

ORIGINAL ARTICLE

Obesity and the extent of liver damage among adult New Zealanders: findings from a national survey

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Summary

Objective

Non-alcoholic fatty liver disease (NAFLD), defined as excessive fat accumulation in hepatocytes when no other pathologic causes are present, is an increasingly common obesity-related disorder. We sought to describe the prevalence of elevated liver enzymes, a marker of liver damage, among New Zealand adults, and high-risk subgroups including those with an elevated body mass index and those with pre-diabetes or diabetes, to gain a better understanding of the burden of liver disease.

Methods

A total of 4,721 New Zealanders aged 15+ years participated in a nationally representative nutrition survey. Liver enzymes, alanine transaminase (ALT) and gamma glutamyl transpeptidase (GGT) were measured in serum. Results were available for 3,035 participants, of whom 10.8% were Māori and 4.5% Pacific.

Results

Overall, the prevalence of elevated ALT and elevated GGT was 13.1% (95% confidence interval [CI]: 11.2 – 15.0) and 13.7% (95% CI: 12.0 – 15.4), respectively. Odds ratios for an elevated ALT or GGT markedly increased with increasing body mass index. Men with obesity had the highest elevated ALT prevalence (28.5%; 95% CI: 21.7–35.4), and women with diabetes had the highest elevated GGT prevalence (36.5%; 95% CI: 26.0–47.0). Adding alcohol consumption categories to each of the adjusted models did not meaningfully change any results, although for women, heavy alcohol consumption was associated with an elevated GGT (overall $p = 0.03$).

Conclusions

Obesity-related liver disease is likely to increasingly burden the New Zealand health sector and contribute to health disparities unless effective obesity treatment and prevention measures are given high priority.

Keywords: Ethnic minorities, liver enzymes, non-alcoholic fatty liver disease (NAFLD), obesity.

Introduction

Chronic liver disease (CLD) causes significant morbidity and mortality worldwide and is becoming an increasingly important public health issue (1–3). While hepatitis B, hepatitis C and harmful alcohol consumption are common causes of CLD, obesity is increasingly associated with liver disease (4,5). Non-alcoholic fatty liver disease (NAFLD) has emerged in parallel with the obesity

epidemic and is the most common CLD worldwide, affecting up to 30–35% of adults (6) and up to 70% of people with type 2 diabetes (7). NAFLD, defined as hepatic fat accumulation exceeding 5–10% of liver weight when no other pathologic causes such as excess alcohol intake are present (8), is considered to be part of the metabolic syndrome (9). While simple fatty liver disease can progress to more severe non-alcoholic steatohepatitis,

cirrhosis, end-stage liver disease and hepatocellular cancer (6), the most common manifestation of NAFLD is an increased risk of extrahepatic conditions, especially cardiovascular disease and type 2 diabetes (10). Cardiovascular disease is the most common cause of death among these patients (10,11).

In New Zealand, hepatitis B and C infections are important causes of CLD (12). However, recent laboratory data suggest hepatitis B incidence is declining, the result of a universal infant hepatitis B vaccination programme implemented in the late 1980s (13) and a hepatitis B screening programme in areas with high rates of hepatitis B (14). While hepatitis C infection has increased since the 1990s, particularly among intravenous drug users and Asian communities, the prevalence in New Zealand is estimated to have peaked at about 1% in 2010 (15,16).

Harmful alcohol consumption is common and contributes to liver disease in New Zealand. A recent survey identified 18% of adults had harmful or hazardous drinking behaviours (17). Similarly, excess body weight is prevalent in New Zealand. In 2012/2013, 31% of New Zealand adult men and women were obese, and a further 38% of men and 30% of women were overweight (18). The extent of excess weight-related liver disease or NAFLD is not established in New Zealand.

A blood sample taken as part of the 2008/2009 New Zealand Adult Nutrition Survey (2008/2009 NZANS) (19) provided the opportunity to subsequently measure liver enzymes commonly used as markers of liver (hepatocyte) dysfunction, among a nationally representative sample. The aim of this study was to describe the prevalence of elevated alanine transaminase (ALT) and gamma glutamyl transpeptidase (GGT) among the New Zealand adult population, and high-risk subgroups, to gain a better understanding of the burden of liver disease.

Methods

The 2008/2009 NZANS was a nationally representative, cross-sectional survey of 4,721 New Zealanders aged 15 years and above, conducted from 27 October 2008 to 28 October 2009 (18,19). Additional blood analyses for this study were completed in 2013. Ethical approval to undertake the survey was obtained from the New Zealand Health and Disability Multi-region Ethics Committee (MEC/08/04/049).

The survey methods are described in detail elsewhere (19). In brief, participants were recruited using a three-stage area-based sampling frame. Firstly, 607 small geographically defined areas (meshblocks) were selected using probability-proportional-to-size sampling. Meshblocks in rural areas contained approximately

60 individuals, and meshblocks in urban areas contained approximately 110 individuals. Within each selected meshblock, private dwelling households were randomly selected, and for each of these households, a single individual was randomly selected. Increased sampling occurred for Māori, Pacific and the age groups 15–18 and 71+ years to ensure adequate sample sizes for subgroup analyses. Informed written consent was obtained from each participant. The participation rate was 61%.

Data

Trained interviewers obtained data at participants' homes. They used computer-assisted personal interview software to complete the questionnaire and calibrated instruments for blood pressure and anthropometric measurements. Data collected included demographics, alcohol consumption and medical history. Ethnicity was self-reported, with the option to choose multiple groups using the Statistics New Zealand standard ethnicity question (19). For this analysis, participants who selected more than one ethnic group were assigned to a single ethnic category using the following prioritized order: Māori, Pacific, New Zealand European and Other (including South Asian, South-east Asian, Latin American and African ethnic groups). Socioeconomic status was assessed using the 2006 New Zealand Index of Deprivation (20). For this index, each meshblock is assigned a score that reflects the extent of material and social deprivation and is used to construct deciles from 1 to 10. These deciles were divided into quintiles. Quintile I represented participants residing in the least-deprived areas (lowest 20%) and quintile V those in the most-deprived areas (highest 20%).

Standing height was measured to the nearest 0.1 cm using a stadiometer (Seca 214, Seca, Hamburg, Germany). Weight was measured to the nearest 0.1 kg using electronic scales (Tanita HD-351, Tanita Corporation, Arlington Heights, IL, USA; maximum weight 200 kg). Height and weight were both measured at least twice. If the duplicate measurements differed by more than 1%, a third measurement was taken. The mean of the two closest measurements (or the mean of all three, if they were equally spaced) was calculated and used in analyses. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

A non-fasting blood sample was obtained from 3,348 non-pregnant participants (71% of the survey participants) at a local health clinic. For each participant, the blood was collected into three vacutainers (two containing ethylenediaminetetraacetic acid [EDTA] and one with no additive). The blood in one EDTA vacutainer was used to determine a complete blood count at the local

laboratory. The other two blood samples were transported to Canterbury Health Laboratories, Christchurch, New Zealand, at 4°C, for separation of whole blood and serum. Blood analyses completed at the time of the survey included glycated haemoglobin (HbA1c) (19). Remaining aliquots of serum and whole blood samples were transported to the Diabetes and Lipid Laboratory, University of Otago, Dunedin, New Zealand, where they were stored at -80°C.

In 2013, liver enzymes ALT and GGT were measured from 3,035 stored frozen aliquots of serum using Roche Diagnostics GmbH (Mannheim, Germany) kits on a Roche Cobas C311 Chemistry Autoanalyser. The accuracy and precision of the analysis were assessed using Roche Diagnostics controls. The coefficient of variation (CV) for the ALT analysis was 1.8% and 1.7% for the Precinorm U and Precipath U controls, respectively. For GGT, the CVs for Precinorm U and Precipath U controls were 1.4% and 0.9%, respectively. Multiple aliquots of pooled serum were analysed within each batch to assess between-batch variability (CV 7.2% for ALT and 1.2% GGT; $n = 180$).

Definitions

Elevated ALT was defined as $>29 \text{ IU L}^{-1}$ for men and $>22 \text{ IU L}^{-1}$ for women (21), and elevated GGT was defined as $>51 \text{ IU L}^{-1}$ for men and $>33 \text{ IU L}^{-1}$ for women (22). The World Health Organization BMI cut-off points were used to define the following categories for participants aged 19 years and over: normal weight (BMI 18.50–24.99 kg m^{-2}), overweight (BMI 25.00–29.99 kg m^{-2}) and obese (BMI 30.00 kg m^{-2}) (23). For participants aged 15–18 years, the Cole gender and age-specific BMI cut-off points were used (24). Self-reports of doctor-diagnosed diabetes and the 2010 American Diabetes Association cut-offs for HbA1c were used to define diabetes and pre-diabetes (25). Participants were included in the diabetes category if they self-reported doctor-diagnosed diabetes or had an HbA1c $\geq 6.5\%$ (48 mmol mol^{-1}). Those with an HbA1c of at least 5.7% (39 mmol/mol) but below 6.5% (48 mmol/mol) and who did not self-report doctor-diagnosed diabetes were classified as having pre-diabetes. All other participants were considered to have normal glucose metabolism. Alcohol consumption habits were determined from the self-reported questionnaire data (19) and New Zealand's safe alcohol consumption recommendations (26). Each participant was allocated to one of four categories: lifetime abstainer (never consumed alcohol in their lifetime), 12-month abstainer (consumed alcohol in their lifetime, but not in the 12 months prior to the survey), 'light to moderate' drinkers (no more than 10 standard drinks for women and no more

than 15 standard drinks for men per week) and 'heavy drinkers' (more than 10 standard drinks for women and more than 15 standard drinks for men per week).

Statistical analysis

Survey strata, primary sampling units and weights (19) were incorporated into all analyses, reflecting the complex survey design. The estimated resident population living in private dwellings in New Zealand in March 2009 was used to derive the weights based on age, sex and ethnicity (19).

Geometric means for ALT and GGT and age-specific rates (95% confidence intervals [CIs]) of elevated ALT and GGT were calculated for men and women by 10-year age groups (15–24, 25–34, 35–44, 45–54, 55–64, 65–74 and ≥ 75 years) and for ethnic groups. Because of small numbers in the older age groups within each of the different ethnic groups, those aged ≥ 65 years were combined when calculating the ethnicity-specific rates. Rates for elevated enzymes were also calculated for BMI categories and glucose metabolism disorder categories, as defined earlier.

We decided *a priori* to investigate associations between liver enzyme elevation and age (continuous), ethnicity (described earlier), BMI (continuous) and glucose metabolism disorder (described earlier). Sex-stratified logistic regression models were used to estimate unadjusted odds ratios (ORs) and 95% CIs. All variables that were potentially associated with elevated liver enzymes ($p < 0.25$) in the unadjusted analyses were included in the subsequent multiple logistic regression models to produce adjusted ORs and 95% CIs. Interactions were examined between sex and each demographic variable. Nonlinearity in associations involving continuous predictors (age and BMI) was tested and, where appropriate, modelled using quadratic terms. For each continuous predictor, commonly used categories were chosen, and the differences between the mid-points of these categories (measured as ORs using change in the continuous predictor) are provided to assist with interpretation. We used the following mid-points: age 20 years (adolescent/young) versus 30 years (young adult), 45 years (middle aged) and 70 years (older); BMI 22 kg m^{-2} (normal) versus 27.5 kg m^{-2} (overweight) and 35 kg m^{-2} (obese). STATA 13.1 (StataCorp, College Station, TX, USA) was used for all analyses, and two-sided $p < 0.05$ was considered statistically significant.

Results

Table 1 shows the demographic characteristics of the population who participated in the 2008/2009 NZANS

Table 1 Characteristics of the survey participants

Demographic and clinical values	All survey participants (<i>n</i> = 4,721)	Survey participants with both ALT and GGT results (<i>n</i> = 3,035)
	Mean (min–max)/No. (%) [*]	Mean (min–max)/No. (%) [*]
Age (years)	44.3 (15–98)	44.3 (15–98)
Men	2,066 (47.8)	1,327 (47.7)
Ethnic group		
Māori	1,040 (11.3)	558 (10.8)
Pacific	701 (4.8)	351 (4.5)
New Zealand European	2,420 (68.4)	1,772 (69.3)
Other	560 (15.5)	354 (15.4)
NZDep [†] quintile		
I	664 (20.1)	463 (19.1)
II	829 (21.5)	568 (21.6)
III	761 (21.0)	524 (21.7)
IV	1,072 (19.3)	686 (19.4)
V	1,395 (18.2)	794 (18.2)
Highest education level		
No school qualification	1,220 (18.4)	793 (18.0)
School qualifications only	1,413 (26.8)	847 (25.4)
Trade qualifications	782 (18.6)	501 (18.9)
Post school, tertiary or professional	1,125 (32.9)	786 (34.5)
Current cigarette smoking [‡]	1,074 (21.2)	570 (18.5)
Current alcohol drinker [§]	3,767 (86.1)	2,480 (87.7)
Self-reported medical history		
Diabetes	341 (4.9)	253 (5.2)
Angina or myocardial infarct	489 (6.5)	375 (6.6)
Hypertension	1,339 (23.5)	989 (24.3)

^{*}Survey weights specific to all survey participants and to those with blood results were used to calculate percentages; therefore, the percentages may not equal the number for each category.

[†]NZDep (16) with quintile I representing participants residing in the least-deprived areas (lowest 20%) and quintile V those in the most-deprived areas (highest 20%).

[‡]Current smoker defined as smoking at least one cigarette per month.

[§]Current alcohol drinker defined as reporting having had an alcoholic drink in the last 12 months.

ALT, alanine transaminase; GGT, gamma glutamyl transpeptidase; NZDep, New Zealand Index of Deprivation.

and the population for whom a blood sample was taken and ALT and GGT measured. The two groups were similar.

Overall, the prevalence of elevated ALT and elevated GGT among adult New Zealanders was 13.1% (95% CI: 11.2–15.0) and 13.7% (95% CI: 12.0–15.4), respectively. Mean ALT and mean GGT levels by 10-year age groups and by ethnic groups for men and women are shown in Table 2. Mean ALT levels were highest among men aged 25–64 years (20.0–21.5 IU L⁻¹) and Māori and Pacific men (20.9 and 21.9 IU L⁻¹, respectively). Mean GGT levels among men were similar across all age groups except those aged 15–24 years for whom it was about 10 IU L⁻¹ lower. In women, mean GGT levels increased with increasing age, peaking among women aged 65–74 years. Among the ethnic groups mean ALT and GGT levels were highest in Pacific, 18.0 and 28.5 IU L⁻¹, respectively, and almost as high in Māori, 16.6 and 26.4 IU L⁻¹, respectively.

Table 3 shows the age-specific elevated ALT rates and elevated GGT rates for men and women. Overall, 16.9% (95% CI: 13.7–20.1) of men and 9.7% (95% CI: 7.7–11.6) of women had an elevated ALT level, whereas for GGT roughly similar proportions of women (14.2%, 95% CI: 11.9–16.5) and men (13.1%, 95% CI: 10.7–15.6) had an elevated level. Men aged 25–54 years had the highest elevated ALT rates, and women aged 55 years and over had the highest elevated GGT rates.

Higher proportions of both Māori and Pacific had elevated ALT or GGT levels compared with the New Zealand European and Other ethnic groups (Table 3). Age-specific elevated GGT rates were particularly high among Pacific peoples aged 45–54 years (44.9%, 95% CI: 30.2–59.7) and 55–64 years (47.1%, 95% CI: 29.5–64.6) (Table 4).

Elevated ALT and GGT levels were high among those categorized as obese, and among those with diabetes (Table 3). Men with obesity had the highest prevalence

Table 2 Geometric means (standard deviation) for ALT and GGT by 10-year age groups and by ethnic groups for men and women aged 15 years and over

Groups	All (<i>n</i> = 3,035)		Men (<i>n</i> = 1,327)		Women (<i>n</i> = 1,708)	
	ALT	GGT	ALT	GGT	ALT	GGT
Age range (years)						
15–24	14.1 (1.6)	16.8 (1.6)	16.7 (1.6)	18.8 (1.6)	12.0 (1.5)	15.1 (1.6)
25–34	16.9 (1.5)	21.6 (1.6)	21.5 (1.4)	28.0 (1.5)	13.5 (1.5)	17.1 (1.6)
35–44	15.5 (1.5)	21.3 (1.7)	20.5 (1.5)	27.2 (1.7)	12.3 (1.4)	17.3 (1.6)
45–54	17.5 (1.5)	23.7 (1.7)	20.9 (1.4)	30.7 (1.7)	14.6 (1.4)	18.4 (1.6)
55–64	17.0 (1.5)	24.3 (1.7)	20.0 (1.5)	28.8 (1.7)	14.8 (1.4)	21.0 (1.7)
65–74	15.2 (1.6)	26.9 (2.2)	16.1 (1.6)	27.5 (2.1)	14.5 (1.6)	26.3 (2.3)
75+	11.9 (1.9)	24.5 (3.3)	12.2 (1.9)	28.8 (3.5)	11.7 (1.8)	21.2 (2.9)
Ethnicity						
Māori	16.6 (2.0)	26.4 (2.4)	20.9 (1.8)	34.0 (2.1)	13.7 (1.9)	21.2 (2.3)
Pacific	18.0 (2.4)	28.5 (3.3)	21.9 (2.1)	36.6 (3.1)	15.1 (2.4)	22.7 (3.1)
New Zealand European	15.5 (1.5)	21.0 (1.8)	18.4 (1.5)	25.0 (1.7)	13.3 (1.4)	18.0 (1.7)
Other	15.5 (1.5)	21.9 (1.7)	18.9 (1.5)	26.8 (1.6)	12.8 (1.5)	18.0 (1.6)

International System conversion factors: To convert ALT and GGT to microkatal per litre, multiply by 0.0167.

ALT, alanine transaminase; GGT, gamma glutamyl transpeptidase.

Table 3 The elevated ALT and GGT rates by 10-year age groups, ethnicity, body mass index category and glucose metabolism disorder for men and women aged 15 years and over

Categories	Men (<i>n</i> = 1,327)		Women (<i>n</i> = 1,708)	
	ALT % (95% CI)	GGT % (95% CI)	ALT (95% CI)	GGT % (95% CI)
Age range (years)				
15–24	14.6 (7.7–21.5)	4.1 (0.6–7.6)	5.1 (1.1–9.1)	7.2 (2.5–11.9)
25–34	23.1 (13.9–32.3)	15.0 (8.2–21.7)	13.7 (8.0–19.3)	12.3 (7.1–17.4)
35–44	19.2 (12.2–26.3)	14.5 (8.5–20.5)	5.8 (2.9–8.8)	9.2 (5.3–13.2)
45–54	22.4 (13.7–31.2)	15.1 (8.3–21.8)	12.3 (6.2–18.5)	12.8 (7.4–18.2)
55–64	17.3 (8.7–25.8)	15.9 (8.4–23.5)	11.5 (5.9–17.0)	18.3 (11.6–24.9)
65–74	4.9 (1.1–8.8)	14.0 (8.7–19.2)	13.5 (7.0–19.9)	32.4 (23.0–41.9)
75+	2.2 (0.4–3.9)	16.2 (11.2–21.1)	5.2 (1.9–8.4)	17.3 (12.5–22.1)
Ethnicity				
Māori	26.3 (17.8–34.8)	27.3 (19.4–35.3)	10.8 (6.8–14.7)	22.9 (16.5–29.3)
Pacific	22.7 (15.3–30.0)	29.7 (21.6–37.8)	14.8 (9.3–20.4)	26.4 (19.0–33.7)
New Zealand European	15.0 (11.2–18.8)	10.1 (7.3–12.9)	8.4 (6.0–10.7)	12.1 (9.4–14.9)
Other	17.2 (9.3–25.1)	12.2 (6.0–18.4)	13.3 (7.1–19.4)	13.8 (7.3–20.4)
Body mass index (kg m ⁻²)				
Normal	7.7 (3.6–11.8)	7.1 (3.4–10.9)	4.9 (2.6–7.2)	6.6 (4.0–9.2)
Overweight	15.8 (11.0–20.6)	12.0 (8.4–15.6)	10.5 (6.5–14.6)	15.1 (10.8–19.4)
Obese	28.5 (21.7–35.4)	20.9 (15.7–26.1)	16.0 (11.4–0.5)	23.3 (18.3–28.4)
Glucose metabolism disorder				
Normal	16.0 (12.0–20.0)	10.1 (7.4–12.9)	7.1 (5.0–9.2)	10.0 (7.6–12.5)
Pre-diabetes	17.3 (11.5–23.1)	16.3 (11.3–21.3)	15.7 (10.6–20.9)	20.9 (15.6–26.2)
Diabetes	23.1 (12.8–33.4)	26.2 (16.7–35.6)	15.2 (7.3–23.0)	36.5 (26.0–47.0)
Total	16.9 (13.7–20.1)	13.1 (10.7–15.6)	9.7 (7.7–11.6)	14.2 (11.9–16.5)

ALT, alanine transaminase; CI, confidence interval; GGT, gamma glutamyl transpeptidase.

of elevated ALT levels (28.5%; 95% CI: 21.7–35.4), and women with diabetes had the highest prevalence of elevated GGT levels (36.5%; 95% CI: 26.0–47.0).

The results of the logistic regression models are shown in Tables 5 and 6. ORs for an elevated ALT or an elevated GGT increased significantly with increasing BMI for both

Table 4 The age-specific rates for elevated ALT and elevated GGT by age group for Māori, Pacific and New Zealand European and Other ethnic groups

Age range (years)	Māori		Pacific		New Zealand European		Other	
	ALT % (95% CI)	GGT % (95% CI)	ALT % (95% CI)	GGT % (95% CI)	ALT % (95% CI)	GGT % (95% CI)	ALT % (95% CI)	GGT % (95% CI)
15–24	12.1 (0.3–24.0)	11.7 (4.0–19.6)	13.1 (3.0–23.1)	9.1 (0.5–17.7)	9.2 (4.1–14.3)	5.3 (0.1–9.7)	8.4 (0–18.1)	No observations
25–34	25.1 (13.9–36.4)	24.0 (13.5–34.4)	26.5 (16.7–36.3)	28.2 (17.7–38.6)	16.1 (9.4–22.9)	9.2 (3.9–14.5)	16.4 (4.2–28.6)	14.6 (3.2–26.0)
35–44	20.4 (10.2–30.6)	37.4 (24.2–50.7)	18.1 (9.0–27.2)	26.5 (15.9–37.2)	9.8 (5.1–14.4)	6.3 (2.5–10.0)	13.8 (2.8–24.9)	10.4 (1.6–19.3)
45–54	15.9 (6.0–25.9)	23.8 (11.6–36.0)	24.5 (11.8–37.2)	44.9 (30.2–59.7)	18.4 (10.8–25.9)	10.9 (5.8–16.1)	13.0 (1.4–24.5)	14.4 (3.3–25.5)
55–64	20.0 (6.2–33.8)	30.7 (17.6–43.9)	14.0 (3.7–24.3)	47.1 (29.5–64.6)	10.6 (5.2–16.0)	13.0 (7.4–18.5)	33.9 (14.3–53.6)	27.4 (7.5–47.4)
65+	6.9 (0–16.7)	34.9 (20.3–49.4)	6.2 (0–12.9)	32.4 (16.4–48.4)	6.2 (3.5–8.8)	20.4 (16.0–24.7)	15.6 (5.3–26.0)	20.4 (10.0–30.7)
Total	18.0 (13.2–22.8)	25.0 (19.9–30.0)	18.6 (14.0–23.1)	27.9 (22.7–33.2)	11.5 (9.2–13.8)	11.1 (9.2–13.1)	15.2 (10.2–20.2)	13.0 (8.7–17.3)

ALT, alanine transaminase; CI, confidence interval; GGT, gamma glutamyl transpeptidase.

men and women. These findings changed little after adjustment and remained statistically significant, except for elevated GGT levels among men. The adjusted odds of an elevated GGT level also significantly increased with increasing age for both men and women. Among the ethnic groups, the adjusted OR of an elevated GGT was highest for Pacific men (OR 3.70; 95% CI: 2.11–6.48) and women (OR 2.20; 95% CI: 1.27–3.81) and was almost as high for Māori men and women. Women with diabetes also had a high adjusted OR of an elevated GGT level (OR 2.49; 95% CI: 1.31–4.76). Adding alcohol consumption categories to each of the adjusted models did not meaningfully change any of the results reported in Table 5. Alcohol consumption category was not statistically significantly associated with elevated ALT for men (overall $p = 0.68$) or women (overall $p = 0.12$) or with elevated GGT for men (overall $p = 0.86$). For women, heavy alcohol consumption was associated with an elevated GGT (overall $p = 0.03$) with *post hoc* pairwise comparisons showing higher odds of an elevated GGT for heavy drinkers compared with 12-month abstainers and light/moderate drinkers (OR 3.21; 95% CI: 1.26–8.13, $p = 0.01$ and OR 2.86; 95% CI: 1.37–5.98, $p = 0.005$, respectively). There was no evidence of a sex-by-alcohol consumption interaction for either outcome (elevated ALT $p = 0.24$ and elevated GGT $p = 0.58$).

Discussion

The burden of liver-related diseases is important and increasing worldwide, much of which is due to the escalating prevalence of NAFLD in parallel with the obesity epidemic (1–3). This study provides the first estimates of liver dysfunction in New Zealand using data from a nationally representative survey. Overall, the prevalence of elevated ALT and elevated GGT among adult New Zealanders was 13.1% and 13.7%, respectively. The rates were exceptionally high among those with excess weight, those with diabetes and Māori and Pacific populations.

Although the causes for elevated ALT levels and elevated GGT levels observed in our nationally representative cross-sectional survey cannot be determined, there are plausible explanations. Excess body weight is associated with increased liver enzyme levels (27) and is most likely a major contributing factor in our study. The odds of an elevated ALT for men and women or elevated GGT for women was two to three times higher among those who were obese compared with those of normal weight. Obesity and overweight are common in New Zealand, which has the third highest obesity rate (31%) in the world behind the USA and Mexico (28). Further, obesity is very common among both Pacific (68%) and Māori (48%)

Table 5 Multivariate regression model for elevated ALT levels

Ethnicity	Men (n = 1,327)			Women (n = 1,708)			Unadjusted interaction	Adjusted interaction†
	Unadjusted odds ratio (95% CI)	p-value	Adjusted* odds ratio (95% CI)	p-value	Unadjusted odds ratio (95% CI)	p-value		
New Zealand European	1.00		1.00		1.00		1.00	
Māori	2.02 (1.18–3.46)		1.39 (0.67–2.89)		1.32 (0.78–2.22)		0.92 (0.49–1.73)	
Pacific	1.66 (0.99–2.76)	0.05	0.95 (0.48–1.87)	0.63	1.90 (1.12–3.24)	0.08	1.06 (0.56–2.00)	0.13
Other	1.17 (0.64–2.16)		1.19 (0.63–2.23)		1.67 (0.91–3.05)		1.97 (1.06–3.66)	
Age, years (5 years)‡								
Linear slope	0.87 (0.81–0.94)	<0.001	0.85 (0.79–0.92)	<0.001	1.05 (0.99–1.13)	0.13	0.99 (0.92–1.06)	0.73
Quadratic slope	0.96 (0.94–0.97)	<0.001	0.97 (0.95–0.98)	<0.001	0.98 (0.97–1.00)	0.02	—§	
30 vs. 20	1.59 (1.18–2.15)		1.31 (0.93–1.85)		1.49 (1.09–2.04)		0.97 (0.84–1.12)	
45 vs. 20	1.68 (0.98–2.88)		1.18 (0.63–2.22)		2.11 (1.16–3.82)		0.93 (0.65–1.33)	
70 vs. 20	0.34 (0.17–0.68)		0.25 (0.11–0.55)		1.87 (0.93–3.78)		0.86 (0.42–1.76)	<0.001
Body mass index (kg m ⁻²)‡								
Linear slope	1.09 (1.03–1.14)	0.002	1.09 (1.02–1.17)	0.02	1.09 (1.06–1.12)	<0.001	1.09 (1.05–1.13)	<0.001
27.5 vs. 22	1.57 (1.18–2.08)		1.59 (1.09–2.33)		1.59 (1.34–1.88)		1.57 (1.29–1.92)	
35 vs. 22	2.89 (1.48–5.65)		2.99 (1.22–7.35)		2.98 (2.01–4.42)		2.90 (1.81–4.66)	
Glucose metabolism disorder								
Normal	1.00		1.00		1.00		1.00	
Pre-diabetes	1.10 (0.67–1.80)	0.39	—¶		2.44 (1.45–4.09)	0.001	2.31 (1.22–4.37)	0.04
Diabetes	1.58 (0.82–3.03)		—¶		2.34 (1.18–4.66)		1.62 (0.74–3.55)	0.13

*Adjusted = controlled for age and all variables in the table with unadjusted p-value <0.25.

†Interactions were examined between sex and each demographic variable. Tests for interactions include quadratic terms for age but not body mass index.

‡Age and body mass index were centred by subtracting raw means.

§There was no evidence of quadratic effects in these models.

¶Glucose metabolism disorder did not pass the screening criteria for men in the ALT model. ALT, alanine transaminase; CI, confidence interval.

Table 6 Multivariate regression model for elevated GGT levels

	Men (n = 1,327)			Women (n = 1,708)			Adjusted interaction†
	Unadjusted odds ratio (95% CI)	p-value	Adjusted* odds ratio (95% CI)	Unadjusted odds ratio (95% CI)	p-value	Adjusted* odds ratio (95% CI)	
Ethnicity							
New Zealand European	1.00		1.00	1.00		1.00	
Māori	3.36 (2.06–5.48)		3.54 (2.05–6.12)	2.16 (1.38–3.38)		2.27 (1.33–3.89)	
Pacific	3.77 (2.30–6.20)	<0.001	3.70 (2.11–6.48)	2.60 (1.63–4.13)	<0.001	2.20 (1.27–3.81)	0.01
Other	1.24 (0.65–2.38)		1.38 (0.70–2.68)	1.16 (0.64–2.11)		1.38 (0.75–2.56)	
Age, years (5 years)‡							
Linear slope	1.09 (1.02–1.15)	0.006	1.08 (1.01–1.16)	1.13 (1.08–1.18)	<0.001	1.11 (1.05–1.18)	0.001
Quadratic slope	0.98 (0.97–1.00)	0.009	0.98 (0.97–1.00)	—§		—§	0.07
30 vs. 20	1.61 (1.20–2.15)		1.52 (1.14–2.03)	1.27 (1.16–1.40)		1.24 (1.09–1.40)	
45 vs. 20	2.51 (1.44–4.37)		2.28 (1.32–3.95)	1.83 (1.45–2.31)		1.70 (1.25–2.30)	
70 vs. 20	2.59 (1.38–4.87)		2.43 (1.17–5.05)	3.35 (2.10–5.34)		2.88 (1.57–5.29)	
Body mass index (kg m ⁻²)‡							
Linear slope	1.08 (1.02–1.14)	0.005	1.03 (0.98–1.09)	1.08 (1.05–1.11)	<0.001	1.06 (1.02–1.09)	0.001
27.5 vs. 22	1.53 (1.13–2.06)		1.19 (0.87–1.61)	1.52 (1.30–1.78)		1.35 (1.13–1.62)	
35 vs. 22	2.73 (1.35–5.54)		1.50 (0.73–3.09)	2.68 (1.85–3.90)		2.03 (1.32–3.13)	
Glucose metabolism disorder							
Normal	1.00		1.00	1.00		1.00	
Pre-diabetes	1.73 (1.10–2.72)	<0.001	1.27 (0.74–2.18)	2.37 (1.57–3.59)	<0.001	1.57 (1.01–2.46)	0.01
Diabetes	3.14 (1.77–5.56)		1.94 (0.95–3.95)	5.16 (3.06–8.69)		2.49 (1.31–4.76)	0.81

*Adjusted = controlled for age and all variables in the table with unadjusted p-value < 0.25.

†Interactions were examined between sex and each demographic variable. Tests for interactions include quadratic terms for age but not body mass index.

‡Age and body mass index were centred by subtracting raw means.

§There was no evidence of quadratic effects in these models.

CI, confidence interval; GGT, gamma glutamyl transpeptidase.

populations in New Zealand (18), which is consistent with their higher rates of elevated ALT and GGT levels compared with the other ethnic groups in this study.

Excess alcohol consumption is known to increase GGT. However, alcohol is not only hepatotoxic but also a concentrated source of energy providing 29 kJ g^{-1} . Although mechanisms by which excess weight affects the liver are not clearly understood, it has been suggested that the pathways by which alcohol intake and obesity affect the liver could overlap (29) and are potentially additive (30). Further, it has been suggested that the effect of an equivalent amount of alcohol on the liver could be greater with increasing BMI (31). In our study, women who consumed alcohol had higher odds of elevated GGT compared with those who did not consume alcohol. No associations between alcohol and GGT elevation were observed for men despite hazardous drinking being more common among New Zealand men than women (17). However, participants' alcohol consumption may have been miscategorized because the 2008/2009 NZANS questionnaire about alcohol intake did not include questions about binge drinking (19). Further, people typically underestimate their alcohol intake, particularly young men and middle-aged women (32).

Ethnicity effects remained statistically significant after adjusting for both BMI and drinking behaviour, suggesting that other factors contribute to these differences. While not available to investigate in the present study, hepatitis B infection may explain some of the difference, as this infection is common among both Māori and Pacific populations in New Zealand (14). Following the introduction of a successful hepatitis B vaccination programme in 1988, the prevalence has since declined among younger-aged New Zealanders (13). Ethnic differences in the prevalence of NAFLD have been observed among the US population, which were not fully explained by known risk factors such as lifestyle, adiposity and metabolic factors (33), suggesting other unknown ethnic specific factors are involved, which may also explain our observed ethnic differences.

Overall, ALT levels decreased with increasing age in this New Zealand population, which is consistent with other recent observations (34–36). The decrease in ALT levels with age was independent of metabolic syndrome components, adiposity signalling, alcohol use and other liver function tests in both the cross-sectional (34) and longitudinal (35) analyses in the Rancho Bernardo Study. Why ALT levels decrease with age is not known, but it does suggest ALT is not an ideal test to monitor the clinical course of liver disease and that appropriate normal ranges need to be established for older ages.

The proportion of women with elevated GGT levels was high among those 55 years and over, compared with

younger women and men of all ages. Although elevated GGT is a commonly used biological marker of excess alcohol consumption, hazardous drinking is infrequent among women in this older age group and is unlikely to explain most of these cases of elevated GGT. Obesity is a more likely explanation because more than one-third of women 55 years and over in the present study were obese. There may be other explanations, as elevated GGT is also an independent marker of other non-liver disorders such as both cardiovascular and all-cause mortality (37,38) and certain cancers, including liver cancer and female cancers, specifically breast, uterine and ovarian cancers (39–41).

This study was based on a national sample with oversampling of Māori and Pacific and younger and older age groups. The 61% participation rate may be considered less than ideal but is good for a national survey with a high respondent burden. Results were weighted so that they were representative of New Zealand's population. While liver enzyme test results were not available for all survey participants, there were no important differences in characteristics between the entire sample and the group for which liver enzyme test results were available. We used data from a nutrition survey, and data that could have informed possible causes of elevated liver enzymes, such as hepatitis infection status, were not collected.

Conclusions

The prevalence of elevated ALT and GGT in New Zealand is high, particularly among Pacific and Māori populations, who also have especially high rates of obesity and diabetes. Obesity-related liver disease is likely to increasingly burden the New Zealand health sector and contribute to health disparities unless effective obesity treatment and prevention measures are given high priority.

Conflict of Interest Statement

No conflict of interest statement

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Author contributions

K.J.C. conceived the study. K.J.C. and J.C.M. designed the study. J.C.M. and A.R.G. analysed the data. All authors interpreted the data. K.J.C., J.C.M. and A.R.G. drafted the manuscript. All authors critically reviewed and approved the final submitted manuscript.

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