Original Research Article

Association of total bilirubin levels with acute coronary syndrome and other risk factors: an observational study

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Received: 27 March 2021
Revised: 05 May 2021
Accepted: 12 May 2021

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ABSTRACT

Background: Acute coronary syndrome (ACS) refers to clinical symptoms pertaining to acute myocardial infarction. Bilirubin is an antioxidant that helps in removal of excessive heme. The aim of the study was to find the association of ACS and other risk factors for ACS with the total bilirubin levels in our setup.

Methods: A cross sectional observational study was conducted on 100 cases attending the department of medicine in a Dr. Panjabrao Deshmukh Memorial Medical College, Amravati, Maharashtra. Patients fitting the eligibility criteria were subjected to data collection which was done using pre-designed case record form. The case record form had details of demography, detailed clinical history, physical examination and relevant investigations.

Results: The mean age of the cases was 55.64±10.23 years with male preponderance. Majority of the patients presented with chest pain (83%) followed by shortness of breath (65%) and nausea/vomiting (33%). There was moderate significant correlation between total bilirubin levels and LDL levels (r=0.703; p value<0.001) and There was mild significant correlation between total bilirubin levels and TGs (r=0.403, p value<0.001) Based on the median value of 0.48 as cut off, 33% had bilirubin levels more than 0.48. Presence of diabetes and hyperlipidemias had significant association with the total bilirubin levels.

Conclusions: Nearly 1/3rd of the patients in our study had high bilirubin levels. Higher bilirubin levels correlated well with presence of diabetes and presence of hyperlipidemias. There was significant correlation between the serum LDL and TG levels with total bilirubin levels in the present study.

Keywords: Acute myocardial infarction, Total bilirubin levels, Risk factors

INTRODUCTION

Acute coronary syndrome (ACS) refers to clinical symptoms pertaining to acute myocardial infarction. Unstable angina, non ST segment elevation and ST segment elevation are the categories of acute coronary syndrome. Several risk factors affect the syndrome like presence of high lipids, hypertension, diabetes and smoking. Basic pathophysiology of the syndrome is myocardial ischemia resulting from endothelial dysfunction and damage to endothelium due to these risk factors. During this process of inflammation various anti-inflammatory and pro-inflammatory factors come into consideration. Free heme is a pro inflammatory and cytotoxic affects mainly a result of release of free radicals. Bilirubin is an antioxidant that helps in removal of excessive heme.

It was considered that bilirubin was waste product of the heme oxygenase action but now reports suggest that it has strong relation with coronary artery lesion types. This basically is because of its major antioxidant action inhibiting both lipid and protein oxidation.

The aim of the study was to find the association of ACS and other risk factors for ACS with the total bilirubin levels in our setup.
METHODS

A cross sectional observational study was conducted among the patients attending the department of medicine in a Dr. Panjabrao Deshmukh Memorial Medical College, Amravati, Maharashtra. During a period of 1 year (September 2019 to October 2020) the patients with acute coronary syndrome admitted were included in the study.

Necessary permissions from the ethics committee were taken before the start of the study. Written informed consent was taken prior to collecting the data from the patients. Patients with hepatitis of any cause, who were drugs like amiodarone, oral hypoglycemics, anti-pileptics, anti-fungal drugs and anti-tuberculosis drugs were excluded from the study. Patients with diagnosed cirrhosis of liver, bile duct obstruction and haemolytic jaundice were excluded from the study.

A study conducted by Vamadaven AS et al inferred that the prevalence of ACS in India was 8%. With this, 95% confidence interval and 5.5% absolute error, we found minimum sample size to be 93. But, for our convenience, we have included 100 cases of ACS in the present study. Data collection was done using pre-designed case record form. The case record form had details of demography, detailed clinical history and physical examination.

Relevant investigations like complete blood count, electrolytes, electrocardiogram, chest X-ray, serum bilirubin levels, etc were done in all the patients. ACS was diagnosed in the patients using standard guidelines. All the patients were treated according to the standard guidelines of management of ACS.

Statistical analysis

The data was collected, compiled and analysed using EPI info (version 7.2). The qualitative variables were expressed in terms of percentages. The quantative variables were both categorised and expressed in terms of percentages or in terms of mean and standard deviations. Difference between two proportions was analysed using chi square or Fisher exact test. To correlate between the quantitative variables we used Pearson’s correlation coefficient (r) and scatter diagram with fit line and 95% confidence interval was plotted. All analysis was 2 tailed and the significance level was set at 0.05.

RESULTS

We included 100 cases of acute coronary syndrome in the present study.

The mean age of the cases was 55.64±10.23 years with male preponderance. About 23% had diabetes, 31% had hypertension, 8% had history stroke or transient ischemic attacks, 4% had previous myocardial ischemia, 12% had hyperlipidemias and 25% were current smokers (Table 1).

| Demographic factors | Frequency | Percentage (%) |
|---------------------|-----------|----------------|
| Age group (years)   |           |                |
| 30 to 40            | 10        | 10             |
| 40 to 50            | 34        | 34             |
| 50 to 60            | 27        | 27             |
| >60                 | 29        | 29             |
| Gender              |           |                |
| Male                | 56        | 56             |
| Female              | 44        | 44             |
| Past history        |           |                |
| Diabetes mellitus   | 23        | 23             |
| Hypertension        | 31        | 31             |
| Stroke/TIA          | 8         | 8              |
| Previous MI         | 4         | 4              |
| Hyperlipidemias     | 12        | 12             |
| Current smoker      | 25        | 25             |

Majority of the patients presented with chest pain (83%) followed by shortness of breath (65%) and nausea/vomiting (33%) (Table 2).

| Chief complaints    | Frequency | Percentage (%) |
|---------------------|-----------|----------------|
| Chest pain          | 83        | 83             |
| Shortness of breath | 65        | 65             |
| Nausea/vomiting     | 33        | 33             |
| Dizziness           | 12        | 12             |
| Loose stools         | 14        | 14             |
| Hypotension          | 10        | 10             |
| Tachycardia          | 14        | 14             |

There was moderate significant correlation between total bilirubin levels and LDL levels in the present study (r=0.703, p value<0.001). There was mild significant correlation between total bilirubin levels and TGs in the present study (r=0.403, p value<0.001) (Figure 1-2).

![Figure 1: Correlation of total bilirubin levels with LDL in the present sample (r=0.703, p value<0.001).](image)
Correlation of total bilirubin levels with TG in the present sample (r=0.403, p value<0.001).

The mean bilirubin levels were 0.48±0.12 in the present study. Based on the median value of 0.48 as cut off, 33% had bilirubin levels more than 0.48 (Table 3).

Table 3: Distribution of study subjects based on total bilirubin levels.

| Total bilirubin levels | Frequency | Percentage (%) |
|------------------------|-----------|----------------|
| <0.48                  | 67        | 67             |
| >0.48                  | 33        | 33             |
| Total                  | 100       | 100            |
| Mean                   | 0.48      |                |
| Median                 | 0.47      |                |
| SD                     | 0.12      |                |
| Range                  | 0.1 to 1.92 |               |

Table 4: Association of different factors with serum total bilirubin levels.

| Factors         | Low TB (n=67) | High TB (n=33) | P value |
|-----------------|---------------|----------------|---------|
| Age             |               |                |         |
| <50             | 31            | 13             | 0.5194  |
| >50             | 36            | 20             |         |
| Gender          |               |                |         |
| Male            | 42            | 14             | 0.0549  |
| Female          | 25            | 19             |         |
| Past history    |               |                |         |
| Diabetes mellitus | 10           | 13             | 0.0061  |
| Hypertension    | 15            | 8              | 0.8354  |
| Stroke/TIA      | 5             | 3              | 0.7777  |
| Previous MI     | 2             | 2              | 0.4605  |
| Hyperlipidemias | 4             | 8              | 0.0081  |
| Current smoker  | 15            | 10             | 0.3900  |

Patients with diabetes mellitus had significantly higher proportion of total bilirubin levels more than 0.48. Patients with hyperlipidemia had significantly higher proportion of total bilirubin levels more than 0.48. Total bilirubin levels were not significantly associated with past history of hypertension, previous MI, stroke/TIA and current smoking status (p>0.05) (Table 4).

DISCUSSION

ACS is as a result of inflammation induced due to the vessel blockage leading to ischemia and infarction. This process is associated with release of free radicals in the blood. Scavenging these free radicals is of utmost importance and is done by some internal antioxidants. One of such antioxidant is bilirubin levels in the blood.1-3,5,7,11 With this background, we conducted a study to understand the total bilirubin levels among the patients with ACS and to find association with risk factors for ACS.

Upon analysis of the data, we found that 33% of the patients had more than the median value of total bilirubin levels. Similar inferences were reported by Sahin et al, Hammur et al and Puroshotham et al.12-14 Presence of diabetes and hyperlipidemias were associated with higher bilirubin levels in the present study. One of unique studies conducted by Okuhara et al reported that change in total bilirubin levels following acute myocardial infarction was related to heme oxygenase activation.15 Another study conducted by Puroshotham et al inferred that there was moderate significant correlation between the serum LDL and triglyceride levels with total bilirubin levels in their study.12 Similar inferences were reported by Xu et al and Hopkins et al in their studies.16,17 Shen et al conducted a meta-analysis of different studies and inferred that higher bilirubin levels were associated with major cardiac adverse events and mortality among majority of the studies.18 Hence, total bilirubin is associated with higher morbidity and mortality in patients with ACS. Various studies conducted across have associated total bilirubin levels with the in mortality and major adverse events during follow up of the patients.19-24 Our study had some limitations. It was a single centre study and an observational study. Follow up studies conducted in this regard would yield better results.

CONCLUSION

Nearly 1/3rd of the patients in our study had high bilirubin levels. Higher bilirubin levels correlated well with presence of diabetes and presence of hyperlipidaemias. There was significant correlation between the serum LDL and TG levels with total bilirubin levels in the present study. Future studies to be conducted to assess the association of total bilirubin levels with all-cause mortality using multivariate models.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee
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Cite this article as: Verma S, Kamble O. Association of total bilirubin levels with acute coronary syndrome and other risk factors: an observational study. Int J Adv Med 2021;8:835-8.