

SERUM BILIRUBIN IS AN IMPORTANT PREDICTOR OF CANCER MORTALITY: RESULTS FROM THE POLISH ARM OF THE HAPIEE STUDY

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Introduction: Bilirubin, a final product of heme catabolism in the intravascular compartment, belongs to the most efficient endogenous antioxidants. Its systemic concentrations are considered to protect from diseases mediated by increased oxidative stress, including cardiovascular, inflammatory of cancer diseases. Thus, the aim of our study was to assess the relationship between serum bilirubin concentrations and overall, cardiovascular and cancer mortality.

Methods: The study was performed on a Polish arm of the HAPIEE study (n=7688 in total, a subsample of 1870 subjects with biochemical parameters), in which the associations between the serum bilirubin concentrations and bilirubin UDP-glucuronosyl transferase (UGT1A1) promoter gene variations with overall, cardiovascular and cancer mortality were analyzed.

Results: Strong negative correlation between serum bilirubin levels and cancer mortality ($p<0.001$) was detected; this association was expressed more in men. Subjects in the lowest bilirubin quartile (again in particular men), had, as compared to other quartiles, significantly higher both overall and cancer mortality ($p<0.001$ for both comparisons). Negative relationship of bilirubin to cardiovascular mortality was surprisingly much less expressed. Similarly, negative relationship to overall and non-cardiovascular mortality was observed in men (but not women) with Gilbert syndrome phenotype (benign hyperbilirubinemia) ($p<0.01$). On the other hand, these associations were not observed with *UGT1A1* promoter gene variations, most likely due to limited penetrance of this gene mutation.

Conclusion: Serum bilirubin concentrations are a significant negative predictor of total mortality; this association is mostly driven by the effect on a cancer, and much less on cardiovascular mortality. These relationships are primarily pronounced in male population, most likely due to physiologically higher systemic bilirubin. *UGT1A1* promoter gene variations do not seem to have any major role on predicting mortality

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