

Mortality from liver cirrhosis in Espírito Santo State, Brazil

Mortalidade por cirrose hepática no Estado do Espírito Santo, Brasil

La mortalidad por cirrosis hepática en estado de Espírito Santo, Brasil

Patricia Lofego Gonçalves ¹
 Carlos Sandoval Gonçalves ¹
 Fausto Edmundo Lima Pereira ²

Abstract

To study mortality from liver cirrhosis in Espírito Santo State, Brazil, we reviewed death certificates (DC) from 2000-2010 and medical records of deceased patients with investigation of alcoholism and hepatitis B or C. From a total of 218,410 DC, 3,554 deaths from liver cirrhosis were retrieved. The annual mortality rate was 19.8/100,000 for men and 4.31/100,000 for women, without significant changes after correction for ICD-R98 and R99 and without a significant increase in the annual percentage change. In 49% of death certificates, the aetiology of cirrhosis was defined: of these alcoholism in 81.5% of cases and viral hepatitis in 15.7%. Aetiology was confirmed in 262 reviewed records, including alcoholism (40.5%); hepatitis B or C (26.7%); other (3.8%); and cryptogenic (10.6%). The mean annual potential years of life lost were 5,946 years and 1,739 years for men and women respectively. The mortality rate from cirrhosis in Espírito Santo State is intermediate in relationship to worldwide data; alcoholism and hepatitis B or C were the main aetiologies; probably alcoholism is overestimated and hepatitis B and C viruses are underestimated as causes of cirrhosis registered on death certificates.

Liver Cirrhosis; Hepatitis; Alcoholism; Mortality

Resumo

Para estudar a mortalidade e conferir a etiologia da cirrose lançada nas Declarações de Óbito (DO) no Espírito Santo, Brasil, foi feita a revisão das DO (2000 a 2011) e de prontuários dos falecidos com investigação de alcoolismo e hepatites B e C. Entre 218.410 DO foram identificados 3.554 mortes por cirrose. A mortalidade anual foi 19,8/100 mil homens e 4,31/100 mil mulheres, sem variação anual significativa e sem alteração significativa após correção por CID R98 e R99. Em 49% dos DO a causa da cirrose foi identificada: alcoolismo 85% e hepatite B ou C 15,7%. As etiologias nos 262 casos revisados foram: alcoolismo 40,5%; hepatite B ou C 26,7%; outras causas 3,8%; criptogênicas 10,6%. A média anual de anos potenciais de vida perdidos foi 5946 e 1739 anos, respectivamente, para homens e mulheres. A taxa de mortalidade por cirrose no Espírito Santo é intermediária em relação a outras regiões do mundo; alcoolismo e hepatites B e C são as principais etiologias. É provável que alcoolismo seja superestimado e hepatites B e C subestimadas como causa de cirrose nas DO.

Cirrose Hepática; Hepatite; Alcoolismo; Mortalidade

¹ Hospital Universitário Cassiano Antônio Moraes, Vitória, Brasil.
² Universidade Federal do Espírito Santo, Vitória, Brasil.

Correspondence

P. L. Gonçalves
 Hospital Universitário Cassiano Antonio Moraes, Av. Marechal Campos 1468, Vitória, ES 29040-100, Brasil.
 patricialofego@gmail.com

Liver cirrhosis is the end stage of a number of diseases, mainly alcoholic liver disease and viral hepatitis, and it is a significant cause of death worldwide.^{1,2} Studies on aetiology and mortality from liver cirrhosis in Brazil are scarce^{3,4,5,6}. For these reasons we studied the mortality and the aetiology of liver cirrhosis in Espírito Santo State by analysing the death certificates from 2000 to 2010.

The official death certificates for all deaths that occurred in Espírito Santo State from January 2000 to December 2010 were reviewed. Lines A, B, C and D of each certificate were searched for the following codes from the International Classification of Diseases, 10th revision (ICD-10⁷: K70.3 (alcoholic cirrhosis), K73.4 (primary biliary cirrhosis), K74.4 (secondary biliary cirrhosis), K74.5 (biliary cirrhosis without other specifications) and K74.6 (other forms of liver cirrhosis and those without specification). A correction of the data was performed by calculating the estimated number of deaths from cirrhosis among those certificates whose cause of death was recorded as ICD-10- R98 or R99 (without medical assistance or an identified cause). Medical records of deceased patients who had been treated at the University Hospital in Vitória (the reference hospital for liver diseases in the state) were reviewed. The inclusion criteria were investigation of alcohol consumption, HBsAg and anti-HCV antibodies.

The crude mortality ratio and the age-adjusted annual mortality ratio for males and females, standardised to the world population were calculated using a direct method⁸.

The Annual Percentage Change was estimated by fitting a regression line to the natural logarithm (nl) of each annual mortality rate using the calendar year as a regressor variable (given $y = a+bx$, where y is nl of rate and x is the calendar year, the APC = $[(e^b-1) \times 100]$ ⁹.

Estimates of the number of potential years of life lost were performed based on the life expectancy at the age of death for the Brazilian population multiplied by the number of deaths that occurred at each age.

All of the statistics are presented with 95% confidence intervals (95%CI). For all comparisons, p-values less than 0.05 were considered significant.

This research was approved by the Ethics Research Committee of the Health Sciences Center of the Federal University of Espírito Santo State (protocol n. 157/08).

A total of 218,410 death certificates were analysed, and 3,554 deaths from liver cirrhosis were retrieved. Age and gender distributions are summarised in Figure 1 (mean of ages: 54.7 ± 13.9 years in men and 57.6 ± 16.9 years in women).

The ethnic distribution was similar in males and females: 47.5% White, 41.1% Mulatto and 11% Negro.

The age adjusted annual mortality rates are presented in Figure 2. The mean annual adjusted mortality rate was 19.8/100,000 for men and 4.31/100,000 for women. Differences of mortality rates with or without correction for R98 and R99 were not significant.

The average annual number of potential years of life lost due to death from liver cirrhosis was 260.1 years/100,000 men and 79.4 years/100,000 women (5,946 and 1,739 potential years of life lost by year respectively for men and women, in the study period).

The aetiology of liver cirrhosis was identified in 49% of death certificates. Alcoholism and viral hepatitis were the main associated factors in 81.5% (95%CI: 79.7-83.4) and 15.7% (95%CI: 17.4-14.0) of the cases, respectively.

Figure 3 summarizes the aetiology of cirrhosis in 262 cases in which the three main aetiologies were simultaneously investigated in each case. In this reviewed sample, age and gender distribution were similar to data observed among the 3,554 deaths retrieved from death certificates (Figure 1), although the mean of ages was significantly higher in men.

The results presented here demonstrate that mortality from liver cirrhosis in Espírito Santo State is similar to that reported in previous Brazilian studies carried out in 1962-1964³ and 1974⁴ in São Paulo state. However mortality is lesser than that reported in the study that included all Brazilian regions⁵. If the mortality from liver cirrhosis in Espírito Santo State was similar to the reported for the Southeast Region in 1989 (34.7 and 6.8/100,000 respectively for men and women)⁵, data presented here suggest that there was a reduction in mortality from cirrhosis in the state in the last 25 years.

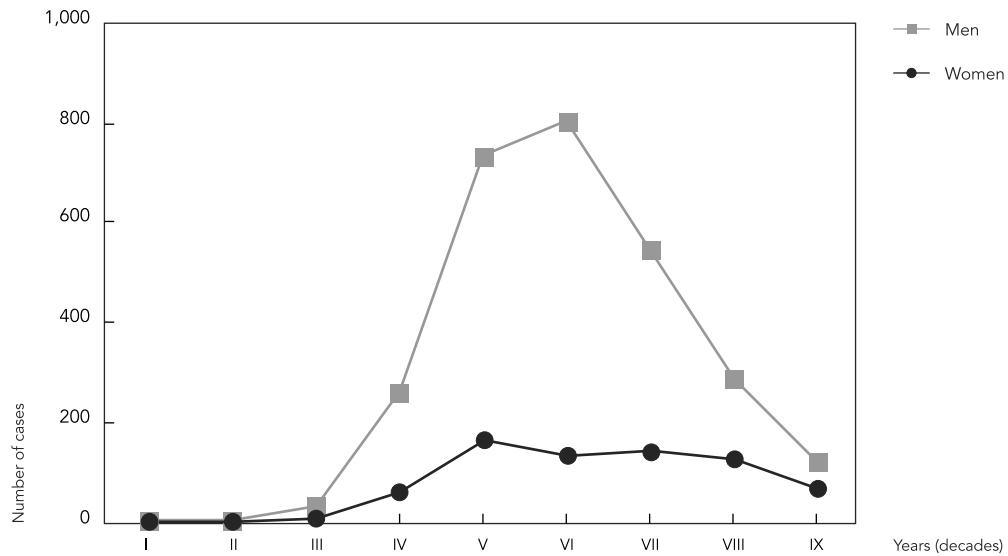
In comparison with data from the Americas, the mortality rate is similar to that reported in Chile¹⁰, and higher than that recently reported in Mexico¹¹, the United States and Canada¹. In comparison with European countries, the mortality ratio is similar to that reported in Western European countries and lower than in the United Kingdom (Scotland) and Eastern Europe^{1,12}.

The age and gender distributions are similar to what has been observed in other countries. Observations on prevalence, incidence and mortality have demonstrated that the risk of developing or dying from liver cirrhosis is higher in men in all countries, although there is large inter-country variation^{1,12,13}. In 262 cases in which the aetiology was confirmed (reviewed sample) the male-to-female ratio was significantly higher and

Figure 1

Mortality from liver cirrhosis in Espírito Santo State, Southeast Brazil: (a) Age and gender distribution in 3,554 deaths occurring between January 2000 and December 2010; (b) Age and gender distribution in a sample of 262 deceased patients who received care at the University Hospital in Vitória in which chronic alcoholism, HBsAg and anti-VHC were simultaneously investigated.

1a) 3,554 deaths



1b) 262 deceased patients

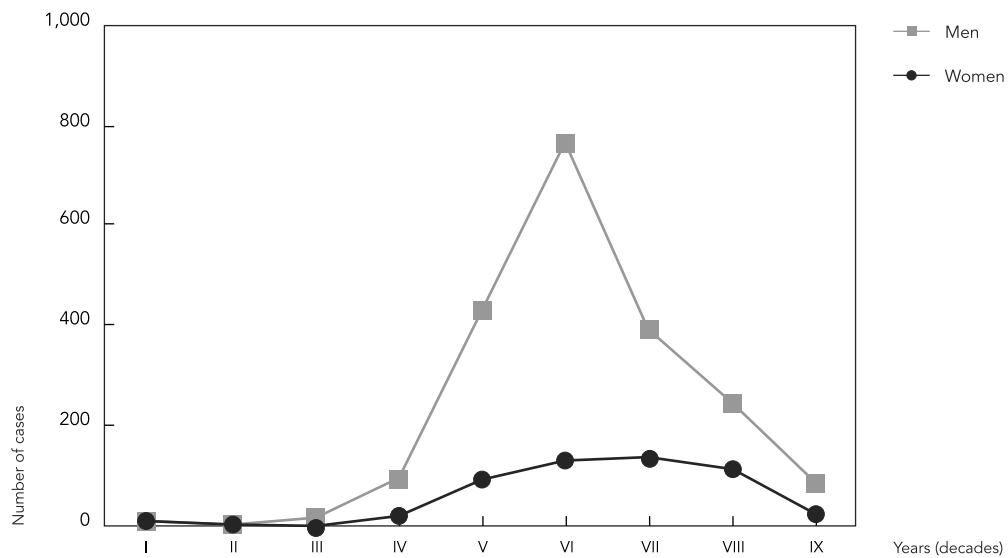


Figure 2

Age adjusted and standardized mortality rates from liver cirrhosis, with or without corrections for death certificates attested as R98 and R99 (without medical care or ill-defined causes), in Espírito Santo State, Southeast Brazil.

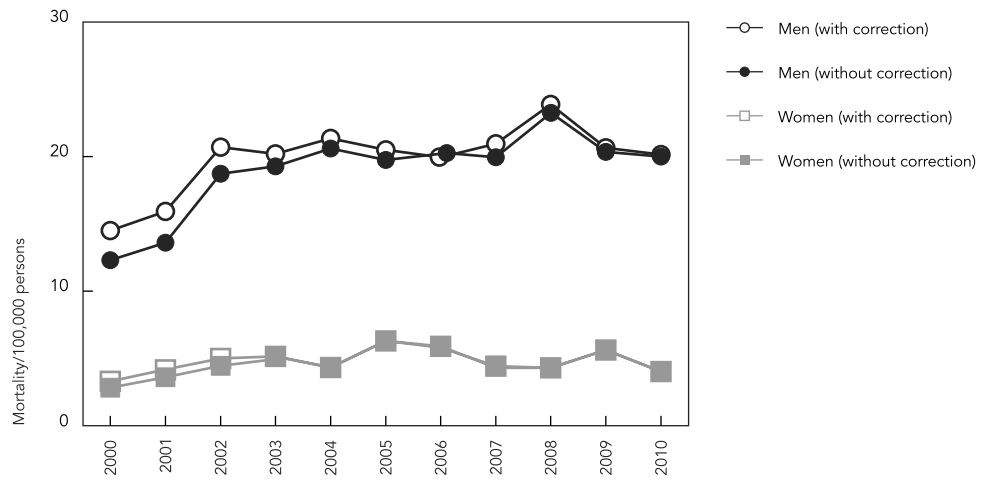
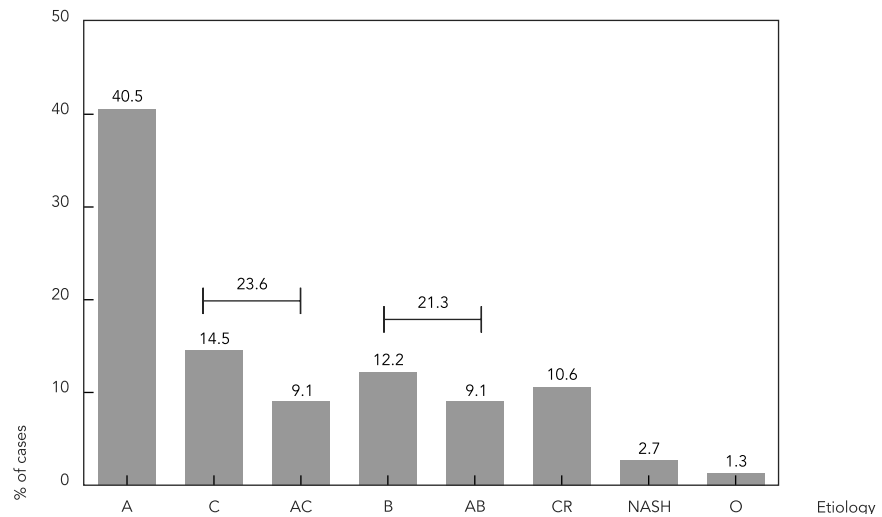


Figure 3

Etiology of liver cirrhosis in 262 cases retrieved from analysis of 3,554 death certificates in Espírito Santo State, Southeast Brazil (period 2000-2010).



These 262 cases were deceased patients who received care at the University Hospital in Vitória in which chronic alcoholism, HBsAg and anti-VHC were simultaneously investigated. The values above the lines indicate the sum of values (in %) shown on the bars.

A: chronic alcoholism; AB: alcoholism plus HBV; AC: alcoholism plus HCV; B: hepatitis B virus; C: hepatitis C virus; CR: cryptogenic; NASH: non-alcoholic steato hepatitis; O: other causes.

the age of death was significantly lower in patients with alcoholic cirrhosis than non-alcoholic cirrhosis (data not shown), as demonstrated in other countries¹⁰.

The Annual Percentage Change indicated a non significant increase in mortality: +2.82 (95%CI: -0.69;+6.39, p = 0.066) for men and + 1.58 (95%CI: -3.35;+4.18, p = 0.589) for women.

The aetiology of liver cirrhosis based on information retrieved from death certificates showed a high frequency of abusive alcohol ingestion and a low frequency of hepatitis virus infection. In the reviewed sample chronic alcoholism was the main isolated aetiology of cirrhosis but with frequency significantly lower than among death certificates in which the aetiology was recorded. Most likely, there was an overestimation of alcoholism and an underestimation of hepatitis virus infection in death certificates, as suspected by other authors¹⁴. This overestimation is probably due to the fact that the physicians give more importance to alcoholism as a cause of cirrhosis, failing to investigate the hepatitis virus, if the patient has a past history of alcohol abuse. On the other hand when the physician who signed the death certificate was not the physician who made the diagnosis on the patient, the abusive use of alcohol is more easily shared by the family than a past history of infection with HBV or HCV. If there are no reports of chronic alcoholism, the death certificate is signed as liver cirrhosis without a specified cause, as occurred in 51% of the reviewed death certificates. In this group a large number of cases of HBV or HCV associated cirrhosis could be included.

The reliability of the reviewed sample is supported by the gender distribution, which was similar to the distribution observed in the 3,554 deaths retrieved from death certificates. This reliability is also reinforced because the three main aetiological factors of cirrhosis were carefully investigated in each patient before death. In addition, the prevalence of different aetiologies observed in this sample was very similar to that observed in 1,516 cases of liver cirrhosis diagnosed at the University Hospital in Vitória between 1993 and 2010⁶. The frequency of chronic alcoholism in the reviewed sample was lower than that retrieved from death certificates, suggesting overestimation of alcoholism and under estimation of hepatitis B or C viruses as aetiology of liver cirrhosis recorded in death certificates.

It is noteworthy that the potential years of life lost due to death from liver cirrhosis is more relevant if we consider that alcoholism played a role in around 58% of the cases, and death occurs earlier in alcoholic cirrhosis than in cirrhosis of other aetiologies

In conclusion, the data presented here demonstrated that the mortality rate from liver cirrhosis in Espírito Santo State have intermediate values in relation to those observed worldwide, without a significant increase in the last 11 years. Chronic alcoholism, HCV and HBV were the main aetiological factors. Although chronic alcoholism is the main isolated cause of cirrhosis in the state of Espírito Santo, probably chronic alcoholism was overrated and hepatitis viruses were underestimated as causes of cirrhosis registered in death certificates.

Resumen

Para el estudio de la mortalidad por cirrosis hepática en el estado de Espírito Santo, Brasil, se revisaron los certificados de defunción entre 2000-2010 y los registros de los pacientes fallecidos con un historial de alcoholismo y hepatitis B y C. De entre 218.410 certificados de defunción, se recuperaron 3.554 muertes por cirrosis hepática. La tasa anual de mortalidad fue de 19,8/100.000 para los hombres y 4,31/100.000 para las mujeres, sin variación anual significativa y sin cambios significativos, después de la corrección por CID-R98 y R99. En el 49% de los certificados de defunción se definió la etiología: alcoholismo 81,5 % y hepatitis viral

15,7%. La etiología se confirmó en 262 registros revisados: alcoholismo 40,5%; hepatitis B o C en un 26,7%; otras causas 3,8% y en un 10,6% la cirrosis era criptogénica. La media de años potenciales de vida perdidos fue 5946 y 1739 años para hombres y mujeres. La tasa de mortalidad es intermedia en relación con el resto del mundo; alcoholismo y hepatitis B o C fueron las principales etiologías; el alcoholismo probablemente está sobrevalorado y la hepatitis B o C se subestiman como causa en los certificados de defunción.

Cirrosis Hepática; Hepatitis; Alcoholismo; Mortalidad

Contributors

P. L. Gonçalves reviewed the death certificates, carried out the tabulation of data, and participated in the data analysis and the write-up of the article draft. C. S. Gonçalves reviewed the hospital forms and participated in the write-up of the article draft. F. E. L. Pereira participated in the data analysis and wrote up the final version of the article.

Acknowledgements

We acknowledge Dr. Sebastião Onofre Sobrinho and Dra. Maria das Graças M R Cavalcante for granting access to the Núcleo Especial de Sistema de Informação em Saúde data bank from the Espírito State Health Secretariat and the Nucleo de Doenças Infecciosas, UFES, for their financial support.

References

1. Bosetti C, Levi F, Lucchini F, Zatonski WA, Negri E, La Vecchia C. Worldwide mortality from cirrhosis: an update to 2002. *J Hepatol* 2007; 46:827-39.
2. Leon DA, McCambridge J. Liver cirrhosis mortality rates in Britain from 1950 to 2002: an analysis of routine data. *Lancet* 2006; 367:52-6.
3. Puffer RR, Griffith GW. Características de la mortalidad urbana. Washington DC: Organización Panamericana de la Salud; 1968. (Publicación Científica, 151).
4. Guimarães C, Pacheco-de-Souza JM, Jorge MH, Laurenti R, Gotlieb SL, Santo AH, et al. Mortality of adults 15 to 74 years of age in São Paulo, Botucatu and São Manoel (Brazil), 1974/1975. *Rev Saúde Pública* 1979; 13 Suppl 2:1-73.
5. Lessa I. Cirrhosis of the liver in Brazil: mortality and productive years of life lost prematurely. *Rev Panam Salud Pública* 1997; 1:125-32.
6. Goncalves PL, Zago-Gomes MP, Marques CC, Mendonça AT, Gonçalves CS, Pereira FE. Etiology of liver cirrhosis in Brazil: chronic alcoholism and hepatitis viruses in liver cirrhosis diagnosed in the state of Espírito Santo. *Clinics* 2013; 68:291-5.
7. World Health Organization. International Statistical Classification of Disease and related Health Problems: 10th revision. Geneva: World Health Organization; 1992.
8. Gordis L. Measuring the occurrence of disease: II. Mortality. In: Gordis L editor. *Epidemiology*. 3rd Ed. Philadelphia: Elsevier Saunders; 2004. p. 48-70.
9. National Cancer Institute. http://seer.cancer.gov/seerstat/WebHelp/seerstat.htm#Trend_Algorithms.htm (accessed on 04/May/2011).
10. Alonso FT, Garmendia ML, Aguirre M, Searle J. Análisis de la tendencia de la mortalidad por cirrosis hepática en Chile: años 1990 a 2007. *Rev Méd Chile* 2010; 138:1253-8.
11. Méndez-Sánchez N, García-Villegas E, Merino-Zeferino B, Ochoa-Cruz S, Villa AR, Madrigal H, et al. Liver diseases in Mexico and their associated mortality trends from 2000 to 2007: a retrospective study of the nation and the federal states. *Ann Hepatol* 2010; 9:428-38.
12. Zatoński WA, Sulkowska U, Mańczuk M, Rehm J, Boffetta P, Lowenfels AB, et al. Liver cirrhosis mortality in Europe, with special attention to Central and Eastern Europe. *Eur Addict Res* 2010; 16: 193-201.
13. Fleming KM, Aithal GP, Solaymani-Dodaran M, Card TR, West J. Incidence and prevalence of cirrhosis in the United Kingdom, 1992-2001: a general population-based study. *J Hepatol* 2008; 49:732-8.
14. Torres-Poveda K, Burguete-García AI, Madrid-Marina V. Liver cirrhosis and hepatocellular carcinoma in Mexico: impact of chronic infection by hepatitis viruses B and C. *Ann Hepatol* 2011;10:556-8.

Submitted on 29/May/2013

Final version resubmitted on 08/Jan/2014

Approved on 22/Jan/2014