

**Table 2.5. Case-control studies of HCV and cholangiocarcinoma and biliary tract cancers**

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	Exposure categories	No. of exposed cases	Relative risk [odds ratio] (95% CI)	Adjusted potential confounders	Comments
<i>Americas</i> Shaib <i>et al.</i> (2007) USA, 1992–2002	246 patients with histologically confirmed cholangiocarcinoma, diagnosed at University of Texas M.D. Anderson Cancer Centre: 83 cases with intrahepatic cholangiocarcinoma (ICC) (46 men, 37 women; mean age: 59.8 ( $\pm$ 11.4) years) and 163 cases with extrahepatic cholangiocarcinoma (ECC) (96 men, 67 women; mean age: 61.1 ( $\pm$ 9.8) years); blood testing at time of diagnosis; participation rate NR	236 healthy individuals (134 men, 102 women), randomly selected from existing database of healthy individuals at same cancer centre, genetically unrelated family members, spouses, and friends of patients without gastrointestinal cancer, interviewed between 1999 and 2004; frequency matched to cases by sex, ethnicity, and age ( $\pm$ 5 years); mean age: 58.1 ( $\pm$ 11.4) years; blood testing at time of inclusion in database	Anti-HCV: second-generation enzyme-linked immunosorbent assay (ELISA)	ICC	78	1.0	Age, sex, ethnicity, HBV markers, and alcohol consumption	
				Anti-HCV				
				Neg	5	7.9 (1.3–84.5)		
				Pos				
ECC	157	1.0						
Anti-HCV								
Neg	6	2.8 (0.3–35.1)						
Pos								
<i>Asia</i> Shin <i>et al.</i> (1996) Korea, 1990–1993	41 consecutive cases of newly diagnosed cholangiocarcinoma (30 men, 11 women), admitted to Inje University Pusan Paik Hospital; mean age: 59.2 ( $\pm$ 8.1) years; histological confirmation: 51%; 29 cases had anti-HCV status	406 control subjects comprised of inpatients and healthy people from same hospital as cases [described in Table 2.4]; individually matched to HCC cases by sex and age ( $\pm$ 4) years	Anti-HCV: ELISA [generation of assay NR]	Anti-HCV	25	3.9 (0.9–17.1)	Age, sex, socioeconomic status, HBsAg positivity, <i>Clonorchis sinensis</i> in stool, transfusion history, hepatitis history, liver fluke history, drinking history, and smoking history	
				Neg				
				Pos	4			

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Yamamoto <i>et al.</i> (2004) Japan, 1991–2002	50 patients with histologically confirmed ICC (29 men, 21 women), treated at 2 major medical centres in Osaka City; mean age: 64.6 ( $\pm$ 9.7) years; participation rate NR	205 other surgical patients without primary liver cancer (121 men, 84 women), from same medical centres as cases; 2–5 controls matched to each case by sex, 5-year age group, and operation date ( $\pm$ 1 year); mean age: 65.3 ( $\pm$ 9.2) years; participation rate NR	Anti-HCV: ELISA [generation of assay NR]	Anti-HCV Neg Pos	32 18	1.0 6.0 (1.5–24.1)	Age, sex, operation date, transfusion, diabetes mellitus, hypertension, liver status at operation, bilirubin, alanine aminotransferase, albumin, and platelet count	
Zhou <i>et al.</i> (2008) China, 2004–2006	312 patients with histologically confirmed ICC (207 men, 105 women), underwent surgical resection at Eastern Hepatobiliary Surgery Hospital of Second Military Medical University in Shanghai; mean age: 53.2 ( $\pm$ 10.4) years; participation rate NR	438 patients unaffected by liver diseases (276 men, 162 women), selected from individuals admitted to Departments of Gastroenterology, Urology, Ophthalmology, Neurology, and Cardiology at Shanghai Hospital of Second Military Medical University; matched to cases by age ( $\pm$ 5 years), sex, and date of hospital admission; mean age: 54.8 ( $\pm$ 11.8) years; participation rate NR	Anti-HCV: ELISA [generation of assay NR]	Anti-HCV Neg Pos	303 9	1.0 0.93 (0.28–3.1)	Age, sex, date of hospital admission, HBsAg, diabetes mellitus, hypertension, hepatolithiasis, cigarette smoking, and alcohol consumption	

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Hsing <i>et al.</i> (2008) China, 1997–2001	417 cases of newly diagnosed biliary tract cancers, recruited using rapid reporting system established between Shanghai Cancer Institute and 42 collaborating hospitals in 10 urban districts of Shanghai; participation rate: 95%, of whom over 90% provided a blood sample; histological confirmation rate NR Diagnostic subtypes: 234 with gallbladder cancer (65 men, 169 women; 61% ≥65 years old), 134 with extrahepatic bile duct cancer (78 men, 56 women; 60% ≥65 years old), and 49 ampulla of Vater cancer (27 men, 22 women; 65% ≥65 years old)	762 healthy population-based controls without a history of cancer (297 men, 465 women), randomly selected from all permanent residents listed in Shanghai Resident Registry; frequency matched to cancer cases on age (± 5 years) and gender; 59% ≥65 years old; participation rate: 82%, of whom 80% provided a blood sample	Anti-HCV: third-generation ELISA, with confirmation by third-generation recombinant immunoblot assay	<u>Gallbladder</u> Anti-HCV	Neg	231	1.0	Age
					Pos	3	0.6 (0.2–2.2)	
				<u>Extrahepatic bile duct</u> Anti-HCV	Neg	132	1.0	
				Pos	2	0.8 (0.2–3.4)		
				<u>Ampulla of Vater</u> Anti-HCV	Neg	48	1.0	
					Pos	1	1.0 (0.1–7.5)	
Lee <i>et al.</i> (2008) Korea, 2000–2004	622 patients with histologically confirmed ICC (69% men), diagnosed during study period at major teaching hospital in Seoul, patients excluded if diagnosed with other cancers within 5 years before cholangiocarcinoma diagnosis; mean age: 60.7 years	2488 healthy controls, chosen from individuals visiting health promotion centre at same hospital during same time period as cases, excluded if diagnosed with cancer or missing data regarding risk factors and cancer; matched 4:1 to cases by age, sex, and date of admission or diagnosis; participation rate NR	Anti-HCV: ELISA [generation of assay NR]	Anti-HCV	Neg	610	1.0	None
					Pos	12	1.0 (0.5–1.9)	

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<i>Europe</i> Donato <i>et al.</i> (2001) Italy, 1995–2000	26 incident cases ICC (21 men, 5 women), admitted to 2 main hospitals in province of Brescia; part of Brescia HCC Study; all born in Italy, residents of Brescia, and less than 76 years of age; mean age: 65 ( $\pm 6.4$ ) years; participation rate NR; histological confirmation rate NR; 24 cases had anti-HCV status	824 patients without liver disease or malignant neoplasms (686 men, 138 women), admitted to departments of ophthalmology, dermatology, urology, surgery, cardiology, and internal medicine of same hospitals as cases; all born in Italy, residents of Brescia, and less than 76 years of age; frequency matched to liver cancer cases on age ( $\pm 5$ years), sex, and date and hospital of admission; mean age: 65.7 ( $\pm 6.3$ ) years; participation rate: 96%	Anti-HCV: third-generation ELISAs	Anti-HCV Neg Pos	18 6	1.0 9.7 (1.6–58.9)	Sex, age, area of residence, HBV infection, alcohol intake, and history of hepatolithiasis	