction from 9.1 to 8.7 days in the average time of hospitalization, our analyzes showed a stationary trend. These variations may be related to health network structure in each country.

Herein, the average and total cost of hospitalizations for PE showed increasing trends in the period studied. These studies show that the implementation of venous thromboembolism (VTE) algorithms in hospitals is important to reduce in-hospital VTE. This education program could decrease costs too.[28,29] A VTE prophylaxis

thrombus prevention program implemented in four hospitals in Salvador/BA showed a significant increase in the use of correct heparin doses (53% before implementation of the program and 75% after).[29]

The increase in the total cost is probably due to the growth in hospitalizations that occurred in the country and its regions. Alternatively, the increase in the average cost per hospitalization may be related to the use of more advanced methods of diagnosis and treatment in hospitals. Although these improvements lead to a reduction in hospital stay, they are more costly to health systems and increase the average and total cost of hospitalizations. Similarly, this growth was also observed in other countries, such as the USA, where all age groups showed an average increase in the cost of hospitalization, ranging from $13,000.00 to $15,000.00.[27] More importantly, patients with PE usually also have some comorbidity, such as pneumonia, femoral neck fracture, stroke, lung cancer, and others.[7,15] The occurrence of PE, along with comorbidities, can aggravate not only the patient's clinical outcome, but also the cost of hospitalization.

Some limitations of our study should be mentioned. An ecological study was conducted using secondary data that could be biased, mainly in relation to differences in the quality of information systems between regions of the country. As a result, both the number of PE cases and the number of deaths may be underreported, especially in the North and Northeast regions. Additionally, errors in data typing in the information systems, as well as the inclusion of suspected but unconfirmed cases, can compromise the quality of the data.

Taken together, our analyses showed increasing trends in the hospitalization rate and in the total and average cost for PE in Brazil and its regions. On the other hand, we identified a decreasing trend in the in-hospital mortality rate, while the average length of hospital stay showed a stationary trend. Additionally, we observed spatial variations in temporal trends between regions and states in Brazil. These findings therefore highlight the urgent need to develop regional and local strategies that promote improvements in hospital infrastructure, diagnostic services, and timely treatment of cases, so that there is a reduction in the time and cost of hospitalizations and, especially in the mortality rate due to PE in the country.

AUTHOR CONTRIBUTIONS

JAG, JEBB and CDFS: substantial contribution to the study design; data analysis and interpretation; drafting and revision of the manuscript; and approval of the final version to be published. CAOR, RFC, MBS, DSC, ALON, JPOA and GBAS: data collection and analysis and drafting and revision of the manuscript.

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