Original Article

Epidemiology and Clinical Evolution of Liver Cirrhosis in Singapore

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Abstract

Introduction: Liver cirrhosis is a common cause of morbidity and mortality and an important burden on the healthcare system. There is limited literature on liver cirrhosis in Singapore. We aimed to describe the epidemiology and clinical characteristics of cirrhotic patients seen in an ambulatory setting in a tertiary referral centre. Materials and Methods: This is a retrospective observational cohort study of cirrhotic patients attending the ambulatory clinic of Singapore's largest tertiary hospital over 5 years. Cirrhosis was diagnosed on characteristic radiological features and/or histology. Aetiology of cirrhosis was determined by history, serology, biochemistry and/or histology. Data on decompensation events and death were retrieved from computerised hospital records. Results: The study included 564 patients with median follow-up of 85 months. Mean age was 60.9 ± 12.5 years with 63.8% males. Main aetiologies of cirrhosis were chronic hepatitis B (CHB) (63.3%), alcohol (11.2%), cryptogenic (9%) and chronic hepatitis C (CHC) (6.9%). CHB was the predominant aetiology in Chinese and Malays whereas alcohol was the main aetiology in Indians. CHC cirrhosis was more common in Malays than other races. Majority had compensated cirrhosis with 76.8%/18.3%/5%; Child-Pugh A/B/C respectively. Decompensation events occurred in 155 patients (27.5%) and 106 of them (18.8%) died. Diagnosis of cirrhosis via surveillance ultrasound was associated with improved 10-year survival. Age at diagnosis, portal vein thrombosis, Child-Pugh class and decompensation within 1 year of diagnosis were independent predictors of mortality. Conclusion: CHB is the primary cause of liver cirrhosis in Singapore. The major aetiologies of cirrhosis vary amongst the different ethnic groups. Cirrhotics with advanced age, portal vein thrombosis, poorer liver function and early decompensation have a higher mortality risk.

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Key words: Aetiology, Ambulatory, Clinical characteristics, Ethnic group, Mortality

Introduction

Cirrhosis is the common end result of chronic damage to liver parenchyma caused by a variety of liver diseases. It results in replacement of liver tissue by fibrotic scar tissue and regenerating nodules, leading to progressive liver dysfunction and clinical complications such as portal hypertension, hepatocellular carcinoma (HCC), liver failure and death. Cirrhosis is a major cause of mortality and morbidity worldwide and represents an important burden on healthcare resources.[1]

The epidemiology of liver cirrhosis varies with geographical location and socioeconomic conditions. The major aetiologies of cirrhosis in Western countries are chronic hepatitis C and alcoholic liver disease.[2-4] In the East, there are variations in epidemiology of liver cirrhosis within different Asian countries. Chronic hepatitis C is the prevalent cause of liver cirrhosis in Japan, whereas chronic hepatitis B is the main aetiology of cirrhosis in China, Korea and parts of Southeast Asia.[5,6] In Nepal and Thailand, alcohol-related cirrhosis is the predominant aetiology.[7,8]

To date, there is little published data on the epidemiology of liver cirrhosis in Singapore. Most were case series involving small numbers of patients and were published more than 25 years ago.[9-13] There is an important need to fill the knowledge gap with regards to the current epidemiology of liver cirrhosis in Singapore. The aim of this study was

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to describe the aetiology and clinical evolution of liver cirrhosis in a cohort of multi-ethnic Asian patients attending an ambulatory liver clinic at a large tertiary care hospital in Singapore.

Materials and Methods

We performed a retrospective observational cohort study of cirrhotic patients attending the ambulatory clinics of the Singapore General Hospital's Department of Gastroenterology and Hepatology between September 2006 and August 2011. Cases of liver cirrhosis were identified from the department's outpatient cirrhosis registry. Cirrhosis was diagnosed by radiology (presence of coarse echoes and nodular outline of the liver on either ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI) or by histology. The date of diagnosis of liver cirrhosis was based on the earliest record of radiological or histological evidence of liver cirrhosis. Patients' clinical and laboratory data were retrieved from computerised hospital records. The study was approved by the hospital's centralised institutional review board.

Aetiology of cirrhosis was determined by the primary physician and was based on clinical history, serology, biochemistry and/or histology. Cirrhosis was classified as due to chronic hepatitis B (CHB) or chronic hepatitis C (CHC) based on the presence of hepatitis B surface antigen (HBsAg) or anti-HCV IgG, respectively. Alcoholic liver cirrhosis was diagnosed if the patient consumed more than 20 units of alcohol per week for males or 14 units per week for females. Non-alcoholic fatty liver disease (NAFLD) was diagnosed based on presence of hepatic steatosis on imaging or histology, in the absence of significant alcohol consumption and co-existing causes for chronic liver disease. Primary biliary cirrhosis (PBC) was diagnosed based on positive anti-mitochondrial antibodies or corroborative histology. Autoimmune hepatitis (AIH) was diagnosed based on the presence of anti-liver antibodies, raised globulin fraction and/or histological evidence suggesting AIH. Wilson's disease was diagnosed based on a combination of clinical features, low serum caeruloplasmin, positive Kayser-Fleishcer rings, elevated 24-hour urinary copper and histology, where available. Patients were considered to have cryptogenic liver cirrhosis when all the above tests were negative, in the absence of significant alcohol intake and the absence of radiological features of hepatic steatosis. Dual aetiologies were considered when there was equal contribution of 2 aetiological factors. Otherwise, the predominant cause of liver cirrhosis was recorded based on the definitions above.

Compensated cirrhotics were followed up every 6 months and decompensated cirrhotics were reviewed every 3 months or less in the ambulatory clinic. During each clinic visit, patients were evaluated for signs of decompensation and development of new complications. Abdominal ultrasound and alfa-fetoprotein (AFP) were performed every 6 months for HCC surveillance. Outcome parameters recorded were development of decompensation events (jaundice, ascites, spontaneous bacterial peritonitis (SBP), variceal bleeding, hepatic encephalopathy), HCC and death. Mortality data were retrieved from hospital records and was censored on 31 August 2011. Deaths from complications of cirrhosis, progressive liver failure and HCC were considered to be liver-related. Patients who had a record of a recent clinic attendance within 6 months of the census date were deemed to be alive. Patients who had no record of a recent clinic attendance within 1 year of the census date and no record of death were deemed to be lost to follow-up and were excluded from the survival analysis. We were unable to determine if these patients were still alive or may have passed away outside of our hospital.

Statistical analysis was performed using SPPS version 19 (Chicago, USA). Continuous variables were compared between groups using unpaired t-test and Mann-Whitney U test. Categorical variables were compared using chi-square test (or Fisher's exact test where applicable). Survival from time of diagnosis of cirrhosis was analysed using the Kaplan-Meier method and compared by the log-rank method for variables of interest. Logistic regression analysis was performed to identify factors associated with mortality. Multivariate analysis was performed using Cox's proportional hazard regression model to evaluate for independent factors predictive for patient survival. Missing data was addressed by using the population means. A P level of less than 0.05 was taken to be significant.

Results

Our study included 564 patients with a median follow-up period of 85 months (range, 3 to 273). The baseline characteristics of the study cohort are described in Table 1. Majority of the subjects were Chinese (89.7%) and 76.8% had Child-Pugh A cirrhosis.

Aetiology of Liver Cirrhosis

CHB was the most common cause of liver cirrhosis in Singapore, accounting for almost two-thirds of the entire cohort (63.3%). This was followed by alcohol (11.2%), cryptogenic (9%) and CHC (6.9%).

Comorbid Conditions

Hypertension was present in 42.9%, diabetes mellitus in 34.6% and hyperlipidaemia in 22.7% of the cirrhotic cohort

Table 1. Baseline Characteristics of the Study Cohort (n = 564)

Variable		Mean ± SD/n (%)
Age	Mean age (years)	60.9 ± 12.5
Gender	Male	360 (63.8%)
Race	Chinese	506 (89.7%)
	Malay	27 (4.8%)
	Indian	25 (4.4%)
	Others	6 (1.1%)
Aetiology	Chronic hepatitis B	357 (63.3%)
	Alcohol	63 (11.2%)
	Cryptogenic	51 (9%)
	Chronic hepatitis C	39 (6.9%)
	Primary biliary cirrhosis	21 (3.7%)
	Non-alcoholic fatty liver disease	10 (1.8%)
	Autoimmune hepatitis	9 (1.6%)
	Wilson disease	2 (0.4%)
	Hepatitis B + hepatitis C	4 (0.7%)
	Hepatitis B + alcohol	2 (0.4%)
	Hepatitis C + alcohol	1 (0.2%)
	Others	5 (0.9%)
Comorbidities	Diabetes mellitus	195 (34.6%)
	Hypertension	242 (42.9%)
	Hyperlipidaemia	128 (22.7%)
	Coronary artery disease	68 (12.1%)
	Renal impairment	94 (16.7%)
	Smoking	65 (11.5%)
Laboratory tests	Albumin (G/L)	35.3 ± 6.8
	Bilirubin (μmol/L)	28.1 ± 39.2
	Alkaline phosphatase, ALP (U/L)	106.7 ± 73.3
	Alanine transaminase, ALT (U/L)	69.6 ± 152.9
	Asparatate transaminase, AST (U/L)	72.3 ± 137.1
	Gamma glutaryltransferase, GGT (U/L)	126.7 ± 165.4
	Prothrombin time, PT (seconds)	12.6 ± 2.3
	International normalised ratio, INR	1.2 ± 0.3
	Haemoglobin, Hb (g/dL)	12.8 ± 2.2
	Platelets (x 10^9/L)	150 ± 75
	Alfafetoprotien, AFP (μg/L)	294 ± 3761
Child-Pugh class	A/B/C	433 (76.8%)
		103 (18.3%)
		28 (5%)

(Table 1). Diabetes, hypertension and hyperlipidaemia were significantly more common in patients with cryptogenic liver cirrhosis and NAFLD-related cirrhosis compared to those with CHB, CHC and alcoholic cirrhosis. There was no significant difference in the frequency of coronary artery disease amongst the different aetiologies. Renal impairment was more common amongst patients with CHC cirrhosis. Smoking was significantly more common in patients with alcoholic cirrhosis (data not shown).

Ethnic Differences in Aetiology of Liver Cirrhosis

The aetiologies of liver cirrhosis were different between ethnic groups (Table 2). In Chinese, CHB was the commonest aetiology of cirrhosis, followed by alcohol and cryptogenic cirrhosis. In Malays, CHB was likewise the most common aetiology, followed by CHC and cryptogenic cirrhosis. Among Indians, however, alcohol was the predominant cause of liver cirrhosis, followed by cryptogenic cirrhosis and CHB. We observed a high rate of CHC cirrhosis in Malays compared to Chinese and Indians (P <0.001 for both comparisons). We also observed that the prevalence of cryptogenic cirrhosis was higher in Malays and Indians compared to Chinese. There were no significant differences in the prevalence of PBC and NAFLD-related cirrhosis amongst the different ethnic groups.

Clinical Presentation

Eighty-three percent of the study cohort had compensated disease at diagnosis (Table 3). Amongst these, the most common mode of diagnosis of cirrhosis was via surveillance ultrasound in patients on regular follow-up for chronic viral hepatitis (CHB and CHC). Conversely, compensated patients with alcoholic cirrhosis, cryptogenic cirrhosis and NAFLD were more commonly diagnosed through evaluation of abnormal liver function tests, low platelet counts or incidentally on imaging for unrelated indications (Fig. 1).

A small proportion (17%) of this ambulatory cohort of cirrhotics presented with decompensated cirrhosis (Table 3). Of these, the most common clinical presentations were elevated bilirubin and ascites. A greater proportion of alcoholic cirrhotics presented with decompensated disease at initial diagnosis compared to other aetiologies of cirrhosis. They were more frequently jaundiced and had a higher incidence of ascites and variceal bleeding. HCC was diagnosed in 52 patients (9.2%) at the time of diagnosis of cirrhosis and was more common in CHB compared to other aetiologies.

Development of Decompensation during Follow-up

A total of 155 patients (27.5%) developed clinical decompensation during the follow-up period. Of those who presented with compensated cirrhosis at diagnosis, 102 patients (21.8%) experienced their first decompensation

Table 2. Comparison of Major Aetiologies of Liver Cirrhosis Based on Ethnic Groups

Aetiology	Chinese (n = 506)	Malays (n = 27)	Indians (n = 25)	Others (n = 6)
Chronic hepatitis B (CHB)	336 (66.4%)	12 (44.4%)	4 (16%)	5 (1.4%)
Alcohol	52 (10.3%)	0 (0%)	10 (40%)	1 (1.6%)
Cryptogenic	38 (7.5%)	6 (22.2%)	7 (28%)	0
Chronic hepatitis C (CHC)	33 (6.5%)	6 (22.2%)	0 (0%)	0
Primary biliary cirrhosis (PBC)	20 (4%)	0 (0%)	1 (4%)	0
Non-alcoholic fatty liver disease	7 (1.4%)	2 (7.4%)	1 (4%)	0

Table 3. Clinical Presentation of Cirrhosis Based on Different Aetiologies of Liver Disease

	Overall (n = 564)	HBV (n = 357)	HCV (n = 39)	Alcohol (n = 63)	NAFLD (n = 10)	Crypt (n= 51)
Compensated cirrhosis	468 (83%)	319 (89.4%)	30 (76.9%)	34 (54%)	8 (80%)	45 (88.2%)
Abnormal liver function tests	77 (13.7%)	24 (6.7%)	4 (10.3%)	9 (14.3%)	3 (30%)	17 (33.3%)
Thrombocytopenia	26 (4.6%)	10 (2.8%)	1 (2.6%)	5 (7.9%)	1 (10%)	8 (15.7%)
Incidental diagnosis on imaging	81 (14.4%)	41 (11.5%)	6 (15.4%)	12 (19%)	3 (30%)	16 (31.4%)
Screening for chronic liver disease	283 (50.2%)	244 (68.3%)	19 (48.7%)	8 (12.7%)	1 (10%)	3 (5.9%)
Decompensated cirrhosis	96 (17%)	38 (10.6%)	9 (23.1%)	29 (46%)	2 (20%)	6 (11.8%)
Elevated bilirubin	55 (9.8%)	19 (5.3%)	4 (10.3%)	23 (36.5%)	1 (10%)	0 (0%)
Variceal bleeding	27 (4.8%)	7 (2%)	3 (7.7%)	8 (12.7%)	1 (10%)	4 (7.8%)
Ascites	39 (6.9%)	22 (6.2%)	2 (5.1%)	9 (14.3%)	0 (0%)	3 (5.9%)
Hepatic encephalopathy	3 (0.5%)	1 (0.3%)	0 (0%)	1 (1.6%)	1 (10%)	0 (0%)
Hepatocellular carcinoma	52 (9.2%)	43 (12%)	2 (5.1%)	2 (3.2%)	0 (0%)	4 (7.8%)

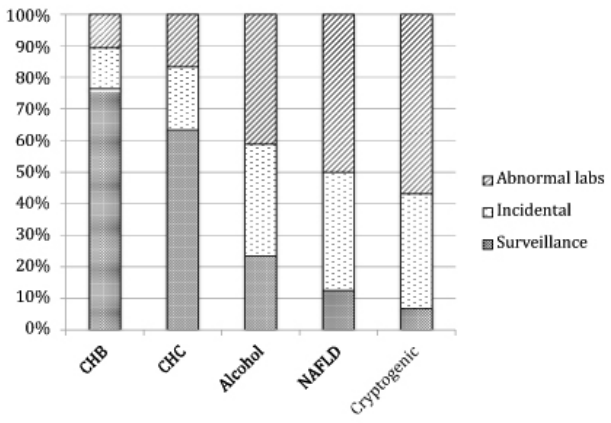

Fig. 1. Graph showing the mode of diagnosis in patients with compensated cirrhosis (n = 468).

event during follow-up. In the group who presented with decompensated cirrhosis at diagnosis, 53/96 (55.2%) experienced a further decompensation event. The most common decompensation events were development of ascites (16.8%) and hepatic encephalopathy (14.4%). Variceal bleeding (9.8%), jaundice (6.7%) and SBP (4.6%) occurred less often. Median time to the first decompensation event was 32 months (range, 0 to 244), and was significantly shorter in Child-Pugh C patients (6 months) versus Child-Pugh B (17 months) and Child-Pugh A (43 months), P <0.001 by log-rank comparison. There was no significant difference in the time to first decompensation based on different races or aetiologies of cirrhosis.

Survival Data

A total of 106 cirrhotic patients died (18.8%) over a median follow-up period of 85 months (range, 3 to 273). The cause of death was related to liver cirrhosis and/or HCC in 74.5%. Majority of the liver-related death were due to advanced HCC and hepatic decompensation complicated by sepsis. Patients who died from non-liver related causes

of death were excluded from the survival analysis.

A total of 388 patients (68.8%) remained compliant to follow-up and attended the ambulatory clinic within 6 months of the census date. A further 70 patients (12.4%) were deemed to be lost to follow-up as they had not visited the hospital in the 1 year prior to the census date and had no record of death. These patients were excluded from the survival analysis. In a comparative analysis of baseline characteristics of patients who were lost to follow-up versus those who completed the study, the former had a significantly higher proportion of alcoholic cirrhosis and more advanced cirrhosis.

The median survival of the cohort was 17.5 ± 5 years, with a 5-year survival rate of 90% and a 10-year survival rate of 73%. There was no difference in survival based on gender or ethnic group, but we observed significant differences in survival based on aetiology. Patients with alcoholic cirrhosis had significantly poorer survival compared to other aetiologies of cirrhosis with a median survival of 11.1 years versus 17.5 years respectively, $P = 0.005$ by log-rank comparison (Fig. 2).

The 10-year survival rate of cirrhotics diagnosed through surveillance ultrasound was significantly better compared to those who presented with abnormal laboratory findings such as abnormal liver function and low platelet count (Fig. 3). Cirrhotic patients with diabetes mellitus had significantly reduced survival compared to non-diabetics (OR 2.32, 95% CI, 1.53 to 3.52). A similar reduced survival trend was seen in cirrhotic patients who actively smoked (OR 2.62, 95% CI, 1.58 to 4.35) (Table 4).

Mean survival of Child-Pugh A cirrhotics (16.5 ± 0.9 years) was significantly better compared to Child-Pugh B (9.8 ± 0.6 years) and Child-Pugh C (8.6 ± 0.8 years) patients. There was no significant difference in the survival between Child-Pugh B and C patients, even after excluding 11 patients who underwent liver transplantation. Patients with compensated cirrhosis had a 10-year survival rate of 82% compared to 59% in those with decompensated disease at diagnosis (Fig. 4).

On multivariate analysis, only age at diagnosis of cirrhosis, presence of portal vein thrombosis, Child-Pugh class and decompensation within 1 year of diagnosis were identified as independent predictors for mortality (Table 4).

Discussion

Our study is the first to provide comprehensive data on the epidemiology and clinical evolution of liver cirrhosis in Singapore. The main aetiology of liver cirrhosis in Singapore is CHB infection, which accounted for 63%

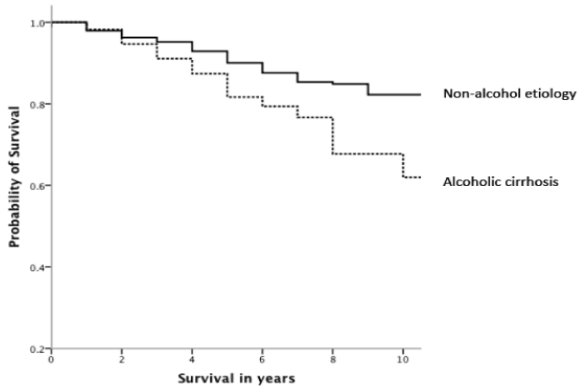

Fig. 2. Graph showing the Kaplan-Meier analysis of survival between patients with alcoholic cirrhosis (dotted line) and other aetiologies of liver cirrhosis (solid line), adjusted for age and race.

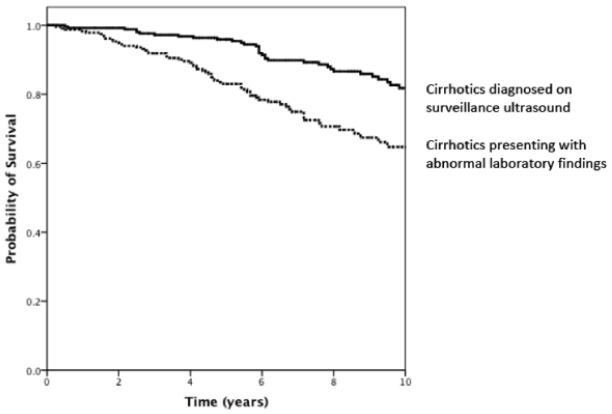

Fig. 3. Graph showing the comparison of 10-year survival between compensated cirrhotics diagnosed through surveillance (solid line) versus those presenting with abnormal laboratory findings (dotted line), P <0.001 by log-rank comparison.

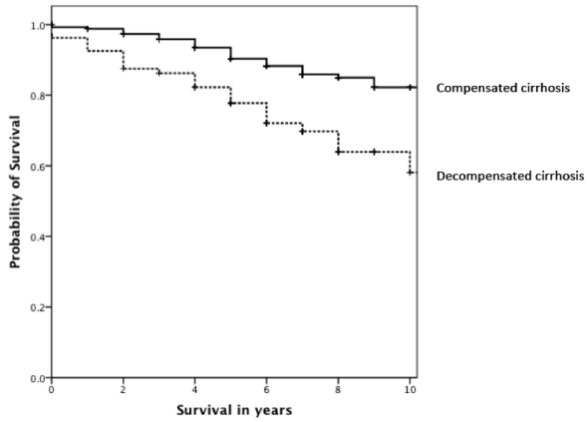

Fig. 4. Graph showing Kaplan-Meier analysis of 10-year survival between patients diagnosed with compensated cirrhosis (solid line) and decompensated cirrhosis (dotted line), P <0.001 by log-rank comparison.

Table 4. Univariate and Multivariate Cox Regression Analysis of Factors Associated with Survival in Cirrhotic Patients

Variable	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age	1.04 (1.02 – 1.06)	<0.001	1.04 (1.02 – 1.06)	0.001
Alcohol aetiology	2.34 (1.40 – 3.90)	0.001	-	NS
CHB aetiology	0.53 (0.35 – 0.81)	0.003	-	NS
Diabetes mellitus	2.32 (1.53 – 3.52)	<0.001	-	NS
Active smoking	2.62 (1.58 – 4.35)	<0.001	-	NS
ALT	0.99 (0.99 – 1.00)	0.048	-	NS
Platelet count	0.99 (0.99 – 1.00)	0.011	-	NS
Portal vein thrombosis	4.51 (1.81 – 11.19)	0.001	10.94 (3.62 – 33.06)	<0.001
HCC at diagnosis of cirrhosis	2.69 (1.52 – 4.77)	0.001	-	NS
Child-Pugh A vs Child-Pugh B/C	0.33 (0.22 – 0.51)	<0.001	0.41 (0.21 – 0.78)	0.006
Decompensated at presentation	2.39 (1.49 – 3.83)	<0.001	-	NS
Cirrhosis diagnosed on surveillance	0.55 (0.36 – 0.84)	0.006	-	NS
Decompensation within 1 year	6.77 (4.37 – 10.48)	<0.001	4.60 (2.74 – 7.74)	<0.001
New HCC on follow-up	2.39 (1.57 – 3.64)	<0.001	-	NS

ALT: Alanine transaminase; CHB: Chronic hepatitis B; HCC: Hepatocellular carcinoma

of cases identified from the largest tertiary referral centre in the country. The high proportion of CHB cirrhosis reflects the endemicity of CHB in the region. In Singapore, approximately 4% to 6% of the population is chronically infected with hepatitis B.[14] However, the hepatitis B carrier rate in adults has steadily declined from 9.1% in 1975 to 4.1% in 1999 and 2.7% in 2005 as a result of a compulsory nationwide hepatitis B virus (HBV) immunisation programme.[15] Nonetheless, the prevalence of CHB-related liver cirrhosis remains a significant challenge as a significant proportion of the adult hepatitis B carriers diagnosed in the 1970s would have developed cirrhosis by now.

Our data are similar to that reported by neighbouring Asian countries such as Hong Kong, Taiwan and Malaysia where hepatitis B is the predominant aetiology of liver cirrhosis.[16-18] The epidemiological pattern of liver cirrhosis is likely to be related to the ethnic profile of the various Asian populations. Countries in which a substantial proportion of the populations comprise of immigrants originating from Southern China have a high CHB prevalence.[12] The results of our study thus contribute towards the growing body of data on the epidemiology of liver cirrhosis in Asia. Information regarding aetiology of liver cirrhosis in different countries and different populations is important for optimal distribution of national healthcare resources.[19]

We observed significant differences in the predominant aetiology of liver cirrhosis amongst different ethnic groups. Singapore is a multi-ethnic country with 74.2% Chinese, 13.3% Malays and 9.2% Indians, based on the latest national population statistics. We observed that the ethnic distribution in the cirrhotic cohort was different from that of the general population, with a higher proportion of Chinese (89.7% vs 74.2%) and a corresponding lower proportion of Malays (4.8% vs 13.4%) and Indians (4.4% vs 9.2%). The prevalence of CHB cirrhosis was significantly higher in Chinese whereas alcoholic cirrhosis was significantly higher in Indians. CHC cirrhosis was more common in Malays compared to the other ethnic groups.

Alcoholic liver cirrhosis was the second commonest aetiology of cirrhosis in our study, accounting for 11% of the cohort. While significantly lower than rates in the West, this rate is comparable to data from neighbouring Asian populations.[18] In Singapore, alcoholic cirrhosis was most prevalent among Indians, in keeping with data from the Singapore National Health Survey on trends in alcohol consumption.[20] The Muslim religion forbids the consumption of alcohol, thus explaining the absence of alcoholic cirrhosis amongst Malays. The high incidence of CHC cirrhosis amongst the Malay population may be related to a higher incidence of intravenous drug abuse among young Malay males in Singapore.[21]

Our findings on the racial distribution of specific aetiologies of liver cirrhosis validate those published by Qua et al in a similar multiracial Asian population.[18] However, while theirs was a point-in-time prevalence study, our study provides long-term follow-up data on the clinical evolution and survival of the different ethic and aetiological cohorts. Our study confirms that there is no significant difference in the rate of decompensation or overall survival amongst the different ethnic groups. However, the underlying aetiology

of cirrhosis appears to affect long-term outcome. We showed that patients with alcoholic cirrhosis have poorer survival compared to cirrhosis from other aetiologies. On multivariate analysis however, alcohol aetiology was not found to be an independent predictor for mortality in cirrhosis. The poor outcome in alcoholic cirrhosis is related to delayed presentation, as shown in our study by a significantly higher rate of decompensation, large esophageal varices and poorer liver function at diagnosis.

The 5-year survival rate of 90% in our study cohort exceeds the rate reported in similar studies on the natural history of cirrhosis.[22,23] The favourable survival profile is likely because our study focused on an ambulatory cohort of cirrhotics, in which a large proportion had compensated, Child-Pugh A cirrhosis. Half the cohort was diagnosed via surveillance ultrasound during regular follow-up for chronic viral hepatitis. Secondly, we used ultrasound features of echogenicity and surface nodularity to diagnose cirrhosis in our study. Transient elastography was not routinely available for confirmation of cirrhosis at the time and liver biopsy for histological confirmation of cirrhosis was not routinely performed. Given that the accuracy of ultrasound for diagnosis of cirrhosis is only 65%,[24] it is plausible that a proportion of the cohort may not have had true cirrhosis but advanced fibrosis. This may explain the longer than expected survival rates observed in our study. However, our observational study is based on routine clinical practice, in which ultrasound is routinely used for diagnosis of cirrhosis. We thus believe that the results reflect the true, "on-the-ground" survival rates seen in patients diagnosed with liver cirrhosis via ultrasound. Our study highlights that the use of ultrasound to diagnose cirrhosis is not ideal due to poor specificity. When the clinical pretest probability of cirrhosis is low, we recommend that ultrasound findings of cirrhosis be confirmed with the use of transient elastography before a diagnosis of cirrhosis is conclusively made. In situations of ambiguity, liver biopsy should be performed to make a confirmatory diagnosis of cirrhosis.

We observed a poorer survival in cirrhotic patients with diabetes mellitus and in those who actively smoked. Both factors have been shown to be associated with higher risk of progressive fibrosis and development of HCC.[25-29] Screening of cirrhotics with oral glucose tolerance test has been shown to predict prognosis of cirrhotics.[30] However, neither factor was an independent predictor of mortality on multivariate analysis.

We acknowledge that the retrospective nature of our study is a limitation to the validity of the observations made. However, approximately 70% of the study cohort remained compliant to follow-up through to the end of the study period. Hence, despite being identified retrospectively, the high compliance to follow-up allowed us to collect comprehensive data on the clinical evolution of the study cohort. Secondly, this study was designed as an observational study of a cohort of cirrhotics identified from an ambulatory clinic. Expectedly, a majority of the patients included in the cohort had early-compensated cirrhosis and were diagnosed on surveillance. As such, the conclusions derived from this study are not applicable to advanced cirrhotics who are inpatients or too ill to attend clinics. Thirdly, the prevalence of non-alcoholic steatohepatitis (NASH) is likely to be under-reported in this study. A large number of patients were diagnosed more than decade ago at a time when the role of NASH in liver cirrhosis was not routinely recognised. The observation that concomitant diabetes mellitus, hypertension and hyperlipidaemia were significantly more common in the cryptogenic group suggests that some of these patients were likely NASH patients who were misclassified as cryptogenic cirrhosis.

Conclusion

In conclusion, CHB is the major aetiology of liver cirrhosis in Singapore, accounting for almost two-thirds of the cirrhotic population. The prevalence of specific aetiologies of cirrhosis varies amongst the various ethnic groups, reflecting different exposures to cirrhosis risk factors due to inherent hereditary, socioeconomic and cultural differences. Overall survival in this ambulatory cohort of cirrhotics is excellent, owing to early diagnosis of compensated Child-Pugh A patients through active surveillance. Advanced age, Child-Pugh class, presence of portal vein thrombosis and development of decompensation within 1 year of diagnosis are independent predictors of mortality in patients with liver cirrhosis.

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