

Study of serum bilirubin for prevention of risk factor of cardiac disease in hospitalized patients

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Abstract

Background: Elevated serum bilirubin has been associated with reduced risk of cardiovascular disease (CVD). However, serum bilirubin is also related with several potential confounders related to CVD, such as obesity.

Methodology: This study includes 120 male Indian subjects between 30 to 50 years of age. Biochemical test like Lipid profile, bilirubin and blood sugar were measured on a fully automated analyzer along with quality control sera.

Results: Positive correlation is found between serum bilirubin and HDL cholesterol level while it was negatively correlated with Fasting blood sugar there were no statically significance present between serum total cholesterol and serum triglyceride in hospitalized patients, not in healthy subjects.

Conclusions: From my study it will be conclude that level of serum bilirubin is important parameter for defining risk of cardiovascular disease.

Key words: Bilirubin, HDL, Cardiac disease

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Introduction

Bilirubin is considered a strong reducing agent and a potential physiological antioxidant¹. There's new hope for the fight against cancer and cardiovascular disease, following breakthrough research identifying a pigment in our bile. A fluid produced by the liver and stored in the gallbladder, bile's function was simply thought to aid in the digestion process. However, in conjunction with the University of Vienna and the Heart Research Institute in Sydney, Dr. Andrew Bulmer from the Griffith Health Institute has found that a pigment in bile called bilirubin could help to stave off cancer and cardiovascular disease.

Published in the leading journal *Free Radical Biology and Medicine*, the scientific report details how Dr. Bulmer and his team conducted a study with 44 participants, half of whom had Gilbert Syndrome.²

People with this syndrome show naturally elevated levels of bilirubin in the blood and also higher concentrations of antioxidants, which can protect against disease.²

In view of aforementioned controversial literature, we were aimed to evaluate the different biochemical lipid parameters with HbA_{1c}, related to risk of CVD/

CAD and serum Bilirubin, in the healthy and admitted subjects.

Materials and Methods

This retrospective study was conducted at the GMERS medical college and hospital, Patan, Gujarat (India) on 120 male [60 healthy OPD and 60 IPD admitted in the hospital for clinically different complaints instead of CVD/CHD] subjects which were tested for Blood sugar(FBS), lipid profile, and serum bilirubin, were considered for our study.

The exclusion criteria were (a) females, (b) men below 30 or above 50years and (c) subjects who had TG > 400 mg/dl.(d) patients on known lipid altering medications, (e) diabetics, patients with chronic kidney disease, liver disease and CVD.

Collection of blood sample: 5 ml venos blood was collected from all participants in a fasting condition. From them blood was distributed in Fluoride and plain vacutainer for estimation of various biochemical parameter. Blood samples were centrifugated at 3000 RPM for a period of 10 minutes after giving uniq ID to all participants and same ID was mentioned on eppendorf cup to hide identity of participants.

Blood glucose was estimated by GOD-POD method from fluoride sample in semi-automated biochemistry analyser. Cholesterol was measured by CHOD-PAP method, TG was estimated by GPO-PAP method, HDL was estimated by Phospho tungstate precipitation method and bilirubin was measured by diazotized sulfanilic acid method in biochemistry analyser with using randox quality control material.

Serum LDL and VLDL was calculated by Friedwald's formula. All obtained data were analysed statistically by calculating p-value by using online student t-test calculator.

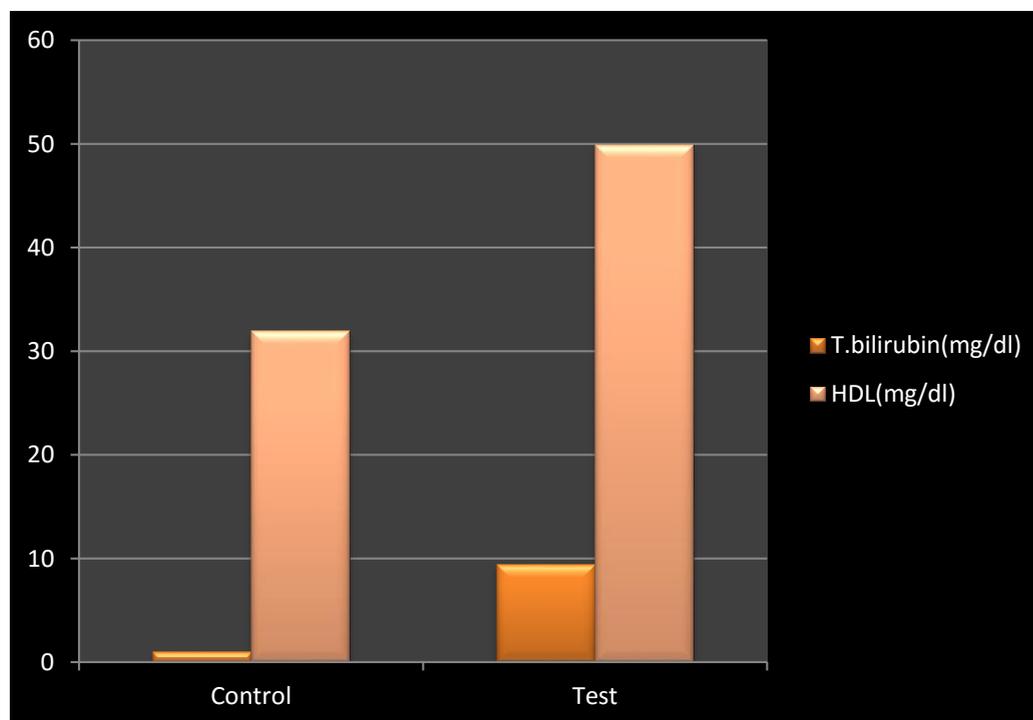
Results

In our study Table represented the biochemical lipid parameters, with serum total bilirubin.

Table 1: Different Lipid and Biochemical Parameters in OPD and Admitted (IPD) Subjects

parameter	Subject Group		P-value
	OPD(60)	IPD(60)	
T.cholesterol(mg/dl)	215.92 ± 40.21	213.45 ± 39.90	0.7362(NS)
S.Triglyceride(mg/dl)	121.83 ± 25.90	123.52 ± 31.23	0.7475(NS)
HDL(mg/dl)	31.92±4.25	49.92±7.23	0.0001(S)
LDL(mg/dl)	159.46±47.29	146.52±45.39	0.1289(NS)
D.bilirubin(mg/dl)	0.43±0.21	5.41±1.92	0.0001(S)
T.bilirubin(mg/dl)	0.94±0.41	9.42±4.1	0.0001(S)
I.bilirubin(mg/dl)	0.51±0.29	4.01±1.6	0.0001(S)
FBS(mg/dl)	123.23±5.2	118.12±4.5	0.0001(S)

Table 1 showed a great difference between OPD and IPD (31.92 ± 4.25 , 49.92 ± 7.23) subjects in serum HDL level, respectively. In the same manner this table also showed a higher level of FBS 123.23 ± 5.2 in OPD subjects. It was represented that the OPD subjects were more prone to risk of CVD. While in IPD subjects it was represented a lower level of 118.12 ± 4.5 .



Graph 1: Graphical presentation of S.bilirubin(mg/dl) and HDL(mg/dl) in test and control group

Table showed there were no statically significant differences between serum TC and serum TG (215.92 ± 40.21 ; 213.45 ± 39.90 and 121.83 ± 25.90 ; 123.52 ± 31.23) in both groups, respectively. Along with this there were found no statically significant differences in serum LDL in both groups.

Discussion

In this investigation we have confirmed and extended a previous observation that increases in serum bilirubin concentration within the normal range are associated with a significant and marked reduction in CAD risk.

Bilirubin has been shown to be an effective antioxidant both *in vitro*^{3,4,5} and *in vivo*⁶. As an antioxidant, it has been shown to suppress the oxidation of lipids and lipoproteins, especially LDL cholesterol (5), and to be directly related to the total serum antioxidant capacity in humans.⁶

When arteries are damaged, smooth muscle cells in blood vessels become activated and grow at the injury sites creating lesions inside the arteries. These lesions can block the flow of blood in arteries of the heart leading to chest pains or deadly heart attacks, Durante said. Arterial lesions can occur due to genetics or because of bad lifestyle choices such as a lack of exercise, unhealthy diet or smoking.⁷

"We found that bilirubin could limit the size of arterial lesions by blocking the growth of vascular smooth muscle cells," Durante said. "Importantly, bilirubin inhibits cell growth without causing cell death, an undesirable side effect of drugs. Cell death creates cellular debris in the arterial network and leads to inflammation and possible rupture of the lesions resulting in even bigger clinical problems."⁸

Smaller studies on bilirubin and CVD events have reported magnitudes of association similar to those seen in the present study. A meta-analysis of 11 studies conducted in men and published up to 2001 reported a 6.5% decrease in atherosclerotic disease rates per 1- $\mu\text{mol/L}$ increase in bilirubin level.⁹ The Framingham Offspring Cohort Study (n=1780) reported a statistically significant 10% reduction in CVD events per 1.7- $\mu\text{mol/L}$ (0.1-mg/dL) increase in bilirubin, a 13% reduction in CHD, and a 13% reduction in MI over a 24-year follow-up after adjustment for conventional risk factors¹⁰. These findings are similar in magnitude to our results of an $\approx 3\%$ to 5% decrease per 1- $\mu\text{mol/L}$ increase at bilirubin levels <10 to 15 $\mu\text{mol/L}$. The slightly weaker associations in THIN data may be due to adjustments for additional risk factors such as social deprivation or possibly the presence of some reverse causation in which bilirubin was measured closer to the event date than in other cohorts, and any stimulation of heme oxygenase in response to advancing yet undiagnosed disease may dilute the observed associations¹¹.

In our study we were not found any statically significant differences between serum TC, TG and LDL in both groups. But we were found a negative relation between serum bilirubin and glycosylated hemoglobin in admitted patients, while there were a positive relation in OPD patients who had normal or lower Bilirubin concentration.

Conclusions

From my study conclusion is that serum HDL and serum bilirubin is found to be higher in hospitalized patients as compared to healthy subjects while there is no difference in level of TC, TG and LDL between hospitalized and healthy controls. According to this we were concluded that admitted patients with higher serum total Bilirubin concentration had a lower risk of CVD/CAD in comparison to OPD subjects. Extensive study is required because sample is small in our study.

Conflict of Interest: None

Source of Support: Nil

References:

1. Stocker R, John F, Keaney J: Role of Oxidative Modifications in Atherosclerosis, *Physiol. Rev.* 2004; 84:1381-1478.
2. <http://medicalxpress.com/news/2012-06-bilirubin-heart-disease.html>
3. Neuzil J, Stocker R. Free and albumin-bound bilirubin are efficient co-antioxidants for alphas-tocopherol, inhibiting plasma and low density lipoprotein lipid peroxidation. *J Biol Chem* 1994; 269:16712-9.
4. Stocker R, Glazer AN, Ames BN. Antioxidant activity of albumin-bound bilirubin. *Proc Natl Acad Sci U S A* 1987;84:5918-22.
5. Wu TW, Fung KP, Wu J, Yang CC, Weisel RD. Antioxidation of human low density lipoprotein by unconjugated and conjugated bilirubins. *Biochem Pharmacol* 1996;51:859-62.
6. Vitek L, Jirsa M, Brodanova M, Kalab M, Marecek Z, Danzig V, et al. Gilbert syndrome and ischemic heart disease: a protective effect of elevated bilirubin levels. *Atherosclerosis* 2002;160:449-56
7. <http://www.sciencedaily.com/releases/2012/12/121206094705.htm>
8. Kelly J, Peyton, Ahmad R, Shebib, Mohammad A, Azam, Xiao-ming Liu, David A. Tulis, William Durante. Bilirubin Inhibits Neointima Formation and Vascular Smooth Muscle Cell Proliferation and Migration. *Frontiers in Pharmacology*, 2012; 3 DOI: 10.3389/fphar.2012.00048
9. Novotny L, Vitek L Inverse relationship between serum bilirubin and atherosclerosis in men: a meta-analysis of published studies. *Exp Biol Med* (Maywood). 2003;228:568-571
10. Lin JP, O'Donnell CJ, Schwaiger JP, Cupples LA, Lingenhel A, Hunt SC, Yang S, Kronenberg F Association between the UGT1A1*28 allele, bilirubin levels, and coronary heart disease in the Framingham Heart Study. *Circulation*.2006;114:1476-1481.
11. Chen SM, Li YG, Wang DM Study on changes of heme oxygenase-1 expression in patients with coronary heart disease. *Clin Cardiol*.2005;28:197-201.