

Ethnic perception of obesity in fatty liver disease

Beshoy Yanny¹, Matthew Viramontes², Lisa M. Najarian², Youssef Challita², Sammy Saab^{1,2}

¹Department of Medicine, ²Department of Surgery, the University of California at Los Angeles, Los Angeles, CA, USA

Contributions: (I) Conception and design: S Saab, B Yanny; (II) Administrative support: S Saab; (III) Provision of study materials or patients: S Saab; (IV) Collection and assembly of data: M Viramontes, LM Najarian, Y Challita; (V) Data analysis and interpretation: S Saab, B Yanny; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Sammy Saab, MD. Pfleger Liver Institute, UCLA Medical Center, 200 Medical Plaza, Suite 214, Los Angeles, CA 90095, USA. Email: SSaab@mednet.ucla.edu.

Background: The prevalence of non-alcoholic fatty liver disease (NAFLD) have been increasing along with the obesity epidemic. Although there is a strong association with diabetes and metabolic syndrome, NAFLD, the disease remains poorly understood. We sought to compare the prevalence, dietary habits, and characteristics of NAFLD patients across different ethnicities.

Methods: Patients with diagnosis of NAFLD or non-alcoholic steatohepatitis (NASH) were administered a demographic survey in this cross-sectional study. Laboratory values was obtained from chart review. Medical charts were reviewed for liver enzyme tests, documented metabolic disorders, body mass index (BMI), age, and transaminase levels. The findings were recorded and the combined data was analyzed.

Results: Eighty-three people participated in the study. Most participants were women. Over 80% of patients had cirrhosis. Ethnicities/race included: Hispanic white, White non-Hispanic, African American, Asian, and Middle Eastern and represented 36%, 29%, 6%, 17%, and 10% respectively. Diabetes was present in 38% of the entire group; 14% of patients had a BMI less than 25 and 100% of patients with normal BMI presented with NASH *vs.* NAFLD. When white Hispanics were compared to other populations. White Hispanics had female predominance (P value 0.01). More Hispanics self-reported DM, HTN, hypercholesterolemia, and obesity when compared to other populations (P value 0.012, 0.03, 0.05, 0.04, respectively). Obesity was under reported by all populations on the survey. Only 12% of Hispanics reported obesity on the survey compared to over 16% in all other populations.

Conclusions: A cross-sectional look at a diverse population reveals gross under reporting of obesity specially in the white Hispanic population. Patients with severe NASH and cirrhosis reported obesity the least. Relative differences of affected NAFLD-NASH patients with DM only present in less than 35%. White Hispanics had more metabolic complications than all other populations including DM, obesity, HTN and hypercholesterolemia at diagnosis. All races/ethnicities under reported obesity despite having a BMI consistent with obesity. Most patients were unaware of their obesity diagnosis at the time of the survey.

Keywords: Non-alcoholic steatohepatitis/non-alcoholic fatty liver disease (NASH-NAFLD); NASH epidemiology; fatty liver disease

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Introduction

Non-Alcoholic fatty liver disease (NAFLD) incidence is expected to rise with the increase of the global epidemic of obesity (1). Obesity has been established as a risk factor for NAFLD (1-3). NAFLD includes a spectrum of liver disease process that encompass non-alcoholic steatohepatitis (NASH) and non-alcoholic fatty liver (NAFL) (1-5). It has been established that patients with NASH portend a worse prognosis compared with those with bland steatosis

only. It has also been well documented that NAFLD is more prevalent in the Latino population. Prevalence of NAFLD in White Hispanic vs. White non-Hispanics vs. African Americans were noted to be 45%, 33% and 23% respectively (4,6-10). The higher prevalence of NAFLD in the Latino population is likely multifactorial secondary to genetics, socioeconomic status, education level, and the presence of multiple metabolic syndrome risk factors. Latino patients develop NAFLD at a much younger age than non-Latino whites and African Americans (5-10). Despite multiple efforts in studying NASH-NAFLD, the disease remains poorly understood, and the characteristics of affected patients are dynamically and rapidly changing. More studies are needed to improve our understanding of NASH-NAFLD epidemiology and relative differences among different races/ethnicities.

Multiple studies have associated NASH and NAFLD with obesity and diabetes (5,11,12). More recent studies have associated food consumption and dietary habits to have an impact on the development or improvement of NASH-NAFLD. Light alcohol intake, dark chocolate intake, and coffee consumption were found to have a positive impact (10,13-15), while consumption of lipopolysaccharides (LPS) and artificial sweeteners in general were associated with a negative impact (14). Our study is unique in prospectively evaluating the demographics, dietary habits and family history from the patient's prospective and truly reporting a random cross section of all comers to the liver clinic with the diagnosis of NASH and NAFLD in an effort to better understand this evolving and prevalent disease. In our study. We sought to compare the prevalence, dietary habits, and characteristics of NAFLD patients across different ethnicities in a random cross section of outpatient clinic patients at a large academic institution with a diverse population.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi. org/10.21037/dmr-2020-05).

Methods

Participants and procedures

Patients screened for clinic visits at UCLA Pfleger liver institute were evaluated. After informed consent was obtained, a survey was filled out by the patients prospectively. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). IRB approval was obtained UCLA IRB FWA 00004642. Patient charts were then retrospectively reviewed for liver enzyme tests, documented metabolic disorders, body mass index (BMI), age, and transaminase levels. Participants in this cross-sectional study were patients who patients who carry the diagnosis of NAFLD or NASH with and without liver cirrhosis presenting to liver clinic for evaluation at the University of California, Los Angeles Pfleger Liver Institute between June 2016 and June 2018. Surveys and informed consent were administered in both English and Spanish, and translation services were provided for patients whose native language was neither English nor Spanish. All eligible patients seen in the Pfleger Liver Institute were invited by investigators to participate in the study during their visit at the clinic.

Following a short verbal explanation of the study, participants were administered a demographic questionnaire and family history questionnaire (see below). Participation in the study was completely voluntary and there was no compensation offered. The University of California, Los Angeles Institutional Review Board approved the study. Prior medical records of all study participants were accessed in order to obtain information about the patients including medical records, medications, and laboratory test results.

Demographic questionnaire

Each participant completed one self-administered questionnaire, which was separated into a section for demographics and family history. The demographics section included questions including inquiries regarding their age, gender, ethnicity/race, how long the patient had known about their liver disease, and risk factors such as time spent driving per day, activity levels, dietary habits such as consuming beverages containing a high level of sugar, family history and past medical history including the presence of diabetes, hypertension, dyslipidemia, and obesity. High sugar level drinks were defined as Juice, nondiet Soda drinks, Sweetened smoothies, sweetened shakes, and sweetened coffee drinks. Race/ethnicity were selfdefined. Supplement I shows the survey contents obtained from patients.

Operational definitions

We defined hypertension as a blood pressure value greater than 140/90 mmHg measured on two separate occasions,

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Table 1 Features of NASH-NAFLD affected path	ients per population
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Population % present		Gender predominance	Mean BMI (± SD)	Mean age at diagnosis (± SD)	Presence of DM
White-Hispanic, n=30	36	Female: 70%	30.8 (±2.2)	62.9 yo (±1.3 y)	50%
White non-Hispanic, n=25	29	Male: 67%	30.8 (±3.5)	62.6 yo (±1.5 y)	33%
Asian, n=14	17	Female: 71%	30.7 (±2.7)	62.6 yo (±2.7 y)	50%
Middle Eastern, n=9	10	Male: 55%	30.6 (±3.5)	62.7 yo (±1.7 y)	22%
African American, n=5	6	Male: 80%	31.9 (±1.7)	63.5 yo (±1.8 y)	20%

NASH, non-alcoholic steatohepatitis; NAFLD, non-alcoholic fatty liver disease; BMI, body mass index; DM, diabetes mellitus; yo, years old; y, years; SD, standard deviation.

based on current Joint National Committee hypertensive guidelines, or as current use of anti-hypertensive medications. A diagnosis of diabetes mellitus was made if the patient met at least one of the following three criteria: (I) fasting blood sugar equal to or greater than 126 mg/dL measured on two occasions; (II) hemoglobin A1c level greater than or equal to 6.5%; and (III) if the patient was currently taking medications for a prior diagnosis of diabetes mellitus. Hypercholesterolemia for liver transplant recipients was defined by an elevated lowdensity lipoprotein cholesterol (LDL-C) level greater than 100 mg/dL, as recommended by treatment guidelines by the American Association for the Study of Liver Diseases (AASLD), and/or individuals being treated with cholesterollowering medication. Hypertriglyceridemia was defined as a triglyceride levels greater than 200 mg/dL or the use of triglyceride lowering medications. Obesity was defined using the World Health Organization definition BMI classification. BMI between 18.5-24.99 was classified as normal, 25-29.99 as overweight, 30-34.99 as class I obesity, 35–39.99 as class II obesity, and >40 as class III obesity (15).

Data analysis

Descriptive statistics mean and standard deviations (SD) were utilized to describe distribution of results. A P value below 0.05 was considered statistically significant and all statistical tests were two-sided.

Inclusion criteria

Patients >18 years old presenting to the liver clinic previously diagnosed with NASH-NAFLD with or without liver cirrhosis were included.

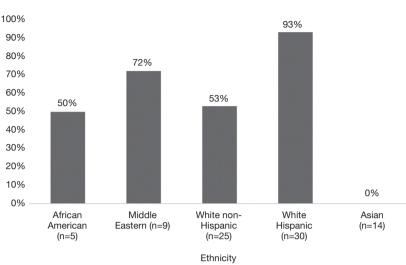
Exclusion criteria

Patients with other etiologies of liver disease including viral hepatitis, cholestatic liver diseases, metabolic liver disease, genetic liver diseases, and patients who consume more than 20 g of alcohol per day.

Results

A total of 83 patients were included in the study. Male 42%, female 58%, and 82% of patients had liver cirrhosis at the time of the study. The ethnicity/race of the study population is shown in Table 1. African Americans, Middle Eastern, White non-Hispanic had male predominance with 80%, 55%, and 67% respectively. Diabetes was present in less than 35% of patients in the Middle Eastern, White non-Hispanic and African Americans group and in less than 30% of African Americans and Middle Eastern patients with present in 50% of white Latino patients (Figure 1). Diabetes was present in 38% of the study cohort in total. Fourteen percent of patients had a BMI less than 25 and 100% of patients with normal BMI presented with NASH vs. NAFLD. More Hispanics self-reported DM, HTN, and hypercholesterolemia when compared to other populations (P value 0.012, 0.03, 0.05 respectively). Obesity was under reported by all populations on the survey. Only 12% of Hispanics reported obesity on the survey compared to over 16% in all other populations (*Tables 1,2*).

The mean (\pm SD) age at diagnosis for the entire cohort was 62.5 (\pm 1.7) years. Eighty percent of our patient cohort was over 60 years old. White Hispanics self-reported age at the time of diagnosis was 62.9 \pm 1.3 vs. 62.7 \pm 5.7 for the rest of cohort (P=0.057). The mean (\pm SD) BMI for the entire patient cohort was 30.7 \pm 3.2. Detailed demographics and



Percent with cirrhosis

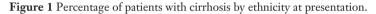


Table 2 Features of NASH-NAFLD patient profile

Population	% present	% family Hx of NAFLD	Gender predominance	Sugar drink daily	Mean BMI (± SD)	Mean age at diagnosis (± SD)	Presence of DM
White-Hispanic, n=30	36	75	Female: 70%	100%	30.8 (±2.2)	62.9 yo (±1.3 y)	50%
White non-Hispanic, n=25	29	15	Male: 67%	100%	30.8 (±3.5)	62.6 yo (±1.5 y)	33%
Asian, n=14	17	12	Female: 71%	100%	30.7 (±2.7)	62.6 yo (±2.7 y)	50%
Middle Eastern, n=9	10	5	Male: 55%	80%	30.6 (±3.5)	62.7 yo (±1.7 y)	22%
African American, n=5	6	0	Male: 80%	82%	31.9 (±1.7)	63.5 yo (±1.8 y)	20%

NASH, non-alcoholic steatohepatitis; NAFLD, non-alcoholic fatty liver disease; BMI, body mass index; DM, diabetes mellitus; yo, years old; y, years; SD, standard deviation.

clinical characteristics of the entire cohort is represented in *Table 3*; 68% of patients drink at least 1 high sugar containing beverage per day, and 64% percent of patients drive for less than half an hour daily. Demographics collected via survey are noted in *Tables 1,4*.

When white Hispanics were compared to other populations White Hispanics had female predominance P value 0.01, were diagnosed with NASH or NAFLD at age over 60 years of age which was not significantly different from other populations P value 0.03. More Hispanics selfreported DM, HTN, and hypercholesterolemia when compared to other populations (P value 0.012, 0.03, 0.05, 0.04. respectively). The self-reported co-morbidities of the entire population is reported in *Table 3*.

Metabolic features

Hypertension

Hypertension at the time of NASH-NAFLD diagnosis was present in 24.7% of the entire cohort. Hypertension was self-reported in 43% of White Hispanics *vs.* 12% of other populations collectively. White Hispanics with NASH had more HTN compared to all other populations (P value 0.03). The presence of hypertension was self-reported and chart verified.

Hypercholesterolemia

Hypercholesterolemia reported and verified by chart review at the time of NASH-NAFLD diagnosis was 24%

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 Table 3 Disease characteristics of 83 patients with NASH (continued)

	1	, ,		
Characteristic	Number of responses			
Characteristic	Yes	No		
History of				
Heart disease	6 (7%)	77 (93%)		
Stroke	0 (0%)	83 (100%)		
Peripheral vascular disease	3 (4%)	80 (96%)		
Diabetes Mellitus	9 (11%)	74 (89%)		
Vitamin D deficiency	1 (1%)	82 (99%)		
Family history of				
Fatty liver	11 (13%)	72 (87%)		
Hypertension	30 (36%)	53 (64%)		
Diabetes	19 (23%)	64 (77%)		
Hyperlipidemia	20 (24%)	63 (76%)		
Obesity	13 (16%)	70 (84%)		
Manifestations of portal hypertension				
Esophageal varices	30 (36%)	53(64%)		
Encephalopathy	59 (71%)	24 (29%)		
Ascites	61 (82%)	22 (26%)		
NAOLI				

NASH, non-alcoholic steatohepatitis.

 Table 4 Demographic characteristics patients with non-alcoholic fatty hepatitis or non-alcoholic fatty liver disease

Characteristic	Number of responses
Gender	
Female	48 (58%)
Male	35 (42%)
Age, years, mean (± standard deviation)	62.5 (±1.7)
Stratification	
18–40	5 (6%)
41–60	22 (27%)
60+	56 (67%)
How many drinks with sugar do you drink daily?	
0–1 drinks a day	58 (70%)
2–3 drinks a day	20 (24%)
4–5 drinks a day	4 (5%)
6+ drinks a day	1 (1%)

in the entire group, which was verified by chart review. Hypercholesterolemia was self-reported in 38% of White Hispanics *vs.* 7% of other populations collectively. White Hispanics with NASH had more hypercholesterolemia (P value 0.05).

Diabetes mellitus

The reported prevalence of diabetes mellitus was 34.4% for the entire group, which was verified by chart review. Diabetes was present in 50% of White Hispanics *vs.* 22% of all other populations. Diabetes was present in more White Hispanics with NASH *vs.* all other populations (P=0.012).

Obesity

The self-reported prevalence of obesity in our sample was 16%. However, the chart review revealed obesity was documented in 43% of the cohort based on BMI calculation. White Hispanics self-reported obesity was 12.1% vs. 16.7% in all other populations. Based on self-reported data White-Hispanics with NASH were less obese than all others however this was not statistically significant (P=0.157). Based on chart review all populations under reported obesity. Based on chart review 58% of white Hispanics with NASH-NAFLD had a BMI over 35 and 38% of the rest of the population had a BMI of over 35. Based on chart review White Hispanics with NASH-NAFLD were more obese than other populations (P=0.053).

First degree family members with fatty liver disease, sugar containing drink consumption and self-reported liver cirrhosis

The self-reported prevalence of first degree relatives with NASH-NAFLD was 18.3%. White Hispanics reported 32% vs. 13.1% in all other populations. White Hispanics had more first degree family members with NASH-NAFLD compared to the rest of the populations in this study (P=0.953). The reported prevalence of ingesting at least one sugar containing drink was 100% and did show a statistically significant association with NASH-NAFLD with no difference between White Hispanics vs. all other populations in the study (P=0.0654). Finally liver cirrhosis was present in 82% of our patient population. Cirrhosis was present in 93% of White-Hispanics vs. 73% of all other populations at diagnosis. White-Hispanics had more liver cirrhosis at the time of diagnosis compared to all other populations (P=0.047).

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Discussion

NASH-NAFLD is an evolving disease, which is becoming more prevalent worldwide (1,12-14). The pathophysiology, prevalence of the disease, NASH-NAFLD patient profile, and comparison of the disease characteristics and progression in different populations all remain poorly understood (14,15). Out study looked at a cross section of a diverse population in a large academic center. Our findings suggest that the NASH-NAFLD is present in more White-Hispanics and White non-Hispanic population over all other populations reported in the study. Overall the age at the time of diagnosis was similar in all populations. White Hispanics had more self-reported and chart verified DM, HTN, and hypercholesterolemia, and low self-reported obesity at the time of diagnosis compared to all other populations which was statistically significant. White Hispanics also had a statistically significant more female predominance over all other populations in our study and reported more firstdegree family members with NASH-NAFLD. Cirrhosis was also present in more White Hispanics at diagnosis vs. all other populations. Our data suggests that risk factors for NASH-NAFLD are unique in different ethnicities and that some ethnicities are more prone to NASH-NAFLD vs. others. In this case White Hispanics had more metabolic diseases at were more likely to have liver cirrhosis at the time of diagnosis vs. all other populations. More interestingly White Hispanics had lower perception of obesity than all other populations may be contributing the late diagnosis and increased complication risk.

It has been reported that in high income western countries NAFLD prevalence is as high as 20-40% making it the most prevalent chronic liver disease (5,14). It has also been reported that NAFLD is 3-5 times more prevalent in men than women in the United States (4,12,14). Multiple studies have also reported that NASH-NAFLD is more prevalent in the Hispanic population. Our study is unique in that it prospectively evaluates the prevalence and characteristics of patients with NASH-NAFLD in a random cross section of outpatient clinic patients at a large academic institution with a diverse population. Our study implicates that NASH-NAFLD exhibits different gender predominance and is more prevalent in certain populations such as the White-Hispanic and White non-Hispanic population. This is not different from previously reported studies (4). Our study did show male predominance in white non-Hispanics, Middle Eastern, and African American populations which is also no different from

previous studies. Despite multiple retrospective studies showing an association between diabetes and NASH-NAFLD our prospective study shows that less than 35% of patients have diabetes concurrently with NASH-NAFLD. In certain populations the association with diabetes was noted in less than 25% of patients. Diabetes was more prevalent in White-Hispanics at the time of diagnosis vs. all other populations, and cirrhosis was diagnosed at the time of presentation in more white Hispanics vs. white non-Hispanic as suggested by previous studies. The age at diagnosis was similar in the entire population which was different from what was previously reported that White Hispanics are diagnosed at an earlier age (15). Interestingly the self-reported prevalence of obesity in our sample was 16% however chart review revealed obesity was documented in 43% of the cohort. White Hispanics self-reported obesity was 12.1% vs. 16.7% in all other populations. Based on self-reported data White-Hispanics with NASH were less obese than all others however this was not statistically significant (P=0.157). Based on chart review all populations under reported obesity. Based on chart review 58% of white Hispanics with NASH-NAFLD had a BMI over 35 and 38% of the rest of the population had a BMI of over 35. Based on chart review White Hispanics with NASH-NAFLD were more obese than other populations (P=0.053). This shows that despite our best efforts in patient education we may be falling short in discussing the obesity diagnosis, its implications, and prevention in certain populations.

To our knowledge this one of the largest prospective studies to date looking at the prevalence of NASH-NAFLD in a large diverse population. Our clinic is located in diverse area of Los Angeles and therefore encounters patients of multiple ethnicities and cultures which is a strength of our study. The limitation to our study is that patients with NASH-NAFLD were clinically diagnosed and lack a histological diagnosis as liver biopsy is not commonly performed to diagnose NASH-NAFLD at our institution. Due to the lack of a widely accepted scoring system for NASH-NAFLD none were used as well. This does not undermine the strength of our findings as all other etiologies of liver disease were excluded appropriately and imaging studies confirmed steatosis on all NASH-NAFLD patients.

The natural history of NAFLD in the general population remains poorly understood as most of the data comes from selected patient populations (16,17). Our study in a large diverse population shows that NASH-NAFLD is more prevalent in certain population over others, and risk factors for NASH-NAFLD are continuing to evolve. In our paper we show that risk factors for NASH-NAFLD are unique in different races/ethnicities. This study also highlights that certain populations perceive obesity differently. For in instance white Hispanics self-reported obesity in only 12% however obesity was present in 50% per chart review. Perhaps this discrepancy in self-reporting obesity may be secondary to health illiteracy, poor access to care or cultural differences. This population specifically was diagnosed later in life, and were found to have cirrhosis at that time of diagnosis. Perhaps if patients in this population knew about obesity early on liver cirrhosis may have been slowed down or prevented all together. Overall this crosssectional look at a diverse population in a large academic center also shows predominance of NASH vs. NAFLD in patients with normal BMI, and male predominance in African American, Middle Eastern and White non-Hispanic populations. Our study suggests that white Hispanics have a higher prevalence of metabolic diseases such as DM, hypercholesterolemia and obesity as well as other factors such as HTN and liver cirrhosis at the time of diagnosis which confirms what has been reported in previous studies. All races/ethnicities under reported obesity, which shows that despite our best efforts in patient education we are still falling short in discussing the obesity diagnosis, and its implications. We suggest that health care providers should discuss the diagnosis of obesity with patients to improve the patient's understanding. More prospective studies are needed elucidate the risk factors contributing to NAFLD-NASH patients in different ethnicities and personalize screening and treatment for certain populations.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by The University of California, Los Angeles Institutional Review Board (FWA 00004642) and informed consent was taken from all individual participants.

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Supplement I Metabolic complication in non-alcoholic steatohepatitis (NASH) patients survey

Section A: Medical history

1)	How would you define your ethnicity? Please check one box					
	 Non-Hispanic White Hispanic White 	□ African Ameri □ Asian		rican Indian r:		
2)	What year were you told yo	ou have fatty liver?				
3)	Do you have high blood pro □ Yes	essure? □ No				
	↓ What year were you diagno	osed?				
4)	Do you have diabetes? □ Yes ↓ What year were you diagno	□ No osed?				
5)	Do you have high cholester □ Yes ↓ What year were you diagno	□ No				
6)	How much did you weigh 5	years ago?		_lbs		
7)	How much did you weigh 1	0 years ago?		lbs		
8)	How much driving do you o □ 0–29 min □ 3	do a day on average? 0–60 min	□ 60–120 min	□ >	120 min	
9)		ar do you drink daily? –3 drinks a day			inks, coffee, sports drinks, energy drin + drinks a day	ıks)
10	 Have you changed your life Yes If No, please circle what a A. Did not think it was a r B. It required too much ch C. Financially I am not ab D. Financially I do not hav E. I could not abide by thit F. I was not given enough G. I was too embarrassed H. Other reason 	□ No pplies: eal disease, I felt norm hange in my lifestyle le to afford healthier we the ability to follow s diet plan for person instruction on how to	nal food options v up with a physic al reasons (exampl o change my diet c	an for this pro e: I ate whatev r how long I n	blem er my wife cooked)	

Section B: Family bistory

11)	How many brothers do you have?
	How many have fatty liver?
	How many have high blood pressure?
	How many have diabetes?
	How many have high cholesterol?
	How many are overweight?
12)	How many sisters do you have?
,	How many have fatty liver?
	How many have high blood pressure?
	How many have diabetes?
	How many have high cholesterol?
	How many are overweight?
13)	Mother
	Does your mother have fatty liver?
	Does your mother have high blood pressure?
	Does your mother have diabetes?
	Does your mother have high cholesterol?
	Is your mother overweight?
14)	Father
,	Does your father have fatty liver?
	Does your father have high blood pressure?
	Does your father have diabetes?
	Does your father have high cholesterol?
	Is your father overweight?