

Prevalence of cirrhosis/advanced fibrosis among HBsAg-negative and HBcAb-positive US adults: a nationwide population-based study

Shuai-Wen Huang^{1,3}, Chen Chen², Hong-Yan Kong^{1,3}, Jia-Quan Huang^{1,3*}

¹Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China;

²Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, USA;

³National Medical Center for Major Public Health Events, Wuhan, China.

***Correspondence to** Jia-Quan Huang, MD, Department and Institute of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, P. R. China.

Email: huangjiaquan21@aliyun.com

Table S1. Trends analyses for cirrhosis[#] in the US adults with HBsAg-negative and HBcAb-positive from 2001-2018. *

	% With cirrhosis ^{&}
Rao-Scott χ^2	P=0.19
Linear regression	R ² =0.00045, P=0.77

*Adjusting for sampling weights and accounted for complex survey designs; [#]defined as FIB4 >3.25.

Table S2. Prevalence of cirrhosis (defined as APRI>1) by selected characteristics in US adults with HBsAg-negative and HBcAb-positive, NHANES, 2001–18. #

Characteristics	NHANES 2001-2018	NHANES 2001-2006	NHANES 2007-2012	NHANES 2013-2018
	(Total)	(Era 1)	(Era 2)	(Era 3)
	Adjusted %(95%CI)	Adjusted %(95%CI)	Adjusted % (95%CI)	Adjusted % (95%CI)
Overall	4.13(3.12-5.13)	3.47(2.30-4.64)	5.33(3.36-7.30)	3.75(1.60-5.90)
Sex				
Male	5.78(4.02-7.53)	4.63(2.44-6.82)	8.25(4.44-12.05)	5.00(1.59-8.41)
Female	2.05(1.18-2.93)	1.96(-0.02-3.95)	2.20(1.15-3.25)	2.01(0.70-3.31)
Age groups (years)				
20-39	0.93(0.24-1.74)	0.33(-0.32-0.99)	1.50(-0.32-3.33)	1.50(-0.26-3.27)
40-59	5.29(3.67-6.91)	5.53(3.33-7.74)	7.56(3.28-11.83)	2.65(0.93-4.37)
60+	4.22(2.20-6.24)	2.21(0.86-3.56)	4.20(1.82-6.58)	5.62(1.09-10.15)
BMI:				
<25	3.22(2.15-4.29)	3.07(1.96-4.18)	3.93(1.57-6.29)	2.39(-0.09-4.88)
25-30	5.40(2.97-7.82)	3.46(0.94-5.99)	8.67(4.45-12.89)	4.49(-2.33-11.33)
>30	3.34(1.65-5.02)	3.72(0.34-7.10)	3.76(0.77-6.74)	2.26(0.34-4.19)

Ethnicity:				
Non-Hispanic white	5.60(3.23-7.96)	4.77(2.51-7.02)	8.29(2.28-14.30)	4.45(-0.37-9.27)
Non-Hispanic black	4.01(2.80-5.22)	3.03(1.48-4.57)	4.90(2.41-7.41)	4.26(1.88-6.65)
Others	2.50(1.59-3.40)	1.76(0.53-2.98)	2.92(1.09-4.74)	2.71(1.15-4.26)
Education:				
Less than high school	4.87(3.43-6.32)	3.85(2.29-5.41)	7.64(3.73-11.55)	3.50(1.40-5.61)
High school or above	3.86(2.57-5.37)	3.33(1.81-4.85)	4.51(2.04-6.98)	3.84(1.09-6.60)
Income-poverty ratio level:				
0-1.0	5.03(3.03-7.02)	3.18(0.39-5.96)	7.16 (2.58-11.74)	4.83(1.71-7.95)
>1.0	4.13(2.89-5.37)	3.68(2.23-5.13)	5.26(3.00-7.52)	3.62(0.72-6.51)
Alcohol drinking:				
Non-drinker	1.71(0.74-2.68)	0.84(-0.15-1.85)	2.54(0.27-4.82)	1.95(-0.01-3.93)
drinker	5.29(3.78-6.82)	4.49(3.05-6.92)	6.48(3.34-9.62)	4.64(1.62-7.65)
Smoking status:				
Never smoker	2.13(0.98-3.27)	1.22(0.11-2.33)	3.61(0.43-6.78)	1.61(0.53-2.68)
Former smoker	5.04(2.47-7.61)	6.63(3.37-9.89)	2.48(0.17-4.80)	5.62(-0.83-12.09)
Current smoker	6.82(4.41-9.22)	4.00(1.52-6.48)	11.86(5.80-17.92)	6.40(1.77-11.03)
Liver disease				
No	2.72(1.88-3.56)	2.27(1.06-3.48)	3.97(2.13-5.80)	2.07(0.65-3.49)
Yes	14.41(8.64-20.18)	12.91(5.19-20.62)	15.20(5.74-24.65)	15.17(2.86-27.48)
Diabetes				
No	3.88(2.87-4.95)	3.79(2.47-5.11)	4.80(2.48-7.13)	3.14 (1.06-5.21)
Yes	5.90(2.90-8.90)	0.86(-0.43-2.16)	8.97(4.40-13.55)	7.68(0.67-14.69)
Hypertension				
No	3.66(2.62-4.69)	3.91(2.38-5.44)	4.81(2.21-7.41)	2.15(1.01-3.29)

Yes	5.18(3.02-7.34)	2.20(0.79-3.62)	6.57(4.60-8.54)	6.40(1.37-11.45)
HBsAb negative				
No	3.09(2.13-4.05)	2.69(1.22-4.16)	4.17(2.11-6.24)	2.56(0.97-4.15)
Yes	7.93(4.60-11.26)	6.90(1.92-11.83)	9.11(4.09-14.13)	7.74(0.66-14.83)

All estimates accounted for complex survey designs and sampling weights of NHANES.

Table S3. Prevalence of cirrhosis (defined by LSM, APRI, or FIB-4) in US adults with HBsAg-negative and HBcAb-positive, NHANES, 2017–2018. #

Cirrhosis	Cirrhosis defined by LSM/APRI/FIB-4		
	LSM (>13.4 kPa) *	APRI (>1.0) %	FIB-4 (>3.25) §
	N=352	N=367	N=367
Adjusted prevalence (%)	4.89	3.94	1.62

* Cirrhosis defined as median liver stiffness measurement (LSM) >13.4kPa; % Cirrhosis defined as APRI>1.0; § Cirrhosis defined as FIB-4>3.25;

All estimates accounted for complex survey designs and sampling weights of NHANES.

Table S4. The proportion of awareness of hepatitis B virus infection and received therapy for hepatitis B in US adults with HBsAg-negative and HBcAb-positive, NHANES, 2013-2018 (N=1150).#

	Awareness of HBV infection(N=75)	Ever received therapy for hepatitis B (N=10)
Adjusted Proportion (%)	8.84	1.68

All estimates accounted for complex survey designs and sampling weights of NHANES.

Table S5. Prevalence of cirrhosis (FIB>3.25) by awareness of HBV infection or not in US adults with HBsAg-negative and HBcAb-positive, NHANES, 2013–18. #

	Awareness of HBV infection(N=75)	Unawareness of HBV infection(N=1062)
Adjusted prevalence (%)	3.54	3.29

All estimates accounted for complex survey designs and sampling weights of NHANES.

Table S6. Prevalence of cirrhosis by the controlled attenuated parameter (CAP) in US adults with HBsAg-negative and HBcAb-positive, NHANES, 2017–18. #

Cirrhosis	Cirrhosis defined by LSM/APRI/FIB-4		
	LSM (>13.4 kPa) *	APRI (>1.0) %	FIB-4 (>3.25) \$
CAP≥238 dB/s	6.61	5.62	1.56
CAP<238 dB/s	1.81	1.52	1.52

All estimates accounted for complex survey designs and sampling weights of NHANES.