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Correlation between elevated serum bilirubin levels and coronary artery disease risk - An institutional study

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ABSTRACT

Background and objectives. Coronary artery disease (CAD) is a major public health problem resulting in profound morbidity and mortality. Recent research studies have suggested that bilirubin may play a role in preventing coronary artery disease. The purpose of this study was to determine the association between increased levels of bilirubin in the blood and risk for developing coronary artery disease (CAD).

Material and methods. For the course of this study, an observational method was used where 30 participants were enrolled from our department's general medicine unit. We collected demographic data and patient's medical history. Moreover, we carried out complete blood count to measure serum levels of bilirubin such as total, direct and indirect, lipid profile, fasting blood glucose, C-reactive protein (CRP). Several statistical analyses were done to find out whether there is any relation between blood bilirubin levels and CAD related risk factors.

Results. The current findings showed average serum concentration for bilirubin at 1.5 ± 0.5 mg/dL.In this regard, hypertension was prevalent among 40% of respondents while diabetes took up 20%. This present study indicates that there is strong negative relationship between cardiovascular risks indicator blood-bilirubins.

Conclusion. Consequently, this study produces great proof that shows strong support for a negative relationship between the levels of bilirubin in the blood and the likelihood of getting affected by coronary arteries. This might be due to different roles played by bilirubin such as being an antioxidant and having anti-inflammatory properties. These findings suggest that there is a need for more investigations into bilirubin as its importance as a potential biomarker for assessing and mitigating cardiovascular risk has been highlighted.

Keywords: serum bilirubin, coronary artery disease, cardiovascular risk factors, antioxidative properties, inflammatory markers

INTRODUCTION

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality globally, meaning it has become a significant challenge to public health. Recognition of the multifactorial nature of CAD risk factors is necessary for early diagnosis, prevention and efficient management of the condition. However, it is emerging that high serum bilirubin levels may be involved in CAD pathogenesis thereby increasing the number of potential biomarkers for CAD risk assessment [1]. This institutional study aims at determining the association between elevated serum bilirubin and coronary artery disease as well as finding out whether or not they can be used as predictors for this condition.

Bilirubin, an orange-yellow pigment produced during heme catabolism is commonly associated with liver function and jaundice. Nevertheless, recent studies have indicated its antioxidant and anti-inflammatory properties suggesting its multifunctional role beyond hepatocyte metabolism [2]. Bilirubin's ability to scavenge reactive oxygen species largely explains its antioxidant effects hence reducing oxidative stress related injuries within endothelial cells, lipids and proteins in the vascular system. Furthermore, some studies suggest that bilirubin has been shown to inhibit the proliferation of vascular smooth muscle cells, suppress pro-inflammatory cytokine production, and promote vasodilation, all of which are key processes in the development and progression of atherosclerosis [3].

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In a number of epidemiologic studies, blood bilirubin concentrations have shown an inverse association with the likelihood of CAD, implying a probable defensive role against atherosclerosis-related cardiovascular disease [4]. For instance, Schwertnerand and colleagues (1994) conducted a prospective population study that showed individuals who had low serum bilirubin levels were more likely to develop coronary artery disease than those with high levels even when traditional cardiovascular risk factors were controlled for. Similarly, Novotný and Vítek (2003) carried out a meta-analysis which had significant results in relation to the negative relationship between serum bilirubin amounts and coronary artery disease risk factors across various populations [5,6].

However, the mechanisms through which blood bilirubin levels may be associated with CAD susceptibility are not well understood. Evidence suggests that its antioxidant potential may provide protection against endothelial dysfunction, oxidative stress and inflammation. These processes are central to development of plaques and their instability. However, there are contradictory data on this issue which calls for further investigations into molecular signaling as well as proof of causality. The purpose of this study was to determine the association between increased levels of bilirubin in the blood and risk for developing coronary artery disease.

MATERIALS AND METHODS

Study design and setting

A study was undertaken within our department of general medicine under observation. Its core aim was to find out how the levels of serum bilirubin correlate with the chances or odds of coronary artery disease (CAD) among adult patients. The study protocol was reviewed and approved by Institutional Review Board (IRB) of this institution. After written informed consent, all participants were included in the study. All procedures were in accordance with ethical standards of Helsinki Declaration.

Enrollment occurred at the outpatient clinic in the Department of General Medicine where 30 participants were selected for the study based on specific criteria. Inclusion criteria consisted of consenting adults over 18 years who had come for check-ups or treatment pertaining to chronic illnesses as a routine requirement while exclusion criteria incorporated individuals with diagnosed liver ailments such as hepatitis, cirrhosis, hemolytic disorders and non-consenting ones respectively.

Data collection: On enrolment, each participant was subjected to an elaborate medical history that included age, sex, smoking status, hypertension record, diabetes mellitus and any known heart diseases. Information about height, weight, and blood pressure measurements came from physical examinations.

Sample collection: Blood samples were taken from all subjects after fasting overnight for 12 hours. Serum bilirubin levels (total, direct, and indirect) were measured using the van den Bergh reaction. Additional biochemical parameters, including lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), fasting blood glucose, and C-reactive protein (CRP), were also assessed using standard laboratory techniques.

Statistical analysis

Data were analyzed using SPSS version 25. Descriptive statistics (mean ± SD for continuous variables, frequencies, and percentages for categorical variables) were used to summarize the participants' baseline characteristics. The correlation between serum bilirubin levels and CAD risk factors was assessed using Pearson's correlation coefficient for continuous variables and Spearman's rank correlation for ordinal variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The Table 1 presents the baseline demographics of the 30 participants who were recruited for our institutional research study addressing elevated serum bilirubin levels related to risks of coronary artery disease. The mean age was 51.2 with a standard deviation of 9.5 years, suggesting that it is a middle-aged sample. In general, males comprised more than half of this sample population since there was 40 percent female and 60 percent male participation rates respectively. The majority of them was comprised of non-smokers; only few reported being smokers.

TABLE 1. Baseline features of participants in the study (n=30)

Variable	Mean ± SD (or %)
Age (years)	51.2 ± 9.5
Gender (%)	
Male	61%
Female	39%
Smoking status (%)	
Non-smoker	72%
Smoker	28%

It is important to note that these demographic factors though may be illustrations or explanations for future outcomes on coronary artery disease risk factors, but rather, they provide a context as to how one can analyze further outcomes relating to CAD risk factors. However, in view of other clinical and bio-

chemical indices that would form part of comprehensive analysis of study results, we would then explore the specific impact of these demographic variables on coronary artery disease risk.

The Table 2 provides details of the number of cases of hypertension and diabetes that are found in the study population, which consists of 30 participants aimed at assessing whether there is any correlation between high levels of serum bilirubin and risk for coronary artery disease. Hypertension is present among 40% of subjects, thus indicating a good proportion of this research population suffering from this condition, which is known to be associated with coronary artery disease. Furthermore, in 20% of subjects, diabetes was also reported showing enough evidence about significant cardiovascular risk factors in the cohort. This information will help to understand health characteristics regarding these conditions besides their association with CAD risks alongside serum bilirubin levels.

TABLE 2. Prevalence of hypertension and diabetes among study participants (n=30)

Variable	Prevalence (%)
Hypertension	40%
Diabetes	20%

The laboratory results for participants in our study are excellently summarized in Table 3. An average level of total serum bilirubin was found to be 1.5 mg/dL, with an average direct and indirect bilirubin being 0.4 mg/dL and 1.1 mg/dL respectively which indicated normal bilirubin metabolism in our study population. Total cholesterol was at 200 mg /dL while LDL (bad) cholesterol were at 130 mg /dL and HDL (good) cholesterol levels were at 45 mg /dL. Cardiovascular risk among the participants is represented by these cholesterol levels portrayed as having a mixed picture. Also, Triglyceride levels were on average around 150 mg /dL, which also contributes to the cardiovascular risk profile.

TABLE 3. Revised laboratory results for study participants (n=30)

Variable	Mean ± SD
Total Serum Bilirubin (mg/dL)	1.5 ± 0.5
Direct Bilirubin (mg/dL)	0.4 ± 0.2
Indirect Bilirubin (mg/dL)	1.1 ± 0.4
Total Cholesterol (mg/dL)	200 ± 45
LDL Cholesterol (mg/dL)	130 ± 35
HDL Cholesterol (mg/dL)	45 ± 5
Triglycerides (mg/dL)	150 ± 60
Fasting Blood Glucose (mg/dL)	100 ± 20
C-reactive Protein (mg/L)	2.5 ± 1.5

Those fasting blood glucose levels that were measured show that there is a potential for some subjects to have glucose metabolism problems because they averaged at about 100 mg/dL. Meanwhile C-reactive protein, which is an indicator of inflammation, had a mean of 2.5 mg/L indicating mild to moderate inflammation within the group.

This detailed laboratory breakdown is important in studying how risk factors for coronary artery disease like serum bilirubin concentration correlate with other cardiovascular risks highlighted by lipid profiles; glucose metabolism and systemic inflammation such as CRP levels (Table 3).

DISCUSSION

The present study aimed to determine the relationship between increased blood bilirubin levels and the incidence of coronary artery disease (CAD) in 30 patients from our Department of General Medicine. The results imply that high bilirubin levels could serve as a protective factor against CAD, which is consistent with literature evidence on its antioxidative and anti-inflammatory functions.

Additionally, Novotny and Vitek (2003) found a negative association between bilirubin levels in serum and heart attacks; thus, demonstrating how higher amounts of bilirubin might provide total protection against developing CAD [6]. Furthermore, Lin et al. (2010) revealed that serum bilirubin could be utilized as potential biomarker for low risk of cardiovascular diseases, indicating its ability to mitigate oxidative stress and inflammation that are major causes of atherosclerosis [7].

Our findings are also in line with those by Suhand et al. (2018), who showed that there were fewer occurrences of cardiovascular events among individuals with high blood bilirubin within a big statin treated population [8]. This may imply that antioxidants produced by this substance reduce lipid peroxidation as well as vascular inflammation leading to reduced chances of having CAD

Additionally, the study's findings of slightly higher bilirubin levels in the normal range also affirm the belief that even a slight increase in bilirubin levels may be significant for cardiovascular protection. Kundurand group [9] discussed the therapeutic application of bilirubin to cardiovascular disease suggesting that individuals with mild unconjugated hyper bilirubinemia associated with Gilbert syndrome have a low risk of CAD.

Nevertheless, our research reveals how difficult it is to understand and diagnose CAD by means of total bilirubin as regards its interaction with different variables such as lipid profile, fasting glucose level and C-reactive protein level. The lipid profiles and glucose levels among our subjects demonstrate a mixed

cardiovascular risk thus reflecting an aspect of CAD as multifactorial disorder that requires comprehensive approaches to preventions and management.

CONCLUSION

The results of this study provide more evidence that the risk of coronary artery disease is negatively correlated with blood bilirubin levels. This could be because of the anti-inflammatory and antioxidant effects of bilirubin, among its other functions. These results emphasize the necessity for further research into bilirubin as a possible biomarker for evaluating and reducing cardiovascular risk.

Conflict of interest:
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Investigation: N. Krishna Geetha; K.I.S.N. Vaishnavi
Data curation: K.I.S.N. Vaishnavi; Gowri Shankar;
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