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Social inequalities in the temporal trend of mortality from sickle cell disease in Brazil, 1996-2019

Desigualdades sociais na tendência temporal de mortalidade por doença falciforme no Brasil, 1996-2019

Desigualdades sociales en la tendencia temporal de la mortalidad por enfermedad de células falciformes en Brasil, 1996-2019

Karen Cordovil [1]
Wagner Tassinari [2]
Raquel de Vasconcellos Carvalhaes de Oliveira [3]
Yara Hökerberg [3]

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Abstract

Contrary to international trends, the mortality rate of sickle cell disease increased in Brazil after the implementation of the neonatal screening program, probably due to improving access to diagnosis. This study aimed to assess differences in the temporal trend of the mortality rate and median age at death from sickle cell disease in Brazil, considering implemented measures to expand diagnosis, and improve health care access in-country and in the international scenario. Time series were extracted from the Brazilian Mortality Information System from 1996 to 2019. Changes in the mortality rate and median age at death were verified via segmented regression models, which were stratified by sex, region of residence, and age. Most deaths occurred in non-white people, young adults, and the Southeast and Northeast population. Sickle cell disease mortality rate increased until 2010 (13.31%; 95%CI: 6.37; 20.70), particularly in individuals aged 30 years or more (12.78%; 95%CI: 2.98; 23.53) and in the Northeast (12.27%; 95%CI: 8.92; 15.72). Most deaths occurred in the second decade of life (3.01 deaths/million), with a 59% increase in the median age of death in Brazil, from 27.6 to 30.3 years, more pronounced in females and the North Region. The observed gain in the survival of sickle cell disease in Brazil is still much lower than in developed countries and presents regional disparities, probably due to the lack of access to health care and recent treatments, such as hydroxyurea, still restricted to hematological referral centers in Brazilian capitals.

Sickle Cell Anemia; Mortality; Interrupted Time Series Analysis; Regression Analysis

Correspondence
K. Cordovil
Programa de Epidemiologia em Saúde Pública, Escola Nacional de Saúde Pública Sergio Arouca, Fundação Oswaldo Cruz. Rua Leopoldo Bulhões 1480, Rio de Janeiro, RJ 21041-210, Brasil.
karensouz@gmail.com

[1] Escola Nacional de Saúde Pública Sergio Arouca, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil.
[2] Instituto de Ciências Exatas, Universidade Federal Rural do Rio de Janeiro, Seropédica, Brasil.
[3] Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, Brasil.

Introduction

Sickle cell disease is a type of structural hemoglobinopathy of genetic origin defined by the presence of S hemoglobin (HbS) [1]. Individuals with homozygous genotype HbSS (referred as sickle cell anemia) tend to have greater morbimortality and manifest chronic anemia, frequently accompanied by recurrent vaso-occlusive crises, pain, and multiple organ failure [1,2]. Individuals with double heterozygotes (HbSC, HbSD, HbSE, and HbStal) tend to present mild or moderate clinical forms [3,4], whereas those with sickle cell trait (HbAS) are more prone to be asymptomatic [5].

Global estimates suggest 5.7 million live births with HbS and 300,000 live births with HbSS per year, 75% of them in Sub-Saharan Africa [6]. An estimate shows approximately one case of sickle cell disease per 1,000 live births in Brazil [7], with the highest incidence in Bahia State (1:650), Rio de Janeiro (1:1,300), and Minas Gerais (1:1,383) [4,8]. From 1996 to 2016, 6,749 people died because of sickle cell disease, mostly in the Southeast (48.7%) and Northeast (31.6%) [9]. Sickle cell disease inpatients treated with hydroxyurea presented higher survival rates in public hospitals of Mato Grosso do Sul State [10]. Mean survival reached the third decade of life, with the median age at death ranging from 26.5 years in Bahia State to 30 years in São Paulo and 31.5 years in Rio de Janeiro [11], below the survival rates in the United States and England [4,12,13].

Some of those actions include universal access to neonatal screening [14], including sickle cell disease and other hemoglobinopathies in the screening, as well as pneumococcal immunization [15], prophylactic penicillin [15,16], and hydroxyurea [15], recently indicated for children older than three years [17]. Studies suggested that these measures reduce mortality in children with sickle cell disease [18,19,20,21].

Contrary to international trends [20,22], sickle cell disease mortality rate increased in Brazil after the implementation of the neonatal screening program, probably due to a greater access to diagnosis [23,24]. Most of these studies were limited to one region of Brazil, the pediatric population, or hospital samples [23,25,26].

Thus, this study aims to assess the temporal trend in mortality from sickle cell disease in a longer period (1996 to 2019) to evaluate the effect of age and regional inequalities on the annual mortality rates and the median age at death.

Methods

Time-series study using data from the Brazilian Mortality Information System (SIM) of the Ministry of Health [27]. Inclusion criteria were deaths from Brazilian residents diagnosed with sickle cell disorders, coded as D57 – Sickle cell disorders (specifically, D57.0 – HbSS disease with crisis; D57.1 – HbSS disease without crisis; D57.2 – Sickle cell/Hb-C disease; D57.3 – Sickle cell trait; D57.8 – Other sickle cell disorders) according to the 10th revision of the International Classification of Diseases (ICD-10) [28], in any field of the death certificate, from 1996 to 2019. Dead individuals aged 70 years or older (outliers) were excluded.

Outcomes were sickle cell disease mortality rates (per million inhabitants) and the median age at death. The population of mortality rates was retrieved from the census (2000 and 2010) and intercensus estimates (up to 2012) and projections (2013-2019), obtained at Brazilian Health Informatics Department (DATASUS) [29]. The exposure variables included age (years), sex, years of schooling (none, 1-7, 8-11, and 12 or more), marital status (single, married/stable union, widowhood/separated/divorced), skin color/race (white, black, brown, yellow, or indigenous), and geographic region of residence (North, Northeast, Southeast, South, or Central-West). Causes of death were classified according to genotype and ICD-10: HbSS (D57.0 – Sickle cell anemia with crisis and D57.1 – Sickle cell anemia without crisis), and other genotypes, which include HbSC (D57.2 – Sickle cell/Hb-C disease), HbAS (D57.3 – Sickle cell trait), HbS-beta (D57.4 – Sickle cell thalassemia), and D57.8 – Other sickle cell disorders [28].

Statistical analysis

To describe the deaths, absolute and relative frequencies of sociodemographic variables and the median age at death (and interquartile range) according to genotype were estimated. Line graphs to assess the temporal trends of sickle cell disease mortality rates and the median age at death were built.

To identify changes in the magnitude or direction of the temporal trend of the mortality rates and median age at death, two different segmented regression models (called joinpoint) were performed – the first using Poisson distribution with the quasi-likelihood estimator (mortality rate) and the second using Gaussian distribution with maximum likelihood estimator (median age at death) [30]. The joinpoint regression model aims to identify one or more breakpoints in presence of change in the magnitude or direction of the time series and allows jointly estimating the beta coefficients for the different segments in time [31]. Population was an offset for mortality rate, and the analysis was stratified by sex, region of residence, and age group. The median age at death was stratified by sex and region. The year was the linear predictor for both models. Then, the annual percent change (APC) defined by a constant percent variation per year during a time range in comparison to the previous year was estimated [32]. Also, it was estimated the average annual percent change (AAPC), in order to summarize the trend over the study period 1996 to 2019, which allows comparisons among groups [32]. APC and AAPC statistical significance were considered when the 95% confidence interval (95%CI) did not include zero [32]. Comparisons among groups were valued when there was a difference of five or more percentage points in the AAPC estimates or an absence of overlap between their 95%CI.

The segmented packages of the R software, version 3.5.1 (http://www.r-project.org), were used for statistical analyses [30].

Results

Of 10,276 deaths caused by sickle cell disease in Brazil from 1996 to 2019, 468 were excluded due to other causes of death unrelated to sickle cell disease (ICD-10: D-05.7 – Other carcinoma in situ of breast) or individuals aged ≥ 70 years. Thus, the final sample totaled 9,808 deaths from sickle cell disease, 9,499 (96.8%) of which were HbSS, and 309 (3.2%) included other genotypes, such as HbSC (n = 52), HbAS (n = 39), HbS-beta (n = 1), and other sickle cell disorders (n = 217).

HbSS deaths were frequent in adults aged 20-39 years (43.3%), up to 7 years of schooling (59.2%), single (73.8%), brown skin color (53.4%), who lived in the Southeast (43.7%) and Northeast (31.9%) of Brazil. More than 40% of deaths from other genotypes occurred at the extremes of age: 21% in children and 23% in individuals 50 years or older (Table 1). The median age at death ranged from 20.5 in the North to 30.4 years in the South (Table 2).

From 2006 to 2019, the average mortality rate in Brazil was 2.2 deaths of sickle cell disease per one million inhabitants, highest values were found for individuals aged 20-29 years and those who lived in the South, the lowest in the North (Table 3). In the study period, there was an average annual increase of 4.6% in the mortality rate in Brazil due to sickle cell disease (AAPC = 4.58, 95%CI: 3.73; 5.43). The APC showed a 13% annual increase from 1996 to 2000 and subsequently reduced to 5% until 2010 (Table 3, Figure 1a). The trends were similar for both sexes ($AAPC_{Females}$ = 4.68, 95%CI: 3.72; 5.65; $AAPC_{Males}$ = 4.45, 95%CI: 3.25; 5.67) (Table 3, Figure 1b). All age groups and Brazilian regions showed an increase in the mortality rate (Figures 1c and 1d), with higher average annual percentage changes in individuals aged 30 years or more ($AAPC_{30}$ or + = 4.76, 95%CI: 3.47; 6.07) and those who lived in the North ($AAPC_{N}$ = 5.76, 95%CI: 4.32; 7.22) and Northeast ($AAPC_{NE}$ = 6.53, 95%CI: 5.45; 7.62) (Table 3). The latter presented a 12.3% annual increase in the mortality rate until 2006, the only region where it lasted until 2019, but with a lesser variation. In individuals aged 30 years or more, the mortality rate decreased after 2015 (Table 3, Figure 1d).

Table 1

Sociodemographic characteristics of the deaths (N = 9,808) due to sickle cell disease. Brazil, 1996-2019.

Characteristics	HbSS		Others *		Total
	n	%	n	%	n
Age groups (years)					
< 10	1,611	17.0	65	21.0	1,676
10-19	1,306	13.7	31	10.0	1,337
20-29	2,296	24.2	54	17.5	2,350
30-39	1,810	19.1	46	14.9	1,856
40-49	1,310	13.8	42	13.6	1,352
50 or older	1,166	12.3	71	23.0	1,237
Total	9,499	100.0	309	100.0	9,808
Sex					
Female	4,758	50.1	140	45.3	4,898
Male	4,739	49.9	169	54.7	4,908
Total	9,497	100.0	309	100.0	9,806
Years of schooling					
None	699	11.6	33	16.7	732
1-7	2,864	47.6	79	39.9	2,943
8-11	1,866	31.0	64	32.3	1,930
≥ 12	588	9.8	22	11.1	610
Total	6,017	100.0	198	100.0	6,215
Marital status					
Single	5,784	73.8	149	59.8	5,933
Married or stable union	1,692	21.6	82	32.9	1,774
Divorced, separated, or widowhood	361	4.6	18	7.2	379
Total	7,837	100.0	249	100.0	8,086
Race/Skin color					
Brown	1,027	53.4	138	50.7	1,165
Black	466	24.2	66	24.3	532
White	425	22.1	65	23.9	490
Yellow or indigenous	7	0.4	3	1.1	10
Total	1,925	100.0	272	100	2,197
Region of residence					
North	502	5.3	26	8.4	528
Northeast	3,026	31.9	95	30.7	3,121
Southeast	4,154	43.7	122	39.5	4,276
South	934	9.8	29	9.4	963
Central-West	883	9.3	37	12.0	920
Total	9,499	100.0	309	100.0	9,044

HbSS: D57.0 – Sickle cell anemia with crisis and D57.1 – Sickle cell anemia without crisis, 10th revision of the International Classification of Diseases (ICD-10).

* ICD-10: D57.2, D57.3, and D57.8.

Table 2

Median age at death (N = 9,808) due to sickle cell disease. Brazil, 1996-2019.

Characteristics	N	%	Median	Interquartile range	Minimum-Maximum
Total sample	9,808	100.0	26.8	15.8-40.1	0.0-68.9
Genotype					
HbSS	9,499	96.8	26.8	15.8-40.1	0.0-68.9
Others *	309	3.2	29.6	14.3-46.5	0.0-68.0
Sex					
Female	4,898	49.9	26.8	15.8-40.1	0.0-68.9
Male	4,908	50.0	25.5	14.4-37.7	0.0-68.9
Region of residence					
North	528	5.4	20.5	7.7-32.3	0.0-68.1
Northeast	3,121	31.8	24.4	12.0-37.8	0.0-68.8
Southeast	4,768	48.6	28.7	18.5-41.7	0.0-68.9
South	422	4.3	30.4	19.9-41.0	0.0-68.8
Central-West	969	9.9	27.2	16.2-40.2	0.0-68.9

HbSS: D57.0 – Sickle cell anemia with crisis and D57.1 – Sickle cell anemia without crisis, 10th revision of the International Classification of Diseases (ICD-10).
* ICD-10: D57.2, D57.3, and D57.8.

Table 3

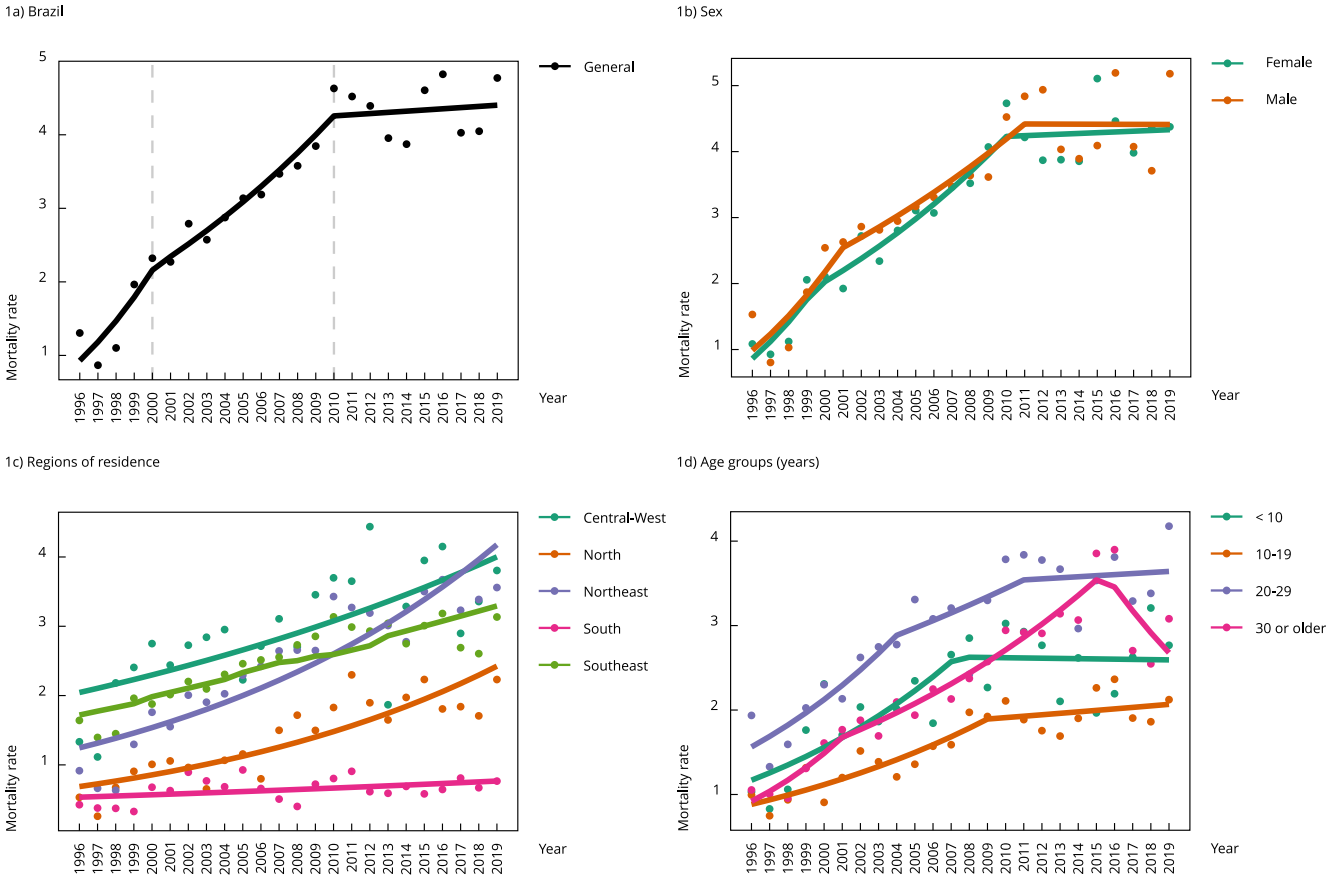
Annual percent change (APC) and average annual percent change (AAPC) of mortality rate (*10^6) and the median age (MA) at death of sickle cell disease. Brazil, 1996-2019.

Characteristics	AMR (per million)					MA (in years)				
	AMR	Period	APC	95%CI	AAPC	MA	Period	APC	95%CI	AAPC
Brazil	2.20	1996-2000	13.13	6.20; 20.52	4.58	26.8	1996-1998	-69.96	-92.46; 19.77	23.73
		2000-2010	5.15	3.40; 6.94			1998-2016	59.13	44.44; 75.30	
		2010-2019	0.30	-1.43; 2.07			2016-2019	-24.16	-68.37; 81.87	
Sex										
Female	2.15	1996-1999	13.98	3.41; 25.63	4.68	26.8	1996-2005	25.72	-8.43; 72.59	34.34
		1999-2010	5.62	3.70; 7.57			2005-2010	93.17	21.47; 207.20	
		2010-2019	0.21	-1.34; 1.79			2010-2019	9.23	-25.21; 59.53	
Male	2.23	1996-2001	12.45	2.76; 23.05	4.45	25.5	1996-2000	-9.74	-71.20; 182.90	32.36
		2001-2011	4.33	1.86; 6.86			2000-2019	43.29	29.78; 58.21	
		2011-2019	-0.02	-2.47; 2.50						
Region										
North	1.46	1996-2011	9.04	6.19; 11.96	5.76	20.5	1996-1999	-99.64	-100.00; -55.27	-11.00
		2011-2019	-0.12	-4.01; 3.93			1999-2019	103.20	33.82; 208.50	
Northeast	2.50	1996-2006	12.27	8.92; 15.72	6.53	24.4	1996-2001	-16.10	-73.38; 164.40	37.08
		2006-2019	2.16	0.53; 3.81			2001-2019	61.12	29.54; 100.40	
Southeast	2.52	1996-2010	3.66	2.67; 4.66	1.61	28.7	1996-2003	21.99	-26.73; 103.10	48.94
		2010-2019	-1.49	-2.80; -0.15			2003-2019	62.52	42.21; 85.75	
South	6.48	1996-2002	13.83	1.21; 28.02	3.08	30.4	1996-2009	107.80	5.64; 308.80	59.20
		2002-2019	-0.46	-2.24; 1.34			2009-2019	12.59	-63.39; 246.30	
Central-West	2.99	1996-2007	5.64	1.76; 9.67	3.20	27.4	1996-2008	74.13	-22.40; 290.70	28.17
		2007-2019	0.83	-2.22; 3.97			2008-2019	12.08	-15.63; 48.90	

95%CI: 95% confidence interval; AMR: average mortality rate.

Figure 1

Trends of the mortality rate (per 1 million inhabitants) of sickle cell disease, 1996-2019.



From 1998 to 2019, the median age at death increased annually by 24% in Brazil (AAPC = 23.73, 95%CI: 11.36; 37.47) (Table 3, Figure 2a). Although the AAPC was similar for both sexes ($AAPC_{Females}$ = 34.34, 95%CI: 22.15; 47.75; $AAPC_{Males}$ = 32.36, 95%CI: 19.23; 46.45), the period of the upward trend differed. Females had an annual increase of 93% from 2005 to 2010, and males had an annual increase of 43% from 2000 to 2019 (Table 3, Figure 2b). The South had the best survival improvement with an average annual increase of 59% ($AAPC_S$ = 59.20, 95%CI: 12.81; 124.67) in the median age at death, markedly until 2009 (Table 3, Figure 2c).

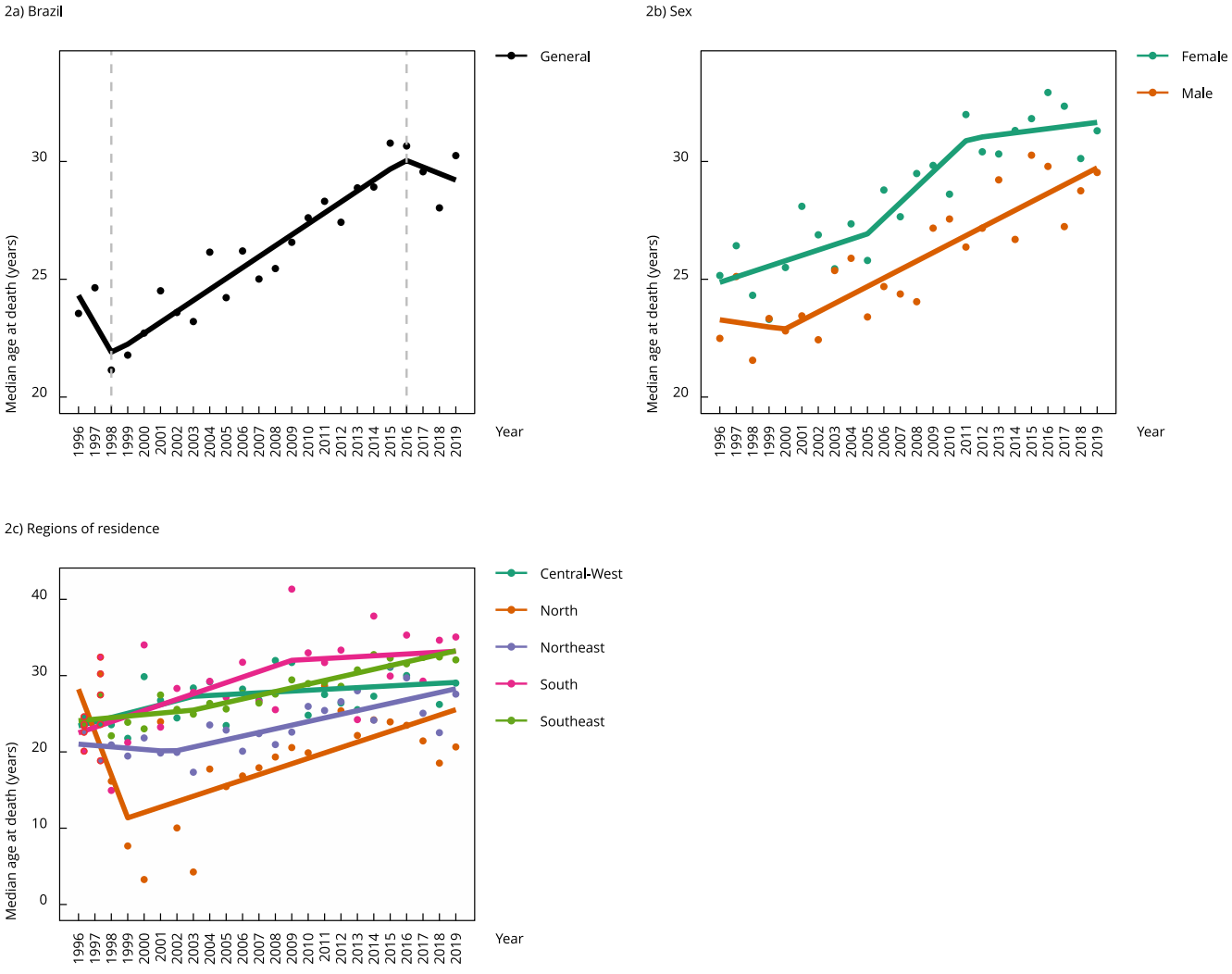
Discussion

The study results showed an upward trend in the mortality rate from sickle cell disease in Brazil until 2010, accentuated in the Northern Brazil and those aged 30 or more years (1996 to 2019). Most deaths from sickle cell disease occurred in the second decade of life and the median age of death in Brazil increased by 24% from 1998 to 2019, more pronounced in the South and Southeast.

The upward trend in sickle cell disease mortality in Brazil in both sexes, all age groups, and regions may reflect the improvement in the quality of the mortality information system, particularly in the first decade of 2000 [33]. Previous Brazilian studies suggest that neonatal screening for sickle cell dis-

Figure 2

Trends in median age at death from sickle cell disease, 1996-2019.



ease did not improve its access and quality of care and, consequently, has had no effect on mortality from this disease [19,24,34,35,36]. On the other hand, international studies suggest a downward trend in the mortality rate, particularly among children under five years of age [24,37].

A study in the United States identified a reduction in the mortality rate of children and adolescents from 1983 to 2002, more pronounced among children under three years of age (68% reduction, 95%CI: 58; 75) and progressively lower in children aged 4-14 years [22]. Although the authors had attributed this reduction to the universal access to the newborn screening programs for hemoglobinopathies and the prophylactic penicillin, only one retrospective cohort study conducted in Jamaica provided robust evidence on the performance of newborn screening, followed by measures to prevent infection and orient parents about the disease [38,39].

From 1990 to 2015, general mortality rate decreased in all regions and age groups in Brazil, and higher decreases occurred among children under 15 years of age [40,41]. However, our results suggested

that individuals with sickle cell disease did not benefit from poverty reduction, improvement in access to health services, and quality of life observed in Brazil [42].

The National Neonatal Screening Program in Brazil encompasses six diseases, including sickle cell disease and other hemoglobinopathies that were first screened in 2001 [43]. In 2005, the coverage rate reached 80%, but only in 2013, a universal access to screening for sickle cell disease was implemented in all regions of the country [44]. However, access to these tests in different regions of Brazil was unequal. São Paulo, Minas Gerais, and Rio de Janeiro were the first states to universalize access to the diagnosis of sickle cell disease, whereas the states in the North and Northeast regions were the last [44]. This disparity might explain the higher increase in the mortality due to sickle cell disease in the North and Northeast compared to the Southeast.

After 2010, the mortality rate of sickle cell disease stabilized in Brazil, except in the Southeast, which presented a slight decrease. The latter might relate to the approval and access regulation of hydroxyurea in the public health system [15,45,46,47]. Evidence suggests that hydroxyurea has improved hematological parameters and reduced hospitalizations and deaths [48,49]. Despite efforts to expand access and improve the quality of care, the treatment of sickle cell disease is still restricted to blood centers in Brazilian capitals.

From 1998 to 2016, an increase of 9.6 years occurred in the median age at death from sickle cell disease in Brazil, reaching 31 years. A multicenter study carried out in the United States from 1978 to 1998 showed a median of 48 years for females and 42 years for males with the HBSS genotype and 68 and 60 years for females and males with the HbSC genotype [50,51]. Another study revealed that the median age at death increased from 28 to 46 years from 1979 to 2017 [52], showing Brazil's disadvantage compared to developed countries like the United States and the United Kingdom [4,52].

Brazil has more than 100,000 cases of sickle cell disease [7,51], showing an incidence of approximately 1:1,000 live births [7], comparatively lower than in the United States (1:360) [4]. The worse indicators in Brazil are probably related to lack of treatment access and restricted hematology services, as well as a delay in the use of new technologies in the Brazilian Unified National Health System (SUS), such as hydroxyurea, recommended for treatment since 2002, but freely available only in 2010.

One of the study strengths is the universal recording of the SIM, a tool for health surveillance in Brazil [53] that may allow the generalizability of results. The trend analysis on mortality by the Joinpoint regression covered more than 20 years, including the period before and after implementing diagnosis and treatment for sickle cell disease in Brazil and explored demographic and regional heterogeneities. Moreover, the joinpoint regression model is a user-friendly statistical technique with simple interpretation [30].

Although previous studies have assessed mortality from sickle cell disease in Brazil, most have used hospital samples in referral centers [11,54,55,56]. Compared to two recent studies [9,56], our study covered a broader period, assessing the time before and after the adoption of policies targeting sickle cell disease, relevant to describe their effect and potential inequalities across sex, ages, and regions of Brazil.

Limitations include potential classification bias related to the cause of deaths, in the population used to estimate mortality rate as well as to the ecological design. The SIM is subject to classification errors in the cause of death, which was minimized by considering the recording of sickle cell disease in any field on the death certificate. Despite being used in previous studies [24,57], the general population incorrectly estimated individuals at risk of death from sickle cell disease. Studies in the United States and Europe use the Afro-descendant population, mostly affected by this genetic hemoglobinopathy [4]. Alternatively, one study estimated the at-risk population using population-based records of sickle cell disease surveillance [57]. However, Brazil lacks more accurate estimates of the population affected by this hemoglobinopathy and is hampered by miscegenation, heterogeneity in the coverage of screening programs, and potential disparities in the incidence of this disease across country regions. Moreover, since this was an ecological study, it does not allow inferring the effects of the specific public health actions on mortality of sickle cell disease [58].

Conclusions

In conclusion, our study showed an increase in the mortality rate and that the gain observed in survival with sickle cell disease in Brazil was lower than in developed countries, particularly for patients who live in the North or Northeast regions. Thus, government measures to expand the diagnosis and treatment of sickle cell disease in Brazil must be improved and put in force in a decentralized manner. These findings can contribute to the management of resources for these patients of the SUS. Future studies may assess hospitalizations for sickle cell disease to investigate factors related to the quality of hospital care for individuals with this hemoglobinopathy.

Contributors

K. Cordovil contributed to the study conception and design, data analysis and interpretation, writing, and critical review; approved the final version to be published; and is responsible for all aspects of the paper, ensuring the accuracy and completeness of any part of the study. W. Tassinari contributed to the study conception and design, data analysis and interpretation, writing, and critical review; approved the final version to be published; and is responsible for all aspects of the paper, ensuring the accuracy and completeness of any part of the study. R. V. C. Oliveira contributed to the study conception and design, data analysis and interpretation, writing, and critical review; approved the final version to be published; and is responsible for all aspects of the paper, ensuring the accuracy and completeness of any part of the study. Y. Hökerberg contributed to the study conception and design, data analysis and interpretation, writing, and critical review; approved the final version to be published; and is responsible for all aspects of the paper, ensuring the accuracy and completeness of any part of the study.

Additional information

ORCID: Karen Cordovil (0000-0003-1573-7796); Wagner Tassinari (0000-0002-3799-1261); Raquel de Vasconcellos Carvalhaes de Oliveira (0000-0002-8293-8603); Yara Hökerberg (0000-0003-1573-7796).

Conflict of interest

The authors declare no potential conflict of interest, including political and/or financial interests associated with patents or ownership, provision of materials and/or inputs, and equipment used in the study by the manufacturers.

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Resumo

Ao contrário dos estudos internacionais, houve um aumento da taxa de mortalidade por doença falciforme no Brasil após a implantação do programa de triagem neonatal, provavelmente devido à melhoria do acesso ao diagnóstico. O objetivo deste estudo foi avaliar as diferenças na tendência temporal da taxa de mortalidade por doença falciforme e idade mediana ao morrer no Brasil, considerando as medidas implementadas para ampliar o diagnóstico e melhorar o acesso à saúde no país e no cenário internacional. As séries temporais foram extraídas do Sistema de Informação sobre Mortalidade de 1996 a 2019. Mudanças na magnitude da taxa de mortalidade e na idade mediana ao morrer foram verificadas via modelos de regressão segmentada, estratificados por sexo, região de residência e idade. A maioria dos óbitos ocorreu entre jovens, pretos ou pardos, e habitantes das regiões Sudeste e Nordeste. Houve um aumento da taxa de mortalidade por doença falciforme até 2010 (13,31%; IC95%: 6,37; 20,70), especialmente em indivíduos com 30 anos ou mais (12,78%; IC95%: 2,98; 23,53) e habitantes do Nordeste (12,27%; IC95%: 8,92; 15,72). A maioria dos óbitos ocorreu durante a segunda década de vida (3,01 óbitos/milhão), com um aumento de 59% na idade mediana ao morrer no Brasil (de 27,6 para 30,3 anos), mais acentuada entre mulheres e na Região Norte. O aumento observado na sobrevivência da doença falciforme no Brasil ainda é muito menor do que em países desenvolvidos e com disparidades regionais, provavelmente pela falta de acesso aos serviços de saúde e aos tratamentos recentes, como a hidroxiureia, que ainda é restrita aos centros de referência hematológicos das capitais brasileiras.

Anemia Falciforme; Mortalidade; Análise de Séries Temporais Interrompida; Análise de Regressão

Resumen

A diferencia de los estudios internacionales, en Brasil se produjo un aumento de la tasa de mortalidad por enfermedad de células falciformes tras la implantación del programa de tamizaje neonatal, probablemente debido a la mejora del acceso al diagnóstico. El objetivo del estudio es determinar las diferencias en la tendencia temporal de la tasa de mortalidad y la edad media de muerte por enfermedad de células falciformes en Brasil, teniendo en cuenta las medidas implementadas para ampliar el diagnóstico y mejorar el acceso a la atención sanitaria en el país y en el escenario internacional. Las series temporales fueron extraídas del Sistema de Información sobre de Mortalidad de 1996 a 2019. Los cambios en la magnitud de la tasa de mortalidad y la edad media de la muerte se identificaron con modelos de regresión segmentados, estratificados por sexo, región de residencia y edad. La mayoría de las muertes ocurrieron en personas de color, adultos jóvenes y los habitantes del sureste y noreste. Hubo un aumento de la tasa de mortalidad por enfermedad de células falciformes hasta 2010 (13,31%; IC95%: 6,37; 20,70), sobre todo en individuos de 30 años o más (12,78%; IC95%: 2,98; 23,53) y en el Noreste (12,27%; IC95%: 8,92; 15,72). La mayoría de las muertes ocurrió en la segunda década de la vida (3,01 muertes/millón), con un aumento del 59% en la edad media de muerte en Brasil, de 27,6 a 30,3 años, más pronunciado en las mujeres y en el Norte. La ganancia observada en la supervivencia de la enfermedad de células falciformes en Brasil es todavía muy inferior a la de los países desarrollados y con disparidades regionales, probablemente debido a la falta de acceso a la asistencia sanitaria y a los tratamientos recientes, como la hidroxiurea, todavía restringidos a los centros de referencia hematológica de las capitales brasileñas.

Anemia de Células Falciformes; Mortalidad; Análisis de Series de Tiempo Interrumpido; Análisis de Regresión

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