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Original Research Article

Correlation of various cardiac markers in diagnosed case of acute MI

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ABSTRACT

Introduction: The ischemic injury to the heart and its extent of damage is directly associate with the length of ischemia. For the post mortem diagnosis of MI during an autopsy poses a challenge, particularly in cases of very minute myocardial infract. Biochemical markers provide a very useful tool for the assessment of acute coronary syndrome. These are total creatinine kinase, the MB isoforms and myoglobin,as well as the troponin I(cTnI) and cardiac troponin T (cTnT). The aim of the present study was to study status of cardiac markers like CPK-MB, LDH, Trop-I in diagnosed case of acute MI.
Material and Methods: In this prospective study, 35 cases of sudden death that were studied at tertiary care government hospital attached to post-mortem centre during the period from April 2017 to July2018 for the underlying pathology for the sudden death by the assessment of various biochemical markers.
Results: It was observed that out of 35 cases, CPK-MB levels were elevated in 29 cases. LDH levels were raised only in 4 cases. Troponin-I levels were raised in 33 cases. Of all the enzymes Troponin-I levels were raised in 94% cases as compared to the other two. It was observed that the sensitivity and specific for CPK-MB, LDH and Trop I were 84% and 30%, 72% and 20 %, 92% and 74% respectively.
Conclusion: It was concluded that for the diagnosis of myocardial infarction it is important to perform serial measurement of cTnI because the first measurement may still be negative when the case presents early after the onset of symptoms.

1. Introduction

The heart is a muscular pump that has a remarkable capacity to work through out a human lifetime. As per the requirements, heart can augment its blood flow as compared to normal. This is possible because of the capacity of the coronaries to modify its blood flow as and when required. Ventricle cope up to the increased workload by modifying itself. This compensatory mechanism sometimes cannot match up to the requirements and the heart is no longer able to supply the required blood to the body which translates in to congestive heart failure. Another reason for the same is the impaired blood supply to the heart resulting in to the limitation of the capacity of the left heart to function which again results in to heart failure.[1]

Myocardial infraction (MI) is an ischemic necrotic injury to the heart tissue. It is directly associated with the length of the ischemia as well as the requirement of the myocardial tissue. It was shown that 20 minutes of blood supply occlusion results in the development of a foci of necrosis which intensifies as the time lengthens.[2] MI is one of the most commonly observed ailment in the patients who are hospitalized particularly in the developed countries. In US, there are approx. 6,50,000 patients who develop new MI and 450,000 experience recurrent MI every year. Ischemic Heart Diseases (IHD) is one of the most common cause of sudden death in adults over the age of 30 years.[3] Early mortality rate of MI is approximately 30%, more than half of these death occurs with before the hospitalization.[4]

Historically, the criteria used for coronary artery disease are mainly ECG and biochemical markers assessment. The Troponin complex (I, C, T) regulates the calcium

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homeostasis in the striated muscles. Cardiac troponin I (cTnI) is a specific marker to the cardiac ischemia and it is without any cross reactivity. The marker is sensitive enough to allow the detection of even a very small infract well before the commencement of ischemia.[5]

Biochemical markers provide a very useful tool for the assessment of acute coronary syndrome. These are total creatinine kinase, the MB isoforms and myoglobin,as well as the troponin I(cTnI) and cardiac troponin T (cTnT).[6]

The aim of the present study was to study status of cardiac markers like CPK-MB, LDH, Trop-I in diagnosed case of acute MI.

2. Material and Methods

This is a prospective study. All cases of sudden death that were received by at tertiary care government hospital attached to post-mortem centre during the period from April 2017 to July2018, were investigated for myocardial infraction as the underlying pathology for the sudden death by the assessment of various biochemical markers. The required permissions for the conduction of the study were obtained from the Institutional Ethics Committee. Once a sudden death occurred, the case was reported to the judicial investigator in that area who's in turn arranges for a post mortem examination to be performed. Patients having increased level of cTnI because of conditions like cardiac surgery, renal failure, hypothyroidism, severe burns and sepsis were excluded from the study. The age of the sudden death cases enrolled in the study were 18 years and above. All the cases were studied by detailed autopsy protocol.

The study included 35 post mortem blood samples from brought dead patients in casualty. Medico-legal post-mortem cases brought to the post-mortem centre attached to the Tertiary Care Hospital, for autopsy included in the study.

Medico-legal hospitalized case (death within 24 hours of admission) with history of heart disease brought to centre within 24 hours of death, patients dying within one hour of onset of symptoms and reaching our centre within 24 hours of death, patients with acute myocardial infarction admitted in hospital and died within one week to one month were included in the study. Decomposed bodies/mutilated bodies/skeletonized bodies/ burn bodies, bodies brought to hospital more than 24 hours of death were excluded.

2.1. Biochemical analysis of cTnI, CPK-MB& LDH

The blood was collected from the heart during the autopsy. About 10 ml of blood was collected from heart artery and placed in airtight vial or test tube and was immediately centrifuged at 3,000 round/minute until separation of plasma and were stored at 4°C for not more than 24 hours in central biochemistry laboratory, and analysing them by Micro Lab RX-50 system based on the Biomarker Enzyme Linked Fluorescent Assay (ELFA) principles). Once the assay is completed, results were analysed automatically by the computer. The results are automatically calculated by the instrument and the concentrations were expressed in (or ng/mL) for troponin and (ng/ml) for CPK-MB (U/L) and LDH (IU/L).

2.2. Estimation of cardiac troponin I CPI

The measurement range for Semi automated analyser Micro Lab RX-50 TnI is 0.2-30 ng/ml. We chose a cut-off value of 0.2 ng/ml as the minimal detectable concentration of cardiac troponin I. Observations of cardiac troponin I falling below the cut off value were considered negative results. Sensitivity of this enzyme kit is 88%.

2.3. Estimation of cardiac CPK-MB

The plasma sample that were analysed for cTnI were also studied for CPK- MB in the Cardiac Serum Marker Core Laboratory by a mass assay to permit the consistent comparison with cTnI levels in a single reference laboratory. Once the assay is completed, results are analysed automatically by the computer. The RFV (Relative Fluorescence Value) is derived by subtracting the reading from the last observation. The measurement range for Micro Lab RX-50 is CPK-MB is0 to 25(U/L). All the measured levels of CPK-MB that fell below the cut-off value 1 (U/L) were collectively expressed negative result. Sensitivity of this enzyme kit is 82%.

2.4. Estimation of LDH

Serum lactate dehydrogenase more than 460(IU/L) related to analyse clinical outcome. . LDH is found in all the cell. Lactate dehydrogenase catalyse the conversion of lactate to pyruvic acid and back as it converts NAD to NADH and back. Quantitative estimation of LDH done on semi-automated analyser Micro Lab RX-50.Normal range value of LDH is 230 – 460 IU/L. More than 460 IU/L value of LDH indicates raised level OR positive test. LDH sensitivity of this enzyme kit is 74%.

2.5. Observations

The present study investigated serum LDH, cardiac troponins and creatinine phosphokinase in the blood from medico legal autopsy cases with regard to cause of sudden death.

The study included the subjects of both the genders. Out of a total of 35, 20 were males and 15 females (ratio - 4:3). All the subjects were of 30 years or above in age. Maximum numbers of cases were observed in age group of 50-59 years. Mean age was 55.02 years.

When compared with the body mass index (BMI), troponin I levels shown a positive correlation. There was a significant increase in number of cases and troponin I levels

Table 1: The kits used in the study were the following

Kits	Company	Country
Troponin I	Beckman Coulter	India
CK-MB	Unicel Dx 600	India
LDH	Unicel DX 600	India

Table 2: Sensitivity and specificity of cardiac markers CPK MB, LDH AND TROPONIN I with respect to time

No.	Cardiac marker	1st detection	Duration of detection	Sensitivity	Specifity
1	CPK-MB	4 to 6 hours	2 – 3 days	70%	50%
2	Trop-I	3 to 4 hours	7-10 days	94%	98%
3	LDH	6 to 10 hours	5 – 7 days	60%	50%

Table 3: Gender Distribution of cases

Gender	Frequency	Percentage
Male	20	57.1
Female	15	42.9
Total	35	100

Table 4: Body mass index in relation to troponin enzyme marker

			Troponin		Total
			Positive	Normal	
BMIGR	Normal	Count	4	2	6
		% within BMIGR	66.7%	33.3%	100.0%
	Overweight	Count	21	8	29
		% within BMIGR	72.4%	27.6%	100.0%
Total		Count	25	10	35
		% within BMIGR	71.4%	28.6%	100.0%

Table 5: Body mass index in relation to CPK-MB

			CPKMB		Total
			Positive	Normal	
BMIGR	Normal	Count	5	1	6
		% within BMIGR	83.3%	16.7%	100.0%
	Overweight	Count	23	6	29
		% within BMIGR	79.3%	20.7%	100.0%
Total		Count	28	7	35
		% within BMIGR	80.0%	20.0%	100.0%

with respect to the rise in the BMI.

When the comparison between BMI and CPK-MB levels were observed, there was mild negative correlation found between the two variables. This may be attributed to the fact that CPK levels rise late as compared to troponin-I levels and also troponin-I is comparatively heart specific.

The comparison between body mass index and LDH levels show mild negative correlation. This could be attributed to late rise and non-specificity of LDH enzyme.

2.6. Enzyme markers evaluation

It was observed that out of 35 cases, CPK-MB levels were elevated in 29 cases. LDH levels were raised only in 4 cases. Troponin-I levels were raised in 33 cases. Of all the enzymes Troponin-I levels were raised in 94% cases as compared to CPK-MB and LDH.

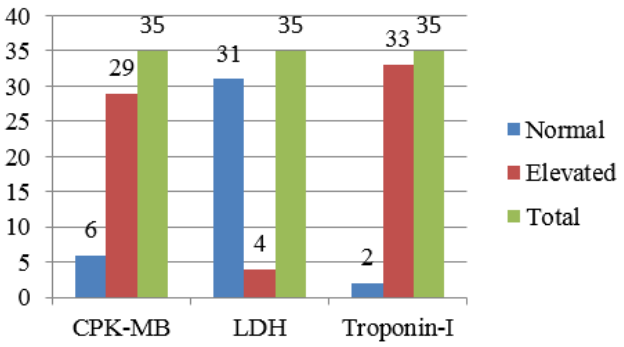

Fig. 1: Evaluation of enzyme marker readings

Table 6: Body mass index in relation to lactate dehydrogenase

			LDH		Total
			Positive	Normal	
BMIGR	Normal	Count	5	1	6
		% within BMIGR	83.3%	16.7%	100.0%
	Overweight	Count	21	8	29
		% within BMIGR	72.4%	27.6%	100.0%
Total		Count	26	9	35
		% within BMIGR	74.3%	25.7%	100.0%

Table 7: Evaluation of enzyme marker readings

	CPK-MB	LDH	Troponin-I
Normal	6	31	2
Elevated	29	4	33
Total	35	35	35
Percentage%	74	14	94

Table 8: Statistical analysis of coronary arteries block with standard deviation

		CPK-MB	LDH	TROPONIN_I
N	Valid	35	35	35
	Missing	0	0	0
Mean		30.7714	431.6	0.3014
Std. Deviation		4.55093	46.9187	0.04306
Minimum		23	320	0.22
Maximum		40	490	0.4

Table 8 Shows the statistical analysis of blocked coronaries and corresponding enzyme values. The mean CPK-MB level was found to be 30.77 with standard of deviation 4.55. Where as the mean LDH level was 431.6 with standard of deviation 46.91. The mean Troponin-I level was 0.3 with standard of deviation 0.04. These observations were suggestive that Troponin-I is more specific as compared to CPK –MB and LDH. On application of Chi square test on this mean and standard deviation of cardiac markers sensitivity and specificity of the cardiac markers calculated as below: For CPK-MB: Sensitivity is 84% and specificity is 30%. For LDH: Sensitivity is 72% and specificity is 20 %. For Trop I Sensitivity is 92% and specificity is 74%.

3. Discussion

The selection of the most appropriate diagnostic modality plays an important role for the forensic experts to conclude the cause of death. Sudden cardiac death due to acute due to acute myocardial infarction constitutes a significant portion of the autopsies that are conducted by forensic pathologist. The role of enzyme marker become significant as the recognition of infarction by light microscopy using routine Haematoxylin –eosin staining is possible only if death has occurred at least 6 to 12 hours after the onset of ischemic injury.

Cardiac troponin, creatinine phosphokinase and are sensitive markers of myocardial damage within 48 hours of chest pain. The lactate dehydrogenase (LDH) isoenzyme has been the established marker for late diagnosis of myocardial infarction. Among the unexpected and undiagnosed sudden death, incidence of sudden death, incidence of ischemic heart disease is very high. As such ,opining as to cause of death at autopsy also becomes not easy, So as after keeping in mind many studies are conducted to evaluate the roll of gross morphological, histopathological and biochemical (cardiac Troponin-I) parameters in ascertaining the cause of death to ischemic heart disease as per Mustafa GH et al.[7]

As per the study conducted by Gary Ross et al Creatine phosphokinase similar to other serum marker is not highly specific for cardiac disease. Several condition that can cause false elevation of CPK-MB levels include Rhabdomyolysis, Renal failure, Hypothyroidism, Heart failure. According results of this study, sensitivity of cardiac troponin was 85% which is highly significant and sensitive and used to definite positive value, and when there is skeletal muscle injury, the troponin I level is only elevated if there is concomitant myocardial damage. The same results are noted in my present study as out of 35 cases, in 29 cases CPK-MB levels are elevated and on after application of statistical analysis sensitivity of CPK-MB is found 84% and specificity is 30%. The results of the present study are correlated and similar with the Gary Ross et al study.[8]

Steen Hansen et al determined the Troponin-I expression in 46 autopsied hearts using an immunohistochemical technique. In result of this study Troponin-I is like myoglobin, Myosin and other protein muscle component of the normal myocardial cells and appear in elevated serum concentrations after acute myocardial infarction because of leakage from the damaged myocardial cells and then stated that cardiac troponin-I is specific for heart muscle cells and if not found in other tissues. The results of this study are consistent with the present study as Troponin-I is elevated in serum in postmortem examination of deceased having history of chest pain and myocardial infarction. In conclusion it can be said that evaluation of immunohistochemical expression of cardiac troponin-I apparently represent the highly sensitive marker of early myocardial infarction.[9]

Luciano Babuin et al showed that the Troponin I is an established marker and also provides robust prognostic information of myocardial infarction, abnormally the cardiac troponin I define the use of present state of the art biomarkers for the diagnosis of patients with cardiovascular disease, and also states that because of the maximum sensitivity of cTroponin I, elevations are common in serum in postmortem examination in case of cardiovascular disease, the results of the Luciano Babuin study are similar with the present study with regard to cardiac marker Troponin I study, as per the present study result cardiac Troponin I marker is highly sensitive and specific ,so as Troponin I carries significant prognostic importance in the diagnosis of myocardial infarction or heart disease.[10]

Roderic P.MacDonald et al showed that the determination of serum lactic dehydrogenase as an aid in the diagnosis of acute myocardial infarction, and LDH determination, not ordinarily necessary for the diagnosis of acute myocardial infarction. It is helpful when the ECG patterns masks the recent changes of acute MI. It was demonstrated that the value of LDH determination as an aid in the diagnosis of acute myocardial infarction and LDH determinations are most useful in the diagnosis of coronary artery disease. The present study found that the lactate dehydrogenase is elevated in 4 number of cases out of 35 cases, so as per study Lactate dehydrogenase enzyme evaluation is not useful also not aid in diagnosis of myocardial infarction. As per results of the present study, after analysis sensitivity and specificity of lactate dehydrogenase are 70% and 28%, so due to poor specificity of lactate dehydrogenase, LDH is not helpful and having poor prognostic importance in diagnosis of myocardial infarction.[11]

Mellisa A et al stated that a cardiac troponin I marker kinetics dictate the sensitivity of troponin-I which improves with time. The sensitivity of troponin I at the time of hospital admission ranges from 25 to 65% and increase to 59 to 90% at 6 to 8 hour after death. They observed that troponin kinetics can complicate very early detection of myocardial infarction, the specificity of Troponin-I does not vary significantly over time. The specificity of Troponin-I is on the order of 83 to 98%. The early detection of MI is crucial to the to the preservation of cardiac function, troponin I is an extensively sensitive marker of myocardial necrosis and is necessary for establishing the diagnosis of myocardial infarction. On the other hand in the present study after data analysis it was concluded that troponin I is highly sensitive. In analysis of troponin-I readings in 35 cases it was calculated that sensitivity of troponin I is 92% which is similar to the study by Mellisa et al.[12]

Christopher Heeschen et al, stated that by using defined threshold values and the employed test systems, single testing of cTnI within 12 hours after chest pain onset was appropriate for risk stratifications. In results it is revealed that cardiac Troponin are essential markers for the diagnostic and therapeutic risk stratification of patients suspected of having acute coronary syndrome. For this clinical challenge, the evaluated troponin assay provide convincing analytical sensitivity and specificity when the defined threshold values are used. The results of the study by Christopher Heeschen et al, are similar to the present study, as due to high sensitivity and specificity of cardiac Troponin-I it can be used for analytical convincing diagnosis of heart pathology in sudden death patients.[13]

4. Conclusion

It was concluded that for the diagnosis of myocardial infarction it is important to perform serial measurement of cTnI because the first measurement may still be negative when the case presents early after the onset of symptoms. There is need for further studies on the larger scale with multiple variables. Considering the sample size of the present, this pilot project is the first attempt in this comparatively less explored area. Further exploratory work is recommended.

5. Source of Funding

None.

6. Conflict of Interest

None.

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