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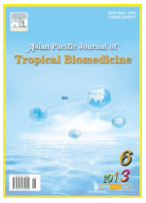

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Correlation between lipid profile and troponin I test results in patients with chest pain in Nepal

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PEER REVIEW

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Comments
Overall I find the paper is worth publishing as it carries a key message and it must be employed in most of the diagnostic laboratories and Intensive coronary care unit.
Details on Page 491

ABSTRACT

Objective: To study the usefulness of traditional lipid profile levels in screening subjects who had developed chest pain due to cardiac event as indicated by a positive troponin I test. **Methods:** In this retrospective study data of the 430 patients presented to the emergency department with symptoms of cardiac ischemia who underwent both troponin and lipid profiles tests were compared with the lipid profiles of 165 normal healthy subjects (controls). The troponin was detected qualitatively when a specimen contains troponin I (cTnI) above the 99th percentile (TnI>0.5 ng/mL). The total cholesterol, high density lipoproteins cholesterol, very low density lipoproteins and triacyl glycerol levels were also analyzed and low density lipoprotein level was calculated using Friedewald's formula. **Results:** Patients with chest pain and positive troponin test (with confirmed cardiac event) were found to have significantly elevated levels of total cholesterol, triacyl glycerol levels, low density lipoprotein level and significantly reduced high density lipoproteins cholesterol levels when compared to the patients who experienced only chest pain (negative troponin) and healthy controls. **Conclusions:** Traditional lipid profile levels is still can be used in screening populations to identify the subjects with high risk of developing cardiac event in case if the laboratory set up has not troponin test facilities.

KEYWORDS
Troponin, Chest pain, Cardiac event, Lipid profile, Nepal

1. Introduction

The assessment of patients with acute chest pain of possible cardiac cause continues to be a challenge and positive diagnosis has psychological, social and legal implications[1,2]. The presence of ST segment elevation in the ECG is highly specific (but only about 50% sensitive[1]) for acute myocardial infarction (MI). However, many patients presenting to coronary care units have chest pain without ST elevation in the ECG. The diagnostic possibilities in these cases include: acute coronary syndrome in evolution, or 'non-ischaemic' chest pain.

The World Health Organization defines for diagnosing AMI, the presence of two of the three enlisted features namely, symptoms of myocardial ischemia, elevated levels of cardiac marker (protein or enzyme) concentrations in the blood, and a typical electrocardiographic pattern involving the development of Q waves or persistent T wave changes[3]. Further the American Heart Association case definition for acute myocardial infarction (AMI) requires an "adequate

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set" of biomarkers: two measurements of the same marker at least 6 h apart[4-6].

Traditionally the cardiac enzymes used in the assessments for the detection of MI includes the triad of lactate dehydrogenase, aspartate transaminase (serum glutamate oxaloacetate transaminase) and creatine kinase-MB (CK-MB) which is of heart origin. However the use of biochemical 'gold-standard' CK-MB levels has limited prognostic power[1,2] compared to the serum troponins (both I and T) which are considered to be more specific and sensitive over CK-MB in the setting of acute coronary syndromes and have been validated for post operative risk stratification for non-cardiac surgical procedures. With CK-MB being used as a marker, it has limitations to identify the future risk of acute coronary syndromes hence, many of the patients are kept in ICCU and occupy beds unnecessarily, and other who are presumed to be safe and are discharged, returns to ICCU with recurrent coronary events[1,2].

The assessment of smaller molecular mass proteins such as myoglobin (1 600 kD) derived from the cytosol of both skeletal and cardiac muscle, heart-type fatty acid binding protein (hF-ABP) are considered to be more cardio specific, is a promising novel marker for early detection of acute or persistent myocardial damage, however in clinical practice neither of these proteins are considered as cardiac markers[3].

Highly sensitive and specific immunoassays for myocardial proteins, such as troponins T and/or I which are components of the thin filaments of the sarcomere are used in the identification of subjects with small areas of myocardial necrosis[3].

The magnitude of troponin elevations has correlated with the risk of death and composite risk of death or non-fatal MI, irrespective of whether the patients had ST elevation or non-ST elevation acute coronary syndromes by observations of the recent studies[3].

Troponin I testing had better sensitivity, specificity and prognostic value than troponin T testing. A positive troponin I result was a strong predictor of cardiac events (death from cardiac causes or MI) in the next 30 d. The predictive value of a negative troponin I result was also high, with a total 30 d event rate of 0.3%, regardless of the admission ECG[1, 2].

The new diagnostic criteria include a characteristic rise and fall in blood concentrations of cardiac troponins and/or CK-MB in the context of spontaneous ischemic symptoms or coronary intervention[3]. Cardiac troponin I and T are highly sensitive and highly specific and may be elevated when CK-MB concentrations are not even mildly elevated. In addition, they may predict recurrent cardiac events in patients with acute coronary syndromes. However, use of troponin testing has been limited by availability of laboratory-based diagnostic techniques and by relatively long processing times[1,2].

Even minor elevations of troponin concentrations in the blood are indicative of myocyte necrosis and not due to leakage of proteins through the myocyte cell membrane. The current immunoassays assays for troponins T and I reliably detect cardiac (as distinct from skeletal muscle) forms of these proteins[3]. Furthermore, troponins have greater sensitivity and specificity for the diagnosis of MI in acute myocardial ischemia.

However it is important to note that some patients who were diagnosed of MI did not have elevated troponins or CK values[3]. Some patients had died even much before the cardiac markers reach the threshold for detection[2].

Further troponin concentrations are found to be elevated in tachycardia, percutaneous coronary intervention, pulmonary emboli with right ventricular infarction, cardiac surgery, myocarditis and renal failure, in which the cause of myocyte necrosis is not known[3].

In this study we proposed to evaluate the association between lipid profile levels of the subjects with chest pain with positive or negative troponin test.

2. Materials and methods

In this retrospective study, the data of the registry maintained in the department of biochemistry of the Manipal Teaching Hospital, Pokhara, Nepal were analyzed. The WHO case definition[2] was used to retrospectively assign a diagnosis in 430 patients presenting to the emergency department with symptoms of cardiac ischemia. The inclusion criteria was the subjects (n=430) who were admitted to the intensive care unit of the hospital complaining severe chest pain and who were requested by the medical staff to get both troponin and lipid profiles done.

In addition to that, reports of 165 healthy subjects who had got their lipid profiles checked using the medicare facility were assessed as controls.

The troponin was detected qualitatively when a specimen contains troponin I (cTnI) above the 99th percentile (TnI>0.5ng/ml) method[7-10]. The total cholesterol (TC), high density lipoproteins cholesterol (HDL), very low density lipoproteins (VLDL), and triacyl glycerol levels (TG) were analyzed, using the kits provided by HUMAN Diagnostics and the low density lipoprotein level (LDL) was calculated using Friedewald formula[11].

All the estimations were done using HUMAN 300 semi-auto analyzer and data was analyzed using Epi Info windows version. Significance of the difference of parameters among different groups was analyzed using Z-test.

The reports of the subjects with any of the missing data were excluded. The selection of the reports was done without the prior knowledge of both the subjects and the staff of the intensive care unit. So that healthcare workers and the study subjects were not influenced anyway during the study. Therefore no written consent was obtained from any of the

subjects. The ethical clearance was granted by the ethical committee of the Manipal College of Medical Sciences, Pokhara.

3. Results

Of the 430 subjects with the chest pain and tested for the presence of troponin in the serum qualitatively, only 79 (18.4%) subjects were detected positive. The larger proportion of the subjects (81.6%) with severe chest pain was found to be troponin negative. Initially, the differences in various lipid parameters among the subjects with chest pain and with or without a troponin were compared (Table 1). In addition to that these two groups were compared for the same parameters with those levels of normal healthy subjects (controls).

Table 1
Comparison of lipid parameters of the subjects with chest pain and with or without a positive troponin test.

Variables	Subjects with chest pain (n=430)		
	Troponin−ve (n=351)	Troponin+ve (n=79)	Significance P value
Age (years)	58.06±13.55	56.21±9.94	0.318
TC (mg/dL)	176.00±46.17	221.00±35.80	0.001
TG (mg/dL)	148.20±54.79	163.74±48.22	0.001
LDL (mg/dL)	102.49±44.29	152.26±39.41	0.001
HDL (mg/dL)	43.49±6.72	39.37±4.98	0.076
VLDL (mg/dL)	28.65±11.82	35.38±6.98	0.437

All values are mean±SD. Values in the parenthesis indicate the number of subjects.

No significant difference was observed for age among the two groups of subjects (Table 1). However except for VLDL all other parameters of the lipid profiles were significantly different in two groups. Among the subjects with chest pain total cholesterol, triacyl glycerol, low density lipoproteins levels were higher in the subjects with troponin positive than the subjects with a negative troponin. Further HDL levels in the subjects with troponin positive were lower than troponin negative.

Of the subjects with chest pain, a significantly (P<0.001) higher levels of TC, LDL and TG, have been observed in subjects with positive troponin test, when compared to the healthy subjects (Table 2) and the subjects with a negative troponin test (Table 1).

The data of Table 2 shows the comparison of biochemical data of the subjects with chest pain and with or without a positive test for troponin against the healthy controls.

Further HDL level of the subjects with chest pain and positive troponin was significantly lower than the HDL levels of controls (Table 2) and that of the subjects with a negative troponin test (Table 1).

The effect of sex on having only chest pain (when troponin is negative) was evaluated and data are given in Table 3. In the subjects with chest pain which is not due to cardiac event as indicated by negative troponin test a significantly greater levels were observed for TG and for VLDL in males than in females. However all these parameters were within the normal levels. The all other parameters including TC, LDL and HDL levels were the same for both sexes.

The effect of sex of the subjects in having chest pain with a positive troponin, *i.e.* chest pain due to cardiac event, was not evaluated as the numbers are not sufficient.

Table 2
The comparison of lipid profiles of the subjects with chest pain and with and without positive troponin against healthy controls.

Variables	Control (165)	Chest pain (430)		P^* Value
		Troponin	Mean±SD	
Age (years)	55.84±12.61	P (79)	56.21±9.94	0.236
		N (351)	58.90±13.55	0.034
TC (mg/dL)	182.24±52.59	P (79)	221.05±5.79	0.001
		N (351)	175.9±46.17	0.234
Triglycerides (mg/dL)	158.08±58.89	P (79)	163.74±48.22	0.298
		N (351)	148.20±54.79	0.169
LDL (mg/dL)	105.31±48.26	P (79)	152.26±39.41	0.001
		N (351)	102.50±44.29	0.458
HDL (mg/dL)	41.56±17.09	P (79)	39.37±4.98	0.047
		N (351)	43.49±6.72	0.456
VLDL (mg/dL)	31.39±12.09	P (79)	35.38±6.98	0.023
		N (351)	28.65±11.82	0.046

All values are mean±SD; Controls: Healthy subjects; Values in the parenthesis indicated the number of subjects; P: Subjects with chest pain and troponin positive; N: Subjects with chest pain and troponin negative; P^*: Significance between control and P and N groups separately.

Table 3
The effect of sex on the variables in subjects only with chest pain (when troponin is negative).

Variables	Males (245)	Females (106)	Significance
Age (years)	57.46±11.37	56.48±12.47	NS
TC (mg/dL)	172.43±27.41	181.2±52.0	NS
TG (mg/dL)	142.19±25.05	138.89±32.13	0.05
LDL (mg/dL)	99.89±36.78	101.4±43.65	NS
VLDL (mg/dL)	29.84±12.37	28.47±8.59	0.03
HDL (mg/dL)	40.86±7.10	43.46±7.83	NS

NS: Not significant.

4. Discussion

In a previous study of subjects with chest pain it was reported that troponin was positive in 79 subjects (18.4%) and negative in 351 (81.6%) subjects[4-6]. They also reported higher incidence of acute myocardial infarction, acute heart failure, and death due to cardiac event in the subjects with chest pain and positive troponin confirming that it is a powerful, independent and valuable tool for risk stratification in patients with acute chest pain. Our data indicated that, of the subjects with chest pain (430) only 79 subjects (18.4%) were detected positive and a larger proportion of subjects (81.6%) were detected negative for troponin. Accordingly, those seventy nine subjects with chest pain are at high risk of developing cardiac event though the incidence of cardiac event is lower (18.4%).

It is well known that increased levels of LDL, TG and TC and decreased levels of HDL are also indicative of increased incidence of cardiac events and are considered as risk factors[12]. Therefore in this retrospective study the relationship between levels of lipid profile parameters and the results of troponin test in predicting cardiac events was evaluated.

The mean TC level of the subjects with positive troponin (221±35.80) was well above the recommended desirable level (<200 mg/dL) thus indicating those subjects are susceptible to develop cardiac event[12]. The level of total cholesterol of the subjects with negative troponin test but with chest pain (176±46.17) was significantly lower than that of the subjects with positive troponin above confirming the importance of maintaining total cholesterol levels below the recommended level[12].

Similarly the mean TG level of the subjects with positive troponin (163.74±48.22) was well above the both the recommended desirable level[6] (<150 mg/dL) and the level of TG of the subjects with negative troponin test but with chest pain (148.20±54.79). Further the TG level of the subjects with only chest pain was slightly lower than the recommended safe level.

Increased level of LDL is highly atherogenic as it could get oxidized and initiates the atheroma formation. Thus it is believed that increased level of LDL than the recommended level is a high risk factor in the development of cardiac event. The mean LDL level of the subjects with positive troponin (152.26±39.41) was well above the recommended desirable level (<130 mg/dL)[12].

Further the mean LDL level of the subjects with negative troponin test but with chest pain (102.49±44.29) was well below the recommended level and confirmed the importance of maintaining lower levels of LDL in preventing future cardiac event.

Thus our data indicated that the subjects who developed chest pain due to cardiac event as confirmed by positive troponin test had significantly greater levels of TC. TG, LDL when compared to those levels in subjects without cardiac event as indicated by negative troponin test.

On the other hand lower HDL level (<40 mg/dL) is also regarded as a cardiac risk factor6and the mean HDL level of the subjects with positive troponin (39.37±4.98) was lower than the recommended safe level. This also indicates that the development of cardiac event was associated with reduced levels of HDL than the recommended level. Further the subjects with negative troponin test (No cardiac event) had a mean HDL level above the cut off value suggestive of safe levels and that value was (43.49±6.72) significantly (P<0.076) greater than the mean HDL levels of the subjects who had a cardiac event.

These lipid parameters were also compared with the values of aged matched hundred and five (165) healthy subjects without any known disease condition. All the values of lipid parameters are within the safe levels for healthy subjects indicating they were having a minimum possibility of developing any cardiac event.

The total cholesterol level and LDL levels of the subjects with positive troponin was significantly (P<0.001) greater than the healthy subjects and no significant difference was observed for TC between healthy subjects and subjects with a negative troponin test but with chest pain. However no significant differences were observed for TG and VLDL between these groups.

Significantly lower (P<0.047) mean HDL level was observed in the subjects with positive troponin when compared to healthy subjects and the subjects only with chest pain but with negative troponin test.

These data indicated that the chest pain due to cardiac event as determined by positive troponin test is closely associated with elevated levels of TC, LDL, TG and also with significantly reduced HDL. However the comparison of lipid parameters of males and females in the sub group of negative troponin tests in the present study revealed that there were no major significant difference of those parameters due to differences in sex.

Therefore our data clearly shows that patients who developed chest pain due to cardiac event as confirmed by positive troponin test had lipid parameters in the risk levels as suggested by ATP III[12]. Therefore the subjects who had lipid profile levels within risk level were at a greater risk of developing chest pain due to cardiac event. Thus it is advisable to screen and identify subjects with risk levels of lipid profile parameters and advise them to control their lipid profiles to maintain within the levels as recommended[12].

Lack of previously published research papers on the relationship between lipid profiles and troponin test for comparison and the fewer number of subjects in our study are the two major limitations in our study. Thus a larger study on this topic should be carried out in the future to extrapolate our observation to the total population.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

We acknowledged the ethical clearance committee and the CEO and Dean of Manipal college of Medical Sciences for granting us the approval to carry out this study.

Comments

Background

The current study was based on the assessment of troponin test in acute chest pain patients along with the lipid profile. Since troponin test are done qualitatively most of the time the clear cut ruling out of AMI patients cannot be established just because of chest pain and troponin test being positive. Sometimes the troponin test can be negative in case of AMI patients. Based on the current concept this results discussed in this paper, develops a strong evidence that only those patients whose troponin test are positive followed by additional findings of abnormal lipid profile can rule out the true AMI patients from others who develops chest pain due to various reasons.

Research frontiers

With the concept of troponin being adjunct to lipid profile determination and those with higher lipid levels would be having AMI with supportive Trop I positive.

Related reports

This work has not published earlier as it is not googled and searched in engines. The author establishes a strong link with the troponin and lipid profile in chest pain patients diagnosed of AMI.

Innovations and breakthroughs

All patients with chest pain cannot be having AMI except those who have established troponin positive with hyperlipidemia and not with troponin positive with normolipidemia.

Applications

In laboratories where the troponin test cannot be done or if it is expensive and cannot be affordable by the patients than only lipid profile test especially the ratio of TG/HDl-c would give a tentative diagnosis of chest pain due to AMI or without AMI.

Peer review

Overall I found the paper is worth publishing as it carries a key message and it must be employed in most of the diagnostic laboratories and intensive coronary care unit.

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