A Descriptive Study on Levels of Serum Bilirubin and Gamma-Glutamyl-Transferase (GGT) in Patients of Acute Coronary Syndrome Visiting a Tertiary Care Hospital of Southern Bihar

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ABSTRACT

BACKGROUND

Most cases of ACS (Acute Coronary Syndrome) are caused by rupture of an atherosclerotic plaque in a coronary artery, resulting in the formation of a thrombus. Atherosclerosis results from an over balance between radical generating, compared with radical scavenging systems, a condition called oxidative stress. Bilirubin had some role in mechanism of ACS. We wanted to evaluate the association between raised total bilirubin level and GGT levels with different subsets of acute coronary syndrome.

METHODS

The present descriptive cross-sectional study was conducted at Narayan Medical College and Hospital from July 2019 to April 2020. Total serum bilirubin was measured in the laboratory by spectrophotometry method. Gamma glutamyl transferase levels were measured in all the patients using a standardized photometric method.

RESULTS

In our study the mean value of triglyceride is 159.86 ± 42.36 with range 60 - 246. Total bilirubin 2.23 ± 0.827, with range 1 - 4. The value of gamma glutaraldehyde was 56.67 ± 26.48 with range 22 - 104. On studying the correlation of serum bilirubin and serum triglyceride in our study subjects, we found very mild correlation with an R square of 0.028. On finding correlation of GGT and serum triglyceride in our study subjects. We found almost no correlation with R square 0. When we do multivariate analysis of effect of serum bilirubin, GGT on total cholesterol level we found that there is very mild correlation with R square 0.031.

CONCLUSIONS

In our study there was very mild correlation between serum bilirubin and gamma glutamyl transferase with marker of acute coronary syndrome such as serum triglyceride level and total cholesterol level but the association was significant.

KEYWORDS

Acute Coronary Syndrome, Triglyceride, Bilirubin, Gamma Glutaraldehyde

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BACKGROUND

Acute coronary syndrome refers to a spectrum of clinical presentations caused by acute myocardial ischemia. It is believed that the rupture or erosion of unstable atherosclerotic plaques is the main pathological basis of the incidence of ACS. At present, Percutaneous Coronary Intervention (PCI) is the principal revascularisation strategy employed in the treatment of ACS. The prognosis of PCI in patients with ACS is a key clinical issue, and some studies have indicated that C-Reactive Protein (CRP), Troponin (Tn), and D-dimers are associated with the prognosis, however, a gold standard has not been established.[1]

Thus, it is crucial to conduct the early diagnosis and effective treatment by combining with enquiry about patients' medical history, as well as physical and laboratory examination.[2]

Most cases of ACS are caused by rupture of an atherosclerotic plaque in a coronary artery, resulting in the formation of a thrombus. Atherosclerosis appears to result from an over balance between radical generating, compared with radical scavenging systems, a condition called oxidative stress. Reactive Oxygen Species (ROS) can damage endothelial cells in many ways, either directly or indirectly. They can also increase endothelial cell permeability and there by accelerate the accumulation of atherogenic factors, such as Low Density Lipoprotein (LDL) in the sub endothelial space.[3]

The oxidation of lipids and the formation of oxygen radicals are important elements in relation to arterial plaque formation and atherosclerosis and are involved in the pathophysiology of coronary artery disease (CAD).[4]

Bilirubin is the end product of haem catabolism, which has 2 forms: Indirect Bilirubin (IDB) and Direct Bilirubin (DB). IDB is converted to DB in hepatic cells and excreted into bile acid. Considered to be a waste product at first, bilirubin now has been known to have antioxidative, anti-inflammatory, and antithrombotic effects.[5]

Gamma-Glutamyl-Transferase (GGT), a widely used biomarker for excessive alcohol consumption and fatty liver disease, is reportedly associated with an increased risk of cardiovascular disease. Our prior study showed that the Oxidized Low-Density Lipoprotein (ox-LDL) level is an important risk factor for CAD in young patients. Interestingly, GGT was detected within atherosclerotic plaques of coronary arteries, where it colocalises with ox-LDL. However, the correlation between GGT and ox-LDL levels has not been evaluated in patients with ACS, and whether the effect of GGT on the incidence of ACS is mediated by or independent of ox-LDL is unclear.[6]

Some researchers believe that serum GGT is partially adsorbed onto LDL lipoproteins, which can carry GGT activity inside the plaque (in proportion with serum GGT levels), in which free iron has also been described. GGT-mediated reactions catalyse the oxidation of LDL lipoproteins, likely contributing to oxidative events influencing plaque evolution and rupture.[7]

The aim of the study was to determine the possible association between raised total bilirubin level and GGT levels with different subsets of acute coronary syndrome.

METHODS

The present descriptive cross-sectional study was conducted at Narayan Medical College and Hospital from July 2019 to April 2020.

Institutional ethical clearance was obtained prior to the beginning of the study and informed consent was obtained from patients. Total 100 patients who fulfils the inclusion and exclusion criteria were included in the present study during study duration. A detailed history, general physical examination, systemic examination and investigations was performed on all patients selected.

Total serum bilirubin was measured in the laboratory by spectrophotometry method. In the Jendrassik-Grof allied methods, total bilirubin is reacted with diazotized sulfanilic acid in an acidic medium to form azobilirubin. The absorbance of the azo pigment is then measured as direct bilirubin and the total bilirubin is measured after treatment with alkaline tartrated solution, which shifts the maximum absorption of the azo pigment towards longer wavelength. Gamma glutamyl transferase levels were measured in all the patients using a standardised photometric method with the normal value noted as 0 - 45 IU / L. Blood samples were taken uniformly six hours from the time of presentation. Cases were divided into three subsets based on electrocardiographic and troponin T measurement**;**

1. ST (Segment) elevation MI (Myocardial Infarction),
2. Non ST elevation MI and
3. Unstable angina.

The following investigations were done in all the patients entering into the study:

- Gamma glutamyl transferase levels
- 14 lead electrocardiogram
- 2D echocardiography with Doppler
- Total cholesterol
- LDL and HDL cholesterol
- FBS and PPBS
- Troponin T estimation
- Total bilirubin test

Following inclusion and exclusion criteria were used for selecting study subjects.

Inclusion Criteria

All patients with acute coronary syndrome, coming to OPD (Out-Patient Department) of Narayan Medical College and Hospital.

Exclusion Criteria

1. History of any alcohol intake
2. History of hepatobiliary disease

3. Surgical conditions causing obstructive jaundice
4. History of taking drugs such as barbiturates, phenytoin, anti-tubercular drugs

RESULTS

Characteristics	Frequency	Percentage
Gender		
Male	72	72
Female	28	28
Age		
≤ 30 yrs.	7	7
31 - 40 yrs.	8	8
41 - 50 yrs.	31	31
51 - 60 yrs.	28	28
61 - 70	22	22
≥ 71 yrs.	4	4

Table 1. Basic Characteristics of the Study Subjects

Table 1 shows the basic demography of study subjects. 72 % of study subjects were males, 28 % were females, 31 % study subjects were in the range of 41 - 50 yrs., 28 % were in the range of 51 - 60 yrs., 22 % were in the range of 61 - 70 yrs. Whereas only 4 % study subjects were above 70 yrs. The mean age of study subjects were 52.10 yrs. ±1 2.28 yrs. with range 26 - 80 yrs.

Variable	STEMI	NSTEMI	UA	Total	P-Value
TGL	165.24 ± 44.38	155.44 ± 40.05	158.84 ± 43.28	159.86 ± 42.36	F-0.57, P = 0.56, non-significant
T. Chol.	205.65 ± 28.99	206.32 ± 31.72	212.06 ± 37.79	207.94 ± 32.73	F-0.37, P = 0.69, non-significant
Total Bilirubin	2.66 ± 0.78	1.99 ± 0.58	2.01 ± 0.65	2.23 ±0.827	F = 10.72, P = < 0.001, significant
GGT	73.15 ± 26.94	51.32 ± 23.56	44.84 ± 20.05	56.67 ± 26.48	F = 13.01, P = < 0.001, significant

Table 2. Value of TGL, T. Chol., Total Bilirubin and GGT between Different Types of Coronary Syndrome in the Study Subjects

In our study the mean value of triglyceride is 159.86±42.36 with range 60 - 246, for STEMI (Segment Elevation Myocardial Infarction) it was 165.24 ± 44.38, for NSTEMI (Non Segment Elevation Myocardial Infarction) it was 155.44±40.05, for UA (Unstable Angina) it was 158.84 ± 43.28. The mean value of total cholesterol is 207.94 ± 32.73 with range 151 - 290, for STEMI it was 205.65 ± 28.99, for NSTEMI it was 206.32 ± 31.72, and for UA it was 212.06 ± 37.79. Total bilirubin 2.23 ± 0.827, with range 1 - 4. For STEMI it was 2.66 ± 0.78, for NSTEMI it was 1.99 ± 0.58, for UA it was 2.01 ± 0.65. When we apply ANOVA (Analysis of Variance) we found significant difference among different subtypes of coronary syndrome. The value of gamma glutaraldehyde was 56.67 ± 26.48 with range 22 - 104. For STEMI it was 73.15 ± 26.94, for NSTEMI it was 51.32 ± 23.56, and for UA it was 44.84 ± 20.05, here also when we apply ANOVA we found significant difference among different subtypes.

Figure 1 shows correlation of serum bilirubin and serum triglyceride. In our study subjects, we found very mild correlation with R square 0.028. When we do multivariate analysis of effect of serum bilirubin, GGT on serum triglyceride level we found there is very mild correlation with R square 0.08, after regression analysis we found F value 4.22 with p value 0.017 that is significant.

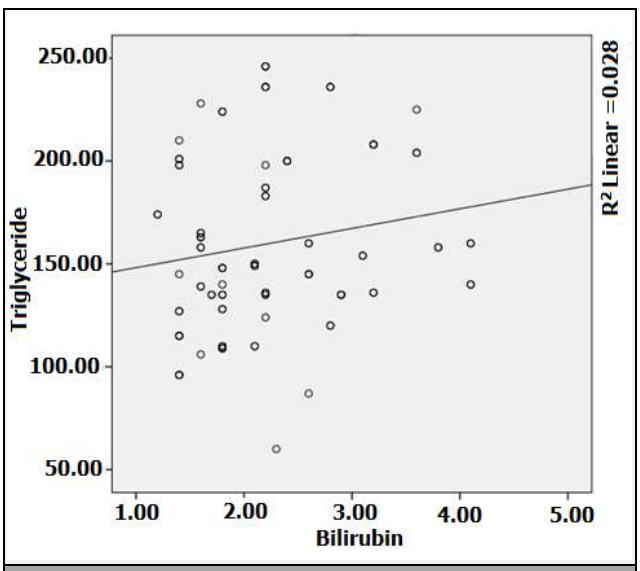

Figure 1. Correlation between Total Bilirubin and TGL

Figure 2 shows correlation of GGT and serum triglyceride. In our study subjects, we found almost no correlation with R square 0. When we do regression analysis we found F value 0.008 with p value 0.931 that is non-significant

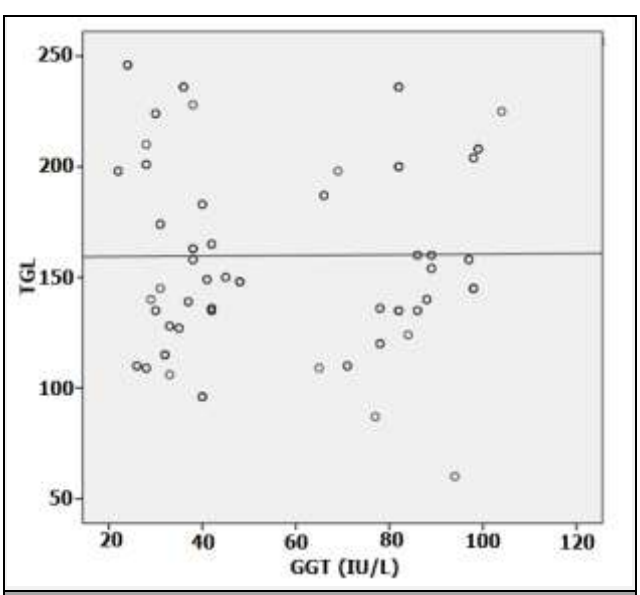

Figure 2. Correlation between TGL and GGT

Figure 3 shows correlation of total cholesterol and serum bilirubin. In our study subjects, we found almost no correlation with R square 0.002. When we do multivariate analysis of effect of serum bilirubin, GGT on total cholesterol level we found there is very mild correlation with R square

0.031, after regression analysis we found F value 1.57 with p value 0.213 that is non-significant.

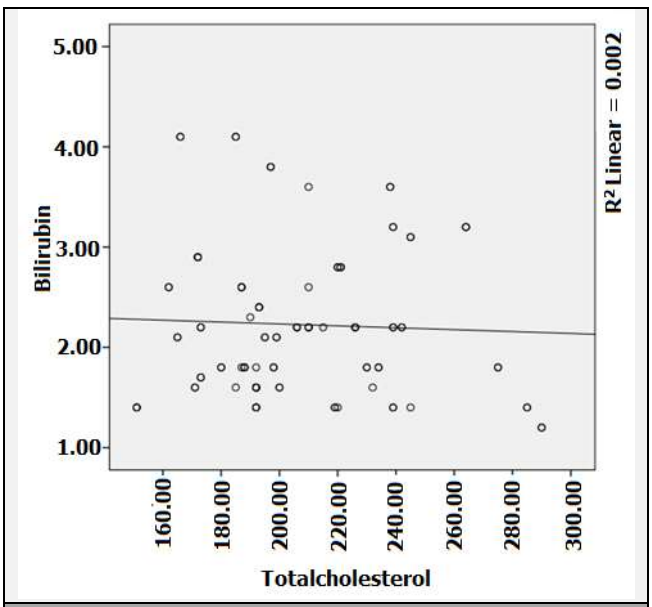

Figure 3. Correlation of GGT and Bilirubin to Total Cholesterol

DISCUSSION

In our study 72 % were males and 28 % were females. The male preponderance was similar to other studies like, Puroshottam R et al[3] had 72.6 % male and 27.4 % were female. Sahin O et al[8] were 66 % of participants were male and 34 % were female. Hopkins et al[9] had 75.6 % males and 24.4 % females. The age ranged from 26 to 80 years. The mean age of the group was 52.1 + 12.28. The maximum (31 %) study subjects were in the range of 41 - 50 yrs., followed by 51 - 60 yrs. Tang C et al[1] in their study found that there were no statistical differences in age, sex, and BMI among the three groups. This finding was similar to other studies and accepted fact that the incidence of ACS increases with age.

In our study total cholesterol and triglyceride vary with the type of MI but when we apply ANOVA test the difference was statistically non-significant. Whereas value of total bilirubin and gamma glutamyl transferase was also different in different type of coronary syndrome but this difference was statistically significant.

Bilirubin has been long postulated to have antioxidant properties and thus its correlation with ACS is of interest. This study tried to find association of serum total bilirubin levels in patients with acute coronary syndrome. The mean bilirubin values in mg / dl for STEMI was 2.66 ± 0.78 SD, for NSTEMI it was 1.99 ± 0.58 and for unstable angina it was 2.01 ± 0.65 SD. Study by FU R et al[2] found that compared with the normal control group, the serum levels of serum bilirubin in groups STEMI, NSTEMI and UAP (Unstable Angina Pectoris) were lower, and the differences were statistically significant ($p < 0.05$). Moreover, the serum bilirubin levels in groups STEMI and NSTEMI were lower than those in group UAP, and the differences were statistically significant ($p < 0.05$). There was no statistically significant difference in comparison with serum bilirubin level between groups STEMI and NSTEMI ($p > 0.05$). Study by Puroshottam R et al[3] found The mean bilirubin values in mg / dl for STEMI was 0.48 + 0.30 SD, for NSTEMI it was 0.45 + 0.16 and for unstable angina it was 0.28 + 0.1 SD. In our study, when we do multivariate analysis of effect of serum bilirubin, GGT on serum triglyceride level we found there is very mild correlation with R square 0.08, after regression analysis we found F value 4.22 with p value 0.017 that is significant. Study by Sahin O et al[8] found high serum total bilirubin level is independently associated with severity of coronary artery disease in patients with NSTEMI. Kim KM et al[10] did cross-sectional study on 19,792 Koreans and found serum total bilirubin concentration inversely correlated with Framingham risk score and it may be helpful to decrease the future risk of coronary artery disease.

Bilirubin has proven to be a potent antioxidant under physiological conditions by inhibiting both lipid and protein oxidation. In several studies it was found that different circulating forms of bilirubin are powerful antioxidants: Free bilirubin, albumin-bound bilirubin, conjugated bilirubin, and unconjugated bilirubin were all noted to be effective scavengers of peroxyl radicals and to be able to protect human LDL against peroxidation. Additionally, bilirubin exerts anti-inflammatory effects on vasculature and inhibits proliferation of vascular smooth muscle cells.

CONCLUSIONS

In our study there was very mild correlation between serum bilirubin and gamma glutamyl transferase with marker of acute coronary syndrome such as serum triglyceride level and total cholesterol level but the association was significant. This reinforces the fact that bilirubin acts as an antioxidant and has cardio-protective action and patients with ACS have lower levels of bilirubin.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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