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ORIGINAL ARTICLE

Ischemic Stroke and Acute Myocardial Infarction: Trends in in-Hospital Mortality in Brazil from 1998 to 2018

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Abstract

Background: Ischemic stroke and acute myocardial infarction (AMI) are cardiovascular diseases with high morbidity and mortality rates in Brazil and worldwide. Their outcomes are influenced by public policies aimed at mitigating risk factors and by investments in infrastructure of emergency support and quality of hospital care.

Objective: To analyze the trend in the proportion of in-hospital deaths from ischemic stroke and AMI in Brazil as a way of evaluating the effectiveness of urgency and emergency services.

Methods: Ecological time series study using data from the Hospital Information System. The outcome was the proportion of in-hospital deaths from ischemic stroke and AMI with stratification by sex and state. Prais-Winsten regression was used to analyze the trend between 1998-2018 with $\alpha \leq 0,05$.

Results: The proportion of deaths from AMI and ischemic stroke declined in the time series ($p<0.001$), decreasing annually by 0.17% and 0.25%, respectively. In 20 years, it reduced 43.76% (ischemic stroke) and 32.39% (AMI) in both sexes. However, the decline was more evident in the South and Southeast regions.

Conclusion: The reduction in hospital deaths from AMI and ischemic stroke was heterogeneous among Brazilian regions, which may be related to inequality in emergency services and hospital support.

Keywords: Stroke; Myocardial Infarction; Hospital Mortality; Time Series Studies.

Introduction

Ischemic stroke and acute myocardial infarction (AMI) are considered cardiovascular diseases (CVD). Their pathophysiology is mostly associated with rupture or detachment of atherosclerotic plaques and clots in vessels, which can lead to occlusion of the arterial lumen and consequent obstruction of blood flow in the brain or heart.[1]

CVDs have high incidence and mortality rates. In Brazil, about 388,000 people died from CVD in 2017, and they are the main cause of death in Brazil and worldwide.[2] The Hospital Information System of the Department of Informatics of the Unified Health System (DATASUS, acronym in Portuguese) showed that between 1998 and 2007, the mortality rates for stroke and AMI were 14.12 and 15.4 per 1000 inhabitants, respectively; after pre- and in-hospital care, between 2008 and 2018, the rates of stroke mortality and AMI were 11.55 and 11.93 per 1000 inhabitants, respectively.[3]

The incidence, risk factors, effectiveness of contingency measures, access to diagnostic tools, and medical assistance influence the mortality of circulatory diseases.[1,4] According to Donabedian, the severity of the situation and the logistical-care strategies play a determining role in the occurrence of deaths; thus, the analysis of mortality in a hospital environment provides an evaluation of the results of actions developed at this

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Central Illustration: Ischemic Stroke and Acute Myocardial Infarction: Trends in in-Hospital Mortality in Brazil from 1998 to 2018

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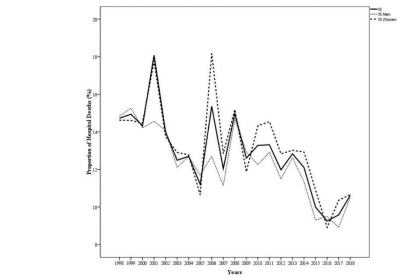
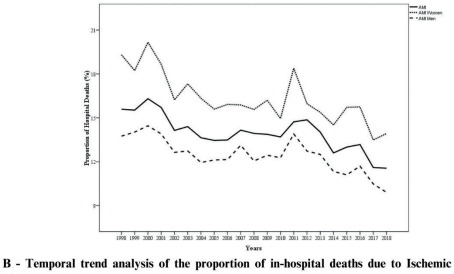


A - Temporal trend analysis of the proportion of in-hospital deaths due to Ischemic Stroke and Acute Myocardial Infarction in Brazil between 1998 and 2018 general and stratified by sex. Ischemic Stroke (IS) general trend lines for men (IS Men) and women (IS Women).



B - Temporal trend analysis of the proportion of in-hospital deaths due to Ischemic Stroke and Acute Myocardial Infarction in Brazil between 1998 and 2018 general and stratified by sex. Acute Myocardial Infarction general trend lines for men (AMI Men) and women (AMI Women).

C - Regionalized scheme of the cumulative trend of the proportion of in-hospital deaths for Ischemic Stroke (IS) and Acute Myocardial Infarction (AMI) in Brazil between 1998 and 2018.

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White downwards arrow means a reduction in AMI; black downwards arrow means a reduction in IS; black upwards arrow means an increase in IS.

level of the health system, such as effectiveness and efficiency.[5]

In-hospital mortality is related, among other social and economic factors, to coverage/access to urgent and emergency services, availability of infrastructure, inputs, and human resources, as well as implementation and adherence to general and specific work processes in hospital support provided.[6-12] Therefore, in-hospital deaths due to ischemic stroke and AMI are more likely to be mitigated when local and national policies seek to assess and intervene in the outcome and its modifiable conditions. [1,6,12]

Considering the significant number of deaths due to stroke and AMI and the fact that understanding the distribution of these diseases within the scope of the hospital health subsystem can provide valuable information to health managers, the objective of this study was to analyze the trend in the proportion of hospital deaths due to ischemic stroke and AMI in Brazil as a means of evaluating the effectiveness of urgency and emergency services in containing these acute events.

Method

Design

This was an ecological time series with analytical approaches. The information analyzed comprises all hospital admissions in the federative units of Brazil between 1998 and 2018 in services owned by or affiliated with the Brazilian Unified Health System (SUS, acronym in Portuguese), which covers more than two thirds of the country's consultations. Authorizations for hospital admissions resulting from ischemic stroke and AMI outcomes were analyzed in all federative units.

Context

Brazil has an estimated population of 213.3 million inhabitants and approximately 94,070 health facilities, of which 52,021 are public, with 152,892 beds for hospitalization, and 42,049 are private, with 279,104 beds. Despite the significant participation of the private sector in Brazilian health, only 26% of Brazilians reported having a medical health plan, according to the National Health Survey in the 2019.[13]

Participants

This is an ecological design; the units of analysis or participants are the federal units that bring together their public and/or contracted hospital services.

Data Sources

The study was carried out using the DATASUS Hospital Information System databases. These data are publicly accessible and can be obtained through tabnet or tabwin on the DATASUS website.[3] There was no database linkage in this investigation.

Variables

To obtain the in-hospital mortality indicator, we used the number of in-hospital deaths due to ischemic stroke and AMI divided by the total number of hospitalizations due to the same diagnosis.

Only the ischemic stroke subtype was used in the study, as this represents about 87% of all cases. The hemorrhagic subtype, which is much less frequent, presents important differences in prognosis compared to the ischemic subtype, and its inclusion could lead to biases in the interpretation of trends.[14]

Data were included in the study by adopting the primary diagnosis of the events in the Hospital Information System and the year of processing and place of residence. The codifications of the conditions studied were based on the Tenth Version of the International Classification of Diseases, which are: G45 (Transient ischemic strokes and related syndromes), G46 (Cerebral vascular syndromes that occur in cerebrovascular diseases), I63 (Cerebral infarction) and I21 (AMI).

The proportion of hospital deaths due to ischemic stroke and AMI was stratified according to federative unit and gender. In order to avoid possible errors in the included data, an audit was carried out by a second group of researchers in a random sample of the bank.

Statistical methods and bias control

A sequence graph and polynomial regression were constructed for data trend analysis, which aims to discover the best curve for the outcomes (Y) of the proportion of hospital deaths due to ischemic stroke and AMI. The independent variable of the regression was the difference between the mean year of the time series and the year of admission processing (X). This procedure minimizes biases in the intercept of equation (β_0).

In order to prevent serial autocorrelation, the Prais-Winsten polynomial regression method was applied in order not to inflate the coefficients (β_1) of the equation ($y = \beta_0 + \beta_1 x$). When β_1 is positive, it indicates an upward trend, and when it is negative, it indicates a downward trend, in addition to informing the average annual evolution rate of the time series. When β_1 presents a value of $p > 0.05$, the trend is considered stationary.

The proportion of period change was also calculated using the following formula: $-1 + 10^{\beta 1}$, where β_1 is the coefficient of the trend equation. The R^2 was used to adjust the polynomial curves, and a significance level of 5% was considered to minimize type I error in the modeling processes.

Ethical aspects

The information extracted from the databases does not refer to the individuals, nor does it identify them. The data refer to conglomerates such as services or federative units, and they are available to the general public, constituting ecological data which do not need to be considered by the Research Ethics Committee, according to Brazilian National Health Council resolution number 466, of December 12, 2012.

Results

At the beginning of the study period, Brazil had an absolute number of in-hospital deaths of 8,844 for ischemic stroke and 5,717 for AMI, with a proportion of hospital deaths of 14.8% and 15.6%, respectively. At the end of the time series, there were 1,873 deaths from ischemic stroke and 13,405 deaths from AMI.

During the 20 years of the time series, the country presented a decline in the proportion of deaths due to ischemic stroke (Central Figure A), with an average annual reduction of 0.25% (Table 1). The percentage of change in the period was 43.76%, with an average rate of decline of 0.24% in men and 0.22% in women per year (Table 1). This decline in the proportion of deaths coincides with the total reduction in deaths from this condition in hospital services between 1998 and 2018.

For AMI, the average annual reduction was 0.17% (Table 1), reaching 11.5% of deaths in 2018 (Central Figure B). The percentage of change in the period was 32.39% for AMI, with an average annual rate of decline of 0.15% in

Table 1 – Trend modeling of the proportion of hospital deaths due to AMI and ischemic stroke in Brazil between 1998 and 2018, overall and stratified by gender

	AMI				Ischemic stroke			
	Model	Trend	p	R^2	Model	Trend	p	R^2
Brazil	-0.17x+13.93	Descending	<0.001	0.38	-0.25x+ 12.87	Descending	<0.001	0.52
Male	-0.15x+12.39	Descending	<0.001	0.39	-0.24x+12.37	Descending	<0.001	0.57
Female	-0.21x+16.36	Descending	<0.001	0.51	-0.22x+13.25	Descending	<0.001	0.35

p: probability that the null hypothesis is true or p-value; R^2: coefficient of determination; AMI: acute myocardial infarction.

men and 0.21% in women (Table 1). Unlike stroke, AMI revealed an absolute increase in hospital deaths with a reduction in the proportion of deaths.

The decline in the proportion of hospital deaths due to ischemic stroke and AMI occurred in a heterogeneous manner among Brazilian federative units (Table 2). For AMI, there was a reduction in hospital deaths in 14 federative units: Bahia, Distrito Federal, Espírito Santo, Goiás, Minas Gerais, Mato Grosso do Sul, Pará, Pernambuco, Paraná, Rio de Janeiro, Rio Grande do Norte, Rio Grande do Sul, Santa Catarina, and São Paulo. For ischemic stroke, a reduction was found in the proportion of deaths in 10 federative units: Acre, Distrito Federal, Espírito Santo, Minas Gerais, Mato Grosso do Sul, Pará, Paraná, Rio de Janeiro, Santa Catarina, and São Paulo. Such reductions are markedly expressed in the South and Southeast Regions (Central Figure C). In Maranhão, the proportion of deaths due to ischemic stroke increased, on average, 0.20% annually (Table 2).

Discussion

Few studies have analyzed hospital mortality due to cerebrovascular diseases in the Brazilian population in long time series. This study covers the entire national territory and used data from a 20-year time series. It was evident that hospital mortality due to AMI and ischemic stroke showed a decreasing trend in general and in both sexes. However, many states showed a stationary trend for at least some of the health conditions, revealing the heterogeneous character at the level of federative entities.

The decline in hospital mortality due to ischemic stroke and AMI seen in Brazil over the last 20 years is corroborated by similar events in other countries. In Italy, De Luca et al. found a reduction in hospital mortality due to AMI by an annual average of 0.23%, being similar in both genders in the 9 years analyzed.[15] In Malaysia, hospital mortality due to ischemic stroke also decreased in an accumulated proportion of 11.58%.[16] Both high- and middle-income countries have revealed mitigation of mortality due to ischemic stroke and AMI in the hospitalized population, including Brazil.[17] Seminog et al., in England, showed a trend towards a reduction in deaths from stroke when intensive care was improved in the acute event, while preventive strategies were more effective in AMI.[6]

However, we observed that there was a reduction in absolute deaths and in their proportion among those hospitalized for ischemic stroke in Brazil, while in cases of AMI, absolute deaths increased with a reduction in the proportion of deaths. Concerning ischemic stroke, the reduction in absolute deaths is probably related to the lower burden of stroke events per se due to greater control of risk factors that are more important in the pathophysiology of the disease and more effectively addressed in the country, such as systemic arterial hypertension, whereas the absolute increasing trend in AMI, despite having a direct relationship with hypertension, may have a greater relationship with risk factors that are growing in Brazil, such as obesity and diabetes.[18]

The adoption of protocols for classifying patients based on the time of onset of symptoms may have contributed to the decline in hospital mortality due to ischemic stroke and AMI in Brazil and in other countries. This action allowed faster access by part of the patients to cerebral and coronary reperfusion therapies with the use of thrombolytics, thrombectomy, and percutaneous coronary intervention, added to the implementation of specialized units for both diseases and the focus on early

Table 2 – Trend modeling of the proportion of hospital deaths due to AMI and ischemic stroke in Brazil by federative unit, between 1998 and 2018

FU	AMI				Ischemic stroke			
	Model	Trend	p	R^2	Model	Trend	p	R^2
AC	0.03x+19.99	Stationary	0.936	0	-0.49x+13.57	Descending	0.028	0.15
AL	0.11x+17.16	Stationary	0.341	0.05	-0.68x+16.77	Stationary	0.213	0.01
AM	-0.03x+9.83	Stationary	0.674	0.10	-0.28x+0.42	Stationary	0.423	0.07
AP*	0.21x+11.11	Stationary	0.086	0.06	-	-	-	-
BA	-0.25+13.68	Descending	0.001	0.38	-0.16x+14.55	Stationary	0.092	0.05
CE	-0.17x+14.34	Stationary	0.109	0.04	-0.08x+14.32	Stationary	0.843	0.10
DF	-0.18+10.10	Descending	0.024	0.16	-0.73x+13.24	Descending	<0.001	0.67
ES	-0.30x+11.70	Descending	<0.001	0.46	-0.44x+15.07	Descending	0.033	0.13
GO	-0.20+12.89	Descending	0.007	0.27	-0.39x+10.52	Stationary	0.172	0.01
MA	0.06x+14.98	Stationary	0.715	0.10	0.20x+7.14	Crescente	0.001	0.39
MG	-0.42x+12.49	Descending	<0.001	0.90	-0.34x+11.20	Descending	<0.001	0.53
MS	-0.54x+16.07	Descending	<0.001	0.50	-0.32x+15.03	Descending	0.008	0.25
MT	-0.03x+15.16	Stationary	0.874	0.11	-0.15x+10.58	Stationary	0.225	0.02
PA	-0.37x+15.06	Descending	<0.001	0.50	-0.55x+14.22	Descending	0.003	0.32
PB	-0.04x+18.60	Stationary	0.743	0.10	0.62x+12.89	Stationary	0.060	0.09
PE	-0.49x+14.80	Descending	<0.001	0.75	-0.25x+14.48	Stationary	0.559	0.09
PI	-0.06x+9.97	Stationary	0.652	0.09	0.06x+6.71	Stationary	0.474	0.07
PR	-0.37x+14.88	Descending	<0.001	0.50	-0.14x+11.67	Descending	0.037	0.13
RJ	-0.16x+15.04	Descending	<0.001	0.59	-0.16x+14.26	Descending	0.009	0.24
RN	-0.34x+14.65	Descending	<0.001	0.56	-0.05x+13.23	Stationary	0.845	0.10
RO	0.02x+14.69	Stationary	0.854	0.10	-0.07x+11.14	Stationary	0.599	0.09
RR*	0.13x+12.91	Stationary	0.437	0.07	-	-	-	-
RS	-0.35x+12.91	Descending	<0.001	0.48	-0.16x+12.38	Stationary	0.083	0.06
SC	-0.32x+12.90	Descending	<0.001	0.90	-0.31x+11.44	Descending	<0.001	0.88
SE*	0.03x+14.28	Stationary	0.815	0.10	-	-	-	-
SP	-0.32x+13.67	Descending	<0.001	0.97	-0.45x+12.38	Descending	<0.001	0.76
TO	0.14x+12.39	Stationary	0.093	0.05	-0.20x+10.95	Stationary	0.588	0.09

*FU: federative unit; p: probability of the null hypothesis being true or p-value; R^2: coefficient of determination; AMI: acute myocardial infarction. *There were no data recorded in the research base for stroke in the states of AP, RR, and SE.*

rehabilitation, in spite of the fact that many patients do not have the opportunity to receive these therapies in a timely manner.[8,9,19,20]

In this sense, Ordinance Number 664 of the Brazilian Ministry of Health established the care protocol for patients with stroke, standardizing the use of the thrombolytic alteplase and implementing the infrastructure of reference centers in the treatment of patients with this outcome,[21] which may have facilitated, in parallel, access to reperfusion therapies for AMI. In

2014, the Basic Life Support Protocol was implemented, aiming to optimize teams' response capacity in the care of acute events such as cardiorespiratory arrest,[22] and its proper management is documented as a predictor of mortality.[8]

It has been established that patients' arrival time at health services is preponderant for a better prognosis, especially with the use of reperfusion therapies in a time shorter than 4.5 hours for ischemic stroke and 12 hours for AMI (ideally, 3 hours for both).[23,24] The Mobile Urgent Care Service (*Serviço de Atendimento Móvel de Urgência* [SAMU]) was implemented in 2003, and its coverage has expanded over time. SAMU may be effective in reducing mortality from AMI and ischemic stroke related to the effect on the gap between the event and therapeutic assistance.[25,26] In 2008, this service reached 52.9% of the Brazilian population, and in 2015 it advanced to 75.92%, functioning as a mobile pre-hospital service, providing regulation and guidance, mainly in external and cardiovascular causes.[25]

Another important factor that may have influenced this drop in hospital mortality due to ischemic stroke and AMI refers to the improvement of medical procedures for diagnosis and intervention. The experimental study by Martins et al. showed that stroke patients treated in the SUS with proximal occlusion of the anterior circulation submitted to thrombectomy resulted in lower mortality than conventional treatments.[26]

With regard to gender, it was possible to identify a small difference in the decreasing trend of deaths due to ischemic stroke and AMI. Research points to higher hospital mortality due to ischemic stroke and AMI among women.[8,9,11,27,28] Women tend to present acute events at an older age,[8,29] which may lead to greater disease severity.[8,9] The multicenter study by Kytö et al. analyzed 31,689 patients with ST-segment elevation AMI in Finland and found that in-hospital mortality in women was 17.5%, much higher than that in men, 8.0%. However, after adjusting for age and comorbidities, it was found that there was no difference in mortality between genders.[29]

Brazilian regions have different in-hospital mortality rates for ischemic stroke (3.13% to 21.6%)[7-9,11,28] and AMI (4.6% to 11.2%)[10,18,29] in different studies. The North and Northeast Regions cover states that are economically less developed than those in the South and Southeast Regions, which is reflected in the resources available for state systems to expand their urgency and emergency network.[11] This situation can be better visualized with the Human Development Index (HDI) of the federative units. In the North and Northeast Regions, mostly with stationary trends, the HDI was 0.660 in Bahia, 0.665 in Sergipe, and 0.639 in Maranhão, which had a growing trend in deaths from strokes. In the states of the South and Southeast Regions, which mostly show a decreasing trend for both diseases, we observed an HDI of 0.783 in São Paulo, 0.774 in Santa Catarina, 0.761 in Rio de Janeiro, and 0.749 in Paraná.[30]

Thus, the most vulnerable regions may have reduced access to health services and products relevant to the resolution of ischemic stroke or AMI events, as well as in low- and middle-income countries.[7] This fact results in differences in the SAMU distribution, where cities the South and Southeast Regions have better structures and greater capacity for monitoring and performance of mobile services, as well as a higher density of physicians per 1000 inhabitants (national average: 2.09; averages in the North and Northeast Regions: 1.09 and 1.30, respectively).[24,31]

As an example, the study by Filgueiras Filho et al., carried out in Salvador, Bahia, revealed that 15.5% of patients with AMI presented more than 12 hours after the onset of symptoms.[31] On the other hand, Alves and Polanczyk in Rio Grande, Rio Grande do Sul, showed that approximately 65% of patients with AMI arrived within 3 hours of the onset of symptoms and 94% within 12 hours, which allowed 80.9% of patients to have reperfusion therapy implemented; this rate of reperfusion is close to that of developed countries and higher than those found nationally, between 40% and 56%.[19]

Limitations

Although the evidence presented in this research serves for possible planning of regional and national public systems, useful limitations for health management and future studies can be identified, including the restriction of data from SUS' own/affiliated services. However, pre- and in-hospital services account for more than 70% of admissions, which suggests representativeness, and the vast majority of private services are insured by the SUS.

Still, there is chronic underreporting in regions of Brazil, with a shortage of human resources and adequate training for information management. Furthermore, the study did not address all cerebrovascular conditions, such as hemorrhagic conditions, which represent a maximum of 13% of events, and causes of malnutrition, defined as the natural history of the disease and

primary/secondary preventive management, which are different.

Caution is required when comparing temporal performance between federative units. This is due to differences in the organization and funding of the emergency system and state emergencies, strongly linked to the economic power of the federative unit as well as age composition. This latter point is due to the non-standardization of outcomes by age.

Finally, the design does not allow us to directly infer individual risk reduction for vulnerable groups, with the risk of committing an ecological fallacy, in addition to not allowing us to state that the cause of death was due to the ischemic stroke or AMI, as this would only be possible with the linkage process with the death certificates, only allowing us to assess not actual mortality, but the number of deaths associated with hospitalizations due to ischemic stroke or AMI, even though deaths caused by other causes, related to the care process, correspond to a small portion compared to the total magnitude of events, making the estimate of the cause of death reliable.

Conclusion

This study evaluated the trend in hospital mortality due to ischemic stroke and AMI between 1998 to 2018, and it is possible to infer that both decreased significantly, regardless of gender. It is possible to state that there is a regionalization of the downward trend in the proportion of hospital deaths, which raises the positive effect of economic development in mitigating deaths.

These data can contribute to the management of the state and federal governments in the planning of short- and long-term actions, notably in regions of greater socioeconomic vulnerability, with possible examples being the encouragement of a healthy lifestyle through primary care services, the expansion of the provision of georeferenced emergency mobile services, financial subsidies from the federal government to health regions with socioeconomic indicators critical to underdevelopment, and the implementation of programs to improve the quality of care aimed at the health conditions that have the most financial impact on health funds such as ischemic stroke and AMI.

Author Contributions

Conception and design of the research, statistical analysis, obtaining financing: Santos JM, Martinez ABR, Lopes JM; acquisition of data and writing of the manuscript: Santos JM, Martinez ABR, Silva EJ, Santana GR, Lopes JM; analysis and interpretation of the data and critical revision of the manuscript for intellectual content: Santos JM, Martinez ABR, Silva EJ, Santana GR, Barbosa RHA, Lima DF, Lopes MR, Lopes JM.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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