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Predictive Role of Cardiac Troponin I, Creatine Kinase-Mb and Electrocardiogram in Early Assessment of Acute Cardiotoxicity in Patients Poisoned by Cardiotoxic Drugs and Toxins

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Authors' contribution

This work was carried out in collaboration among all authors. Author SEDM designed the study, performed the statistical analysis and wrote the first draft of the manuscript. Authors MMS and MAH managed the analyses of the study. Author AMS managed the literature searches and advice of the protocol. All authors read and approved the final manuscript.

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ABSTRACT

Background: In spite speedy development of clinical toxicology researches and protocols cardiovascular failure in severe acute intoxication remains a leading cause of death. Early cardiovascular risk assessment in acutely intoxicated patients is a must nowadays.
This study aims to evaluate the role of ECG, serum cardiac troponin I (cTnI) and creatine kinase myocardial band (CK-MB) for early detection of cardio-toxicity in acutely poisoned patients.
Methods: Prospective study was carried on100 patients with acute cardiotoxicity by drugs and toxins known to cause cardiac injury admitted to Sohag University hospitals, informed written consent has been obtained from each patient; ECG and biochemical analysis of serum cTnI and CK-MB were estimated in all studied patients.

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Results: (90%) of studied patients had complete free recovery, (4%) discharged with complications and (6%) of patients died. ECG test can be used as a predictor of mortality and had sensitivity 100%, specificity 46.8% and negative predictive value (NPV) 100%. Serum cTnI was highly significantly increased with death hence could be used as predictors of outcome. While serum CK-MB couldn't be used as an outcome predictor. ROC curve analysis to assess serum cTnI as a predictor of mortality of acute cardiovascular toxicity with cut off > 1.0 ng/ml had sensitivity 100%, specificity 89.4% and NPV 100% with excellent diagnostic characteristic (accuracy rate 96.4%). There is no significant difference of serum CK-MB and serum cTnI among cardiac drugs toxicity patients and non-cardiac toxins patients.
Conclusion: the study concluded that ECG and serum cTnI can be used as a predictor of mortality. Also, the protocol of management will be same in acute cardiotoxicity by cardiac drugs and non-cardiac drugs and toxins.
Recommendation: the study recommends combining of ECG changes and serum cTnI as they can early detect acute cardiovascular effects in acutely poisoned patients.

Keywords: Cardiotoxicity, ecg; ctni; ck-mb.

1. INTRODUCTION

The annual report of the American association of poison control centres showed that cardiovascular failure remains a leading cause of death in severe acute drug intoxication as accounted for 9.4% of the 2,813 fatalities [1].

Recently, cardiac biomarkers have become important adjuncts to have optimal acute cardiac care [2].

ECG is a non-invasive, relatively inexpensive diagnostic test that provides important information regarding not only the heart but also non-cardiac events impacting the cardiac system [3].

CK-MB has long been used as a biomarker for myocardial injury and reasonably specific as they can be elevated after skeletal muscle injury or vigorous exercise, while cardiac troponins are considered the most specific and highly sensitive markers of myocardial injury, demonstrating superiority in diagnosis as in acute myocardial infarction as shown in many studies [4,5].

There are many studies for using these biomarkers in acute coronary syndrome and many diseases could have myocardial injury also on determining chemotherapeutic drugs cardiotoxicity [6,7,8].

Early cardiovascular risk assessment for acutely poisoned patients is a must nowadays to prevent morbidity and mortality and improving utilization of hospital resources [9].

There is a need nowadays for cardiovascular risk stratification in acutely poisoned patients and future studies should combine a cardiac biomarker approach with an ECG approach for this need [10].

1.1 Aim of Study

This study aims to:

1. Evaluate the role of (ECG, serum cTnI and CK-MB) for early detection of cardio-toxicity in acutely poisoned patients
2. To assess the efficacy of serum CK-MB and cTnI as indicators in assessing the severity of various forms of cardiac injury due acute toxicity.
3. To make a comparison between the increase in serum cTnI and CK-MB caused by acute toxicity with cardiac drugs in compare with non-cardiac drugs or toxins known to have a cardiotoxic effect.

2. MATERIALS AND METHODS

2.1 Study Design

A prospective study was carried out on 100 patients with acute cardiotoxicity by drugs and toxins known to cause cardiac injury admitted to Sohag hospitals during the period from April 2018 to September 2019.

2.2 Patients

According to equation [n = (Z1-α + Zβ) 2(S1 + S2)2/(μ1-μ2)2] by Hassanian et al. [11] in his Iranian study of QT dispersion to determine sample size with significant results by using this equation we need at least 59 patients to have significant results so we decided to collect 100 patients' sheets to have significant results.

2.3 Inclusion Criteria

All patients admitted to Sohag University hospitals with acute cardiotoxicity by drugs and toxins known to cause cardiac injury. The type of medication or toxin was determined according to the history given by the patient him/herself if he/she is conscious of admission. If the patient is unconscious, the history was taken from the relatives.

2.4 Exclusion Criteria

Patients with underlying cardiac diseases like previous myocardial infarction will be excluded. Also, those who take chemotherapeutic drugs will be excluded.

The following data were collected from the sheet of each patient

1. Socio-demographic data
2. Full history
3. Clinical examination
4. Investigations
5. Treatment
6. Outcome

2.5 Electrocardiogram

ECG parameters from the first ECG taken on intensive care unit (ICU) or emergency department (ED) were recorded from all patients as

- Rate
- Rhythm
- QT and PR intervals (QTc interval considered prolonged if greater than 0.45 seconds in men and 0.47 seconds in women) [12]
- QRS complex
- ST segment abnormality
- T wave changes

2.6 Serum CK-MB & cTnI

Venous blood samples (5 ml) were collected from patients on admission to CCU or ICU. The blood samples were collected in vials. Blood allowed to clot then serum was separated by centrifugation. The serum was used for the analysis of CK-MB and cTnI.

- cTnI levels were determined using a Beckman Coulter Access 2 Immunoassay System**.**
- CK-MB measurements were carried out on a Beckman Coulter AU480 Chemistry System**.**

The upper reference limits for the quantitative cardiac markers used in this study were: CK-MB activity ≥25 IU/L; cTnI ≥ 0.4 ng/mL [13].

2.7 Statistical Analysis

The collected data was coded and verified before computerized data entry and were statistically analysed using Statistical Package for the Social Science (SPSS) version 16 program and expressed in tables and charts.

Comparison between outcome groups was tested by using Chi-square test for qualitative data, and by using independent t-test for quantitative data. Linear regression analysis was used to identify significant predictors of Outcomes. P value: level of significance: P >0.05: Non-significant; -P < 0.05: Significant; P < 0.01: Highly significant; P <0.001: Very highly significant. Receiver operating characteristic curve (ROC) was used to assess predictors of outcome with their best cut off points, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The cut-off point with the best sensitivity, NPV and minimizes false positives was chosen. According to Mood et al. [14] AUCs between 0.7 and 0.8 were classified as “acceptable” and between 0.8 and 0.9 as “excellent” discrimination.

3. RESULTS

The prospective study was carried out on 100 patients of acute cardiotoxicity admitted to Sohag Hospitals. In the current study, the mean age was 16.3 years, 51% of the studied patients were males and 49% were females (Table 1). The different toxic agents enrolled in the study shown in (Table 2) it was found that CNS drugs occupied the highest percentages among studied patients (25%) then cardiovascular drugs and pesticides each had (15%), while, CO poisoning in the last just had (1%). The outcome of the patients as shown in (Table 3) revealed that (87%) of patients were discharged with complete recovery and (6%) of patients died, while, (4%) discharged with complication.

ECG changes among studied patients (Table 4)ECG readings during the first 24 hours of admission of the studied patients were normal in (44%), (28%) had sinus tachycardia, (9%) had sinus bradycardia, (4%) with prolonged QT and inverted T, (3%) had ST elevation, (2%) for each

heart block, AF and PVCs and (1%) for both sinus arrest and SVT. ECG test as a predictor of mortality (Table 5), ECG test had a sensitivity (100%) as all non-survivors had abnormal ECG, while, specificity was (46.8%) as only 44 patients had normal ECG among 94 survivors, PPV of ECG was (10.7%) as 6 patients died from total 56 had abnormal ECG and NPV was (100%) as all who had normal ECG survive. Relationship between ECG parameters analysis and mortality (Table 6) showed that all survivors had normal ECG. While, PVCs and SVT were observed as a sign of mortality in (100%), then, elevated ST (33.3%), prolonged QT (25%) and finally sinus bradycardia (11.1%). There was a statistically significant difference between ECG parameters changes as regards mortality by using Chi-square test as $p < 0.001$.

CK-MB measurements of all studied patients during their first 24 hours of admission shown in (Table 7) only (26%)of studied patients had

Table 1. Number and percentage of the studied patients as regard age and sex

Age groups (years)	Number	Percentage (%)
≤15years	57	57%
16-30years	28	28%
31-45years	7	7%
45-70years	8	8%
Total	100	100%
Mean ± standard deviation (SD) = 16.30± 17.392 years		
Sex	**Number**	**Percentage(%)**
Male	51	51%
Female	49	49%
Total	**100**	**100%**

Table 2. Percentages of the different types of toxic agents with cardio-toxic effects encountered in 100 acutely intoxicated studied patients

Toxic agents	No. of patients	Percentages	Total
Cardiovascular drugs (CVS)			
Beta-blockers (BBs)	6	6%	15%
Calcium channel blockers(CCBs)	4	4%	
Digoxin	5	5%	
CNS drugs			25%
Antipsychotics	10	10%	
Tricyclic antidepressants (TCAs)	3	3%	
Anticonvulsants	5	5%	
Benzodiazepines	2	2%	
Anticholinergics	2	2%	
Lithium	1	1%	
Lidocaine spray	1	1%	
Succinylcholine	1	1%	
Animal bites			14%
Scorpion	13	13%	
Snake	1	1%	
Pesticides			15%
Organophosphates (OPs)	8	8%	
Carbamate	7	7%	
Phosphides			5%
Zinc phosphate	2	2%	
Aluminum phosphate	3	3%	
Hydrocarbons	2	2%	2%
Hydrocarbons plus OPs	2	2%	2%
Drugs of abuse			12%
Opioids	4	4%	
Tramadol	3	3%	
Amphetamines	2	2%	
Cannabis	3	3%	
Carbon monoxide (CO)	1	1%	1%
Theophylline	4	4%	4%
Paraphenylenediamines (PPD)	5	5%	5%
Total	100	100%	100%

Table 3. Number and percentage of the outcome of all studied patients

Survivors	Out come	Number	%
Survivors	Complete recovery	87	87%
	Recovery with complications	4	4%
	Escaped	1	1%
	Get out against medical advice	2	2%
Non Survivors	Died	6	6%
Total		100	100%

Table 4. ECG parameters changes among all studied patients

ECG changes	Number	%
Normal	44	44%
Sinus tachycardia	28	28%
Sinus bradycardia	9	9%
Prolonged QT	4	4%
Sinus tachycardia and inverted T wave	4	4%
Elevated ST+ sinus tachycardia	3	3%
Heart block	2	2%
Atrial fibrillation (AF)	2	2%
Premature ventricular contractions (PVCs)	2	2%
Sinus arrest	1	1%
Supra-ventricular tachycardia(SVT)	1	1%
Total	100	100%

Table 5. Chi-Square statistical analysis of ECG changes and survivors versus non survivors and sensitivity, specificity, PPV and NPV of ECG test

ECG changes	Survivors patients	Non Survivors	Fisher exact-test	
	N=94	N=6	Total	p-value
Normal	44 (46.8%)	0 (0%)	44	0.02*
Abnormal	50 (53.2%)	6 (100%)	56	
Total	94(100%)	6(100%)	100	
Sensitivity=100%	Specificity=46.8%	PPV=10.7%	NPV=100%	

**P < 0.05 (significant) **P < 0.01 (highly significant) ***P < 0.001 (very highly significant)NS: Non significant ; PPV: positive predictive value; NPV: negative predictive value*

normal measurements, while, (5%) had shooting measurements. Serum cTnI measurements of all studied patients during their first 24 hours of admission shown in (Table 8) cTnI levels were normal in the majority of patients (74%), while, only (16%) had measurements above 1 ng/ml. Independent t-test statistical analysis of serum CK-MB and cTI about the outcome (Table 9) showed that there was no statistically significant difference between discharged and died patients as regards serum CK-MB (P-value 0>.05), while, there was very highly statistically significant difference between discharged and died patients as regards serum cTnI (P-value 0< .001).Independent t-test statistical analysis of serum CK-MB and cTI among (complicated recovered and died patients) and non-complicated recovered patients(Table 10).Linear regression analysis of serum CK-MB and cTI to detect predictors of mortality(Table 11). Both (Tables 10,11) showed that serum cTnI could be used as predictors of outcome and mortality of acute cardiovascular toxicity as there is the significant increase of serum cTnI in died and complicated recovery patients than patients discharged with complete recovery. While serum CK-MB showed no significant difference and couldn't be used in outcome and mortality prediction. Sensitivity, specificity and accuracy rate of serum cTI as a predictor of mortality in the current study is shown in (Table 12). ROC curve analysis to assess serum cTnI as a predictor of mortality of acute cardiovascular toxicity presented in (Fig. 1). Table (12) and (Fig. 1) revealed that cTnI with cut off > 1.0 ng/ml had sensitivity 100%, specificity 89.4% and NPV 100% with excellent diagnostic characteristic (accuracy rate 96.4%).Table (13) revealed that there is a highly significant difference in the mean of serum cTnI among patients with normal ECG and patients with abnormal ECG. Bar graph of independent t-test shown in (Fig. 2 and 3) highlighted that there was no significant difference of serum CK-MB and serum cTnI among cardiac drugs toxicity patients and non-cardiac toxins patients as (P value > 0.5).

4. DISCUSSION

Referrals to emergency departments due to intoxication remain to be important in terms of mortality and morbidity. Among these intoxications, cases with cardiac involvement should be closely monitored [15].

Studies should combine a cardiac biomarker approach with an ECG approach for risk stratification of drug overdose patients [10].

The present study was undertaken on 100 acutely poisoned patients by drugs and toxins with cardio-toxic effect who admitted to Sohag hospitals.This study aimed to evaluate the role of (ECG, serum cTnI and CK-MB) for early detection of cardio-toxicity in acutely poisoned patients and their efficacy as indicators of mortality.

In the present study the majority of patients (57%) fall in the age group ≤15 years. In contrast to this study Hussien et al. [16] who studied only cardiovascular drugs found that the majority of studied patients were in the age group of (18- 24) years presenting 50% of cases followed by the age group (25-40) years by 37.5%. Also, Karakilic et al. [15] in Turkey found that the mean age was 33.36±12.23 when they studied relationship between BNP and cardiovascular toxicity. This was explained by Hassan and siam [17] as most of the poisonings by medications and pesticides were due to accidental ingestions by infants and young children.

Table 6. Chi-Square statistical analysis showing relationship between ECG parameters analysis and mortality in the current study

ECG parameters	Outcome		Total
	Died(6)	Survivors (94)	
Normal	0	44	44
Sinustachycardia	0	28	28
Sinusbradycardia	1	8	9
Heart block	0	2	2
Atrial fibrillation (AF)	0	2	2
PVCs	2	0	2
Sinus arrest	0	1	1
ProlongQT	1	3	4
Supra-ventricular tachycardia	1	0	1
Sinus tachycardia & inverted T wave	0	4	4
Elevated ST+sinus tachycardia	1	2	3
Total	6	94	100
Chi-aquare	X=59.12		
	P-value=0.000***		

**P < 0.05 (significant) **P < 0.01 (highly significant) ***P < 0.001 (very highly significant)NS: Non significant*

Table 7.CK-MB measurements percentages among all studied patients

CK-MB		
Normal (<25 IU/l)	26	26%
25-100 IU/L	56	56%
100-200 IU/L	9	9%
200-300 IU/L	4	4%
1500-2500	5	4%
Total	100	100%

Table 8.Serum troponin I measurements percentages, mean, mode, median and standard deviation among all studied patients

Serum troponin I		
Normal (<0.4ng/ml)	74	74%
0.4-1ng/ml	10	10%
1-3ng/ml	4	4%
3-6ng/ml	3	3%
6-9ng/ml	5	5%
9-12nglml	3	3%
12-15ng/ml	1	1%
Total	100	100%

Mean ± standard deviation= 1.16± 2.78 Median= 0.1 Mode= 0. 1 Range: 0.01-14.59 ng/ml

Table 9. Independent t- test statistical analysis of serum CK-MB and cTI in relation to outcome

Laboratory parameters		Survivors N=94	Died N=6	Independent t-test T	P-value
Serum CK-MB (Normal<25 IU/l)	Normal (<25 IU/l)	26 (27.7%)	0 (0%)	-0.358	0.721NS
	25-100 IU/L	53 (56.4%)	3 (50%)		
	100-200 IU/L	6 (6.4%)	3 (50%)		
	200-300 IU/L	4 (4.3%)	0 (0%)		
	1500-2500	5 (5.3%)	0 (0%)		
	Mean± SD	1.56±444	91.3±37.66		
	Range	10-2500	30-138		
Serum cTI (Normal<0.4ng/ml)	Normal (<0.4 ng/ml)	74 (78.7%)	0 (0%)	7.143	0.000***
	0.4-1 ng/ml	10 (10.6%)	0 (0%)		
	1-3 ng/ml	3(3.2%)	1(16.7%)		
	3-6 ng/ml	3 (3.2%)	0 (0%)		
	6-9 ng/ml	2 (2.1%)	3 (50%)		
	9-12 ng/ml	1 (1.1%)	2 (33.3%)		
	12-15 ng/ml	1 (1.1%)	0 (0%)		
	Mean± SD	0.75±2.2	7.59±3.23		
	Range	0.01-14.60	1.5-10.70		

**P < 0.05 (significant) **P < 0.01 (highly significant) ***P < 0.001 (very highly significant)NS: Non significant SD: Standard deviation*

Table 10. Independent t-test statistical analysis of serum CK-MB and cTIamong (complicated recovery and diedpatients) and non-complicated recovery patients

Variable		Complicated recovery & died patients N=10	Non complicated recovery N=90	Independent t-test T	p-value
CK_MB	Mean± SD	2.78±641.4	1.38±403	0.972	0.33 NS
cTI	Mean± SD	4.6±4.5	0.7±2.25	4.55	0.000***

**P < 0.05 (significant) **P < 0.01 (highly significant) ***P < 0.001 (very highly significant) NS: Non significant SD: Standard deviation*

Table 11. Linear regression analysis of serum CK-MB and cTnI to detectpredictors of mortality

Predictors	Un-standardized Coefficients		Standardized Coefficients	Independent t-test	
	B	Std. Error	Beta	T	p-value
CK_MB	2	0.00	0.036	0.358	0.721 NS
cTnI	-0.050	0.007	-0.585	-7.143	0.000***

**P < 0.05 (significant) **P < 0.01 (highly significant) ***P < 0.001 (very highly significant)NS: Non significant*

Table 12. Sensitivity, specificity and accuracy rate of serum cTnI as a predictor of mortality in the current study

Variable	Cut off point	AUC (Area under the curve)	p-value	Sensitivity (%)	Specificity (%)	PPV (%) (Positive predictive value)	NPV (%) (Negative predictive value)	Accuracy rate
serum cTI	>1.0 ng/ml	0.964	0.000***	100%	89.4%	37.5%	100%	96.4%

**P < 0.05 (significant) **P < 0.01 (highly significant) ***P < 0.001 (very highly significant) NS: Non significant*

Table 13. Independent t-test statistical analysis of serum cTnI among studied patients showing ECG changes

Variable		Patients with normal ECG N=44	Patients with abnormal ECG N=56	Independent t-test T	p-value
cTnI	Mean± SD	0.21±0.36 ng/ml	1.91±3.5 ng/ml	-3.165	0.002**

**P < 0.05 (significant) **P < 0.01 (highly significant) ***P < 0.001 (very highly significant)NS: Non significant SD: Standard deviation*

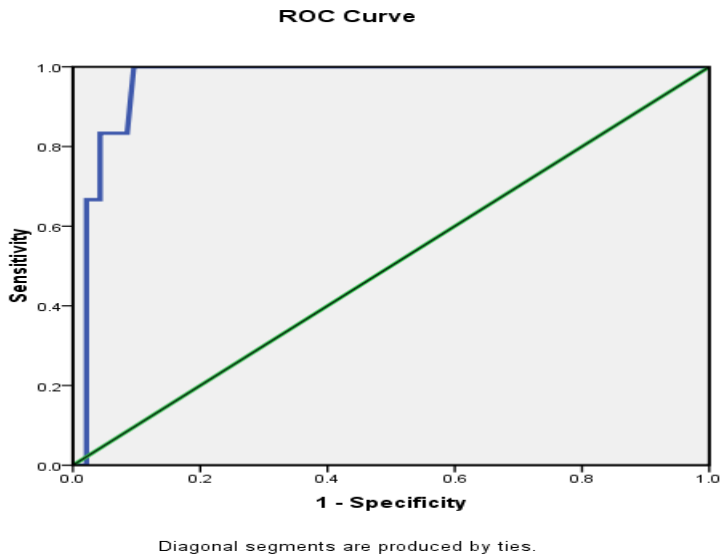

Fig. 1. Receiver Operator Characteristic (ROC) Curve of serum cTnI

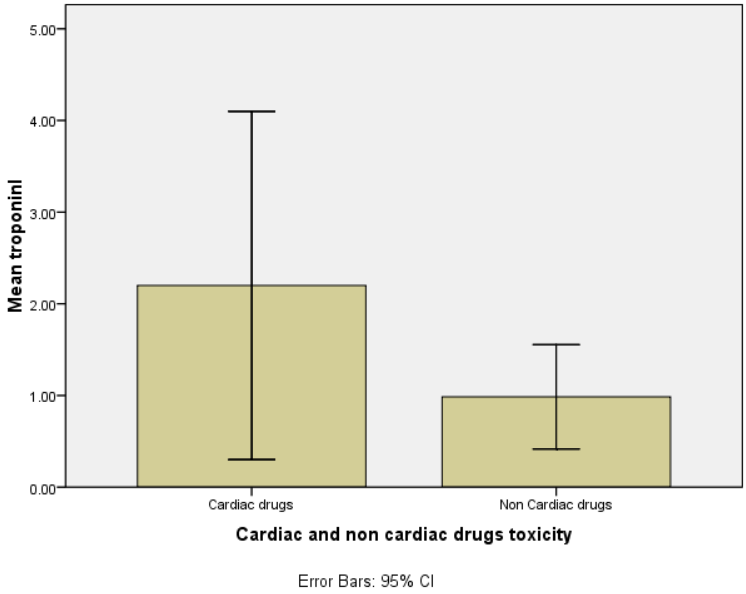

Fig. 2. Bar graph illustrates independent t test statistical analysis of serum cTI among cardiac drugs toxicity patients and non cardiac toxins patients

In the current study 94% survived and 6% of patients died.Varieties of toxins were involved in the study as pesticides and hydrocarbons, therapeutic drugs as (CVS drug, CNS drugs and theophylline), drugs of abuse, bites and PPD. CNS drugs occupied the highest percentages among studied patients 25% then cardiovascular drugs and pesticides each have 15%, while, CO poisoning in the last just have 1% this agree with Tanta study of ECG changes by Heshmat et al. [3] who found that major toxic agents were therapeutic drugs and pesticides. Also, the cardiovascular drugs showed that BBs (6%), digitalis (5%) and CCBs (4%) this agree with *Hussein (*et al. (2018) who showed that beta blockers toxicity was the commonest cardiovascular drug toxicity followed by digitalis and finally calcium channel blockers.

The collected data revealed that ECG readings during the first 24 of admission of the studied

patients were normal in (44%), (28%) had sinus tachycardia, (9%) had sinus bradycardia, (4%) for each prolonged QTc and inverted T, (3%) had ST elevation, (2%) for each heart block, AF and PVCs and (1%) for each sinus arrest and SVT. These results partially coincided with the study conducted on 282 cases of acute poisoning admitted to Tanta Poison Center during the period from the start of July - 2009 to the end of June - 2010 by Heshmat et al. [3] to evaluate the ECG changes they found that 58.51% of patients had ECG changes. These were: sinus tachycardia followed by prolonged QTc interval then sinus bradycardia and lastly nodal tachycardia.

Cardiac toxicity is a common finding in patients who have been poisoned with a wide variety of chemical agents. Both cardiac drugs and other medications can cause ECG changes [18].

In this study ECG test as predictor of mortality had sensitivity 100%, specificity (46.8%), PPV (10.7%) and NPV (100%).PVCs and SVT were observed as a sign of mortality in (100%), then, elevated ST (33.3%), prolong QTc (25%) and finally sinus bradycardia (11.1%). There was very highly statistically significant difference between ECG changes as regards mortality by using Chi-square test as p <0.001.

These findings came with Manini et al. [9] who reported that evidence of abnormality in initial ECG is strongly associated with acute cardiovascular adverse effects in suspected poisoning, with 94.1% sensitivity, 96.2% NPV and 95% specificity and ECG changes that correlate with bad prognosis during suspected acute poisoning include QT prolongation, non-sinus rhythm and ventricular ectopy. Also, in a cohort study by Hirose et al. [19] they also showed how PVCs can be a bad sign as they demonstrated that healthy men with PVCs had significantly increased cardiac mortality compared with participants without PVCs in their study.

In the current study serum CK-MB measurements were normal only in (26%), while, (5%) had shooting measurements with mean 1.56±444 in survivors and 91.3±37.66 in non survivors no statistically significant difference between survivors and died patients as regards serum CK-MB.

While, serumcTnI measurements of all studied patients were normal in the majority of patients (74%), while, only (16%) had measurements above 1ng/ml with mean 0.75±2.2 in survivors and 7.59±3.23 in non survivors there is high statistical significance difference between discharged and died patients as regards serum cTnI (P value 0<.001).

By using linear regression analysis with the indices studied in the current work showed that serum cTnI were significantly increased with death hence could be used as predictors of outcome. While serum CK-MB couldn't be used as outcome predictor.

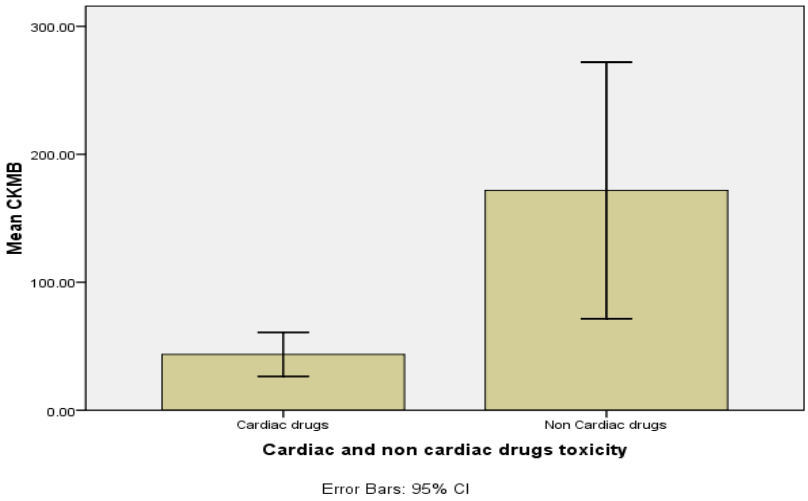

Fig. 3. Bar graph illustrates independent t test statistical analysis of serum CK-MB among cardiac drugs toxicity patientsand non cardiac toxins patients

This came to agree with Manini et al. [10] who reported that cTnI had excellent diagnostic test characteristics to predict acute drug overdose mortality while, CK-MB couldn't be used as a predictor.

This study agree with several studies [5,20,4,21] who reported that cardiac troponins are considered the most specific and highly sensitive markers of myocardial injury, demonstrating superiority in diagnosis as in acute myocardial infarction and should replace CK-MB as the diagnostic 'gold standard' for the diagnosis of myocardial injury.

In contrast Azab and Elawady [22] reported that Increased CK-MB level was found to be predictors of severe scorpion envenomation, also, Mohamed et al. [23] found no association between cTnI elevation as a marker of cardiotoxicity and clinical predictors of severity of acute drug overdose due to TCAs and antipsychotics and *Khater and Sarhan (2015*) mentioned that half of the deaths due to zinc phosphide cardiotoxicity occurred with negative troponin I, while, in harmony with us *Abdel* Wahab et al. [24] recorded that metal phosphides can induce cardiotoxicity and the significant increase in serum cTnI and can depend on it as a predictor of severity.

In the present study ROC curve analysis to assess the predictor of outcome of acute cardiovascular toxicity, the area under the curve for serum cTnI at cut off >1.0 ng/ml had sensitivity 100%, specificity 89.4% and NPV 100%.

In harmony Manini et al. [10] used only serum cTnI initial and peak as predictor of mortality in drug overdose ,his study agree with us as the ROC curve reveals excellent AUC for prediction of mortality using the initial cTnI with accuracy rate 87% while, utilizing the peak cTnI, instead of the initialc TnI, did not improve the AUC 84%.Test characteristics for initial cTnI (90% specificity, 99% negative predictive value and concluded that that the initial cTnI had excellent diagnostic test characteristics to predict acute drug overdose mortality. Also, Abdel Wahab et al. ['24] on their study on metal phosphides found that troponin I at the cut off point ≥2.95ng/ml had sensitivity 100%, specificity 90.06% and accuracy rate 97%.

On the contrary Mohamed et al. [23] who studied the diagnostic ability of troponin to induce cardiotoxicity in acute TCAs and antipsychotics overdose with 100 % specificity, 35.1% negative predictive value and 62.5% accuracy rate at cut-off point>0.02 ng/mL. Besides they concluded from previous studies that in spite advantages of cardiac troponins of high specificity and sensitivity but still raise the number of unanswered questions including the assessment of suitable cut-off for drug-induced cardiotoxicity and determination of critical diagnostic window related to the optimal timing of sample collection, which may be drug-dependent.

Our study revealed that there was a statistically significant difference between patients with abnormal ECG parameters and patients with normal ECG parameters as regards serum cTnI (P value 0<.01). The mean of serum cTnI in normal ECG patients was (0.21±0.36) ng/ml; while, serum cTnI mean in abnormal ECG patients was elevated (1.91±3.5) ng/ ml.

Our results were in accordance with Manini et al. [25] who revealed that combining both ECG and serum cTnI to determine adverse cardiovascular events after acute drug overdose should be current guidelines to optimize the prediction of these patients and he concluded that abnormal ECG parameters such as (eg, QTc prolongation, ST elevation or depression, PVCs) should mandate evaluation of a serum cTnI as part of the initial ED evaluation of acute drug overdose.

The present work highlighted that mean of serum CK-MB was 43.67±31.1 in cardiac drugs toxicity and the mean of non-cardiac drugs toxicity was 1.71±465 with large SD due shooting of CK-MB level in case of PPD toxicity. Serum cTnI mean was 2.2±3.4 in cardiac drugs toxicity and the mean of non cardiac toxicity was 0.98±2.6, this can be due to increase cTnI in scorpion and aluminium phosphide cases.So, there is no significant difference of serum CK-MB and serum cTnI among cardiac drugs toxicitypatients and non cardiac toxins patientsas P value > 0.5.

This can be explained as Hussien et al. [16] who studied only cardiac drugs toxicity revealed that majority of patients had positive cTnI test. Kalawat et al. [26] found that troponin I was elevated in 26% of their studied patients after acute aluminium phosphide toxicity, also, Abdel Wahab et al. [24] revealed increase in serum cTnI in severe toxicity group of metal phosphides toxicity. In addition Sagarad et al. [27] predict myocarditis in scorpion sting envenomation by high serum cTnI.

5. LIMITATIONS OF THE STUDY

We didn't make confirmatory test in all cases, cases of drug abuse toxicity complete screening were done, also, digoxin level in cases of digoxin toxicity. We did not make an adjustment in our results for the intensity of treatment, which may affect the rate of mortality.

Despite these drawbacks, these data still provide important information and the current study is one of few studies in the assessment of serum cTnI and ECG as a predictor of mortality in acute cardiovascular toxicity in both cardiovascular drugs and non-cardiovascular drugs and toxins. Also, we are novel in comparing serum CK-MB and serum cTnI among cardiac drugs toxicity patients and non-cardiac toxins patients showing that there is no significant difference between the two groups and consequent in the management.

6. CONCLUSION

ECG and serum cTnI were significantly increased with death hence could be used as predictors of outcome, while, serum CK-MB couldn't be used as an outcome predictor.ECG changes and serum cTnI together (even qualitative test)promising early prediction of mortality in acute toxicity with improving pathway of care, the protocol of management and best use of hospital resources. The protocol of management will be the same in acute toxicity by cardiac drugs and non-cardiac drugs and toxins.

7. RECOMMENDATION

The study recommends combining of ECG changes and serum cTnI (even qualitative test) as they can early detect acute cardiovascular effects in acute toxicity hoping to improve pathway of care, protocol of management and the best use of hospital resources.We should run on standardize the same protocol of management of acute toxicity by both cardiac drugs and non cardiac drugs. Further studies should focus on how clinicians would be managing patients differentially if they have elevated cTnI during the hospital course. Clearly, patients with elevated cTnI require monitoring and consideration of critical care unit admission. In contrast, a negative cTnI was found to exclude fatality.Further studies are necessary to evaluate whether initiation of certain treatments should be empirically initiated for patients with elevated cTnI. Also, we need further studies to see effects of intensity of treatment on serial cTnI.

CONSENT

As per Sohag University hospitals standard written patient consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

After approval of the director of Sohag University hospitals and the ethical committee all studied patients or relatives signed informed consent before participation and they were allowed to refuse or accept this participation with complete confidentiality.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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