The mapping of ovarian cancer mortality trends in Brazil

O mapeamento das tendências de mortalidade por câncer de ovário no Brasil

El mapeo de las tendencias de la mortalidad por cáncer de ovario en Brasil

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Abstract

Ovarian cancer is the eighth cause of death by cancer in women worldwide. The objective of this study was to analyze trends in the Brazilian ovarian cancer mortality and the relation to age, schooling, and race. Data was collected in the Brazilian Mortality Information System (SIM), from 2006 to 2016. The polynomial regression model was used for the trends analysis, a significant trend was considered when the estimated model obtained a p-value <0.05. Ovarian Cancer caused 34,003 deaths in Brazilian women in this period, the mortality rate (MR) was 0.46 per 100.000 women aged less than 40; 4.2 in women aged between 40 – 59; 12.2 in women aged between 60 – 79 and 19.4 in women 80 years old or more. About Race, 65% were White, others were declared as Black, Asian, Mixed-race, or Indigenous. Only 26% had 8 years or more of schooling. Mortality rates from ovarian cancer seemed to be rising in Brazil, the major increase happened in the South, the Southeast, and the Middle-West Regions. Women aged between 40 to 59 had the most significant increase. Politics are needed to facilitate the Brazilian population's access to health services, consequently minimizing the time to diagnose and start the treatment. Research about mortality rates could help health workers identify gaps in knowledge and consequently decrease the magnitude of the disease.

Keywords: Ovarian cancer; Mortality; Trend.

Resumo

O câncer de ovário é a oitava causa de morte por câncer em mulheres em todo o mundo. O objetivo deste estudo foi analisar as tendências de mortalidade por câncer de ovário no Brasil

e sua relação com idade, escolaridade e raça. Os dados foram coletados no Sistema de Informações sobre Mortalidade (SIM), no período de 2006 a 2016. Para a análise de tendências foi utilizado o modelo de regressão polinomial, uma tendência significativa foi considerada quando o modelo estimado obteve um valor de p <0,05. O câncer de ovário causou 34.003 óbitos em mulheres brasileiras nesse período; a taxa de mortalidade (RM) foi de 0,46 por 100.000 mulheres com menos de 40 anos; 4,2 em mulheres com idade entre 40 - 59; 12,2 em mulheres com idade entre 60 - 79 e 19,4 em mulheres com 80 anos ou mais. Sobre a raça, 65% eram brancos, outros foram declarados negros, asiáticos, pardos ou indígenas. Apenas 26% tinham 8 anos ou mais de estudo. As taxas de mortalidade por câncer de ovário pareciam estar aumentando no Brasil, o maior aumento ocorreu nas regiões Sul, Sudeste e Centro-Oeste. Mulheres de 40 a 59 anos tiveram o aumento mais significativo. Políticas são necessárias para facilitar o acesso da população brasileira aos serviços de saúde, consequentemente minimizando o tempo de diagnóstico e início do tratamento. Pesquisas sobre as taxas de mortalidade podem auxiliar os profissionais de saúde a identificar lacunas no conhecimento e, consequentemente, diminuir a magnitude da doença.

Palavras-chave: Câncer de ovário; Mortalidade; Tendência.

Resumen

El cáncer de ovario es la octava causa líder de muerte por neoplasias en mujeres alrededor del mundo. El objetivo de este estudio fue analizar las tendencias de la mortalidad por cáncer de ovario en Brasil y su relación con edad, educación y raza. Los datos fueron recolectados del Sistema Brasileño de Información de Mortalidad (SIM), entre 2006 y 2016. Para el análisis de las tendencias se utilizó el modelo de regresión polinomial, para el nivel de significancia se consideró un valor de p <0, 05. El cáncer de ovario fue responsable por 34.003 muertes entre las mujeres brasileñas en el período; la tasa de mortalidad (RM) fue de 0,46 por cada 100.000 mujeres menores de 40 años; 4,2 en mujeres entre 40 y 59 años; 12,2 en mujeres entre 60 y 79 años y 19,4 en mujeres con 80 años o más. En cuanto a la raza, el 65% de la muestra eran mujeres blancas y las demás se declararon como negras, asiáticas, mestizas o indígenas. Solo el 26% tenía 8 años o más de estudio. Las tasas de mortalidad por cáncer de ovario parecieron estar en ascenso en Brasil. En las regiones sur, sudeste y medio-oeste presentaron ascensos más expresivos. Entre las mujeres de 40 hasta 59 años, el aumento fue todavía más significativo. Políticas públicas se demuestran necesarias para fomentar el acceso de la población a los centros de salud, disminuyendo, a su vez, el tiempo de diagnóstico y el comienzo del tratamiento. Las investigaciones sobre las tasas de mortalidad pueden ayudar a

los profesionales de la salud a identificar lagunas de conocimiento y consecuentemente, disminuir la magnitud de la enfermedad.

Palabras clave: Cáncer de ovario; Mortalidad; Tendencia.

1. Introduction

Cancer is the cause of one out of six deaths worldwide. More than 18 million people received this diagnosis every year; around 24 million are expected in 2030. Ovarian cancer is a silent disease with low prevalence but high mortality. A better prognosis can be achieved by early diagnosis; nevertheless, frequent metastasis is already present at this point. The estimated world mortality rate from ovarian cancer was 3.9 per 100,000 in 2012. In the same year, in the US, this malignancy was responsible for 14,080 deaths. In Europe, the incidence was 17.1, and the mortality rate was 11.1. (IARC, 2019; Lowry and Lee, 2017; Ervik et al., 2016)

In Brazil, the ovarian neoplasm is the eighth cause of death by cancer. Approximately 6,150 new cases were estimated between 2018 and 2019, and the estimated incidence is 5.79 per 100,000 women. Three thousand seven hundred fifty deaths were registered by ovarian cancer in 2016 (Saúde, 2017). Due to the high mortality rate after five years from the diagnosis, efforts are necessary to achieve it sooner. Exams already used for screening did not reduce mortality, so there is no definitive screening test; hence, acknowledging related factors is essential to propose new strategies for screening it. (Henderson et al., 2018)

Sharifian et al. (2014) mentioned that mortality rates and information about deaths could help determine priorities to control the disease. On the other hand, indicators as incidence and survivorship could help control the screening program's effects.

Despite being long-discussed, there are only a few studies about ovarian cancer mortality trends. One of these showed a slight increase in mortality trends by ovarian cancer among Irian women; it was higher in the elderly. The authors suggest attention to groups of high risk and programs that can decrease rates of this disease. (Sharifian et al.,2014).

Park, Ruterbush, and Cote (2017) analyzed the trend of epithelial ovarian cancer incidence and survival rates by histopathological subtypes and race over the last decade. They could verify a decrease in incidence. However, the survival rates are unpleasant, even more among the US black and Hispanic women. Another trend study showed that the incidence is variable every year, and the survival has been improved after new treatments. Even though quantifying the magnitude of survival is still a challenge. (Wright et al. 2016) The

environment suffers influence by the used space; therefore, the spatial distribution and analysis are essential methods in epidemiologic studies to identify risk areas and understand the disease behavior, enhancing earlier diagnosis.

So far, ovarian cancer mortality trends studies from Brazil with all aged women are unknown. Thus, the study's objective was to analyze Brazilian ovarian cancer mortality trends and the relation to age, schooling, race, and other factors.

2. Methods

It is an exploratory study, following the STROBE guidelines, of a time series of deaths from ovarian cancer listed in the Mortality Information System (SIM) of women living in Brazil, from 2006 to 2016.

Brazil is the largest country in South America, as well as the highest population density. It is 8 million km² divided into five regions, 27 states, and 5.561 towns and cities. According to the Brazilian Institute of Geography and Statistics data, in 2015, the population was over 208 million, with 51.45% women.

The cause of deaths was registered in the Mortality Information System according to the rules of the tenth revision of the International Classification of Diseases and Related Health Problems Statistics (ICD 10). C56 was the code for ovarian cancer. The mortality ratio was determined between the number of deaths from ovarian cancer in women and the female population in that year and location, obtained from the demographic information Census 2000, 2010, and estimates, multiplied by 100,000. Files with the mortality data were extracted from the Department of the Unified Health System (DATASUS). The female ovarian cancer mortality rates were further analyzed based on age groups: less than 40; 40 - 59; 60-79 and more than 80. Schooling was divided into less than eight years or more than eight years. The races were divided as whites and non-whites.

For the trend analysis, a polynomial regression model was used. The ovarian cancer rates were considered dependent variables (y) and the study years as an independent variable (x). The variable "year" was transformed into a year-centralized variable (x-2011).

The polynomial regression models were tested as linear ($y = \beta 0 + \beta 1 x 1$), quadratic ($y = \beta 0 + \beta 1 x 1 + \beta 2 x 2$), and cubic ($y = \beta 0 + \beta 1 x 1 + \beta 2 x 2 + \beta 3 x 3$), considering the significant trend that the estimated model obtained a p-value < 0.05. To choose the best model, analysis of scatter-plots, the value of the coefficient of determination (R^2), and residual analysis (real homoscedasticity assumption) were considered. When all of the criteria were significant for

more than one model, and thof determination coefficient was similar, the simplest model was chosen. Analyses were performed using R software.

Brazil's cartographic basis is publicly available online in shape-file (SHP) at the Brazilian Institute of Geography and Statistics (IBGE) website. Choropleth maps were built to demonstrate the timeline distribution of the general mortality rates of ovarian cancer by age group among the Brazilian States. All of the figures were constructed using QGIS version 2.8. The spatial distribution of the ovarian cancer rates was presented in intervals. The maps were depicted in red scales, setting the lighter colors for lower rates and darker colors for higher rates.
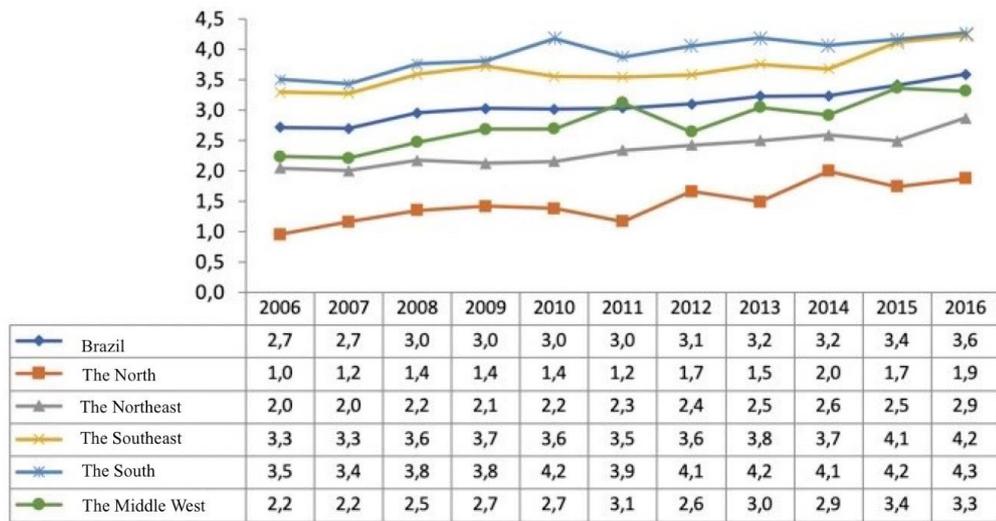
The data were obtained from public databases (http://datasus.saude.gov.br/) and follow the rules for research involving humans in the resolution 466/202 from the National Health Council.

3. Results

Ovarian Cancer was responsible for 34,003 deaths in Brazilian women between 2006 and 2016. The mortality rate (MR) was 0.46 per 100,000 women aged less than 40; 4.2 in women aged between 40 – 59; 12.2 in women aged between 60 – 79 and 19.4 in women 80 years old or more. The race was declared in 94.5% of all notifications, 65% were White, others were declared as Black, Asian, Mixed-race, or Indigenous. Data of schooling was found in ¼ of notifications, and then only 26% had more than eight years of schooling.

The mortality rate from ovarian cancer in Brazil was 2.7 in 2006 and raised to 3.6 in 2016. The Middle-West Region had the highest increase, from 2.2 in 2006 to 3.3 in 2016. On the other hand, the South Region showed higher rates, 3.5 to 4.3, respectively (Figure 1). Trend analysis did not show an increase in the middle West Region, as well as other Regions. (Table1).

Figure 1. Distribution of trend models of ovarian cancer mortality coefficients, from Brazil and Regions, between 2006–2016.

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Brazil	2,7	2,7	3,0	3,0	3,0	3,0	3,1	3,2	3,2	3,4	3,6
The North	1,0	1,2	1,4	1,4	1,4	1,2	1,7	1,5	2,0	1,7	1,9
The Northeast	2,0	2,0	2,2	2,1	2,2	2,3	2,4	2,5	2,6	2,5	2,9
The Southeast	3,3	3,3	3,6	3,7	3,6	3,5	3,6	3,8	3,7	4,1	4,2
The South	3,5	3,4	3,8	3,8	4,2	3,9	4,1	4,2	4,1	4,2	4,3
The Middle West	2,2	2,2	2,5	2,7	2,7	3,1	2,6	3,0	2,9	3,4	3,3

Source: Authors.

Table 1. Coefficients of ovarian cancer mortality trends by age. Brazil and Regions, 2006 -2016.

| Age (years)	North Region Model	R^2	p	T	Northeast Region Model	R^2	p	T	Southeast Region Model	R^2	p	T
< 40	Y= 0.38+0.02x+0.001x²	1.11	0.07	—	Y= 0.39-0.001x+0.005x²	0.19	0.77	—	Y= 0.45-0.02x-0.001x²+0.001x³	0.62	0.34	—
40-59	Y= 3.63+0.11x-0.01x²-0.001x³	0.94	0.14	—	Y= 4.23+0.08x	0.73	<0.01	↑	Y= 4.96+0.02x+0.0099x²	0.69	0.29	—
60-79	Y= 8.62+0.28x+0.01x²	0.98	0.12	—	Y= 11.02+0.15x+0.004x²-0.001x³	0.96	0.13	—	Y=15.31-0.07x+0.02x²	0.66	0.31	—
>80	Y= 18.79+0.96x-0.14x²	1.05	0.09	—	Y= 18.22+0.31x-0.12x²	0.96	0.13	—	Y= 23.65-0.29x+0.02x²	0.47	0.14	—
Total	Y= 1.47+0,08x	0.76	< 0.01	↑	Y= 2.33+0.07x	0.89	<0.01	↑	Y= 3.66+0.07x	0.74	<0.01	↑

Age	South Region Model	R^2	p	T	Middle West Region Model	R^2	p	T	Brazil Model	R^2	p	T
< 40	Y= 0.47-0.01x-0.01x²	0.40	0.03	↓	Y= 0.48+0.06x+0.01x²-0.01x³	0.13	0.26	—	Y= 0.44+ 0.002x	0.70	0.28	—
40-59	Y= 5.28+0.10x-0.01x²-0.003x³	0.88	0.17	—	Y= 4.95+0.07x-0.02x²	0.80	0.21	—	Y= 4.74+0.04x+0.001x²	1.41	<0.01	↑
60-79	Y= 16.87-0.24x-0.001x²+0.01x³	0.26	0.69	—	Y= 14.81+0.19x+0.005x²	0.81	0.21	—	Y= 14.13+0.02x+0.01x²	0.34	0.61	—
>80	Y= 29.03-0.68x-0.20x²	1.12	0.07	—	Y= 26.15+0.06x-0.23x²	0.09	0.89	—	Y= 23.08-0.10x-0.07x²	0.44	0.51	—
Total	Y= 3.93+0.07x	0.77	<0.01	↑	Y= 0.43+0.002x+0.01x²	0.12	0.28	—	Y= 3.09+0.07x	0.92	<0.01	↑

Legend: T=Trend; ─ Constant; ↑ Increasing; ↓ Decreasing. Source: Authors.

A significant increasing trend was observed among women from 40 – 59 years, over the country, but even more in the Northeast Region. A significant decreasing trend was observed among women aged less than 40 in the South Region.

Dispersion graphs present the relevant results extracted from Table 1. The variable Time (years) is a positive determinant to the increasingly significant trends and negative to the South Region in women under 40 years (Figure 2).

Figure 2. Dispersion graphs of the variable with a significant trend to increasing or decreasing of ovarian cancer mortality coefficients. Brazil and Regions, 2006 – 2016.
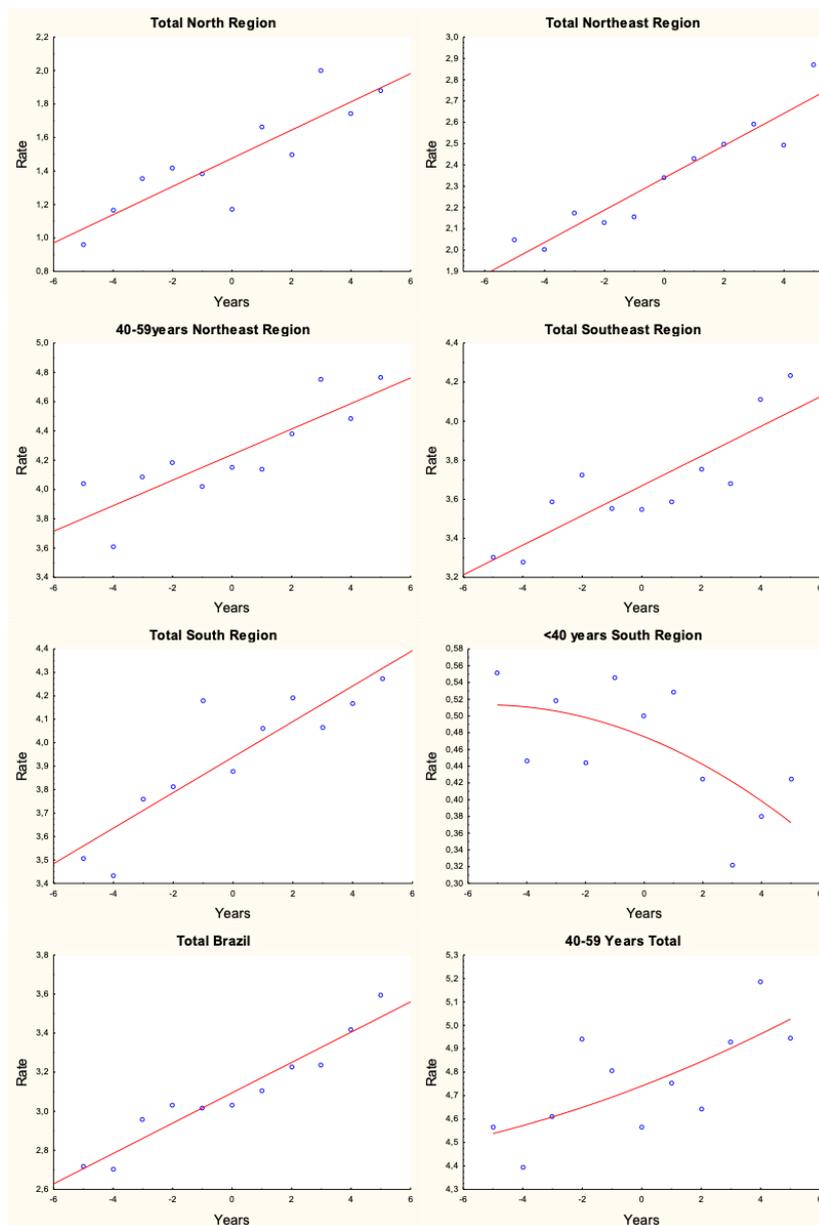
Source: Authors.

The older the women, the greater the mortality rate from ovarian cancer (Figure 3). An increasing trend of deaths is observed with every passing age. Mortality rates are higher in women over 80-year, furthermore, between 2009 – 2011.

Figure 3. Ovarian cancer mortality trends by age and group of years. Brazil, 2006 – 2016.
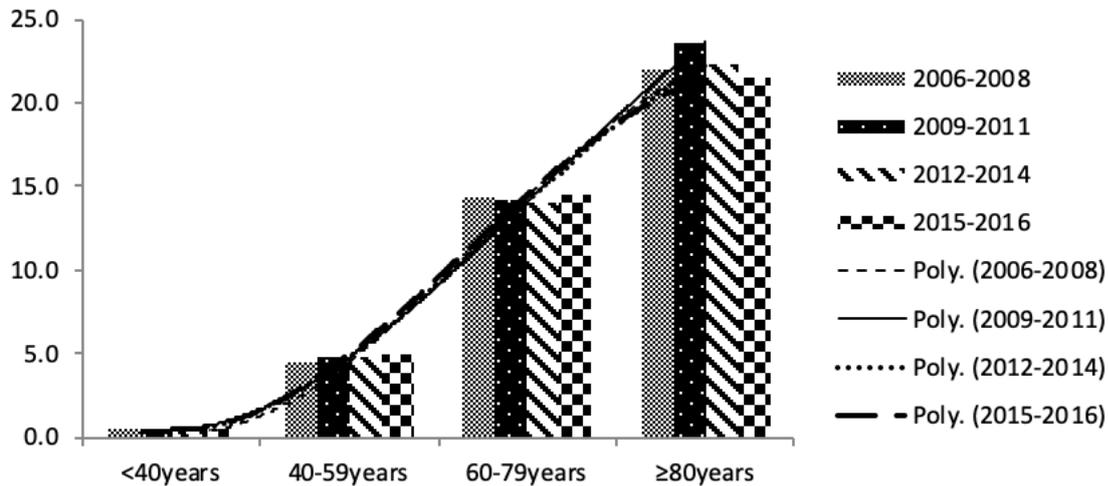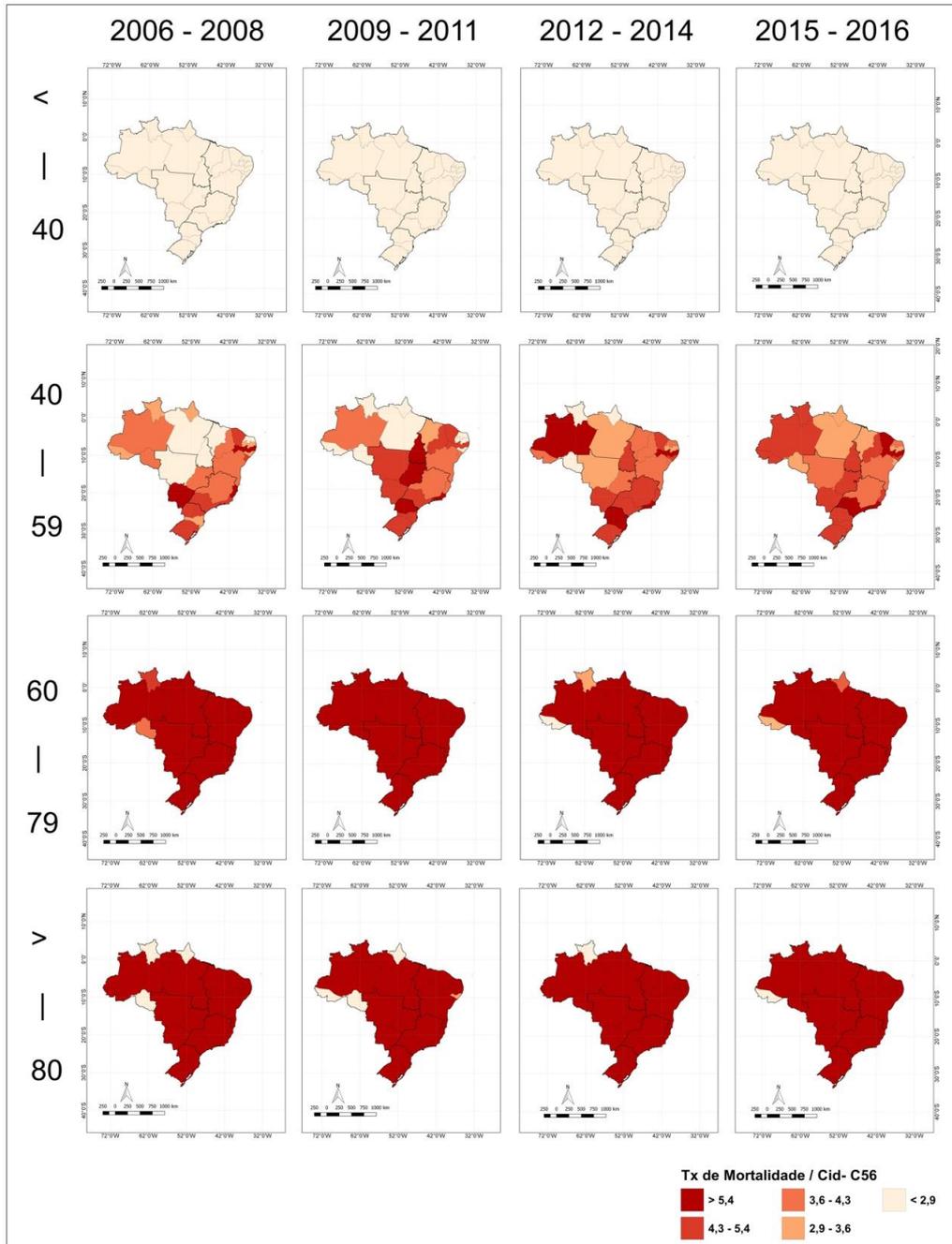

Source: Authors.

The mortality coefficients increased over the years in all Brazilian Regions. However, the highest rates were found as further south as they are on the map. The South and the Southeast have the most significant, while the North Region showed the lower coefficients.

The spatial distribution of the mortality rates by age and group of years from every Brazilian state is presented in Figure 4. The legend is the same as the World Health Organization used to describe the ovarian cancer mortality rates over the world at the GLOBOCAM website.

Figure 4. Spatial distribution of ovarian cancer mortality rates by age and group of years in every Brazilian state.

Source: Authors.

4. Discussion

Mortality trend research from ovarian cancer based on the regional differences is scarce, despite their importance to understanding the disease and the incidence, the screening, and the prevention. Questions related to ovarian cancer survival are significant; there are few

research types about the magnitude of the disease and the relationship with sociodemographic factors such as age, schooling, and race. This research provides a projection of ovarian cancer mortality rates because recent researches have shown improvement in the last years (Chirlaque et al. 2017; Keinan-Boker et al. 2017; Ojamaa et al. 2017).

There was an increased incidence of ovarian cancer in underdeveloped countries in the last years. India is an example (Murthy et al., 2009). On the other hand, there was a decreasing incidence in developed countries, as in the US (IARC, 2019). The main factor responsible for the dramatic reduction of ovarian cancer incidence in the last decades, and consequently in the mortality rates, was the access to the hormonal contraceptive. Since then, it was recognized as a protective factor. Nearly every woman in the US took it at least once, turning the population homogenized, which led other factors to play a significant role in ovarian cancer risk. There is an estimated increase of 37% new cases until 2030 in the US related to other risk factors (Sopik et al. 2015). This growing trend seems to be among older women; they do not commonly use hormonal contraceptives. The risk factors that could be involved are obesity and sterilization; consequently, no deliveries and no breastfeeding (Webb, Green, and Jordan, 2017).

Concerning Brazil, it is necessary to understand the differences between the five Regions. The first paradigm is ethnic origins. Each Region was colonized distinctively. In the South, pronounced immigration from Europe, especially Italians and Germans; in the North, a marked occurrence of indigenous people; in the Northeast Region, a noticeable presence of African descendants. Immigrants from the Middle East and Orient colonized mostly the Southeast Region. Although an important observation is the races mix over the years, resulting in a heterogeneous population (Seyferth, 2013). Secondly, the socio-economic conditions. There is an enormous disparity between classes. The largest part is the low-income population, and a considerable portion depends on government programs as a salary. A Unified Health System is available to every Brazilian citizen. However, vulnerable populations have difficulties accessing this service due to social and economic barriers. Furthermore, the territory dimension makes the resource distribution difficult, enlightening Regions' differences (Landmann-Szwarcwald and Macinko, 2016).

The North and the Northeast Region presents the lower Human Development Index (HDI). Cancers related to infections such as cervix cancer are most frequent in ailing areas. Ovarian and breast cancer are most prevalent in developed areas related to lifestyle and habits. It might be one reason for the lower mortality rates in those regions (Rocha-Brischiliari et al., 2017). Another reason that should be considered is making the diagnosis and determining the

cause of death in areas with restricted access and limited resources. Furthermore, ovarian cancer is a silent disease and hard to be diagnosed even under standard conditions. That could be the reason for different mortality rates between developed and underdeveloped countries.

A decrease in the mortality rate trend of ovarian cancer has happened in women under 40 years old in the South Region. The major access to hormonal contraceptives might explain it or because the social characteristics are similar to developed countries (Malvezzi et al. 2016).

Brazilian life expectancy increased; it could explain increasing deaths in women after the seventh decade. The most critical risk factor for ovarian cancer is the familiar history, strengthening the genetic predisposition (Grossman et al. 2018).

The increasing mortality trend between 40 – 59 years in the Northeast Region could support the differences between Brazilian Regions. Data from Brazil also revealed a significant increased mortality trend, even though; the other four regions have not presented that same pattern when analyzed independently. From a quick observation of the spatial distribution maps of the ovarian cancer mortality rates (Fig. 4), it is possible to note the intensification of the colors as the years went by. Mortality is not just a reflex from incidence, but also the access to diagnoses and treatment. It might be an explanation for the growth observed in this age group. Additionally, as it is already known, the Northeast Region population has limited access to the health system (Sopik et al. 2015; Malvezzi et al. 2016).

In this study, ovarian cancer mortality was more common in White women than to the other races. This information was found in almost the totality of death notifications. Only 35% of deaths occurred on Non-white women, classified by IBGE as Black, Asian, Mixed-race, or Indigenous. According to the 2010 census, over 50% of the Brazilian population was a self-declared as Non-white. The Centers for Disease Control and Prevention (CDC) revealed that White women have more chances to die from ovarian cancer in the US. It also happens in Caucasian countries (Lowe et al. 2013).

Schooling was reported only in 25% of ovarian cancer death notifications, which interposes a better understanding of the disease. Among this, only 26% had eight or more years of schooling. If these data can be extrapolated, Brazilian women with a restricted education would be most susceptible to ovarian cancer's worst outcome.

A hypothesis can be raised that the data founded in the Information System is further incomplete, especially in the regions with the worst access to education and health service. The spatial distribution maps showed lightly colored states that should be painted darker, as the nearby states pointed out inadequate notification. That is expected due to how far away

these states are from the most developed centers. If correctly notified, the data could be even more disappointing than this. Although many data were missing, it was possible to notice essential characteristics such as race, schooling, and privation to health access. Limitations in this study were from secondary data, moreover the years of delay to be available.

5. Final Considerations

This study achieved the objective of analyzing trends in the Brazilian ovarian cancer mortality rates related to age, schooling, and race. Mortality rates studies help to decrease the magnitude of the disease. They can be a tool to identify gaps in knowledge.

Facing the results, future researchers should mainly study screening methods to reach an early diagnosis. Not so far to understand the risk factors and symptoms as an unspecified abdominal pain, which could be a trigger for investigating ovarian cancer. Furthermore, this study allows us to realize that politics are needed to facilitate the population's access to health services, consequently minimizing the time to diagnose and start treatment.

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