Published in final edited form as:

Clin Gastroenterol Hepatol. 2017 August ; 15(8): 1305–1307. doi:10.1016/j.cgh.2017.02.038.

Coffee Drinking and Alcoholic and Nonalcoholic Fatty Liver Diseases and Viral Hepatitis in the Multiethnic Cohort

Veronica Wendy Setiawan^{1,2}, Jacqueline Porcel¹, Pengxiao Wei¹, Daniel O. Stram¹, Nabil Nouredin³, Shelly C. Lu⁴, Loïc Le Marchand⁶, and Mazen Nouredin^{4,5}

¹Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA

²Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA

³Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA

⁴Division of Digestive and Liver Diseases, Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA

⁵Comprehensive Transplant Center, Cedars-Sinai Medical Center, Los Angeles, CA

⁶Epidemiology Program, University of Hawaii Cancer Center, Honolulu, HI

Introduction

Chronic hepatitis C (CHC) and alcoholic liver disease (ALD) are major causes of chronic liver disease (CLD), but nonalcoholic fatty liver disease (NAFLD) has now become the most common cause of CLD¹. Coffee consumption has been inversely associated with CLD severity², but studies were mainly conducted in CHC while fewer studies have been done in other etiologies. We examined the association between coffee consumption and CLD with and without cirrhosis by underlying etiology in African Americans, Native Hawaiians, Japanese Americans, Latinos, and whites in the Multiethnic Cohort (MEC).

Methods

The MEC is a prospective study of >215,000 participants, aged 45–75 years at enrollment between 1993–1996. The study design, baseline characteristics and outcome ascertainment have been described previously^{3, 4}. For this study, we utilized a nested case-control study

Correspondence: 1st: V. Wendy Setiawan, Ph.D., Department of Preventive Medicine, Keck School of Medicine, University of Southern California, 1450 Biggy Street, Room 1517G, Los Angeles, CA 90033, vsetiawa@usc.edu, Phone: 323-442-7806; Fax: 323-442-7749. 2nd: Mazen Nouredin, M.D., Division of Digestive and Liver Diseases, Cedars Sinai Medical Center, Mazen.nouredin@cshs.org.

Conflicts of interest: the authors disclose no related conflicts

Author contributions: study concept and design (VWS, MN); acquisition of data (VWS, LLM); statistical analysis and interpretation of data (VWS, JP, PW, DOS, MN); drafting of manuscript (VWS, NN, MN); critical revision of the manuscript for important intellectual content (VWS, DOS, SCL, LLM, MN); obtained funding (VWS, LLM).

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

derived from MEC participants who were enrolled in the Medicare fee-for-service (FFS) and completed questionnaires on coffee intake and confounders (n=95,197). As previously described⁵, CLD and cirrhosis cases were identified using Medicare claims between 1999–2012. ICD-9-CM codes, BMI, alcohol intake, and history of diabetes mellitus were used to classify cases into etiologic groups⁵. 5,385 CLD cases were identified [ALD (n=1,112), NAFLD (n=2,786), CHC (n=606), CHB (n=165), other (n=357), and cryptogenic (n=359)]. Controls were selected from the eligible participants without CLD and were individually matched to cases (15:1) by age, sex, ethnicity, and length of FFS enrollment.

Coffee drinking was obtained using a quantitative food-frequency questionnaire (QFFQ)³. A calibration study of the QFFQ conducted using three 24-hour recalls from a random subsample revealed an excellent correlation coefficient (0.72) for coffee consumption. Coffee intake was categorized into: never, < 1 cup daily, 1 cup daily, 2–3 cups daily, and 4 cups daily. Associations of coffee intake with CLD were quantified by OR and 95% CI using logistic models conditioned on the sets defined by matching variables and adjusted for education, BMI, diabetes, smoking status, and alcohol intake. Tests for trend were performed by entering the ordinal values representing categories of exposures as continuous variables in the models. Analyses were conducted using SAS 9.3.

Results

The median age at cohort entry of the cases and controls was 61 years old and 44% were male. The ethnicity breakdown was 12% African Americans, 38% Japanese Americans, 5% Native Hawaiians, 22% Latinos, and 23% whites.

The risks for CLD associated with ALD ($P_{\text{trend}}=0.0015$), NAFLD ($P_{\text{trend}}=0.0001$) and CHC ($P_{\text{trend}}=0.0241$) were reduced with increasing coffee consumption (Table 1). The associations of coffee with ALD ($P_{\text{trend}} < 0.0001$) and CHC ($P_{\text{trend}}=0.0215$) were mainly observed in those with cirrhosis. Interestingly, with NAFLD-associated CLD, a significant trend was seen for both cirrhosis ($P_{\text{trend}}=0.0484$) and non-cirrhosis cases ($P_{\text{trend}}=0.0018$). No association was found between coffee drinking and CLD or cirrhosis due to other etiologies (e.g. CHB). No evidence that the coffee associations with ALD, NAFLD, and CHC varied by ethnicity ($P_{\text{heterogeneity}} = 0.20$).

Discussion

In this study with multiple ethnic groups, coffee drinking is associated with reduced risk of NAFLD-, CHC- and ALD-associated CLD. In CHC and ALD, coffee intake was mainly associated with a decrease in risk of CLD with cirrhosis. In NAFLD, it was associated with decreased risk of CLD both with and without cirrhosis.

Our findings support data from studies² showing the effect of coffee on liver enzyme reduction and the association of increased coffee consumption with reduced histological activity, in particular fibrosis in CHC. Our data also suggest a possible effect of coffee intake on the fibrosis process in ALD and CHC and an effect of coffee on multiple pathways in NAFLD, possibly including inflammatory, steatotic and fibrotic processes. The effect of

coffee on fibrosis may be mediated by adenosine receptors⁶. It is possible that coffee constituents have a direct effect on steatosis or steatohepatitis pathways.

Fewer studies have been conducted to assess the effects of coffee consumption in ALD and NAFLD in comparison to CHC². A meta-analysis suggested a protective association for ALD and CHC-related cirrhosis⁷, while another meta-analysis only showed the association in patients with alcoholic cirrhosis⁸.

The study limitations include the likely underestimation of the true prevalence of NAFLD and possibly other etiologies given the lack of biochemical and imaging testing and the use of self-reported coffee intake at baseline which is subject to measurement error. The strengths include its large size, population-based design, validated questionnaire, inclusion of five ethnic, mostly understudied, populations, and information on important confounders.

In conclusion, coffee drinking is associated with reduced CLD risk, particularly for NAFLD, ALD, and CHC, including cirrhosis. We propose that randomized controlled trials should be entertained, in particular in NAFLD patients where coffee consumption seems to affect the entire disease process and no treatments are currently available.

Acknowledgments

Grant support: National Cancer Institute grants CA164973 and CA186203

We thank the MEC participants for their participation and commitment.

Abbreviations

ALD	alcoholic liver disease
BMI	body mass index
CHB	chronic hepatitis B
CHC	chronic hepatitis C
CLD	chronic liver disease
HBV	hepatitis B virus
HCV	hepatitis C virus
NAFLD	nonalcoholic fatty liver disease

References

1. Younossi ZM, Stepanova M, Afendy M, et al. Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2011; 9(6):524–30e1. quiz e60. Epub 2011/03/29. [PubMed: 21440669]
2. Saab S, Mallam D, Cox GA 2nd, et al. Impact of coffee on liver diseases: a systematic review. *Liver international : official journal of the International Association for the Study of the Liver*. 2014; 34(4):495–504. Epub 2013/10/10. [PubMed: 24102757]

3. Kolonel LN, Henderson BE, Hankin JH, et al. A multiethnic cohort in Hawaii and Los Angeles: baseline characteristics. *American journal of epidemiology*. 2000; 151(4):346–57. Epub 2000/03/01. [PubMed: 10695593]
4. Setiawan VW, Virnig BA, Porcel J, et al. Linking data from the Multiethnic Cohort Study to Medicare data: linkage results and application to chronic disease research. *American journal of epidemiology*. 2015; 181(11):917–9. [PubMed: 25841869]
5. Setiawan VW, Stram DO, Porcel J, et al. Prevalence of chronic liver disease and cirrhosis by underlying cause in understudied ethnic groups: The multiethnic cohort. *Hepatology*. 2016; 64(6): 1969–77. [PubMed: 27301913]
6. Dranoff JA, Feld JJ, Lavoie EG, et al. How does coffee prevent liver fibrosis? Biological plausibility for recent epidemiological observations. *Hepatology*. 2014; 60(2):464–7. [PubMed: 24464631]
7. Liu F, Wang X, Wu G, et al. Coffee Consumption Decreases Risks for Hepatic Fibrosis and Cirrhosis: A Meta-Analysis. *PloS one*. 2015; 10(11):e0142457. [PubMed: 26556483]
8. Kennedy OJ, Roderick P, Buchanan R, et al. Systematic review with meta-analysis: coffee consumption and the risk of cirrhosis. *Alimentary pharmacology & therapeutics*. 2016; 43(5):562–74. [PubMed: 26806124]

Table 1

Association between coffee intake and chronic liver disease by underlying etiology in the Multiethnic Cohort

	CHB			CHC [†]			Other			ALD			NAFLD			Cryptogenic		
	No. Cases	OR* (95% CI)	No. Cases	OR* (95% CI)	No. Cases	OR* (95% CI)	No. Cases	OR* (95% CI)	No. Cases	OR* (95% CI)	No. Cases	OR* (95% CI)	No. Cases	OR* (95% CI)	No. Cases	OR* (95% CI)		
Coffee intake (cups/day)	165		606		357		1,112		2,786		359							
All CLD																		
Never	48	1.00 (Ref)	175	1.00 (Ref)	92	1.00 (Ref)	299	1.00 (Ref)	866	1.00 (Ref)	115	1.00 (Ref)				1.00 (Ref)		
<1	36	1.11 (0.69–1.78)	142	1.24 (0.98–1.58)	68	1.08 (0.77–1.52)	226	1.05 (0.86–1.27)	558	1.00 (0.89–1.12)	57	0.85 (0.6–1.19)				0.85 (0.6–1.19)		
1	47	1.08 (0.70–1.68)	169	1.00 (0.80–1.26)	108	1.18 (0.87–1.61)	343	0.98 (0.82–1.17)	759	0.93 (0.84–1.03)	106	0.88 (0.66–1.18)				0.88 (0.66–1.18)		
2–3	27	0.89 (0.53–1.48)	100	0.82 (0.63–1.07)	72	1.18 (0.84–1.65)	201	0.78 (0.64–0.95)	506	0.85 (0.75–0.96)	68	0.82 (0.59–1.14)				0.82 (0.59–1.14)		
4	7	0.78 (0.31–1.95)	20	0.62 (0.37–1.01)	17	1.24 (0.70–2.21)	43	0.60 (0.42–0.86)	97	0.66 (0.53–0.83)	13	0.67 (0.36–1.25)				0.67 (0.36–1.25)		
P trend		0.5964		0.0241		0.2391		0.0015		0.0001		0.1491						
CLD without cirrhosis																		
Never	29	1.00 (Ref)	49	1.00 (Ref)	42	1.00 (Ref)	144	1.00 (Ref)	678	1.00 (Ref)	46	1.00 (Ref)				1.00 (Ref)		
<1	19	0.95 (0.50–1.77)	38	1.38 (0.87–2.20)	35	1.22 (0.75–1.98)	103	1.02 (0.77–1.36)	419	0.94 (0.83–1.08)	21	0.80 (0.46–1.37)				0.80 (0.46–1.37)		
1	24	0.90 (0.50–1.62)	54	1.26 (0.83–1.92)	52	1.24 (0.80–1.94)	171	1.02 (0.80–1.32)	608	0.94 (0.84–1.06)	49	1.06 (0.69–1.64)				1.06 (0.69–1.64)		
2–3	14	0.79 (0.39–1.58)	29	0.96 (0.58–1.59)	43	1.44 (0.91–2.30)	108	0.93 (0.70–1.24)	413	0.86 (0.75–0.98)	32	1.02 (0.62–1.67)				1.02 (0.62–1.67)		
4	5	1.03 (0.36–2.98)	5	0.68 (0.25–1.84)	8	1.29 (0.57–2.94)	25	0.85 (0.52–1.37)	77	0.66 (0.51–0.84)	7	0.99 (0.42–2.33)				0.99 (0.42–2.33)		
P trend		0.6301		0.7035		0.1570		0.5214		0.0018		0.7803						
Cirrhosis																		
Never	19	1.00 (Ref)	126	1.00 (Ref)	50	1.00 (Ref)	155	1.00 (Ref)	188	1.00 (Ref)	69	1.00 (Ref)				1.00 (Ref)		
<1	17	1.36 (0.65–2.86)	104	1.19 (0.90–1.58)	33	0.96 (0.59–1.56)	123	1.04 (0.80–1.36)	139	1.22 (0.95–1.57)	36	0.87 (0.56–1.36)				0.87 (0.56–1.36)		
1	23	1.32 (0.67–2.59)	115	0.92 (0.70–1.21)	56	1.11 (0.72–1.71)	172	0.92 (0.72–1.17)	151	0.90 (0.71–1.14)	57	0.74 (0.51–1.10)				0.74 (0.51–1.10)		
2–3	13	1.02 (0.46–2.24)	71	0.78 (0.57–1.07)	29	0.93 (0.56–1.55)	93	0.64 (0.48–0.85)	93	0.83 (0.63–1.10)	36	0.67 (0.43–1.05)				0.67 (0.43–1.05)		
4	2	0.30 (0.04–2.44)	15	0.61 (0.34–1.08)	9	1.20 (0.53–2.73)	18	0.40 (0.23–0.68)	20	0.74 (0.44–1.23)	6	0.47 (0.19–1.14)				0.47 (0.19–1.14)		
P trend		0.6883		0.0215		0.8403		<.0001		0.0484		0.0220						

OR=odds ratio; CI=confidence intervals.

[†]Include cases with both chronic HCV and chronic HBV.

Include hemochromatosis, primary biliary cirrhosis, primary sclerosing cholangitis, Wilson’s disease, HIV, and autoimmune hepatitis.

* OR stratified by matching factors (age, sex, race/ethnicity, and length of FFS enrollment) and adjusted for education, BMI, diabetes, smoking status, and alcohol intake.