

# Creditability of Cardiac Biomarkers in Sudden Cardiac Death

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## Abstract

**Background:** Natural deaths constitute a significant portion of total deaths cases received for autopsy in general. Cardiovascular system occupies the vast majority of natural death causes. Sudden cardiac death is a catastrophic complication of a number of cardiovascular diseases and affect all ages. Death is mostly unexpected and has a devastating impact on both the surviving family and community. Clinicians use cardiac markers, highly sensitive and specific for detection of myocardial damage to screen living patients for acute myocardial infarction (AMI), however to that point, the utility of those markers for diagnosis of cardiac death in autopsy setting has not been fully established. **Materials and Methods:** A prospective postmortem case control study was carried out on 103 medico-legal cases referred to the Medico-Legal directorate in Baghdad during 6 months period in 2020. The cases under study were classified in to two groups, those died due to cardiac causes (53) as cases group, and those died due to traumatic causes (50) as control group. Blood samples were collected using disposable syringes to withdraw 3-5ml of blood then immediately centrifuged to separate the serum and stored at -20°C till biochemical analysis for cardiac biomarkers (High sensitive troponin I, MB fraction of Creatin kinase and Lactate dehydrogenase). **Results:** Males constituted 77% from the total number while females constituted 23%. The mean age of the total study group was 42.57±15.125 years with a range between 11-72 years. The total number of cases group were 53 case (77% male and 23% female) with a mean age of 48.89±12.566, compared with 50 cases as controls group from the total number (76% male and 24% female) with mean age of 35.88±14.825. Sensitivity of High sensitive troponin I was 96.2% which was acceptable and it's specificity for diagnosis of sudden cardiac causes of death was 22% which was very low. While Sensitivities of MB fraction of Creatin kinase and Lactate dehydrogenase were 96.2% and 94.3% respectively and their specificities were 6% and 14% respectively. There were no correlations between post mortem interval and all three biochemical parameters levels. **Conclusion:** High sensitive troponin I, MB fraction of Creatin kinase and Lactate dehydrogenase were not reliable as diagnostic biomarkers for sudden cardiac deaths without gross postmortem and histopathological examination. There were no correlations between the three biomarkers (High sensitive troponin I, MB fraction of Creatin kinase and Lactate dehydrogenase) and the post mortem interval.

**Keywords:** Biomarkers, Cardiac Death, hs. Troponin I, CK-MB, LDH.

## Introduction

Natural deaths obviously constitute a significant portion of deaths, which are submitted for autopsy and investigation of death daily. In most of the natural

deaths, the death occurs suddenly or unexpectedly without any obvious disease <sup>(1)</sup>. Sudden death account for approximately 2/3 of forensic autopsies <sup>(2)</sup>. Sudden cardiac death is a catastrophic complication of a number of CVD and affect all ages. Death is mostly unexpected and has a devastating impact on both the surviving family and community <sup>(3)</sup>. Cardiac related deaths are increasing in trends and particularly in males <sup>(4)</sup>. Traditional cardiovascular risk factors such as D.M,

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obesity, dyslipidemia, H.T have all been linked to sudden cardiac death<sup>(5)</sup>. Sudden cardiac death is defined as sudden natural and unexpected death due to various existing cardiac pathology if witnessed within 1 hr. of the onset of symptoms, otherwise within 24hrs. after the late was last seen alive<sup>(6)</sup>. Sudden cardiac deaths due to acute myocardial infarction constitutes a significant percentage of caseload for death investigators, coroners, and forensic pathologist.<sup>(7)</sup> The highest risk of fatality occurs within the initial hours of the beginning of AMI<sup>(8)</sup>.

cTn is released from injured cardiomyocytes approximately 3hrs after ischemic event<sup>(9)</sup> and it peaks at 12hrs. and remains high for at least 144hrs<sup>(10)</sup>. CK-MB release occurs from dead cardiac cells within 3-4 hrs. after the onset of MI symptoms, and engaging in a peak between 12-24 hrs. then drops down to ordinary within 48 hrs.<sup>(11,12)</sup>. While LDH started to rise in blood between 12-24 hrs. and peaks within 48-72 hrs. and remains high for 7-12 days then starts to decrease<sup>(13)</sup>. Current study aims: to evaluate the creditability of cardiac biomarkers (Hs. troponin I, CK-MB and LDH) in sudden cardiac death in comparison to postmortem gross and histopathological examinations. Furthermore, to determine the association of cardiac biomarkers (Hs. troponin I, CK-MB, LDH) with post mortem interval.

### Materials and Methods

A prospective postmortem case control study was carried out on 103 medico-legal cases referred to the medico-legal directorate in Baghdad during 6 months period in 2020. Of these 103 cases, 79 cases were males and 24 cases were females. Their age was ranged from (11-72) years, with a mean of  $42.57 \pm 15.125$  years of age.

The cases under study were classified in to two groups, those died due to cardiac causes (53) as cases

group, and those died due to traumatic causes (50) as controls group.

Cases included in this study when death was eye witnessed and circumstances of death was evident and clear as well as when PMI was less than or equal to 12hrs. The study excluded the following cases: when PMI more than 12hrs., decomposed cadavers, infant and children less than 11 years and if blood hemolysis is evident.

Blood samples were collected using disposable syringes to withdraw 3-5ml of blood and were immediately centrifuged to separate the serum and stored at  $-20^{\circ}\text{C}$  till biochemical analysis for cardiac biomarkers.

Gross examination of the heart was conducted in the autopsy room.

In all cases a small piece of tissue sample was taken from suspicious heart muscle (pale and yellowish areas surrounded by an area of hyperemia) and kept in 10% formalin for histopathological examination.

### Results

Males in the total study cases constituted 77% while females constituted 23%. The mean age of the total study group was  $42.57 \pm 15.125$  years with a range between 11-72 years. The total number of cardiac cases were 53 case( 77% male and 23% female) with mean age of  $48.89 \pm 12.566$ , compared with 50 cases as controls group in total number(76%male and 24% female) with mean age of  $35.88 \pm 14.825$ .

Post mortem levels of high sensitive troponin I ( hs.cTnI), CK-MB and LDH were higher in cardiac cases.

Sensitivity of hs. Troponin I was 96.2% which was acceptable and it's specificity for diagnosis of sudden cardiac causes of death was 22% which was very low as shown in table (1).

**Table (1): Sensitivity, specificity, positive and negative predictive value of high sensitive troponin I in total study cases.**

			Histopathology of cases and controls		Total
			negative	positive	
High sensitive troponin I of cases and controls groups(ng/L)	normal	Count	11	2	13
		% within High sensitive troponin I of cases and controls groups(ng/L)	84.6%	15.4%	100.0%
		% within Histopathology of cases and controls	22.0%	3.8%	12.6%
	high	Count	39	51	90
		% within High sensitive troponin I of cases and controls groups(ng/L)	43.3%	56.7%	100.0%
		% within Histopathology of cases and controls	78.0%	96.2%	87.4%

■ Sensitivity, ■ Positive predictive value  
■ Specificity, ■ Negative predictive value

Sensitivity of CK-MB was 96.2 which was acceptable and it's

specificity for diagnosis of sudden cardiac causes of death was 6% which was very low as illustrated in table (2).

**Table (2): Sensitivity, specificity, positive and negative predictive value of CK-MB in total study cases.**

			Histopathology of cases and controls		Total
			negative	positive	
CK-MB of cases and controls groups(U/L)	normal	Count	3	2	5
		% within CK-MB of cases and controls groups(U/L)	60.0%	40.0%	100.0%
		% within Histopathology of cases and controls	6.0%	3.8%	4.9%
	high	Count	47	51	98
		% within CK-MB of cases and controls groups(U/L)	48.0%	52.0%	100.0%
		% within Histopathology of cases and controls	94.0%	96.2%	95.1%

■ Sensitivity, ■ Positive predictive value  
■ Specificity, ■ Negative predictive value

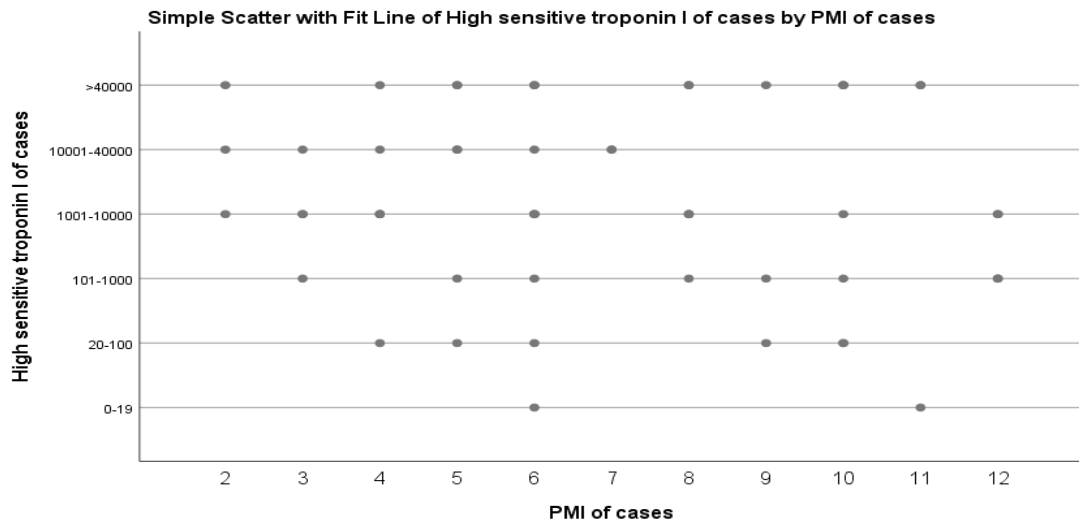
Sensitivity of LDH was 94.3% which was acceptable while it’s specificity for the diagnosis of sudden cardiac causes of death was 14% which was very low as illustrated in table (3).

**Table (3): Sensitivity, specificity, positive and negative predictive value of LDH in total study cases.**

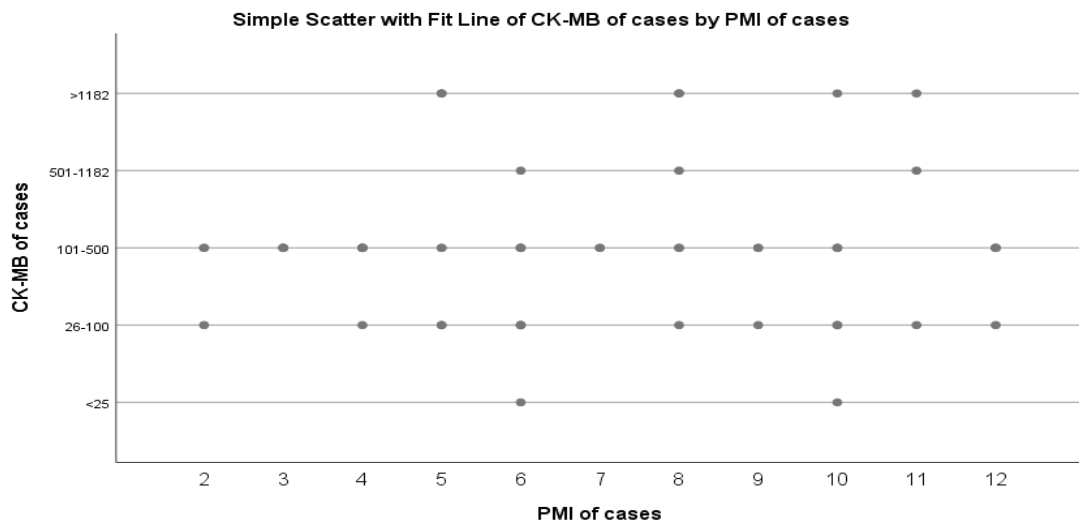
			Histopathology of cases and controls		Total
			negative	positive	
LDH of cases and controls groups(U/L)	normal	Count	7	3	10
		% within LDH of cases and controls groups(U/L)	70.0%	30.0%	100.0%
		% within Histopathology of cases and controls	14.0%	5.7%	9.7%
	high	Count	43	50	93
		% within LDH of cases and controls groups(U/L)	46.2%	53.8%	100.0%
		% within Histopathology of cases and controls	86.0%	94.3%	90.3%

■ Sensitivity, ■ Positive predictive value  
■ Specificity, ■ Negative predictive value

There was no correlation between post mortem interval and all three biochemical parameters levels (p value is significant at 0.05) as shown in figure (1, 2, 3)



**Figure (1): Correlation between Hs. troponin I and PMI.**



**Figure (2): Correlation between CK-MB and PMI.**



**Figure (3): Correlation between LDH and PMI.**

## Discussion

Males in our total study cases were higher than females. This finding was similar to study done previously<sup>(14)</sup>. Males predominance may be due to number of factors include the following: males are more susceptible to emotional and psychological stress because of their higher responsibilities towards their families in our culture, as well as risk factors especially hypertension and smoking are more common in male than in female<sup>(15)</sup>; in addition to the effect of life style. Sensitivity of Hs. Troponin I was high and acceptable (96.2%) while specificity was low (22%). Unfortunately we couldn't found a similar study to compare with. In our study post mortem diagnosis of sudden cardiac causes of death by using CK-MB revealed that the sensitivity of this marker was acceptable while the specificity was very low. This finding agrees with a previous study which showed lack of significance in serum levels of CK-MB between the different groups<sup>(17)</sup>. While the study disagrees with another study which showed that the levels of CK-MB were significantly lower in study group than in control group<sup>(14)</sup>. On the other hand our result disagrees with a previous study that showed a higher specificity percentage and almost similar sensitivity which was closer to our finding<sup>(14)</sup>. This difference might be due to a small number of cases and controls included in their study in addition to the short post mortem interval in comparison to our study. In our study regarding LDH biomarker, there was no statistically significant differences in profile concentrations between the cases group and controls group, confirming the low diagnostic validity of this biomarker. This result was similar to a previous study<sup>(14)</sup>. There were no significant differences in the levels of all the three biomarkers (hs. cTnI, CK-MB and LDH) between cases and controls groups. This may be due to many factors including: the survival time after symptoms started, any other injury to the heart which may cause increase in the levels of biomarkers by diffusion even if the injury was due to non-cardiac injury as well as any degree of hemolysis will affect the results. Regarding the correlation between the biomarkers and post mortem interval, our study showed no correlation

between all three biomarkers and post mortem interval. This finding was similar to the study conducted previously which showed no correlation between CK-MB and PMI, but showed a very weak correlation between PMI and troponin I (cTnI) levels in serum<sup>(16)</sup>. While there were positive correlations between the 2 markers (cTnI & CK-MB) and PMI in a previous study done in Erbil<sup>(17)</sup>. This difference might be due to longer PMI used in their study which ranged between 1-18 hrs., while it was less than or equal to 12 hrs. in this study.

## Conclusions

- Hs. Troponin I, CK-MB and LDH were not reliable as diagnostic biomarkers for sudden cardiac deaths without postmortem gross and histopathological examination.

- There were no correlations between the three biomarkers (hs. Troponin I, CK-MB and LDH) and post mortem interval.

## Recommendations:

Based on the findings and conclusions presented, the following recommendations are suggested:

1. Conducting a further study on a large sample of population of non-cardiac causes of death to create a post mortem normal range of the three biomarkers to be a base for future post mortem studies of sudden cardiac deaths with better accuracy.
2. A comparison study of the three biomarkers on living cardiac inpatients and postmortem cardiac causes of death to evaluate the differences.

**Conflict of Interest:** None

**Funding:** Self

**Ethical Clearance:** Not required

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