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Mortality rate of alcoholic liver disease and risk of hospitalization for alcoholic liver cirrhosis, alcoholic hepatitis and alcoholic liver failure in Australia between 1993 and 2005

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Abstract

Background: Alcoholic liver disease (ALD) is an important contributor to the total burden of alcohol-related harm; however, the morbidity of different types of ALD in Australia has not been described. The aim of this study was to investigate recent trends in hospital admission rates among alcoholic liver cirrhosis, alcoholic hepatic failure and alcoholic hepatitis in Australia, as well as the mortality of ALD.

Method: This is a population-based cohort study including the total 15+ years Australian population. Data were obtained from the Australian Bureau of Statistics and the Australian Institute of Health and Welfare. Main outcome measures: (i) trend of standardized mortality rates and trend of standardized hospital admission rates for males and females for 1993/1994–2004/2005 (fiscal year), (ii) relative risk of alcoholic liver cirrhosis, alcoholic hepatic failure and alcoholic hepatitis hospital admissions for 1999/2000–2004/2005.

Results: The mortality rate of ALD decreased significantly. Significant increases in hospital admissions for alcoholic hepatic failure among older adults and alcoholic hepatitis among younger age groups were observed. There is a significant 10-fold increase in the risk of hospital admissions of alcoholic cirrhosis in 2002/2003 for the 20–29 years population.

Conclusion: Reductions in overall ALD mortality observed are likely the result of advances in disease management. Significant increase in hospital admissions suggests an increase in the prevalence of ALD among the Australian population. Dramatic increases in hospital admissions for alcoholic cirrhosis in 2002/2003 for the 20–29 years population may have been due to an increase in screening of alcohol-related harms in primary care settings.

Introduction

Excessive alcohol consumption is one of the leading causes of morbidity and mortality in Australia. Alcoholic liver disease (ALD) is the most frequent cause of death related to long-term alcohol consumption at high-risk levels. Between 1992 and 2001, ALD caused 6825 deaths in Australia.[1] Deaths due to liver disease have been used as a reliable and robust indicator of overall alcohol-related problems in a range of societies. ALD is a particularly useful indicator for Western countries that have standardized recording procedures for death records.[2]

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The association between alcohol intake and ALD has been well documented. Chronic high levels of alcohol consumption may lead to several types of liver injury, and pathological changes include steatosis, fibrosis, cirrhosis and alcoholic hepatitis.[3] The prognosis of ALD is largely related to continued alcohol consumption, and therefore early detection of the disease has the greatest potential to reduce morbidity and premature mortality.[4]

ALD is an important contributor to the total burden of alcohol-related harm, a large proportion of which can be reliably estimated using hospitalizations for ALD and mortality.[2] The aim of this study was to compare recent trends in hospital admission rates among different types of ALDs, namely, alcoholic liver cirrhosis, alcoholic hepatic failure and alcoholic hepatitis in Australia, as well as describing overall hospital admission rates and mortality rates for ALDs.

Methods

Data sources, coding of diagnosis and selection of cases

Mortality data were sourced from the Australian Bureau of Statistics (ABS) Mortality Data file, which is a compilation of details of all Australian deaths obtained from state and territory Death Registries. Cause of death (primary diagnosis) was recorded according to International Classification of Diseases 9th revision, Clinical Modification (ICD-9-CM) between 1991 and 1997 and according to International Classification of Diseases 10th revision, Australian Modification (ICD-10-AM) between 1998 and 2005. The causes of death information are supplied to the Registrar of Births, Deaths and Marriages in each state and territory by the medical practitioner certifying the death or by a coroner. This information is provided to the ABS by individual Registrars for coding and compilation into aggregate statistics.

State and territory level data on hospital separations (equated here to hospitalizations) were obtained from the Australian Institute of Health and Welfare's National Hospital Morbidity Database (NHMD). The NHMD is an electronic compilation of clinical information on hospital separations (i.e. unit records) from public and private hospitals occurring within each Australian state/territory. This compilation codes information on age at admission, sex, and primary cause of admission and place of residence for all cases. Cause of hospitalization (primary diagnosis) is coded using ICD-9-CM between 1993/1994 and 1997/1998 (fiscal year) and using ICD-10-CM classification system between 1999/2000 and 2004/2005 for all jurisdictions. ICD codes are applied by professional coders and/or the attending clinical staff.

Both ICD-9-CM and ICD-10-CM codes specify liver disease caused by alcohol. For mortality data between 1991 and 2005, and hospital admission data between 1993/1994 and 2004/2005, primary diagnosis of cases matching one of the following codes was included in the analysis: ICD-9-CM codes; 571.0, 571.1, 571.2, 571.3: ICD-10-AM codes; K70.0, K70.1, K70.2, K70.3, K70.4 and K70.9.

Estimated residential population by year, state, gender and 5-year age groups between 1991 and 2005 was sourced from the ABS.

Data analysis

Standardized hospital admission rates and mortality rates of males and females for the 15+ years population were calculated to describe the actual risk of hospital admission and mortality using the direct standardization method. Year, gender and age-specific hospitalization and mortality rates were first calculated for each state/territory and were then directly standardized against the age distribution of the Australian population in 2005 (15+ years, in 5-year age groups).

Multivariate analysis

Multivariate Poisson regression was used to compare the relative risk (RR) of ALD mortality among different years. Models were adjusted for gender, state and age (in 5-year groups) for the overall 15+ years population between 1991 and 2005.

To compare the risk of ALD hospital admissions across different fiscal years, models adjusted for gender, state and age (in 5-year groups) for overall 15+ years population with multivariate analyses performed by 10-year age groups (20–29, 30–39 . . . 70–79 years). Cases younger than 20 years and older than 80 years were excluded because of the very small frequencies. Moreover, in order to detect the potential bias that may be introduced by misclassification between alcohol-specific liver disease and non-specific liver disease, multivariate analysis was also performed on hospital admissions of non-specific liver cirrhosis (K74.6).

Under ICD-10-AM, the specific code for alcoholic hepatic failure is K70.4, but there is no equivalent specific code under ICD-9-CM. Because all jurisdictions had completely switched hospital admission records to ICD-10 by 1999/2000, multivariate analyses of type-specific ALD

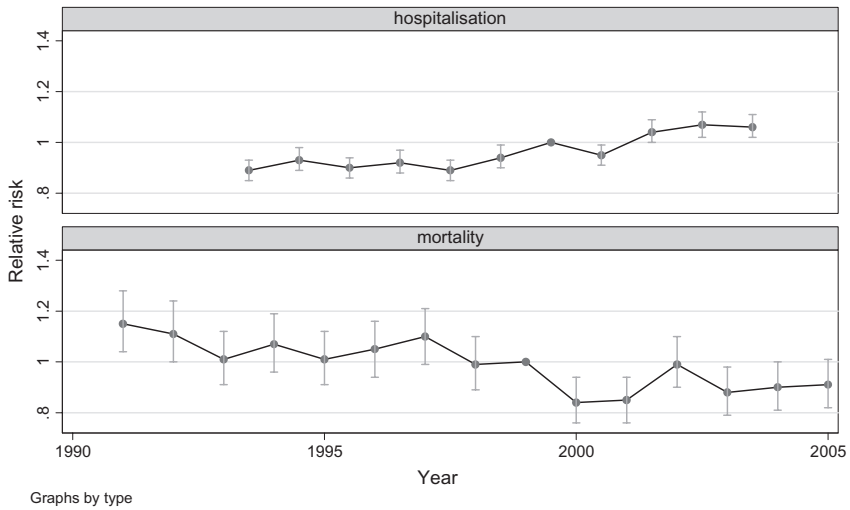

Figure 1 Relative risk of ALD mortality and relative risk of ALD hospital admissions 20+ years estimated from multivariate Poisson regression models (1999 as the reference year). Model adjusted for gender, state and age (in 5-year groups).

hospital admissions were performed for the period 1999/2000 to 2004/2005 with 1999/2000 as the reference year, including: (i) alcoholic hepatic failure (K70.4); (ii) alcoholic fibrosis and sclerosis of liver and alcoholic cirrhosis of liver (K70.2 and K70.3); and (iii) alcoholic hepatitis (K70.1). For deaths, 1999 was used as the reference period.

Results

Overall death and hospital admission trends

Poisson regression models indicated a declining trend in ALD deaths and an increasing trend for hospital admissions (Fig. 1). There was a 21.7% decline in the standardized mortality rate of ALD for males and 8.3% decline for females from 1991 to 2005 (Table 1). The decreasing trend of the risk of dying from ALD was found to be significant (*P* for trend <0.001). The 20% increase in ALD hospital admissions for males and females from 1993 to 2005 was also significant (*P* for trend <0.001) (Table 2).

Trends in ALD type-specific hospital admissions by age group

Between 1999 and 2005, there was a gradual increase in the risk of alcoholic cirrhosis admissions among the 40–49 years age group, while the risk was unchanged for the 50–59 and 60–69 age groups (Fig. 2, Table 3).

Table 1 Standardized alcoholic liver disease mortality (15+ years population)

Year	Male		Female	
	Standardized rates	95% confidence interval	Standardized rates	95% confidence interval
1991	9.2	8.4–10	2.4	2–2.8
1992	9.4	8.6–10.2	2.1	1.7–2.5
1993	7.9	7.2–8.6	2.3	1.9–2.7
1994	8.4	7.6–9.1	2.7	2.3–3.1
1995	8.2	7.5–8.9	2.2	1.9–2.6
1996	8.4	7.6–9.1	2.4	2–2.8
1997	8.8	8.1–9.5	2.4	2–2.7
1998	7.8	7.2–8.5	2.3	1.9–2.6
1999	7.7	7–8.3	2.5	2.1–2.8
2000	6.7	6.1–7.4	2	1.7–2.3
2001	7.1	6.4–7.7	1.7	1.4–2
2002	7.7	7.1–8.4	2.5	2.1–2.9
2003	7.2	6.6–7.8	1.9	1.6–2.2
2004	7.3	6.7–7.9	2	1.7–2.3
2005	7.2	6.6–7.8	2.2	1.8–2.5

Table 2 Standardized alcoholic liver disease hospital admissions (15+ years population)

Year	Male		Female	
	Standardized rates	95% confidence interval	Standardized rates	95% confidence interval
1993/1994	35.6	34.1–37.1	11.6	10.7–12.4
1994/1995	38.2	36.7–39.8	11.5	10.7–12.4
1995/1996	37.2	35.6–38.7	11	10.2–11.8
1996/1997	37.6	36.2–39.1	11.3	10.5–12.1
1997/1998	35.9	34.4–37.3	10.7	9.9–11.5
1998/1999	38.6	37.1–40	11.3	10.5–12.1
1999/2000	40.5	39–42	12.5	11.7–13.3
2000/2001	38.6	37.1–40	12.1	11.3–13
2001/2002	40.9	39.4–42.4	14.3	13.5–15.2
2002/2003	42.8	41.4–44.3	13.1	12.3–13.9
2003/2004	42.4	40.9–43.8	13.4	12.6–14.2
2004/2005	43.3	41.9–44.7	14.2	13.3–15

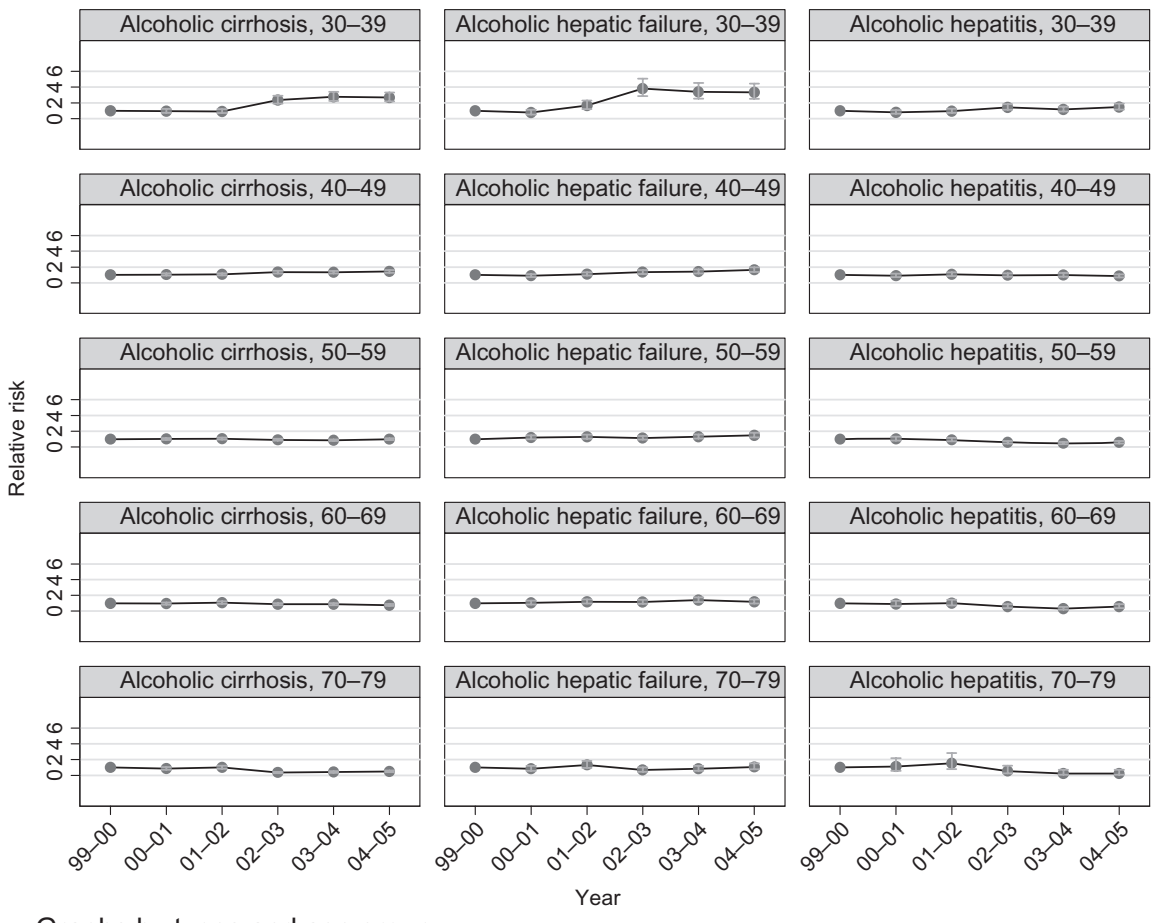

Figure 2 Relative risk of type-specific ALD hospitalization for different age groups (year 1999–2000 was taken as the reference year). Model adjusted for gender, state and age (in 5-year groups).

Table 3 Total number of hospital admissions and trends in the relative risk of type-specific alcoholic liver disease admission for calendar years 1999/2000 and 2004/2005

Age strata	Alcoholic liver cirrhosis		Alcoholic hepatic failure		Alcoholic hepatitis	
	n (%)	Trend direction	*n* (%)	Trend direction	*n* (%)	Trend direction
20–29	154 (31.0)	Increase†	80 (16.1)	Increase†	263 (52.9)	Increase†
30–39	1329 (45.8)	Increase†	839 (28.9)	Increase†	737 (25.4)	NST
40–49	3372 (57.9)	Increase†	1525 (26.2)	Increase†	932 (16.0)	NST
50–59	3346 (62.0)	NST	1390 (25.8)	Increase†	658 (12.2)	Decrease†
60–69	2024 (60.9)	NST	1013 (30.5)	Increase†	288 (8.7)	Decrease†
70–79	821 (65.5)	Decrease†	357 (28.5)	NST	76 (6.1)	NST

†Significant trend $P < 0.05$.
NST, no significant trend observed.

There was a significant gradual increase in the risk of alcoholic hepatic failure admissions among the 40–49, 50–59 and 60–69 age groups. There was a significant decrease in the risk of alcoholic cirrhosis admissions, but not in the risk of alcoholic hepatic failure for the 70–79 age group (Fig. 2, Table 3).

The risk of alcoholic hepatitis admissions remained mostly unchanged between 1999/2000 and 2003/2004 for the 40–49 age group, but there was a significant decrease found among the 50–59 and 60–69 age groups (Fig. 2, Table 3).

For the 20–29 age group, there was a significant 10-fold increase in the RR of hospitalization for alcoholic cirrhosis in the year 2002/2003 compared with years 1999/2000, 2000/2001 and 2001/2002. Hospitalizations were also significantly higher in 2003/2004 and 2004/2005. In addition, for the same age group there was a significant 5-fold increase in the RR of alcoholic hepatic failure in the year 2002/2003, which remained stable for the reminder of the time series. The RR of alcoholic hepatitis showed a gradual significant increase from 1999/2000 to 2003/2004 (Fig. 3, Table 3).

Similarly, among the 30–39 age group, there were substantial increases in the RR of admission for alcoholic cirrhosis and alcoholic hepatic failure in 2002/2003 compared with years 1999/2000, 2000/2001 and 20001/2002. The increase in RR was more striking for alcoholic hepatic failure. The RR of alcoholic hepatitis showed a gradual increase over the six years; however, the trend was not found to be significant in the Poisson model ($P = 0.124$) (Fig. 1, Table 3).

Discussion

The standardized mortality rate of ALD decreased significantly over the studied period. Similar trends over the last two decades were also observed in many European countries,[5] and in the USA.[6] However, mortality may be influenced by improvements in disease management, which usually increases survival rates, and increases hospital re-admissions.[7] In this study, overall hospital

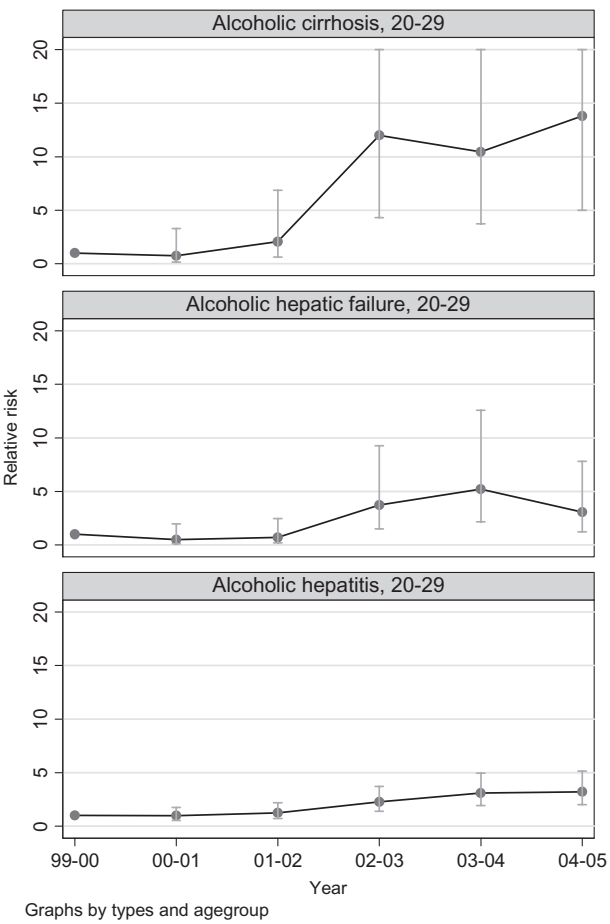

Figure 3 Relative risk of type-specific ALD hospitalization for 20–29 years age groups (year 1999–2000 was taken as the reference year). Model adjusted for gender, state and age (in 5-year groups).

admission rates were found to increase along with a decrease in mortality of ALD. Increasing hospital admission rates suggest an increase in the prevalence of ALD. This suggests that the reductions in ALD mortality observed in this study were more likely due to advances in disease management[4] than an overall decrease in the prevalence of ALD in the general population. The ageing population may be another partial explanation for the apparent decline in ALD mortality.[8] Although the analyses adjusted for 5-year age strata, given that alcohol consumption decreases with age and longevity tends to increase as the Australian population ages, it cannot be ruled out that the observed trend in ALD mortality may be partly due to the residual effect of ageing.

There was a gradual increase in hospital admissions for alcoholic hepatic failure between 1999/2000 and 2004/2005 among the 40–49, 50–59 and 60–69 age groups, while hospital admission rates of liver cirrhosis only increased in the 40–49 age group. This may suggest a real increase in the prevalence of ALD at end stage, and an increase in the prevalence of alcoholic liver cirrhosis for the 40–49 age group.

The development of alcoholic liver cirrhosis is a long-term process. During the early years of the disease when fatty liver, fibrosis and possibly the early stage of cirrhosis (compensated cirrhosis) are presented, symptoms are mild and easily remain undetected during routine general practitioner (GP) visits,[9,10] and the prevalence of undiagnosed cirrhosis is considered to be high.[11] Alcoholic hepatic failure is a life-threatening condition with admissions to hospital usually required. There are two main potential routes to this outcome – serious liver cirrhosis or alcoholic hepatitis (or both).

Given this, and our finding that the risk of alcoholic hepatitis hospitalization decreased between 1999/2000 and 2004/2005 for the population aged 50 to 69 years, we propose that the significant increase in alcoholic hepatic failure was likely due to an increase in the prevalence of total alcoholic liver cirrhosis (diagnosed and undiagnosed) in the older population. It is also possible that the increase in hospitalization for hepatic failure was in part due to the reduction in mortality, which was also observed (i.e. related to better treatment outcomes).

Both alcoholic hepatic failure and alcoholic hepatitis are more likely to lead to detectable symptoms than compensated alcoholic liver cirrhosis.[3] A cohort study of patients with alcoholic liver cirrhosis found that a sub-diagnosis of alcoholic hepatitis was associated with better survival.[12] This suggests that alcoholic hepatitis produces more symptoms with less severe liver injury than alcoholic liver cirrhosis, leading to diagnosis at an earlier stage of liver injury. Thus, hospitalization rates of alcoholic hepatitis are likely to be a more reliable indicator for the prevalence of total (diagnosed and undiagnosed) ALD among the younger age group, while hospitalization rates of alcoholic hepatic failure provide a more reliable estimate of the population prevalence of serious cirrhosis among older age groups.

Taken together, the gradual increase in alcoholic hepatic failure in hospital admissions among older adults, and the gradual increase in alcoholic hepatitis among younger age groups suggests an increase in the prevalence of total (diagnosed and undiagnosed) ALD among the Australia population.

The risk of alcoholic cirrhosis and alcoholic hepatic failure dramatically increased in the year 2002/2003 and remained constant after that for the 20–29 age group (Fig. 2). This rapid increase was not necessarily due to a dramatic increase in the prevalence of alcoholic liver cirrhosis cases in the population. An alternative explanation is that as hospital admissions of alcoholic liver cirrhosis cases are determined by the number of diagnosed cases in primary care settings, the rapid increase may be a result of increased intensity of alcohol-related disease screening. Patients with cirrhosis may only present mild and non-specific symptoms, and diagnosis of liver cirrhosis is usually made at a late stage and at older ages.[11] The successful detection of a young patient with alcoholic cirrhosis is more likely to occur with routine screening for alcohol use disorders in primary care settings. An increase in routine screening by medical practitioners could lead to a considerable increase in diagnosis and hospital admission of asymptomatic alcoholic liver injury.[10,13] The increase in alcoholic hepatic failure admission might be a result of an increase in serious alcoholic hepatitis.

In 2001 the NHMRC released the Australian alcohol guidelines, which were disseminated to GPs and emergency care settings,[14] while the second edition of the alcohol use disorders identification test was also released at about the same time.[15] In 2002, new pharmacotherapies for alcohol dependence also became available.[16,17] The release of the two publications and availability of new treatments may have increased the awareness of alcohol-related diseases among doctors in primary care and thereby increased the likelihood of screening and diagnosis of asymptomatic alcoholic liver injury among younger age groups.

Notably, the number of alcoholic liver cirrhosis admissions among the 20–29 age group is relatively small (154 between 1999/2000 and 2004/2005) compared with the number of admissions for both the 30–39 (1329) and 40–49 (3372) age groups. Thus, the average number of alcoholic liver cirrhosis admissions among the 20–29 age group is about 10% of the number of cases for the

30–39 age group and about 5% of the number of cases for the 40–49 age group. It takes many years for compensated alcoholic liver cirrhosis to progress into the decompensation stage of the disease, at which stage many symptoms are developed. Therefore, a slight increase in early detection of asymptomatic liver cirrhosis could lead to a dramatic shift in the relative risk of hospitalization for alcoholic liver cirrhosis observed in the younger age group. Even so, the proportion of undiagnosed ALD is still likely to be large for the younger and middle-age population. Successful screening of ALD conditions in primary care could aid the prevention of disease progression, and further reduce morbidity and mortality from these conditions in the long term.[13,18]

Study limitations

As discussed above, part of the data used in the analysis of overall ALD mortality and hospitalizations was coded using ICD-9-CM while the later years was coded using ICD-10-CM. Both ICD-9-CM and ICD-10-CM have specific codes for ALD. However, it is very unlikely that the observed gradual increase in ALD hospitalizations or the gradual decrease in ALD mortality was due to changes in coding practice, which occurred at one point in time. During the time period over which the analysis of type-specific ALD hospitalizations occurred, only ICD-10-CM codes were in use and therefore coding alterations would be unlikely to explain substantially any of the large changes that occurred during that time. Nevertheless, the accuracy and consistency of data coding remain a potential methodological weakness in our study, although the possible extent of this is unknown. There may have been variability between coders, clinical staff, hospitals and states in their use of diagnostic terms and interpretation of ICD codes, which may have influenced the outcome. However, we suspect that variability between coders and subsequent diagnoses would be more likely to increase statistical variability (standard error) and thus bias towards the null. We note also that analyses controlled for state and as such, potential differences in coding strategies and staff training among states were adjusted for. Furthermore, as discussed above alcohol misuse is sometimes not recognized or discussed in hospital settings given the huge clinical workload, even when it is relevant to the clinical presentation.[11] Thus, overall, our estimation of ALD hospital admissions and mortality is expected to be lower than the actual rates.

Alcohol-related hepatocellular carcinoma is an important contributor to the morbidity, mortality and cost of medical care. In this study, hospital separation and mortality of alcohol-related hepatocellular carcinoma were not described. As discussed above, this is due to the fact that in general practice a large number of alcohol-related hepatocellular carcinoma cases have not been classified as alcohol-caused. Alcohol-related hepatocellular cancer is likely to be largely under-reported in formal records.

In order to address whether the observed increasing trends in alcoholic liver cirrhosis and hepatic failure may have been due to a change in coding practices incrementally favouring the recording of ALD over non-specific liver disease, a further multivariate analysis was performed for hospital admissions of non-specific liver cirrhosis (ICD10 code K74.6). A significant increasing trend for the risk of non-specific liver cirrhosis was observed for the period between 1999/2000 and 2004/2005 for the 20+ years plus population as well as for the 20–29 age group. Moreover, the RR in 2002/2003 was 5.2 compared WITH the reference period 1999/2000. It is very unlikely therefore that the observed increase in ALD hospitalizations was due to a shift in recording practices, which reduced coding for non-specific liver disease in favour of ALD.

There is some evidence to suggest that alcohol abuse may accelerate the progression of viral hepatitis.[19,20] In this study, coding limitations precluded an ability to identify which cases may have been associated with viral hepatitis infection. However, given diagnostic criteria and difficulties in obtaining patient history of alcohol consumption suggest that, hospitalizations and mortality for patients with viral hepatitis are more likely to be classified as liver disease originating from viral infection than ALD.

Conclusion

In this study, reductions in overall ALD mortality were observed which we argue are more likely the result of advances in disease management rather than a decrease in the prevalence of ALD. In contrast, gradual increases in hospital admissions for alcoholic hepatic failure among older adults and alcoholic hepatitis among younger age groups suggest an increase in the prevalence of total (diagnosed and undiagnosed) ALDs among the Australian population. Dramatic increases in hospital admissions for alcoholic cirrhosis and alcoholic hepatic failure in 2002/2003 may have been due to an increase in screening of alcohol-related harms in primary care settings. The prevention of such long-term disease, which predominates among those of middle age and older, will become increasingly important as the Australian populations continues to age.[21]

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