Table 2.1 Cohort studies of aflatoxin exposure and hepatocellular carcinomas

Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)*	Adjustment for potential confounders	Comments
Ross et al., (1992) Shanghai, PRC	18244 men age 45-64 living in four areas of Shanghai recruited in January 1996 to September 1999 and followed to March 1990. HCC cases identified by linkage to the Shanghai cancer registry and annual follow-up.	Blood sample for HBsAg and urinary sample for aflatoxin metabolites.	HCC (155)	*Aflatoxin biomarkers*				Nested case-control analysis with 22 cases and 140 matched controls.
				None	9	1.0		
				AFB_1-N Gua	6	4.9 (1.5-16.3)		
				AFP_1	6	6.2 (1.8-21.5)		
				AFM_1	6	3.0 (1.0-9.3)		
				AFB_1	10	2.3 (1.0-5.9)		
				Any	13	2.4 (1.0-5.9)		

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Qian et al. (1994) Shanghai, PRC	Update of Ross et al (1992) with follow-up to February 1992	Urinary aflatoxin biomarkers and HBV status. Frequency of consumption of 45 food items	HCC (155)	*Aflatoxin biomarkers*				Nested case-control analysis with 50 HCC cases and 247 controls.
				None	14	1.0		
				Any	36	5.0 (2.1-11.8)	HBsAG positivity and cigarette smoking	
				With adducts				RR for aflatoxin biomarkers and HBsAG positive based on 7 controls.
				AFB_1-N Gua	18	9.1 (2.0-29.2)		
				AFP_1	8	11.1(2.4-50.9)		
				AFM_1	8	16.1(3.6-72.5)		
				AFB_1	6	5.7 (1.3-26.0)		
				AFQ_1	4	9.9 (1.1-135)		
				AFG_1	4	6.0 (0.5-95.3)		RRs for dietary analysis based upon full cohort.
				Negative				
				HBsAG -ve	5	1.0		
				HBsAG +ve	9	7.3 (2.2-24.4)		
				Positive			Cigarette smoking	
				HBsAG -ve	13	3.4 (1.1-10.0)		
				HBsAG +ve	23	59.4 (16.6-212)		
				Estimated dietary aflatoxin exposure (ug/yr)		1.0		
				Low (<71)	14	1.6 (0.8-3.1)		
				Medium (71-113	25	0.9 (0.4-1.9)		
				High (113+)	16			

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Wang et al. (1996) Taiwan, China	12024 males and 13594 females enrolled in a community-based screening project in 7 townships in Penghu islets and 4 in Taiwan island. Recruitment July 1990 to June 1992. Fasting blood and spot urines obtained.	Aflatoxin albumin adducts and HBV status.	HCC (155)	*Male HBsAg-seropositive subjects* Aflatoxin- albumin adducts: Non-detectable Detectable Urinary aflatoxin metabolites: Low High	 13 27 9 20	 1.0 2.8 (0.9–9.0) 1.0 5.5 (1.3–23.4)	Age, residence, cigarette smoking, alcohol drinking	Nested case control analysis of 56 HCC (50 male, 6 female) and 220 matched controls Risk of HCC in HBsAG negative subjects uniformly low.
Ming et al. (2002). Qidong, China.	145 HBsAg-positive men with chronic hepatitis followed for 13.25 years.	Annual average urinary excretion of the AFM1 metabolite of aflatoxin from a pool of at least 8 monthly samples taken in 1987.	HCC (155)	Baseline AFM1: <3.6 ng/L ≥3,6 ng/L	 7/67 24/78	 1.0 3.5 (1.5-8.1)		Attributable risk 57%

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Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)*	Adjustment for potential confounders	Comments
Wu et al. (2007a). Taiwan, China.	Cohort first studied by Wang et al (1996)	Aflatoxin and polycyclic aromatic hydrocarbon (PAH) albumin adducts.	HCC (155)	*High AFB_1 albumin adducts* PAH albumin adducts: Quantile 1 Quantile 2 Quantile 3 Quantile 4 *Low AFB_1 albumin adducts* PAH albumin adducts: Quantile 1 Quantile 2 Quantile 3 Quantile 4	 47 11 12 16 50 5 11 22	 1.0 1.9 (0.6-6.1) 1.7 (0.6-4.9) 2.1 (0.5-8.2) 1.0 0.6 (0.2-2.1) 0.7 (0.2-2.1) 1.5 (0.6-4.0)	HBsAg status, smoking and alcohol consumption	Nested analysis of 174 cases with baseline blood samples of 242 diagnosed from 1991 to 2004 and 776 controls of 1226 with baseline blood samples randomly selected and matched to cases by age, sex, residence and date of recruitment The OR for PAH- and AFB(1)-albumin adducts above the mean in those HBsAg positive was 8.2 (95% CI: 3.6–19.0; $P < 0.0001$), compared to those with low adducts and HBsAg negative.

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Wu et al. (2007b). Taiwan, China	Same cohort as studied by Wang et al 1996 and Wu et al 2007a	Urinary aflatoxin and 8-oxodeoxyguanosine (8-oxodG) biomarkers.	HCC (155)	*Urinary 8-oxodG*			HBsAg status, smoking, alcohol, BMI and urinary AFB1 metabolites.	Nested analysis of 74 HCC cases with baseline urine samples of 241 diagnosed from 1991 to 2004 and 290 controls with baseline urine samples of 1246 randomly selected and matched to cases by age, sex, residence and date of recruitment. Statistically significant positive dose–response relationship between levels of urinary 8-oxodG and urinary aflatoxin metabolites ($P < 0.0001$).
				<25%	20	1.0		
				25-50%	14	0.8 (0.3-2.0)		
				50-75%	21	0.7 (0.3-2.0)		
				>75%	19	0.7 (0.2-1.7)		
				HBsAG negative				
				Urinary 8-oxodG				
				Above median	18	1.0		
				Below median	14	0.6 (0.2-1.7)		
				HBsAG positive				
				Urinary 8-oxodG				
				Above median	22	4.3 (1.9-9.5)		
				Below median	20	11.4 (3.9-33.3)		

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Reference, location, name of study	Cohort description	Exposure assessment	Organ site (ICD code)	Exposure categories	No. of cases	Relative risk (95% CI)*	Adjustment for potential confounders	Comments
Wu et al. (2009) Taiwan, China	Update of the Wang et al (1996) cohort followed to June 2004	Aflatoxin urinary and albumin biomarkers and HBV status.	HCC (155)	*AFB1-albumin adducts*			Batch of aflatoxin biomarker assay, anti-HCV status, habitual smoking, alcohol drinking, and BMI.	Nested case control analysis of 230 HCC (184 male, 46 female) with stored blood and 1052 matched controls The adjusted OR was 7.5 (95% CI 5.1-10.9) for carriers of HBsAg compared with noncarriers, regardless of AFB1 status.
				HBsAG negative:				
				AFB1 <59.8	44	1.0		
				AFB1 ≥59.8	31	1.6 (0.9-3.0)		
				HBsAG positive:				
				AFB1 <59.8	111	7.0 (4.4-11.1)		
				AFB1 ≥59.8	44	10.4(5.7-18.8)		
				Urinary AFB1 Metabolites				
				HBsAG negative:				
				AFB1 <55.2	22	1.0		
				AFB1 ≥55.2	33	2.8 (1.4-5.6)		
				HBsAG positive:				
				AFB1 <55.2	63	11.0(5.8-20.9)		
				AFB1 ≥55.2	80	15.1(7.8-28.2)		