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Mortality due to Malignant Neoplasms of the Liver and Bile Ducts in Brazil: Trends and Projections until 2030

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Mortalidade por Câncer de Fígado e Vias Biliares no Brasil: Tendências e Projeções até 2030

Mortalidad por Cáncer de Hígado y Biliar en Brasil: Tendencias y Proyecciones hasta 2030

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Abstract

Introduction: Intrahepatic liver and biliary tract neoplasm is the seventh most incident and represents the second leading cause of cancer death in the world. Therefore, it is crucial to understand the epidemiology of this disease in relation to the temporal trends of mortality and burden that this disease will present in the future. **Objective:** To analyze the trend in mortality by liver and biliary cancer in Brazil and to calculate mortality projections until 2030. **Method:** An ecological study based in deaths from malignant liver and bile duct cancer (C22) occurred in Brazil from 2001 to 2015 and recorded in the Mortality Information System. Mortality trends were analyzed by Joinpoint regression, while for the calculation of projections, the Nordpred program was used. **Results:** For females, there was a reduction in mortality rates in the Midwest, Southeast and North regions in Brazil; for males, these regions showed increasing but no significant trends. Mortality rates for females will decrease in the future, with emphasis for the rates in the North and Northeast, with a reduction of about 30% by 2030. For males, there will be a 12% increase in mortality rates for the Southern Region. **Conclusion:** Mortality due to liver and biliary cancer in Brazil shows a tendency of reduction for females and stability for males, and this characteristic will be maintained in the coming decades.

Key words: Liver Neoplasms/mortality; Liver Neoplasms/epidemiology; Bile Duct Neoplasms/mortality; Bile Duct Neoplasms/epidemiology; Forecasting.

Resumo

Introdução: A neoplasia de fígado e vias biliares intra-hepáticas é a sétima mais incidente e representa a segunda maior causa de morte por câncer no mundo. Sendo assim, é crucial compreender a epidemiologia dessa doença, no que diz respeito às tendências temporais da mortalidade e da carga que essa doença apresentará no futuro. **Objetivo:** Analisar a tendência da mortalidade por câncer de fígado e vias biliares no Brasil e calcular as projeções de mortalidade até 2030. **Método:** Estudo ecológico baseado em óbitos por neoplasia maligna de fígado e vias biliares intra-hepáticas (C22) ocorridos no Brasil no período de 2001 a 2015 e registrados no Sistema de Informação sobre Mortalidade. As tendências de mortalidade foram analisadas pela regressão *Joinpoint*; para o cálculo das projeções, foi utilizado o programa Nordpred. **Resultados:** Para o sexo feminino, houve redução das taxas de mortalidade nas Regiões Centro-Oeste, Sudeste e Norte no Brasil; para o sexo masculino, essas Regiões apresentaram tendências de aumento, porém não significativo. As taxas de mortalidade para o sexo feminino apresentarão reduções no futuro, com destaque para as taxas das Regiões Norte e Nordeste, com redução de cerca de 30% até 2030. Para o sexo masculino, haverá acréscimo de 12% nas taxas de mortalidade para a Região Sul. **Conclusão:** A mortalidade por câncer de fígado e vias biliares no Brasil apresenta tendência de redução para o sexo feminino e estabilidade para o sexo masculino, e essa característica será mantida nas próximas décadas.

Palavras-chave: Neoplasias Hepáticas/mortalidade; Neoplasias Hepáticas/epidemiologia; Neoplasias dos Ductos Biliares/mortalidade; Neoplasias dos Ductos Biliares/epidemiologia; Previsões.

Resumen

Introducción: La neoplasia intrahepática del hígado y del tracto biliar es el séptimo cáncer más común y representa la segunda causa principal de muerte por cáncer en el mundo. Por lo tanto, es crucial comprender la epidemiología de esta enfermedad con respecto a las tendencias temporales de mortalidad y carga que esta enfermedad presentará en el futuro. **Objetivo:** Analizar la tendencia de la mortalidad por cáncer de hígado y biliar en Brasil y calcular las proyecciones de mortalidad para 2030. **Método:** Un estudio ecológico basado en las muertes por cáncer de hígado y conducto biliar (C22) en Brasil en el de 2001 a 2015 y registrado en el Sistema de Información de Mortalidad. Las tendencias de mortalidad se analizaron mediante regresión de *Joinpoint*, mientras que para el cálculo de las proyecciones se utilizó el programa Nordpred. **Resultados:** Para las mujeres, hubo una reducción en las tasas de mortalidad en las regiones del Medio Oeste, Sudeste y Norte no Brasil; para los hombres, estas regiones mostraron tendencias crecientes, pero no significativas. Las tasas de mortalidad para las mujeres disminuirán en el futuro, con énfasis en las tasas en el norte y el noreste, con una reducción de alrededor del 30% para 2030. Para los hombres, habrá un aumento del 12% en las tasas de mortalidad para las mujeres. **Conclusión:** La mortalidad por cáncer de hígado y biliar en Brasil muestra una tendencia a la reducción de las mujeres y la estabilidad de los hombres, y esta característica se mantendrá en las próximas décadas.

Palabras clave: Neoplasias Hepáticas/mortalidad; Neoplasias Hepáticas/epidemiología; Neoplasias de los Conductos Biliares/mortalidad; Neoplasias de los Conductos Biliares/epidemiología; Predicción.

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INTRODUCTION

Intrahepatic liver and bile ducts neoplasm is the seventh most incident and represents the second leading cause of death by cancer in the world. In 2018, 841 thousand confirmed cases of the disease were registered and 781 thousand related deaths t, which corresponds to 8.2% of all deaths by neoplasm in the world, reaching the global rate of incidence of 9.3 cases/100 thousand inhabitants[1].

Worldwide, the most incident regions of the disease are the poorer and in development countries where nearly 90% of the cases occur, with emphasis in Asia and Sub- Saharan Africa. Among men, the greatest rates are encountered in East and Southeast Asia (31.9 and 22.2 cases/100 thousand inhabitants, respectively), while for women, the most incident regions are Eastern and Western Asia (10.2 and 8.1 cases/100 thousand inhabitants, respectively)[2-4]. In Brazil, 139,530 thousand deaths were registered by liver cancer between 1980 and 2010, with nearly 60% of cases in men and 40% in women[3,5].

Hepatocellular carcinoma represents 70% to 85% of the primary hepatic neoplasms and is the primary liver tumor that occurs more frequently. On the other hand, cholangiocarcinoma that has its origins in the cholangiocytes, epithelial cells lining the biliary ducts, constitute from 10% to 15% of the primary hepatic neoplasms. The other 5% are uncommon tumors as hepatic primary angiosarcoma, the hepatic epithelioid hemangioendothelioma, the hemangiopericytoma or primary hepatic lymphoma[6].

Overall, only the minority of the cases of hepatocellular carcinoma is passible of potentially curative surgical intervention. When there is no intervention on the tumor, it usually grows progressively as a mass that reduces the hepatic function and metastasizes intra and extra hepatic. In these cases, death usually occurs within 10 months in average. Patients with risk factors for hepatocellular carcinoma must undergo periodic screening with widely demonstrated cost-effectiveness[7-9].

The acknowledged risk factors for hepatocarcinoma comprehend chronic infection by the virus of hepatitis B (HBV) and by the virus of hepatitis C (HCV), exposure to aflatoxin in the diet, fatty hepatic disease, alcohol-induced cirrhosis, obesity, tobacco addiction, diabetes and iron overload. For cholangiocarcinoma, the risk factors include liver stroke and cirrhosis[10,11].

As a significant number of risk factors of hepatic cancer is modifiable, there is a strong perspective of reducing its incidence and mortality through preventive strategies as change of lifestyle and immunization against hepatitis. Some of its etiological factors, including infection by hepatitis and cirrhosis are easily identified by tests that can minimize the development of liver cancer[11].

Consequently, it is essential to understand the epidemiology of this disease in what concerns the temporal trends of mortality and the toll this disease will represent in the future. In addition, what can help to understand the extent of the preventive strategies implemented is the analysis of the geographic patterns and identify high risk populations and offer information for policy makers about future perspectives to prevent this cancer in Brazil.

The objective of this study was to analyze the temporal tendency of mortality by liver cancer and intrahepatic biliary ducts and estimate the number of deaths until 2030 for Brazil.

METHOD

Ecological time series study based in secondary data registered at the Mortality Information System (SIM) of the Computer Department of the National Health System (DATASUS). The deaths caused by malignant liver neoplasm and intrahepatic biliary ducts (C22) were analyzed, according to the categories of the International Classification of Diseases and related health problems (ICD), 10^{th} Revision (ICD-10) occurred in Brazil from 2001 to 2015 and reviewed per gender, age range and Brazilian regions.

Despite the recognition that SIM in the last years in Brazil had a quality boost, the use of secondary data about mortality is passible of sub-notification. To correct the sub-notification of deaths by liver malignant neoplasm and intrahepatic biliary ducts, it were used information from the Redistribution per Chapter of Deaths revised by the Active Search, an initiative of the Ministry of Health with data provided at DATASUS website[12].

It was calculated the factor of correction for each age-range[13], period, region and gender based in the percentual difference between the quantity of deaths notified to SIM and the deaths redistributed based in Chapter II (Neoplasms) of ICD-10. This difference was expressed in decimal values with 1 corresponding to a change of 100%, for instance, and the possibility of higher values since in some locations, the redistributed value represented values above those registered in SIM. In addition, cases where the redistributed value was lower than the registered in SIM had negative difference.

Where: D = difference of deaths redistributed, and deaths registered in SIM by Neoplasms in relation to the number of deaths registered in SIM by Neoplasms; NR = number of deaths redistributed by Neoplasms; NS = number of deaths registered in SIM by Neoplasms.

This difference obtained was added to 1 to calculate the factor of correction since the number 1 represents the neutral factor in a multiplication according to the formula below:

$$F = 1 + D$$

Where: F = factor of correction of Chapter II (Neoplasms); D = difference between deaths redistributed and deaths registered in SIM by Neoplasms in relation to the number of deaths registered in SIM by Neoplasms.

This factor was multiplied by the number of deaths by cancer. Therefore, it was assumed that the factor of correction for Chapter II could be applicable to liver cancer and intrahepatic biliary ducts. The formula used for this calculation is described below:

$$OC = F \times NOS$$

Where: OC = number of deaths by malignant liver neoplasm and intrahepatic biliary ducts corrected; NOS = number of deaths registered in SIM by malignant liver neoplasm and intrahepatic biliary ducts; F = factor of correction of Chapter II (Neoplasms).

With the information of the readjusted number of deaths, the standard rates of mortality were calculated, adjusted according to the world population per 100 thousand inhabitants (ASW/100 mil inhabitants). The population data per regions, gender and age were obtained from the demographic census and intercensitary forecasts at the website of "Brazilian Institute of Geography and Statistics (IBGE)".

It was analyzed the time trend of mortality by cancer liver and intrahepatic biliary ducts in Brazil and respective regions and calculated the forecasts of mortality until 2030 per quinquennium for the periods of 2016-2020, 2021-2025 and 2026-2030.

To analyze the mortality trends, it was conducted the regression analysis *Joinpoint,* with the software Joinpoint Regression Program (National Cancer Institute, Bethesda, Maryland, USA), version 4.4.0., January 2017. The objective of the analysis is to identify the occurrence of possible *joinpoints,* a point where a significant change of the trend has occurred.

The method applied identified *joinpoints* based in the model with maximum three points of change. The final model selected was the better adjusted with the Annual Percentage Change (APC) based in the trend of each segment, estimating whether these values are statistically significant at a level of 0.05. The significance tests utilized are based in the Monte Carlo permutation method of and in the calculation of annual percent variation of the ratio utilizing the logarithm of the ratio[14].

In the description of the trends, the terms "significant increase" or "significant reduction" indicate that the trend slope is statistically significant ($p<0.05$).

The predictions were made for each period, utilizing the model age-period-cohort of the program Cancer Registry of Norway (Nordpred), Oslo, Norway, inscribed in the statistical program R. The data were compiled in blocks of five years and the limit age group considered for analysis was the first with more than ten cases for the combined period.

The results of the predictions are presented in the total of deaths observed and anticipated for each period for Brazil and its five regions. For each period, world standard population-based adjusted mortality rates were calculated for global comparisons expressed per 100 thousand inhabitants/year (ASW/100 thousand hab.)[15]. Annual changes of the number of deaths in the last period estimated (2026-2030) were calculated, compared to the last period observed (2011-2015), where the proportion of this change is related to changes of risks or demographic (size or structure of the population). These two components can be different from zero and present a positive or negative direction. The calculation can be expressed as follows [16].

$$\Delta tot = \Delta risk + \Delta\ pop = (Nfff - Noff) + (Noff - Nooo)$$

where: Δtot is the total change, , Δrisk is the change as a function of the risk, Δ pop is the change as a function of the population, *Nooo* is the number of cases observed, *Nfff* is the number of cases estimated and *Noff* is the number of cases expected when the rates of mortality increase during the period studied.

RESULTS

From 2001 to 2015, there were 125,751 deaths by liver and intrahepatic biliary ducts malignant neoplasm in Brazil, 56.9% of which affecting males and 43.1%, females. The standard mortality rate of the world population for Brazilian women varied from 3.57 deaths/100,000 thousand inhabitants in 2001 to 3.39 deaths/100 thousand inhabitants in 2015. For males, this rate varied from 4.23 deaths/100,000 thousand inhabitants in 2001 to 5.84 deaths/100,000 thousand inhabitants in 2015. The ratio for both genders from 2001 to 2015 was, in average, 1.6. The highest mortality rates for both genders were recorded in the North Region, and in the Northeast Region, women presented the highest mortality rates while mortality rates for men were the highest in the South (Figure 1).

The analysis of historical series of female mortality rate showed the trend of significant increase of the mortality in Brazil until 2005 (APC= 3,2% CI95% 0.6-5.9), followed by a period of reduction, but without statistical significance. The reduction in the Central-West (APC = -2.0% CI95% -3.1; -0.8), Southeast (APC = -1.0%

CI95% -1.7; -0.3) and North (APC = -7.6% CI95% -12.7; -2.2) regions stands out. Male mortality presented trend to increase in Brazil (APC = 3.8% CI 95% 0.9-6.8) until 2005 followed by a period of reduction, but not significant. The same pattern was observed for the Northeast Region. For the other Regions, no significant changes occurred (Table 1).

Tables 2 and 3 present the number of deaths and standardized mortality rates for the periods studied and estimated, for females and males, respectively. After the analysis of the data for Brazil in the quinquennium 2026-2030, the estimative is the occurrence of 34,028 female deaths by liver cancer, while for males, the result was 48,819 deaths. The mortality rates for females will show strong reduction in the period from 2016 to 2030, standing out the North and Northeast regions with reduction of 30% when compared to the period from 2001 to 2005. For males, there is another pattern, with rise of the mortality rates until 2030, with bigger increase for the South. The greatest number of deaths concentrates in the age range of over 60 years old.

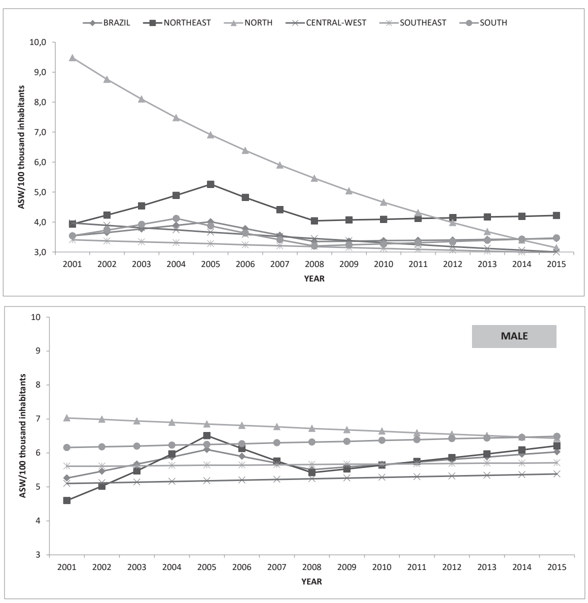

Figure 1. Mortality standard rates of liver and biliary ducts cancer in Brazil and Brazilian Regions per gender, 2001-2015

Captions: Rates of mortality adjusted to the world population (ASW/100 thousand hab.).

Figure 2 shows the rates of mortality by liver cancer in the periods studied and estimated according to the influence of risks and populational structure of Brazil and its regions. For both genders, the differences of rates expected to occur until 2030 will be explained by the change of the Brazilian demographic structure. It stands out the reduction of deaths related to risk factors of the disease in most of the Brazilian regions for both genders, with focus to North and Central-West.

DISCUSSION

The results of the present study show there is a trend of reduction of mortality by liver cancer and biliary ducts for females in most of the Brazilian regions and until 2030, these rates will continue to diminish. For males, the trend is of non-significant increase of the mortality, though this population has the highest rates.

The liver cancer and biliary ducts rates of mortality present relevant regional variations. The current study shows that the rates of mortality for males are similar to those of Central and Southern Asia (3.6 deaths per 100

Table 1. Trends of mortality by liver and biliary ducts cancer in Brazil and Regions: number of deaths, annual percentage change, confidence interval (CI 95%) and year of *joinpoint*

	Number of deaths	APC1 (IC 95%)	*Joinpoint*	APC2 (IC 95%)
FEMALE				
Brazil	54,308	3.2* (0.6; 5.9)	2005	-5.9 (-13.1; 2)
Northeast	17,210	7.5* (2.0; 13.4)	2005	-8.4 (-22.6 ;8.4)
North	3,375	-7.6* (-12.7; -2.2)		
Central-West	2,968	-2.0* (-3.1; -0.8)		
Southeast	23,012	-1.0* (-1.7; -0.3)		
South	8,636	5.1 (-2.6; 13.5)	2004	-6.1 (-13.0; 1.3)
MALE				
Brazil	71,443	3.8*(0.9; 6.8)	2005	-3.3 (-11.6; 5.7)
Northeast	18,583	9.1*(3.1; 15.5)	2005	-5.9 (-21.4; 12.6)
North	5,145	-0.6 (-1.6; 0.3)		
Central-West	4,284	0.4 (-1.1; 1.9)		
Southeast	31,967	0.1 (-0.4; 0.6)		
South	12,522	0.4 (-0.5; 1.2)		

Captions: APC = Annual percentage change *Statistic significance p<0.05.

Table 2. Female mortality by liver and biliary ducts cancer in Brazil and regions: number of deaths observed and estimated per age and rates of mortality adjusted to the world population

	Period observed			Period estimated		
	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025	2016-2030
BRAZIL						
Age (years)						
0-39	812	738	789	774	728	723
40-59	3,856	4,310	4,884	5,355	5,655	5,998
60-85	10,923	12,711	15,293	18,640	22,694	27,307
ASW	3.57	3.42	3.39	3.36	3.33	3.29
NORTHEAST						
Age (years)						
0-39	282	273	274	277	265	252
40-59	1,352	1,324	1,480	1,540	1,615	1,731
60-85	3,498	4,014	4,703	5,537	6,456	7,468
ASW	4,45	4,28	4,17	4,02	3,86	3,7
NORTH						
Age (years)						
0-39	79	87	77	78	76	74
40-59	300	316	340	363	404	469
60-85	628	703	845	994	1,175	1,376
ASW	4.89	4.44	4.11	3.74	3.46	3.25
CENTRAL-WEST						
Age (years)						
0-39	40	59	48	41	39	37
40-59	184	272	326	327	333	332
60-85	425	673	777	950	1,149	1,382
ASW	2.8	3.4	3.08	2.76	2.53	2.35
SOUTHEAST						
Age (years)						
0-39	303	247	297	267	254	247
40-59	1,552	1,828	2,018	2,202	2,280	2,375
60-85	4,761	5,457	6,558	7,885	9,556	11,503
ASW	3.2	3.05	3.02	2.98	2.97	2.96
SOUTH						
Age (years)						
0-39	98	80	95	104	106	106
40-59	550	614	756	879	964	1.049
60-85	1,869	2,034	2,531	3,229	4,126	5,161
ASW	3.59	3.23	3.35	3.52	3.69	3.84

Caption: Rates of mortality adjusted to the world population (ASW/100 mil inhabitants).

thousand inhabitants), Northern Europe (4.0 deaths per 100 thousand inhabitants) and East Africa (4.6 deaths per 100 thousand inhabitants). For females the Brazilian rates were higher than Northern Europe (1.8 deaths per 100 thousand inhabitants), Australia/New Zealand (2.0 deaths per 100 thousand inhabitants), Western Europe (2.1 deaths per 100 thousand inhabitants) and Central-South Asia (2.1 deaths per 100 thousand inhabitants), and in these regions, the lowest mortality rates were reported[11].

The findings about the trends of Brazilian mortality in this study are confirmed by the research results that utilized the Populational Base Cancer Registries of the Latin American countries from 1997 to 2006. For males this research demonstrated the trend of non-significant reduction of the rates of mortality in Argentine (APC = - 1.2%), Chile (APC = -1.8%) and Costa Rica (APC = -1.7%) and non-significant rise in Brazil (APC = 2.0%). This pattern was similar for females with non-significant reduction in Argentine (APC = -2.4%), Chile (APC = -0,3%) and Costa Rica (APC = -3.5%), and non-significant increase in Brazil (APC = 0.9%)[17]. Confirming the findings of this research, the study of mortality by

Table 3. Male mortality by liver cancer and bile ducts in Brazil and Regions: number of deaths observed and estimated per age and rates of mortality adjusted to the world population

	Rates observed			Rates estimated		
	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025	2016-2030
BRAZIL						
Age (years)						
0-39	1,003	1,225	1,206	1,008	834	681
40-59	4,538	7,358	8,156	8,575	8,574	8,552
60-85	9,495	15,044	19,277	25,173	32,102	39,585
ASW	4.23	5.69	5.84	5.97	5.97	5.86
NORTHEAST						
Age (years)						
0-39	442	429	422	404	376	352
40-59	1,448	1,744	1,918	2,113	2,253	2,396
60-85	3,319	3,964	4,885	6,022	7,315	8,711
ASW	5.46	5.76	5.98	6.13	6.12	5.99
NORTH						
Age (years)						
0-39	187	215	218	236	244	246
40-59	486	548	602	640	700.8	804
60-85	798	933	1,158	1,408	1,707	2,029
ASW	6.93	6.76	6.6	6.32	6.07	5.84
CENTRAL-WEST						
Age (years)						
0-39	90	98	75	78	79	79
40-59	370	452	558	596	591	579
60-85	648	876	1,112	1,455	1,889	2,369
ASW	4.94	5.23	5.26	5.26	5.19	5.05
SOUTHEAST						
Age (years)						
0-39	461	426	415	411	400	402
40-59	2,718	3,366	3,618	3,831	3,810	3,817
60-85	5,550	6,688	8,738	11,094	13,931	16,849
ASW	5.42	5.5	5.63	5.67	5.63	5.5
SOUTH						
Age (years)						
0-39	105	111	120	123	122	120
40-59	984	1,332	1,516	1,642	1,686	1,733
60-85	2,173	2,716	3,481	4,488	5,722	7,023
ASW	5.84	6.21	6.35	6.51	6.62	6.65

Captions: Rates of mortality adjusted to the world population (ASW/100 thousand hab.).

cirrhosis, hepatic cancer and disorders because of alcohol use utilizing data about the Global Burden of Diseases in Brazil showed that there was a trend of stability of mortality by hepatic cancer in Brazil from 1990 to 2015[10].

The trend of stability or reduction of the mortality by liver cancer and biliary ducts is not a standard in the European, Asian and American continents. Utilizing the data of Globocam for 184 countries in 2012, the study of Wong et al.[11] showed that there is a trend of increase of mortality by liver cancer and biliary ducts in the United States (Average Annual Percent Change – AAPC = 3.1%, CI 95% = 2.7-3.4 for males; AAPC = 2.3%, CI 95% 1.1-3.5 for females) and in Canada (AAPC = 2.2% CI 95% = 1.5-3.0 for males; AAPC = 1.9% CI 95% = 0.3-3.6 for females); in Norway (AAPC = 5.6% CI 95% = 2.8-8.5), United Kingdom (AAPC = 4.7% CI 95% = 3.6-5.8), Lithuania (AAPC = 2.5% CI 95% = 0.8-4.3) and The Netherlands (AAPC = 2.0%, CI 95% = 0.7-3.3) had increase of mortality for males. In Singapore (AAPC = 7.7, C 95% = 4.1-11.5), there was a significant increase for females.

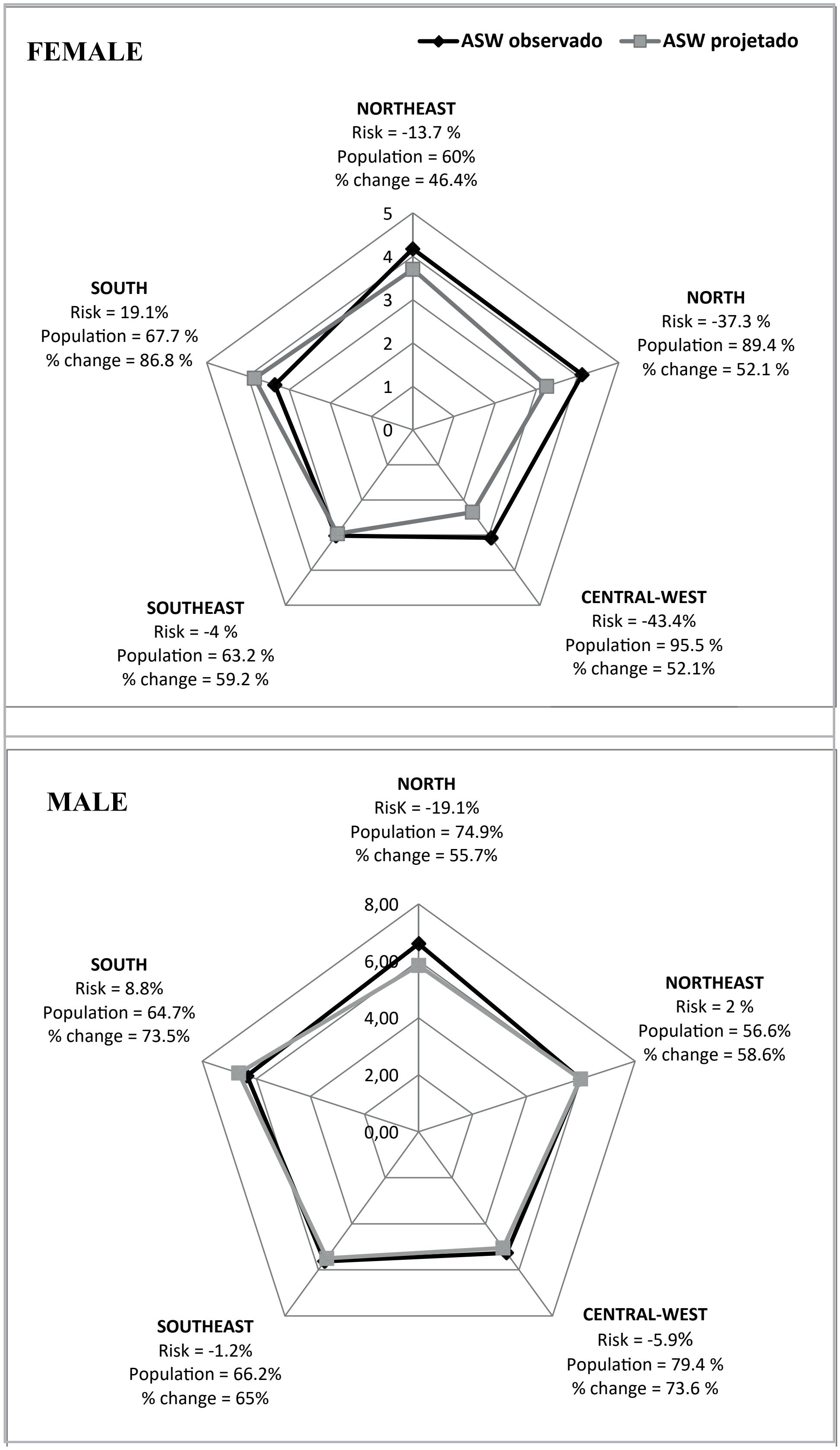

Figure 2. Standard rates by world population, total change (change), relative change for risk factors (risk) and relative change to the structure of the population (population) for both genders, 2011-2015 (observed) and 2026-2030 (estimated) of mortality by liver and biliary ducts in Brazil

Caption: Mortality rates adjusted to the world population (ASW/100 mil hab.).

The rates of mortality by liver cancer and biliary ducts presented by these countries are explained, among other factors, by the variations of the incidence rates for this cancer. In a study that analyzed the database of Cancer Incidence in Five Continents (CI5plus), different patterns of incidence occurred when compared with Europe, Asia and Americas for the period from 2003 to 2007. Countries as Japan (APC = -4.9%), China (APC = -1.7%) and Singapore (APC = -2.0%) had a significant reduction of the rates; Brazil (APC = 3.7%) and Colombia (APC = 2.8%) had a non-significant increase while The Netherlands (APC = 1,9%), Germany (APC = 3.3%) and Switzerland (APC = 1.4%) presented trend of increase of incidence[2].

The epidemiology of this cancer is directly related to the prevalence of risk factors already described that occur unequally in the Brazilian macro-regions. Among the most important exposures, stand out the HBV and HCV infections, alcohol use, hepatic cirrhosis and food contamination with aflatoxins[6,3,10,11]. The analysis of the prevalence of these factors in the Brazilian regions can explain the elevated rates of mortality by hepatic cancer in the North, Northeast and Southern regions and the trend these regions presented in the last decades.

In the end of the XX century, Brazil was classified as having hepatitis B moderate endemicity. The detailed analysis showed a highly heterogeneous distribution of the disease with prevalence increasing from the South to the North, and the Amazon Region has the highest endemicity and the Southeast, Northeast and Central-West regions classified as low to moderate prevalence[18]. In 2010, for the Brazilian population from 10 to 69 years old, the global serum-prevalence for total anti-HBc corresponded to 7.4%, reaching 10.9% in the group of the North regions capitals. For the marker HBsAg, the global prevalence in the Brazilian capitals was 0.37% reaching 0.63% in the North capitals[19,20]. This information are essential since the areas of great prevalence of this risk factor as the North and Northeast of Brazil also present the highest mortality rates of this study.

In Brazil, the National Immunization Program (PNI) has been very successful with the highest world coverage rates of immunization and the Hepatitis B vaccination program is within the routine of universal vaccination. Its coverage was widened in 2001 for the whole country as part of the regular calendar for infants younger than one year and adolescents. The national vaccine coverage between 10 and 19 years old who have received at least one dose of vaccine reaches 30% in the Northeast and Central-West regions and Federal District and for infants younger than 1 year old, the coverage reaches 86.7%. In addition, the Brazilian Health System has a policy in place that defines the standard treatment in cases of chronic infection for hepatitis B and C and all drugs as provided cost-free[21].

The estimates for HCV infection indicate that worldwide, there are nearly 130 to 150 million infected[22]. In Brazil, from three to four million individuals are chronic hosts of the virus As there is no vaccine or immunoglobulin available to prevent HCV infection, the safer method of protection is primary prevention as screening and blood, its derivative and organs tests, sterilization of materials that can be reused and activities of secondary prevention that cover the identification, counseling and testing of individuals at risk, treatment of infected and educative activities[20,23,24].

The alcohol addiction and abuse are also indicated as one of the main causes of development of hepatic cirrhosis. The data of the Health National Research about alcohol use in Brazil shows that 13.7% of the Brazilians older than 18 years abuse this substance, being more prevalent in the Central-West (16.2%) and Northeast (15.6%) regions, more among men (21.6%) than females (6.6%)[25].

In a study that analyzed the use of alcohol as necessary cause of death, elevated rates occurred in the Northeast and Central-West regions and that the adjusted mortality rates were bigger for males in every region, with odds rate of eight (North, Central-West and Southeast regions) to ten-fold (South Region) for males in comparison with women [25]. As a counterpoint to the results of the present study, it is possible to notice that the ratio for both genders and the increase of these rates in the South Region can be related to the behavior of Brazilian men in relation to alcohol abuse. Alcohol abuse resulting damages is diminishing in Brazil demonstrated by the study that reported a drop of the mortality by cirrhosis due to alcohol-use (from 11.4 to 9.5) (16.9%)[10].

The form of prevention of liver neoplasm consists in controlling the most relevant carcinogenic factors with primary prevention, suggesting improvements of vaccine cover of the population against HBV and HCV with wide and effective assistance throughout the national territory as well as safer blood transfusions and hemoderivatives. The fight against alcohol abuse, clarifying the population about its damages, has also significantly contributed to prevent the disease. All these measures have a good cost-effective relation and has direct impact in the incidence of liver neoplasm and biliary ducts.

Nevertheless, while mortality impact by liver cancer reduces in Brazil, in the future there will be more focused effective actions as planning of services, identification of reference units, regionalization of the treatment and organization of the demand flow for treatment per region[26]. Regardless of Brazil relying in a health system with universal coverage, the challenge for the next years will be the development of a system able to respond to the change of health risks and necessity to attend Brazilians based in demographic and epidemiologic alterations through which the country is going through[27].

According to the results of this study, the projection of the mortality indicates reduction/stability of mortality rates by this cancer until 2030, mainly in Brazil's North and Northeast regions. The perspective of reduction of mortality in the poorer regions, reveals, somewhat, how the country copes to control the risk factors for this cancer.

Liver and biliary ducts cancer that are closely connected to the less developed regions and lower socioeconomic levels and is related to viral infections, life and health habits show an auspicious facet for public health in Brazil. The country has shown a considerable reduction of the number of deaths caused by infectious diseases in the last six decades and included the free and universal access to vaccination, to treatment and primary health care, in addition to the establishment of specific policies for vigilance and control of risk factors as the creation of the Plan of Strategic Actions to Cope with Non-Communicable Diseases that has among its goals, the reduction of alcohol abuse[21,28].

Furthermore, there were initiatives focused in the organization of the diagnosis and treatment of cancer in the country from the elaboration of the National Policy for Cancer Prevention and Control, whose objective is the reduction of the mortality and disability caused by this disease and the possibility of diminishing the incidence of some types of cancer among other prerogatives. These policies, programs and actions could together be the foundation to explain the total or partial success to control this disease today and in the future[10,29].

One of the limitations of this study is related to the national register of deaths in Brazil. In the past, there were problems of reliability and completeness of the data, mainly in the North and Northeast regions. It is possible that sub-notifications result from inaccuracy of the cause of death and the lower rates of mortality by the disease are likely the consequence of ill definition or unspecific classification of the deaths. Moreover, the short period of the time series to analyze the projection of the mortality can also be one of the limitations of the present study.

Nonetheless, though there are some limitations about the source of secondary data drawn from the Health Information Systems, some advantages appeared as the broad populational coverage, lower cost during information collection and potential of the data to be used in studies that are able to reflect in programs management, policies and health services.

However, since the creation of the information systems, the Brazilian state has been investing in its improvement, particularly in the last decade with expressive success[30]. In addition, the use of a methodology of correction of sub-notification minimizes the problem, and makes the study robust and representative of the Brazilian populational base.

CONCLUSION

In this study, the analysis of the data shows the favorable epidemiologic status related to liver cancer and bile ducts in Brazil, considering that the regional differences of the distribution of cancer are minimum, in addition to the time trends of reduction and stability observed in the last 15 years and that will continue to be recorded in the upcoming decades. The results of the estimates show that the profile of mortality by this cancer will reduce, mainly for females and that the prevention and control policies of the risk factors must be continuous and strengthened in the country.

CONTRIBUTIONS

Isabelle Ribeiro Barbosa and Dyego Leandro Bezerra de Souza participated ot the study design, analysis of the data, supervision and final wording. Fábia Cheyenne Gomes de Morais Fernandes and Flávia Arichelle Cavalcante dos Santos participated of the data collection, elaboration of the databse and wording of the manuscript. Emelynne Gabrielly de Oliveira Santos and Nayre Beatriz Martiniano Medeiros participated of the wording and/or critical review. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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