Serum bilirubin levels and risk of cancer in the Swedish AMORIS cohort study

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Introduction

- Bilirubin is a by-product of haemoglobin degradation with strong antioxidant properties
- It is thought to be preventive against the development of cancer
- Studies published to date have shown inconclusive results among different cancer types and overall cancer
 We aimed to investigate the association between serum total bilirubin (STB) and risk of overall and site-specific cancers in the large Swedish Apolipoprotein Mortality Risk (AMORIS) cohort

Results: Overall cancer risk

- A total of 21,788 participants developed cancer during a mean follow-up time of 21 years
- Our analyses found a positive association between high levels of STB (≥22µmol/L) and risk of any cancer (Hazard Ratio (HR): 1.08; 95% Confidence Interval (CI): 1.01-1,16, p=0.01), as compared to low STB levels (<11µmol/L).

Whole Population	HR and C.I.s ¹	P for Trend
Bilirubin (μmol/L)	1.00 (1.00, 1.00)	0.01
< 11 (µmol/L)	1 (ref)	
11 to < 22 (μmol/L)	1.03 (1.00, 1.06)	
≥ 22 (µmol/L)	1.08 (1.01, 1.16)	
Men Only	HR and C.I.s2	P for Trend
Bilirubin (μmol/L)	1.00 (0.99, 1.00)	0.001
< 11 (µmol/L)	1 (ref)	
11 to < 22 (μmol/L)	1.05 (1.02, 1.09)	
≥ 22 (µmol/L)	1.10 (1.01, 1.19)	
Women Only	HR and C.I.s2	P for Trend
Bilirubin (μmol/L)	0.99 (0.99, 1.00)	0.86
< 11 (µmol/L)	1 (ref)	
11 to < 22 (μmol/L)	1.00 (0.95, 1.04)	
≥ 22 (µmol/L)	1.05 (0.91, 1.22)	

- This positive association persisted in men (HR: 1.05; 95%CI: 1.02-1.09, p=0.00)
- No statistically significant associations were found in women (HR: 1.05; 95%Cl 0.91-1.22, p=0.86)

Table 1. Hazard ratios and 95% confidence intervals for overall cancer. In thewhole population and following stratification by gender by baseline totalbilirubin and terciles of bilirubin defined by clinical cut-offs

Study population

- The Swedish Apolipoprotein Mortality Risk Study (AMORIS)
- A total of 112,771 cancer-free men and women, aged >20, with baseline measurements of STB
- Incident cases of cancer were identified through the Swedish national cancer register
- Deaths were identified through the Swedish national cancer register up to Dec 31st 2011

Results: Site-specific cancer risk

- A positive association was found between increased STB levels and risk of melanoma (HR: 1.44; 95%CI 1.03-2.02, p=0.01)
- A positive association was also found between increased STB levels and risk of pulmonary cancers (HR: 1.05; 95%CI 0.71-1.55, p= 0.03)

	< 11 (µmol/L)	11 to < 22 (μmol/L)	≥ 22 (µmol/L)	P for Tren
	929	682	27	0.03
00)	1 (ref)	1.13 (1.02, 1.25)	1.05 (0.71, 1.55)	
	1158	1141	85	0.70
01)	1 (ref)	1.03 (0.94, 1.12)	0.99 (0.79 <i>,</i> 1.24)	
	306	277	17	0.73
02)	1 (ref)	1.08 (0.91, 1.28)	0.78 (0.47, 1.31)	
	257	267	22	0.83
03)	1 (ref)	1.05 (0.88, 1.26)	0.72 (0.44, 1.20)	
	235	236	27	0.97
02)	1 (ref)	0.99 (0.81, 1.20)	1.03 (0.67, 1.56)	
	454	548	37	0.28
01)	1 (ref)	1.09 (0.96, 1.24)	1.10 (0.71, 1.41)	
	678	669	63	0.10
01)	1 (ref)	1.12 (1.00, 1.25)	1.06 (0.82, 1.38)	
	386	478	40	0.01
00)	1 (ref)	1.17 (1.01, 1.35)	1.44 (1.03, 2.02)	
	451	567	41	0.19
01)	1 (ref)	1.09 (0.96, 1.24)	1.13 (0.81, 1.56)	
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serum total bilirubin and terciles of bilirubin based on clinical cut-offs

Statistical Analysis

- Multivariable Cox proportional hazards regression was used to analyse associations between STB and overall cancer risk
- In addition to overall cancer risk, we also analysed risk of major cancer types



Conclusions

- Unlike previous studies, our findings suggest that elevated STB is associated with a slightly increased risk of overall cancer
- This association was only found in men
- High STB levels were associated with an increased risk of melanoma and lung cancer
- No significant associations were found with other site-specific cancers
- We are further investigating these results with longer follow-up time





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