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Trend analysis of lung cancer incidence and mortality in Grande Cuiabá, Mato Grosso, Brazil, 2000 to 2016

Análise de tendência da incidência e da mortalidade por câncer de pulmão na Grande Cuiabá, Mato Grosso, Brasil, 2000 a 2016

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ABSTRACT: ***Objective*:** To analyses lung cancer incidence and mortality trends to gender and age group in Grande Cuiabá between 2000 to 2016. ***Methods*:** Study of times series applying incidence data from the Population-Based Cancer Registry of Cuiabá, and mortality data from Mortality Information System. Annual Percentage Change and the Average Annual Percentage Change were calculated in the incidence and mortality rate through the Joinpoint regression. ***Results*:** It was observed between men a decrease of -2,2% in the overall incidence of lung cancer during the term of 2000-2016 and by age range: 40 to 49 years (-4,2%), 60 to 69 years (-2,0%) and 70 to 79 years (-9,4%), in this last age group it was between 2000-2009. The general mortality was stable on historical series, nonetheless, a decline between men of 50 to 59 years (-3,5%) among 2006 to 2016 and of 70 to 79 years among 2002-20011 (-6,3%) were observed. The incidence trends among female individuals maintained stable whereas the overall mortality trends had an increase of 7,2% between 2000-2012 and decrease of -34,1% between 2012-2016. Amid women from 50 to 79 years, there was a raise, ranging from 3,5% to 3,9% between 2000-2016. ***Conclusions*:** There is an evident disparity between the trends analysis of incidence and mortality of lung cancer among men and women, that can be explained by changes in smoking over time, for example, the adherence or not of the smoking withdraw program besides social, cultural, economics differences and even biological.

Keywords: Incidence. Mortality. Lung neoplasms. Tobacco use disorder. Health information systems. Epidemiology.

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RESUMO: ***Objetivo:*** Analisar as tendências de incidência e de mortalidade por câncer de pulmão por sexo e faixa etária, na Grande Cuiabá, Mato Grosso, entre 2000 e 2016. ***Métodos:*** Estudo de séries temporais utilizando informações de incidência do Registro de Câncer de Base Populacional Cuiabá e de mortalidade do Sistema de Informação sobre Mortalidade. Foram calculadas a variação percentual anual e a variação percentual média anual das taxas de incidência e de mortalidade, pela regressão por *joinpoint*. ***Resultados:*** Observou-se entre homens decréscimo de -2,2% na incidência geral de câncer de pulmão entre 2000-2016 e por faixa etária: 40 a 49 anos (-4,2%), 60 a 69 anos (-2%) e 70 a 79 anos (-9,4%), sendo nesta última faixa entre 2000-2009. A mortalidade geral foi estável na série histórica, porém verificou-se decréscimo entre os homens de 50 a 59 anos (-3,5%) entre 2006-2016 e de 70 a 79 anos entre 2002-2011 (-6,3%). Para as mulheres, as tendências de incidência mantiveram-se estáveis, enquanto nas tendências de mortalidade geral houve aumento de 7,2% entre 2000-2012 e decréscimo de -34,1% entre 2012-2016. Entre mulheres de 50 a 79 anos, houve aumento, variando de 3,5 a 3,9% entre 2000-2016. ***Conclusão:*** Existe evidente disparidade nas análises de tendências de incidência e de mortalidade de câncer de pulmão entre homens e mulheres, que pode ser explicada por mudanças do tabagismo ao longo do tempo, por exemplo, adesão ou não ao programa de abandono do tabagismo, além de diferenças sociais, culturais, econômicas e até mesmo biológicas.

Palavras-chave: Incidência. Mortalidade. Câncer de pulmão. Tabagismo. Sistemas de informação em saúde. Epidemiologia.

INTRODUCTION

Cancer ranks second in the number of non-communicable chronic diseases (NCDs) that kill the most in the world[1]. It has stood out for the growth in its incidence and mortality worldwide, mainly due to the rapid aging of the population and increased exposure to risk factors for neoplasms[2]. In 2020, cancer was among the leading causes in 183 countries[3].

Lung cancer (LC) was the most common cancer in the world in 2018[4], coming to second place in 2020, whilst it remained the leading cause of cancer death[3]. In Brazil, for each year, from 2020 to 2022, a total of 17,760 new cases of LC are expected in men and 12,440 in women[5]. Regarding mortality, LC was the first in deaths by type of cancer in men (13.8%/16,733) and the second in women (11.4%/12,621) in 2019[6].

In Mato Grosso, 320 cases of LC were estimated in 2020. Of these, 210 occurred in men and 110 in women[5]. In 2019, there were 314 deaths from this type of cancer, of which 205 were among men and 109 among women[6].

As modifiable risk factors for LC, lifestyle and socioeconomic, demographic, and environmental factors stand out[7]. Among the non-modifiable ones, there are genetic factors and family history of LC[8]. Smoking is the main risk factor for the disease[8], including passive exposure to tobacco as an important point for its occurrence[5].

Considering that LC plays a significant role at the epidemiological level and a public health problem both world- and nationwide[4,5], in addition to its disparate effects between men and women[9,10] and the scarcity of studies on the subject in the central-west region of Brazil and in the state of Mato Grosso, the objective of this article was to analyze trends in incidence and mortality from LC according to gender and age range, in Grande Cuiabá, state of Mato Grosso, from 2000 to 2016.

METHODS

This is a time series study using incidence and mortality information for LC according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10), with code C33-C34, to both genders, between the age groups 40–49, 50–59, 60–69, 70–79, and 80 years old or older, in the Grande Cuiabá area, from 2000 to 2016.

This study is part of the extension project "Surveillance of cancer and its associated factors: updating of population-based and hospital records" (VIGICAN Project) and of a research entitled "Cancer and its associated factors: analysis of population-based and hospital-based records in Cuiabá–MT", in partnership with the Mato Grosso State Health Department (SES-MT) and the Public Ministry of Labor of the 23rd Region.

The incidence information came from the Population-Based Cancer Registry (*Registro de Câncer de Base Populacional* – RCBP) of Cuiabá, available on the RCBP System website (BasepopWeb), developed by the José Alencar Gomes da Silva National Cancer Institute (*Instituto Nacional de Câncer José Alencar Gomes da Silva* – INCA)[11]. Information on deaths from the Mortality Information System (*Sistema de Informação sobre Mortalidade* – SIM) was made available by SES-MT.

The RCBP Cuiabá, whose coverage area is the municipalities of Cuiabá and Várzea Grande, was called the RCBP of Grande Cuiabá. The entire historical series of the registry was used, as cancer evolves slowly and progressively. Therefore, behavior changes are best evaluated over decades.

Incident cases were recorded by the RCBP based on the International Classification of Diseases for Oncology, 3rd edition (ICD-O3), and converted into ICD-10[12-14]. The variables analyzed from the RCBP and SIM databases were: gender (female; male; unknown), age (in years and categorized by age group), specific cause of cancer according to the ICD-O3, morphology and date of diagnosis (exclusive to the RCBP), underlying cause of death according to the ICD-10 and date of death (exclusive to SIM)[12-14]. The quality of the information was assessed using the criteria of the International Agency for Research on Cancer[15].

Cuiabá is the capital of the state of Mato Grosso and the most populous city, according to the latest census[16], with 551,098 inhabitants. Várzea Grande is the second largest city in the state and had a population of 252,596 in 2010.

Crude and age-adjusted incidence and mortality rates were calculated per 100,000 inhabitants. Incidence rates were calculated for each year between 2000 and 2016, dividing the number of new cases of LC by the population over the period and multiplying it by 100,000. Mortality rates for the same period were calculated by dividing the number of deaths from LC by the population over the period and multiplying it by 100,000. Specific crude rates were calculated for each age group, using 10-year intervals, and the incidence and mortality rates adjusted by the direct method, considering the standard world population proposed by Segi[17] and modified by Doll and Cook[18].

Joinpoint regression analysis was used to analyze trends in incidence and mortality. In this method, the annual percentage change (APC) was calculated, which is the direction and

magnitude of the trend results; and the average annual percent change (AAPC), estimated by calculating the weighted geometric mean of the different APCs with weight equal to the segment size for each time interval. Both were estimated by modeling using the jointpoint method, using the calendar year as the regression variable[19,20].

Joinpoint regression analysis is used to find the best model that tests whether multiple line fragments better explain a time trend than a single line (dependent variable: logarithmic rate transformation). It uses Monte Carlo permutation tests to compare different models (with 0, 1, ..., or 5 joinpoints — depending on the size of the time series)[19].

When the model is defined, the APC or AAPC for each segment is calculated and used to describe, quantify the trend, and assess whether it is statistically significant. In this situation, the null hypothesis is APC or AAPC=0, that is, rates are neither increasing nor decreasing. Therefore, they are stable, and their respective 95% confidence intervals are presented[20]. The analyses were performed using the Joinpoint Regression® software, version 8.3.6.1[19]. Individuals over 40 years of age were included in the analyses, to avoid a decrease in the time series, as cases below this age group were rare, an expected fact, since LC is more common in the age groups between 50 and 70 years[21].

SES-MT authorized the use of the data and the publication of the results. The research project was submitted to the Research Ethics Committee of Hospital Universitário Júlio Müller (CEP-HUJM) and approved under opinion number 3.048.183, as well as the Research Ethics Committee of SES-MT, opinion number 3.263.744.

RESULTS

There were 22,345 new cases of all neoplasms, except *in situ* and non-melanoma skin, from 2000 to 2016, in Grande Cuiabá, in patients aged 40 years old and older. Of this total, 6.4% corresponded to lung cancer, that is, 1,436 new cases of LC, of which 63.28% occurred in males and 30.54% in the age group 60 to 69 years. In relation to females, most of the new cases occurred in the age group from 70 to 79 years (26.61%). As for mortality, 1,318 deaths were recorded in the period, 63.88% in males and 29.80% in the 60-69 age group. In women, the incidence was 26.89% also in the age group from 60 to 69 years.

There was a significant decrease in the overall incidence of LC in males over the period 2000–2016, with an APC/AAPC of -2.2 (95% confidence interval — 95%CI -4.0–-0.3). Regarding the trend of incidence of LC by age group in men, there were statistically significant decreasing trends in the age groups from 40 to 49 years — APC/AAPC=-4.2 (95%CI -7.7–-0.6) — and aged 60 to 69 — APC/AAPC=-2 (95%CI -3.7–-0.2) — in the period 2000-2016. In the age group from 70 to 79 years, when analyzing the joinpoints, two trends in the incidence of LC were identified, and a significant decrease was seen in the period 2000–2009 — APC=-9.4 (95%CI -16.6– -1.7) (Table 1).

There was an increase of 1.5% per year in the historical series of the incidence of LC in females in the period 2000-2016, but without statistical significance (95%CI -0.6–3.6). The trends in the incidence of LC among the different age groups of women also tended to be stable (Table 2).

Regarding the trend in general mortality from LC in men, the increase was not significant — APC / AAPC=5.6 (95%CI -3.5–15.5) — in the historical series, however, two joinpoints were observed in the age group from 50 to 59 years, dividing the historical series into three trends in mortality from LC in men (2000–2003; 2003–2006; and 2006–2016), with a significant decrease trend in the period from 2006 to 2016 — APC=-3.5 (95%CI -6.1–-0.9). Three joinpoints were also identified in the 70-79 age group and divided the series into four trends (2000–2002; 2002–2011; 2011–2014; and 2014–2016). In the period from 2002 to 2011, the decrease was statistically significant — APC=-6.3 (95%CI -10.0–-2.6) (Table 3).

Regarding the trend in overall mortality from LC in women, the analysis identified a joinpoint that divided the series into two significant trends: an increase in the period 2000-2012, with APC=7.2 (95%CI 3.0–11.6); and a decrease in the period 2012-2016, with APC=-34.1 (95%CI -51.8–-9.9). In terms of LC mortality trends between age groups, in turn, no joinpoints were seen. The series was considered as a single trend of increased mortality, being significant in the age groups from 50 to 59 years old — APC=3.9 (95%CI 0.6–7.2) —, 60 to 69 years old — APC=3.7 (95%CI 0.3–7.2) —, and 70 to 79 years old — APC=3.5 (95%CI 0.1–7.0) (Table 4).

Table 1. Trend of age-adjusted* lung cancer incidence rates in men from 2000 to 2016.

Overall incidence					
Trend 1			AAPC	95%CI	
Period	APC	95%CI			
2000–2016	-2.2†	(-4.0–-0.3)	-2.2†	(-4.0–-0.3)	
Incidence					
Age range	Trend 1			Trend 2			AAPC	95%CI
	Period	APC	95%CI	Period	APC	95%CI		
40–49	2000–2016	-4.2†	(-7.7–-0.6)	-	-	-	-4.2†	(-7.7–-0.6)
50–59	2000–2016	-1.5	(-5.0–2.1)	-	-	-	-1.5	(-5.0–2.1)
60–69	2000–2016	-2†	(-3.7–-0.2)	-	-	-	-2†	(-3.7–-0.2)
70–79	2000–2009	-9.4†	(-16.6–-1.7)	2009-2016	12.2	(-5.9–33.7)	-0.5	(-8.2–7.8)
≥80	2000–2016	-1.8	(-6.2–2.8)	-	-	-	-1.8	(-6.2–2.8)

*World standard population; †Statistically significant APC or AAPC (p<0.05); APC: annual percentage change; AAPC: annual average percentage change; 95%CI: 95% confidence interval.

Table 2. Trend of age-adjusted* lung cancer incidence rates in women from 2000 to 2016.

Overall incidence				
Trend 1			AAPC	95%CI
Period	APC	95%CI		
2000-2016	1.5	(-0.6–3.6)	1.5	(-0.6–3.6)
Incidence				
Age range	Trend 1		AAPC	95%CI
	Period	APC	95%CI	
40–49	2000–2016	3.5	(-0.9–8.0)	3.5	(-0.9–8.0)
50–59	2000–2016	2	(-1.5–5.7)	2	(-1.5–5.7)
60–69	2000–2016	0.5	(-2.7–3.8)	0.5	(-2.7–3.8)
70–79	2000–2009	0.6	(-2.4–3.6)	0.6	(-2.4–3.6)
≥80	2000–2016	-1.9	(-6.0–2.4)	-1.9	(-6.0–2.4)

*World standard population; APC: annual percentage change; AAPC: annual average percentage change; 95%CI: 95% confidence interval.

Table 3. Trend in age-adjusted* lung cancer mortality rates in men from 2000 to 2016.

Overall mortality	Period	APC	95%CI	AAPC	95%CI
	2000-2016	5.6	(-3.5–15.5)	5.6	(-3.5–15.5)
Mortality by age range	Period	APC	95%CI	AAPC	95%CI
40–49					
Trend 1	2000–2016	0.4	(-4.2–5.2)	0.4	(-4.2–5.2)
50–59					
Trend 1	2000–2003	-21.4	(-49.9–23.4)	-1.6	(-13.3–11.7)
Trend 2	2003–2006	31.6	(-30.0–147.2)		
Trend 3	2006–2016	-3.5†	(-6.1–-0.9)		
60–69					
Trend 1	2000–2016	0.9	(-1.2–2.9)	0.9	(-1.2–2.9)
70–79					
Trend 1	2000–2002	38.2	(-63.2–418.7)	-2.4	(-22.3–22.7)
Trend 2	2002–2011	-6.3†	(-10.0–-2.6)		
Trend 3	2011–2014	22	(-35.1–129.1)		
Trend 4	2014–2016	-40.5	(-87.8–191.4)		
≥80					
Trend 1	2000–2016	5.2	(-0.8–11.5)	5.2	(-0.8–11.5)

*População padrão mundial; †APC ou AAPC estatisticamente significativo (p<0,05); APC: variação percentual anual; AAPC: variação percentual média anual; IC95%: intervalo de confiança de 95%.

Table 4. Trend in age-adjusted* lung cancer mortality rates in women from 2000 to 2016.

Overall mortality							
Trend 1			Trend 2			AAPC	95%CI
Period	APC	95%CI	Period	APC	95%CI		
2000–2012	7.2†	(3.0–11.6)	2012–2016	-34.1†	(-51.8–-9.9)	1.5	(-5.5–9.0)
Mortality							
Age range			Trend 1			AAPC	95%CI
			Period	APC	95%CI		
40–49			2000–2016	1.5	(-5.5–9.0)	1.5	(-5.5–9.0)
50–59			2000–2016	3.9†	(0.6–7.2)	3.9†	(0.6–7.2)
60–69			2000–2016	3.7†	(0.3–7.2)	3.7†	(0.3–7.2)
70–79			2000–2016	3.5†	(0.1–7.0)	3.5†	(0.1–7.0)
≥80			2000–2016	1.7	(-5.3–9.4)	1.7	(-5.3–9.4)

*World standard population; †Statistically significant APC or AAPC (p<0.05); APC: annual percentage change; AAPC: annual average percentage change; 95%CI: 95% confidence interval.

DISCUSSION

The analysis presented in this study allowed us to assess trends in incidence and mortality from LC in male and female individuals by their respective age groups in the years 2000 to 2016 in the Grande Cuiabá area. The results showed that there was a decrease of -2.2% per year in the analysis of the incidence of LC in the studied period in males, but it was not statistically significant for females. Regarding the historical trend of deaths, there was stability of specific mortality by LC among males throughout the study period, while in females there was an increase of 7.2% per year in deaths between the years 2000 and 2012 and a decrease of -34.1% between 2012 and 2016.

The main risk factor for LC is smoking[22]; over two thirds of deaths from this cancer are related to tobacco use[23]. Considering only the effect of tobacco, studies estimate the attributable risk of smoking as a causative agent of LC close to 90%[9].

Regarding the incidence of LC in men, there is a worldwide trend toward a decrease in smoking, contrary to what has been observed in women, which may reflect the patterns of adherence and cessation of smoking[10]. It is important to highlight that the tobacco control policy in Brazil has achieved positive results, and the prevalence of male smokers has been reduced by more than 50% between 1989 and 2008[24].

When comparing the incidences of LC between male age groups, a greater reduction was identified in older age groups, especially in the population aged 70 years old

and older, as well as among those aged between 40 and 49 years. It was noticed that the downward trend in smoking between the years 1989 and 2009 has been higher among men, although the prevalence is still higher than among women. Possibly, anti-smoking actions and programs such as increased taxes on cigarettes, mandatory display of warning images, restriction of advertising at specific times, among others, have had a positive impact on men's decision to quit smoking[25].

Considering the effect of age and birth cohort, the aged population may tend to be more impacted by quitting smoking, as they are more fragile and have a greater number of health comorbidities[26]. Among younger men, the implementation of tobacco regulation policies, control over tobacco advertising and the increase in taxes on cigarettes seem to have contributed to younger adults having awakened to the harmful effects of smoking, since younger age groups are the most affected by such laws[27]. Also, in relation to men, passive exposure to smoke, dust and fumes at work and the concomitant use of alcohol and other drugs tend to be higher than in women, impacting the incidence of LC[28,29].

However, the incidence of LC among women showed a tendency toward stability, even in the analysis stratified by age group. In this sense, still considering smoking as a risk factor, a national survey that analyzed people's perception of pro-tobacco media identified that advertisements were more perceived by men (32.4%) than by women (25.4%)[30]. Although there are fewer female smokers compared to men, the decrease in the number of smokers is smaller and may be associated with their physical characteristics, hormonal influence, and emotional factors[31]. It seems that the decision to quit and to seek a solution to tobacco dependence is also different between men and women. One study found that women were 31% less likely to quit compared to men, and actual successful quitting was also lower[32].

The general trend of LC mortality in men in the present study showed a historical trend toward stability. In Brazil, mortality from LC in men tends to decrease, as in several other countries in the world[9,29]. Although LC has one of the shortest survival times compared to other cancers, it is also necessary to consider a cohort effect according to age group in relation to deaths, the pre-pathogenic period for the incidence of the disease, taking into account the time between the onset of the disease and the death of the individual.

Possibly, the effects of smoking prevention campaigns have had less influence on mortality than on the incidence of LC. As an example, the Tobacco Control Program was implemented in the state of Mato Grosso only after 2008[33] and the law that prohibited smoking in places of collective use was only implemented in 2009[34]. Despite the positive effect in the reduction of overall incidence and in some age groups of this cancer, the same may not have occurred with regard to mortality, although, in the analysis stratified by age group, significant mortality decline trends were identified in the age group from 50 to 59 years (2006-2016) and from 70 to 79 years old (2002–2011).

Unlike men, the historical series of general mortality from LC in women shows significant trends of increase in the period from 2000 to 2012 and of decrease between 2012 and 2016. At the beginning of the historical series[35], analyzing mortality data and population data of the World Health Organization and the Pan American Health Organization of Latin American countries using joinpoint models, mortality rates were increasing due to LC in most of the countries evaluated, including Brazil. This phenomenon was also observed in most countries of the world[29]. Also in this sense, a study that analyzed mortality rates in the regions of Brazil (1996-2011) identified that in the Southeast, South, and Midwest regions, the risk of mortality was higher among women and mortality tended to increase in females[9].

As for the downward trend in female deaths from 2012 to 2016, recent NCDs prevention campaigns and programs launched in the world and in Brazil in recent decades may have helped[36,37]. A systematic review showed a reduction in global smoking rates from 34.9 to 25% in men and from 8.2 to 5.4% in women, mainly in developed countries and Latin America, reflecting the effects of efforts made by tobacco control programs, as in Panama and Brazil[38]. In relation to the latter, the Ministry of Health, through INCA, has been developing national actions that make up the National Tobacco Control Program in an attempt to reduce the prevalence and deaths of smokers, articulating a tobacco treatment network in the Unified Health System (*Sistema Único de Saúde* – SUS), impacting the reduction of smoking on the reduction of mortality from LC[39].

Recently, anti-smoking actions have been developed, such as the Global Action Plan for the Prevention and Control of NCDs 2013–2020[37,40]. A national survey carried out in Brazilian capitals concluded that in the period 2006–2019 there was a favorable evolution of some health indicators, such as the decrease in smoking in both genders[41].

The general mortality trend by age group in women grew 7.2% per year between 2000 and 2012 and fell -34.1% between 2012 and 2016. It can be inferred that the anti-smoking actions initiated in the late 1990s have not produced a protective effect on the origin of the historical series and, as expected, this occurred between the last years evaluated (from 2012 to 2016).

In the evaluation by age group, there was a decreasing trend of -3.5% per year in the period from 2000 to 2016 among women aged 70 to 79 years. In the strata of older age groups, the prevalence of smoking showed a decrease with increasing age in non-institutionalized aged people[18]. Intrinsic characteristics of gender and socioeconomic and cultural profile lead older women to smoke less[42], which may be a possible explanation for the decrease in deaths from LC in women. This same decrease was also found in the years 2006 to 2016 in women aged 50 to 59 years, possibly also due to the later protective effect of anti-smoking campaigns and a decrease in deaths from LC.

According to INCA[8], mortality rate decreased by 3.8% in men and 2.3% per year in women in Brazil between 2011 and 2015, due to the reduction in smoking in this period. The institute also claims that the five-year survival rate is 15% in men and 21% in women. When the disease is diagnosed at an early stage, this rate increases to 56%.

Some considerations about the limitations of the present study must be made. The research used information from the RCBP and SIM. As for the first, one can consider the improvement of data quality control procedures and the search for improvement in the record, with routines of criticism that analyze the validity and consistency of the information, however, some problems of incompleteness and inconsistency of the data are not excluded[43].

Regarding the SIM, there may have been errors in filling out the death certificates. Physicians often record only the pathophysiological events that preceded death, such as cardiorespiratory arrest, heart failure, pulmonary edema, among others, but fail to correctly inform the underlying cause of death, according to the ICD-10[44] criteria, leading to underreporting of some conditions. In addition, in many cases, the underlying cause of death is filled only as a malignant neoplasm, without specifying its location (C80)[45].

Differences are observed between the trends of incidence and mortality from LC between men and women, considering in a special way certain age groups and periods of the historical series. These differences are due to changes in tobacco use over time, such as adherence or not to the smoking cessation program, in addition to social, cultural, economic, and even biological differences.

Men and women respond differently to calls from health promotion and care services, which may explain the behavior of historical LC trends in relation to gender, but smoking is recognized as the main risk factor related to LC incidence trends.

The results of this study can guide the design and implementation of campaigns and strategies in the fight against smoking, resulting in a decrease in morbidity and mortality from LC in Mato Grosso and in Brazil.

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