Medicolegal Study of Serum C-Reactive Protein and Troponin I in victims with Head Injury

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Biological markers.

ABSTRACT

Traumatic head injury is a major concern to neurosurgeons and forensic experts. The aim of this study was firstly to determine the pattern of traumatic head injuries and its contributing factors, and secondly to investigate the clinical and forensic importance of serum C- reactive protein (CRP) and cardiac troponin I (cTnI) as promising diagnostic and prognostic biomarkers in victims with traumatic head injuries. Sixty head injured victims were categorized according to Glasgow coma scale into two groups: mild (13-15) and moderate-severe (3-12). Levels of CRP and cTnI were measured on admission and 24 hours later. Serum levels of CRP and cTnI were significantly higher in moderate-severe group (than mild group) and showed significant changes after 24 hours. Elevated CRP serum level after 24 hours above 12 mg/L was associated with poor victims' outcome. Both CRP and cTnI levels - whether on admission or after 24 hours - correlated significantly with hospital stay. In conclusion, serum CRP and cTnI can be used as markers to investigate severity and outcome of head injured victims.

Introduction

Traumatic head damage is considered a major problem worldwide as head injury is the most widely recognized crisis experienced in emergency units. It is viewed as a main source of death and handicap (Patil and Vaz, 2010; Ghoneim et al., 2012).

In United States of America, traumatic head injury is a contributing element to around 33% of all traumatic deaths (Faul et al., 2010). In Egypt, although there is a lack of updated statistical records for traumatic head injury (Montaser and Hassan, 2013), Ghoneim et al. (2012) revealed that 1300 victims with head injuries were admitted to Tanta Emergency Hospital from May 2009 to June 2010.

Various cerebrospinal fluid or serum biomarkers in cases of traumatic head injuries were evaluated by both neurosurgical and forensic researches, including neuron specific enolase (NSE) (Vázquez et al., 1995; Böhmer et al., 2011) and S-100B protein (Li et al., 2006; Li et al., 2009; Li et al., 2010; Egea-Guerrero et al., 2012; Shahin et al., 2016). However, these biomarkers are expensive and require particular kits and expertise. Hence, the search has to continue for other serum biomarkers of traumatic head injuries that are readily accessible and less in cost.

Victims with severe head damage show many biochemical reactions of acute phase response including the elevation of acute phase reactants (Kalabalikis et al., 1999). C-receptive protein (CRP) is one of the acute-phase

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reactants, which rises quickly in response to infection, injury, ischemia, burns, and other inflammatory conditions. It is widely available in all laboratories and reasonably cheap (Sesso et al., 2003).

Cardiac troponin I (cTnI) is a regulatory protein that controls the calcium- mediated interaction of actin and myosin. It is commonly utilized as a biochemical marker of myocardial damage. Troponin levels might be increased in non cardiac conditions such as pulmonary embolism, sepsis, chronic renal failure and acute non traumatic subarachnoid hemorrhage (SAH), stroke, and intracerebral hemorrhage (Salim et al., 2008).

From a medicolegal point of view, it is essential to determine whether death occurred due to head injury or its complications; to assess the circumstances and time under which head injury was sustained and to recognize the type of intracranial lesions. Therefore, the aim of this study was firstly to determine the pattern of traumatic head injuries and its contributing factors, and secondly to investigate the clinical and forensic importance of serum C- reactive protein and cardiac troponin I as promising diagnostic and prognostic biomarkers in victims with traumatic head injuries.

Material and Methods

This prospective study was conducted on victims with traumatic head injury who were admitted into Neurosurgery Department, Tanta University hospital, in the period from the 1st of February 2015 to the 31st of August 2015. Tanta University Hospital is a tertiary health care facility that receives victims from El-Gharbia governorate and adjoining regions in the Nile Delta. The study was approved by Research Ethics committee of Tanta Faculty of Medicine (approval code: 30341/15) and was conducted in accordance with the Code of Ethics of the World Medical Association. A written informed consent was obtained from each participant or his/her guardian in case of unconscious victims. The privacy and confidentiality of human subjects were observed by assigning code numbers to each patient - known only to the investigators - and the data were analyzed anonymously.

Inclusion criteria:

All victims above 18 years of either sex, who had traumatic head injuries within less than 24 hours on admission, were included in this study.

Exclusion criteria:

Victims were excluded if they: 1) had co-morbid associated disorder as heart, renal, liver diseases, chronic inflammatory disease and malignancies; 2) had a history of previous neurological illness or psychiatric impairment; 3) were under the influence of illicit substance at the time of injury; and 4) died within less than 24 hours.

Methods

Data collection:

All victims were subjected to history taking: personal data: (age, sex, residence and time of admission); circumstances of trauma (type & time of injury and time elapsed between infliction of injury and admission "pre-hospitalization period"). Findings of Glasgow Coma Scale (GCS), physical examination, and computerized tomography (CT) scan of the head were also recorded.

Victims were categorized into two groups based on their GCS on admission: moderate to severe group (GCS 3-12) and mild group (GCS 13-15) (Lee et al., 2005).

The victims were followed up during their hospital stay. The method of treatment (either conservative or operative), hospitalization period and outcome of victims (either survivor or non-survivor) were also recorded in the data sheet.

Sample collection:

A three ml venous blood sample was collected from each victim on admission and another sample was obtained 24 hours after admission. These samples were used for estimation of serum CRP and cTnI. Quantitation of CRP was performed by immunoturbidimetric assay using AVITEX® CRP latex agglutination test kit (Omega Diagnostics Ltd, Scotland, UK) according to the method described by Singer et al. (1957). Cardiac troponin I was measured using the enzyme-linked fluorescent assay technique by one step immunoassay sandwich method and with a final fluorescent detection with VIDAS Troponin I Ultra (by BioMerieux, France) as described by Apple (1998).

The normal range for serum CRP and cTnI differ according to the laboratory performing the assay and the kits used. Our laboratory reference ranges in healthy subjects are less than 6 mg/L for CRP and up to 1 ng/ml for cTnI.

Statistical analysis:

The collected data were organized and statistically analyzed using SPSS software statistical computer package version 22. The distribution of numerical variables was found by Shapiro-Wilk test to be skewed from normality; therefore the data were expressed as median and interquartile range (IQR= 25^{th} - 75^{th} percentiles); Mann-Whitney U and Kruskal Wallis tests were used for comparison between groups; and Spearman's rank order correlation was performed. For qualitative data, comparison between groups was performed using Chi-square and Fisher's exact tests as appropriate. Receiver–operating characteristic (ROC) curve for predicting mortality was generated from the data. Area under ROC curve, sensitivity and specificity were calculated. Significance was adopted at $p< 0.05$ for interpretation of the results of tests of significance (Dawson and Trapp, 2001).

Results

Sixty victims were enrolled in this study and were categorized according to their GCS into mild group (GCS 13-15) that represented 61.7% of total cases and moderate to severe group (GCS 3 -12) that included 38.3% of cases. The median age of all victims was 35.5 years (ranged from 18 - 66 years). The highest incidence of head injuries (53.3% of all cases) was in age group "18- 40 years" followed by age group ">40 - 60 years" (43.3%). Males outnumbered females (96.7% and 3.3 % respectively). Most victims (70%) belonged to rural areas. There was no statistically significant association between the severity of head injury and each of age, sex and residence ($p = 0.151$, 0.693 and 0.072 respectively) as shown in table (1).

Additionally, table (1) demonstrates that the majority of cases were sustained during daytime (70%). The most common causes of head trauma were road traffic accident (RTA) (46.7%) followed by falls (36.7%). A significant association was detected between injury severity and each of time and cause of head trauma ($p <0.001$, $p = 0.002$ respectively) as higher frequencies of moderate to severe cases were caused by RTA (73.9%) and were sustained during night (60.9%). On the other hand, the majority of mild cases were caused by falls (43.3%) and occurred during daytime (89.2%).

Table (1): Sociodemographic data and circumstances of trauma in the studied victims (n=60)

		Studied groups (GCS)						Test of significance	
		Mild(13-15) n= 37		Moderate to severe (3-12) n= 23		Total n = 60			
		n	%	n	%	n	%	Test statistic	p
Age (years)	18- ٤0	19	51.4	13	56.5	32	53.3	X^2_{FE}= 3.413	0.151
	>40- 60	18	48.6	8	34.8	26	43.3		
	> 60	0	0.0	2	8.٧	2	3.3		
Sex	Male	35	94.6	23	100.0	58	96.7	X^2_{ChS}= 1.286	0.693
	Female	2	5.4	0	0.0	2	3.3		
Residence	Urban	8	21.6	10	43.5	18	30.0	X^2_{ChS}= 3.226	0.072
	Rural	29	78.4	13	56.5	42	70.0		
Time of injury	Day	33	89.2	9	39.1	42	70	X^2_{ChS}=19.440	<0.001*
	Night	4	10.8	14	60.9	18	30		
Cause of head trauma	Fall	16	43.3	6	26.1	22	36.7	X^2_{FE}=18.854	0.002*
	Violence	8	21.6	0	0%	8	13.3		
	RTA	11	29.7	17	73.9	28	46.7		
	Work	2	5.4	0	0%	2	3.3		

GCS: Glasgow coma scale; n: number; RTA: road traffic accident; X^2_{ChS}: Pearson's Chi square test; X^2_{FE}: Fisher's exact test; * significant.

Table (2) shows that half the cases had skull fractures with no statistically significant association between the severity of injury and presence of fractures (p = 0.426). More than half the cases had meningeal hemorrhages (56.7%). Brain contusions/lacerations and brain edema were observed in 15 % of all cases each. All cases of intraventricular hemorrhage and brain edema were in moderate -severe group (p = 0.005, p <0.001 respectively). More than half the cases (56.7%) were treated conservatively, with no statistically significant difference between the two groups (p = 0.276). The majority of mild cases (94.6%) had a 7 days hospital stay or less; whereas a significantly higher percentage of moderate to severe cases had a prolonged hospital stay for more than 7 days (p <0.001). Most cases survived till discharge from the hospital (80%) while only 20% of cases died during hospital stay. All non-survivors belonged to moderate-severe group (p <0.001).

Examination of the cardiovascular system revealed no clinically abnormal data. There was no significant difference between mild and moderate - severe group as regards systolic and diastolic blood pressures and heart rate (p = 0.395, 0.160 and 0.331 respectively).

Table (2): Findings of CT scan head and clinical course in the studied victims (n=60)

		Studied groups (GCS)						Tests of significance	
		Mild(13-15) n= 37		Moderate to severe (3-12) n= 23		Total n = 60			
		n	%	n	%	n	%	Test statistic	p
Skull Fracture	**Absent**	20	54.1	10	43.5	30	50.0	X^2_{ChS}= 0.635	0.426
	Present	17	45.9	13	56.5	30	50.0		
Intracranial hemorrhage	**Absent**	13	35.1	7	30.4	20	33.3	X^2_{FE}= 10.471	0.005*
	Meningeal hemorrhage	٢٤	64.9	10	43.5	34	56.7		
	IV HGE	0	0.0	6	26.1	6	10.0		
Brain injury	**Absent**	28	75.7	14	60.9	42	70.0	X^2_{FE}= 21.171	<0.001*
	Contusion/laceration	9	24.3	0	0.0	9	15.0		
	Brain Edema	0	0.0	9	39.1	9	15.0		
Treatment	**Conservative**	23	62.2	11	47.8	34	56.7	X^2_{ChS}=1.187	0.276
	Operative	14	37.8	12	52.2	26	43.3		
Hospital stay	**≤ 7 days**	35	94.6	12	52.2	47	78.3	X^2_{FE}= 14.545	<0.001*
	> 7-14 days	0	0.0	3	13.0	3	5.0		
	>14 - 21 days	0	0.0	2	8.7	2	3.3		
	> 21 days	2	5.4	6	26.1	8	13.3		
Outcome	**Survivor**	37	100.0	11	47.8	48	80.0	X^2_{FE}=20.980	<0.001*
	Non-survivors	0	0.0	12	52.2	12	20.0		

GCS: Glasgow coma scale; n: number; EDH: extradural hemorrhage; SDH: subdural hemorrhage; SAH:subarachnoid hemorrhage; IVHGE: intraventricular hemorrhage; X^2_{ChS}: Pearson's Chi square test; X^2_{FE}: Fisher's exact test; * significant.

Serum CRP levels were elevated above the normal value in 45% of total cases on admission and in 88.3% after 24 hours. Increased serum cTnI were observed in 20% of cases, both on admission and after 24 hours (Figure 1).

Table (3) reveals that after 24 hours, there was a significant elevation of serum CRP level ($p < 0.001$), whereas serum cTnI level was significantly decreased ($p = 0.002$).

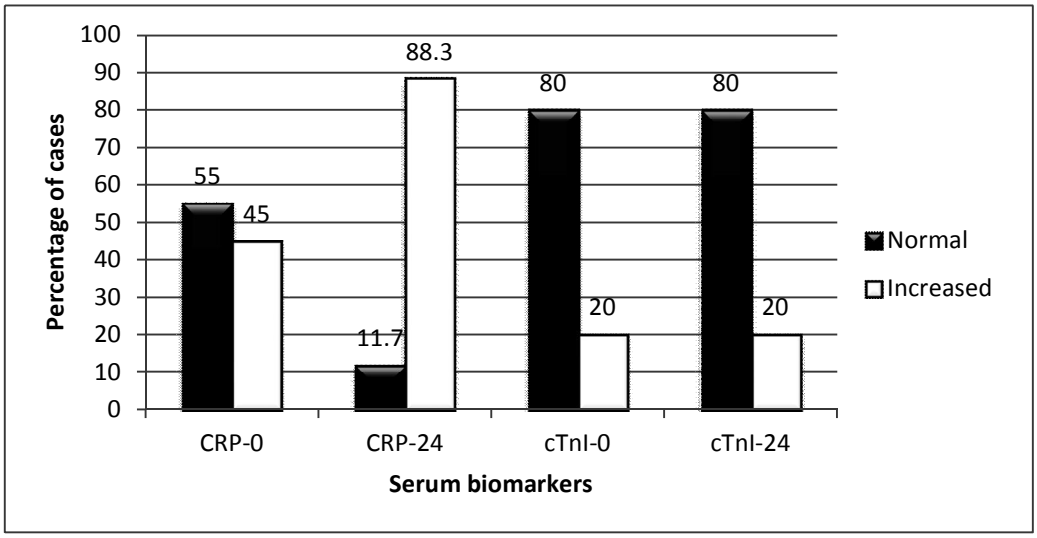

Fig.(1): Bar chart showed increased serum biomarkers in the studied victims. CRP-0: CRP on admission; CRP-24: CRP after 24 hours; cTnI-0: cTnI on admission; cTnI-24: cTnI after 24 hours (n=60).

Table (3): Comparison between C -reactive protein and troponin I levels on admission and after 24 hours (n=60)

	Minimum	Maximum	Median	IQR	Wilcoxon signed rank test	
					Z	p
CRP on admission	0.00	96.00	0.00	0.00- 12.00	-5.798	<0.001*
CRP after 24 hours	0.00	96.00	24.00	6.00- 48.00		
cTnI on admission	0.00	10.70	0.02	0.01- 0.50	-3.104	0.002*
cTnI after 24 hours	0.00	8.29	0.02	0.01- 0.46		

n: number; CRP: C-reactive protein; cTnI: cardiac troponin I; IQR: interquartile range; * significant.

Serum CRP levels on admission and after 24 hours were significantly higher in moderate-severe group than mild group (p = 0.007, <0.001 respectively). On admission, serum CRP level was significantly elevated in cases with skull fractures versus intracranial hemorrhage (p=0.011). The CRP level after 24 hours showed no statistically significant difference between the different types of head injuries (p = 0.668). The CRP serum level on admission showed no significant difference between survivors and non-survivors (p = 0.768), while after 24 hours CRP was significantly higher in non-survivors (p<0.001) as shown in table (4).

Table (4): Association between CRP and Glasgow Coma Scale, CT scan findings, and outcome of victims (n=60)

		CRP on admission				CRP after 24 hours			
		Median	**Mean ranks**	**Test statistic**	**p**	**Median**	**Mean ranks**	**Test statistic**	**p**
GCS	**Mild**	٠.00	26.16	Z_{MW}=-2.686	0.007*	12.00	20.95	Z_{MW}=-5.528	<0.001*
	Moderate-Severe	12.00	37.48			48.00	45.87		
CT scan Findings (Single lesions)	**Skull fracture**	12.00	24.14	Z_{KW}=8.952	0.011*	48.00	18.75	Z_{KW}=0.806	0.668
	Intracranial hemorrhage	٠.00	15.25	Significant difference between skull fracture versus intracranial hemorahge		12.00	17.73		
	brain injury	٠.00	11.50			48.00	24.50		
Outcome	**Survivor**	٠.00	30.20	Z_{MW}=0.295	0.768	12.00	26.68	Z_{MW}=3.488	<0.001*
	Non-survivors	٠.00	31.71			48.00	45.79		

n: number ; CRP: C -reactive protein; GCS: Glasgow coma scale; CT scan: computerized tomography scan; Z_{MW}:Mann Whitney test; Z_{KW}: Kruskal Wallis test; * significant.

Table (5) demonstrates that there was no significant association between cTnI levels; whether on admission or after 24 hours; and injury severity (p = 0.505, 0.779), CT findings (p = 0.082, 0.233) or patient outcome (p = 0.955, 0.806).

Table (6) shows a significant positive correlation between all the four studied serum markers and hospital stay (longer hospital stay in victims with increased levels of markers). Correlation was moderate as regards CRP on admission and after 24 hours and cTnI after 24 hours (r_s = 0.491, 0.409 and 0.344 respectively), while the correlation was weak between cTnI on admission and hospital stay (r_s = 0.265).

Figure (2) shows ROC curve of serum CRP level after 24 hours as a predictor of mortality; the area under the curve (AUC) = 0.819 and p = 0.001. At a cut off value > 12 mg/L, serum CRP level after 24 hours had a sensitivity of 100 % (was able to identify all cases that died) and a specificity 52.08% (identified 52.08% of survivors)

Table (5): Association between Troponin I and Glasgow Coma Scale, CT scan findings, and outcome of victims (n=60)

		cTnI on admission				cTnI after 24 hours			
		Median	Mean ranks	Test statistic	p	Median	Mean ranks	Test statistic	p
GCS	**Mild**	0.01	29.34	Z_{MW}=0.666	0.505	0.01	30.01	Z_{MW}=0.280	0.779
	Moderate-Severe	0.03	32.37			0.02	31.28		
CT scan Findings (Single lesions)	**Skull fracture**	0.47	21.14	Z_{KW}=5.007	0.082	0.24	19.32	Z_{KW}=2.918	0.233
	Intracranial hemorrhage	0.02	15.55			0.02	16.83		
	Brain injury	4.17	29.50			3.97	29.50		
Outcome	**Survivor**	0.02	30.56	Z_{MW}=-0.056	0.955	0.02	30.77	Z_{MW}=-0.246	0.806
	Non-survivors	0.88	30.25			0.46	29.42		

n: number; cTnI: cardiac troponin I; GCS: Glasgow coma scale; CT scan: computerized tomography scan; Z_{MW}:Mann Whitney test; Z_{KW}: Kruskal Wallis test; * significant.

Table (6): Spearman's correlation between the studied serum markers and hospital stay (n=60)

		Hospital stay
CRP on admission	r_s	0.491
	p	<0.001*
CRP after 24 hours	r_s	0.409
	p	0.001*
cTnI on admission	r_s	0.265
	p	0.040*
cTnI after 24 hours	r_s	0.344
	p	0.007*

n: number; CRP: C-reactive protein; cTnI: cardiac troponin I; r_s: Spearman's correlation coefficient; * significant.

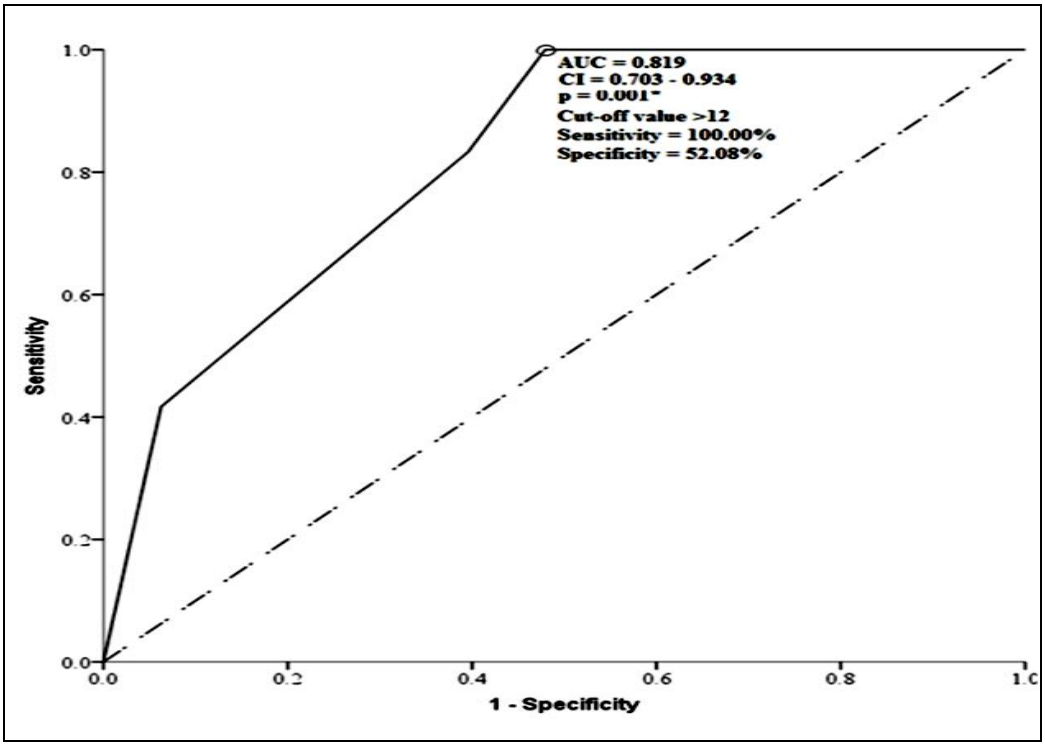

Fig. (2): ROC curve analysis of CRP level after 24 hours as predictor of mortality. Area under the curve = 0.819, P <0.001*, sensitivity 100.00% & specificity 52.08% at cut off value > 12 mg/l (n=60).

Discussion

Head injury constitutes one of the main causes of disability and mortality in Egypt (Zaki et al., 2011). The relationship between head trauma and changes in serum biomarkers presents great interest to both the fields of neurosurgery and forensic practice. For neurosurgeons, serum biomarkers can enhance the prediction and early recognition of victims with poor prognosis to provide the best available standard of care for them to improve their outcome. As regards the medicolegal field, on evaluating claims of malpractice of head injured victims, the serum biomarkers can help forensic experts to conjecture in these cases that the poor outcome of victims was related directly to the effects of trauma, provided that breach of the standard of care is suspected but could not be proved. Besides, more valuable inferences may be withdrawn from studying serum biomarkers in traumatic head injuries concerning the type of intracranial injuries (Cervellin et al., 2012) or determination of the time of trauma (Zaki et al., 2011).

Hence, the aim of this study was firstly to determine the pattern of traumatic head injuries and its contributing factors, and secondly to investigate the clinical and forensic importance of serum C- reactive protein and cardiac troponin I as promising diagnostic and prognostic biomarkers in victims with traumatic head injuries.

Sixty victims were included in this study and the frequency of victims with mild head injuries was higher than the moderate to severe group (61.7% and 38.3% of cases respectively). These findings are in partial agreement with

Farghaly et al. (2007) who found that 46% of traumatic head injuries were mild cases. On the contrary, Sogut et al. (2010) reported a higher frequency of moderate and severe cases compared with mild cases (65% versus 35% respectively). This variation may be due to the inclusion of both children and adults in their study while the present study was conducted on adults only.

The present study demonstrated that more than half the victims were young adults (in the age from 18 to 40 years old). The median age was 35.5 years and the majority of them were males. These findings are in accordance with results of Patil and Vaz (2010); Sogut et al. (2010), Zaki et al. (2011); Ghoneim et al. (2012), Montaser and Hassan (2013) and Hasanin et al. (2016). The higher frequency of young male victims in this study and other comparable studies could be explained by the fact that young males are considered the main breadwinners in society and subsequently are involved in many outdoor activities and use transportation, exposing them to a higher risk of trauma than other age groups.

The cuurent study demonstrated that RTAs (46.7%) and falls (36.7%) were the most common causes of head trauma. These results are in accordance with Sogut et al. (2010) and Zaki et al. (2011). Moreover, the current study demonstrated that there was a significant association between injury severity and each of time and cause of head trauma as a higher frequency of moderate to severe head injuries resulted from RTAs and occurred during night times. These findings are in agreement with El - Gindi et al. (2001) who demonstrated that road traffic collisions were associated with severe and multiple head trauma especially at night as many vehicles sometimes travel without turning on lights.

In this study, half the cases had skull fractures with no statistically significant association between the severity of injury and presence of fractures. This finding is in line with Munteanu et al. (2014). More than half the cases had meningeal hemorrhages (56.7%) and all cases of intraventricular hemorrhage were in moderate-severe group. The occurrence of intraventricular hemorrhage indicates severe traumatic head injury and is usually associated with poor outcome (Atzema et al., 2006). Brain contusions/lacerations and brain edema were observed in 15% of cases each. In partial agreement to these findings, Sogut et al., (2010) stated that brain edema occurred in 16% of cases while meningeal hemorrhages occurred in only 21% of cases. Hasanin et al. (2016) reported a high incidence of intracranial hemorrhage in their study (72% of cases, the commonest was EDH, then SDH) and brain contusion in 16% of cases.

In the present study, more than half the cases were treated conservatively (56.7%) while the remaining required operative intervention (43.3%). This result is consistent with Patil and Vaz (2010) and Hasanin et al. (2016).

Regarding patient outcome, most cases in this study survived till discharge from the hospital (80%) while only 20% of cases died during hospital stay. All non-survivors belonged to moderate - severe group. Similarly, Farghaly et al. (2007) and Sogut et al., (2010) reported a mortality rate of 22.3% and 27% respectively. The higher percentage of conservative management and survivors could be attributed to high frequency of mild head injury cases in the present study and similar studies.

In this study, the heart rate and blood pressure measurements were within normal ranges and cardiovascular examination did not reveal any clinically abnormal data which is in line with Salim et al. (2008).

The CRP is an acute phase reactant, which is secreted by the liver in response to trauma and inflammation. The inflammation in cases of head injury is due to a reaction to the tissue damage which has been extensively documented previously in experimental and clinical studies

of traumatic head injuries (Cederberg and Siesjö, 2010). Peak levels are reached usually after 24 to 48 hours and persist elevated for 5 to 7 days (Sesso et al., 2003).

The present study demonstrated that serum CRP level was elevated above the normal value in 45% of total cases on admission and in 88.3% after 24 hours. Moreover, serum CRP level showed a significant elevation after 24 hours than its initial level on admission. This elevation of CRP levels is a strong evidence of an active tissue damage process; therefore, CRP level increases more as long as the process of tissue damage and the resultant inflammation continue (Kalabalikis et al., 1999).

In accordance with these results, Meisner et al. (2005) studied CRP levels in multiple trauma victims and reported that initial CRP levels increased above 10 mg/L in 98% of victims. Du et al. (2005), Sun et al. (2013) and Naghibi et al. (2017) found that the initial CRP level was significantly higher than normal values and reached its peak three days after trauma.

The present study revealed that the initial CRP level was significantly higher in moderate-severe group and in cases with skull fractures versus intracranial hemorrhage; while it was nearly similar in survivors and non-survivors. These results are in line with those of Sogut et al. (2010) and Sun et al. (2013) who found a significantly higher initial levels of CRP in victims with severe head injuries. Moreover, Meisner et al. (2005) found that initial CRP levels showed no differences between survivors and non survivors in multiple trauma victims. On the contrary, Lee et al. (2005) found no statistically significant differences in CRP measured during the first 2 days after head trauma and GCS. In the current study, CRP serum level after 24 hours was significantly higher in moderate-severe group and in non-survivors. Lee et al. (2005) reported similar findings, but they were detected on a later onset (from day 3). On the other hand, Naghibi et al. (2017) reported that the mean serum CRP level after 48 hours was not significantly higher in non-surviving compared with surviving victims.

Therefore, the measurement of CRP can be used not only to monitor various inflammatory states and many different disorders, but also to assess the severity of tissue damage and victims' outcome. Moreover, the changes observed in serum levels of CRP over time in this study and other studies suggest a probability of their value for determining time of trauma.

As regards cardiac troponin (ctnI), the present study revealed increased serum cTnI level in 20% of cases, both on admission and after 24 hours. This elevation of cTnI level could be attributed to a leakage from the free cytosolic pool through a reversibly damaged myocyte membrane due to ischaemia (Wells and Sleeper, 2008). Some studies postulated that damage inflicted to hypothalamic, insular, or brainstem regions may result in activation followed by dysfunction of the autonomic nervous system, increased circulating catecholamines and an acute inflammatory response (Naidech et al., 2005). The systemic inflammatory response that occurs following head trauma may increase serum cTnI level through direct cytotoxic effect exerted by circulating inflammatory markers (such as tumor necrosis factor α, interleukin 6 and reactive oxygen species) on myocardial cells (Korff et al., 2006; Lu et al., 2008).

Serum cTnI in this study showed a significant decrease 24 hours after admission. Similarly, elevated serum levels of cardiac markers including troponin I were reported by Salim et al. (2008) in 29.8% of traumatic head injuries cases; Miketic et al. (2010) in approximately one third of victims after aneurysmal subarachnoid heamorrhge; Busl et al. (2013) in 10% of victims with subdural hemorrhage; and Prathep et al. (2014) in 24 % of victims with traumatic head injuries. However, Cai et al. (2016) and Hasanin et al. (2016) found

a higher frequency of elevated serum troponin I level 24 hours after trauma (30.9% and 54 % of cases respectively).

In the current study, there was no significant association between cTnI levels; whether on admission or after 24 hours; and injury severity, CT findings or patient outcome. On the other hand, previous studies reported an association between cTnI levels and each of injury severity (Salim et al., 2008; Busl et al., 2013) and patient outcome (Salim et al., 2008; Hasanin et al., 2016). These discrepancies may be attributed to the differences in sample size and exclusion criteria. Additionally, the majority of victims in this study had mild traumatic head injury with normal cardiovascular examination data.

In the present study, there was a significant positive correlation between all the four studied serum markers and hospital stay (longer hospital stay in victims with increased levels of markers). In addition, Naghibi et al. (2017) demonstrated a positive moderate correlation of CRP after 48 hours post trauma with the length of ICU stay. The prolonged hospital stay was found to be significantly associated with severe traumatic head injury and poor patient outcome (Godbolt et al., 2013).

Analysis of receiver operating characteristics (ROC) curve of serum CRP level after 24 hours as a predictor of mortality in the present study showed that victims with CRP level above 12 mg/L had a greater risk for poor outcome (sensitivity of 100 % and specificity of 52.08%). Up to the best of the authors' knowledge, no other studies identified a cut off value of CRP level; for the prediction of mortality in head trauma. Only one study by Hergenroeder et al. (2008) demonstrated that CRP levels may predict the increase in intracranial pressure with an AUC = 0.89.

Conclusions and recommendations

From this study, it could be concluded that elevated serum levels of CRP and cTnI showed significant changes after 24 hours. Elevated CRP serum level after 24 hours was associated with increased severity of head trauma and poor patient outcome. It was found that CRP level 24 hours after head trauma above 12 mg/L was able to identify all non-survivors. Both CRP and cTnI levels correlated significantly with the length of hospital stay. Therefore, serum CRP and cTnI can be regarded as valuable tools to evaluate severity and outcome of head injured victims. The authors recommend exploring the association of these markers with the type of intracranial injury and following up over longer time to evaluate their role in determining time of trauma.

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References:

Apple, F.S. (1998): Cardiac troponin I. In: A. H. B. WU (Ed.) Pathology and Laboratory Medicine: Cardiac Markers. New York: Springer Science Business Media, LLC. P.P. 229 - 231.

Atzema, C.; Mower, W.R.; Hoffman, J.R.; et al. (2006): "Prevalence and prognosis of traumatic intraventricular hemorrhage in patients with blunt head trauma . J. Trauma Acute Care Surg., 60(5): 1010-1017.

Böhmer, A.E.; Oses, J.P.; Schmidt, A.P.; et al. (2011): "Neuron-specific enolase, S100B, and glial fibrillary acidic protein levels as outcome predictors in patients

with severe traumatic brain injury". Neurosurgery, 68(6): 1624-1631.

Busl, K.M.; Raju, M.; Ouyang, B.; Garg, R.K. and Temes, R.E. (2013): "Cardiac abnormalities in patients with acute subdural hemorrhage". Neurocrit. Care, 19(2): 176-182.

Cai, S.S.; Bonds, B.W.; Hu, P.F. and Stein, D.M. (2016): "The role of cardiac troponin I in prognostication of patients with isolated severe traumatic brain injury". J. Trauma Acute Care Surg., 80(3): 477-483.

Cederberg, D. and Siesjö, P. (2010): "What has inflammation to do with traumatic brain injury"? Childs NervSyst., 26(2): 221-226.

Cervellin, G.; Benatti, M.; Carbucicchio, A.; et al. (2012): "Serum levels of protein S100B predict intracranial lesions in mild head injury". Clin. Biochem., 45 (6): 408-411.

Dawson, B. and Trapp, R.G. (2001): Basic and Clinical Biostatics. Lang Medical Book. 3rd ed. New York: McGrow Hill Medical Publishing Division. P.P. 161-218

Du, H.G.; Yin, L.C.; He, M.; et al. (2005): "Application of ulinastatin in severe craniocerebral injuries". Chin. J. Traumatol., 8(4): 236-239.

Egea-Guerrero, J.; Revuelto-Rey, J.; Murillo-Cabezas, F.; et al. (2012): "Accuracy of the S100 β protein as a marker of brain damage in traumatic brain injury". Brain Inj., 26(1): 76-82.

El-Gindi, S.; Mahdy, M. and Abdel Azeem, A. (2001): "Traumatic brain injuries in developing countries. Road war in Africa". Rev. Esp. Neuropsicol., 3 (3): 3-11.

Farghaly, A.; El-Khayat, R.; Awad, W. and George, S. (2007): "Head injuries in road traffic accidents". The annual meetings of International Council on Alcohol, Drugs, and Traffic Safety (ICADTS), The International Association of Forensic Toxicologists (TIAFT), and the 8th Ignition Interlock Symposium (IIS), Seattle, Washington.

Faul, M.; Xu, L.; Wald, M.M. and Coronado, V. (2010). "Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths.". Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Available at: http://www.cdc.gov/traumaticbraininjury/pdf/blue_book.pdf. Accessed 12/4 2015.

Ghoneim, N.I.; Elden, S.M.A.; Okab, M.E. and Elsaay, O.E.A. (2012): "Impact of Implementing Nursing Care Protocol on Moderate Head Injured Patient's Outcome". Am. J. Sci., 8(7): 649 - 664.

Godbolt, A.K.; DeBoussard, C.N.; Stenberg, M.; et al. (2013): "Disorders of consciousness after severe traumatic brain injury: A Swedish–Icelandic study of incidence, outcomes and implications for optimizing care pathways". Journal of Rehabilitation Medicine, 45(8): 741-748.

Hasanin, A.; Kamal, A.; Amin, S.; et al. (2016): "Incidence and outcome of cardiac injury in patients with severe head trauma". Scand. J. Trauma Resusc. Emerg. Med., 24: 58.

Hergenroeder, G.; Redell, J.B.; Moore, A.N.; et al. (2008): "Identification of serum biomarkers in brain-injured adults: potential for predicting elevated intracranial pressure". J. Neurotrauma, 25(2): 79-93.

Kalabalikis, P.; Papazoglou, K.; Gouriotis, D.; et al. (1999): "Correlation between serum IL-6 and CRP levels and severity of head injury in children". Intensive Care Med., 25 (3): 288-292.

Korff, S.; Katus, H.A. and Giannitsis, E. (2006): "Differential diagnosis of

elevated troponins". Heart, 92(7): 987-993.

Lee, K.; Shim, J.; Yoon, S. and Bae, H. (2005): "Prognostic value of the C-reactive protein levels in the head injury". J. Kor. Eurotraumatol. Soc., 1(1): 57-60.

Li, D.R.; Ishikawa, T.; Quan, L.; et al. (2010): "Morphological analysis of astrocytes in the hippocampus in mechanical asphyxiation". Leg. Med., 12 (2): 63-67.

Li, D.R.; Michiue, T.; Zhu, B.L.; et al. (2009): "Evaluation of postmortem S100B levels in the cerebrospinal fluid with regard to the cause of death in medicolegal autopsy". Leg. Med., 11 (Suppl. 1): S273-S275.

Li, D.R.; Zhu, B.L.; Ishikawa, T.; et al. (2006): "Postmortem serum protein S100B levels with regard to the cause of death involving brain damage in medicolegal autopsy cases". Leg. Med., 8 (2): 71-77.

Lu, J.; Goh, S.J.; Tng, P.; et al. (2008): "Systemic inflammatory response following acute traumatic brain injury". Front Biosci (Landmark Ed), 14: 3795-3813.

Meisner, M.; Adina, H. and Schmidt, J. (2005): "Correlation of procalcitonin and C-reactive protein to inflammation, complications, and outcome during the intensive care unit course of multiple-trauma patients". Crit. Care, 10 (1): R1.

Miketic, J.K.; Hravnak, M.; Sereika, S.M. and Crago, E.A. (2010): "Elevated cardiac troponin I and functional recovery and disability in patients after aneurysmal subarachnoid hemorrhage". Am. J. Crit. Care, 19(6): 522-528.

Montaser, T. and Hassan, A. (2013): "Epidemiology of moderate and severe traumatic brain injury in Cairo University Hospital in 2010". Crit. Care, 17 (Suppl 2): 320.

Munteanu, P.L.; Rosu, M.; Panaitescu, V. and Punga, A. (2014): "Patterns of head injuries in lethal road traffic accidents in Buzau County". Rom. J. Legal Med., 22 (1): 9-12.

Naghibi, T.; Mohajeri, M. and Dobakhti, F. (2017): "Inflammation and outcome in traumatic brain injury: does gender effect on survival and prognosis?". Journal of Clinical and Diagnostic Research: JCDR, 11(2): pc06-pc09.

Naidech, A.M.; Kreiter, K.T.; Janjua, N.; et al. (2005): "Cardiac troponin elevation, cardiovascular morbidity, and outcome after subarachnoid hemorrhage.". Circ. Res., 112 (18): 2851-2856.

Patil, A.M. and Vaz, W.F. (2010): "Pattern of fatal blunt head injury: A two year retrospective/prospective medico legal autopsy study". J. Ind. Acad. Forensic Med., 32 (2): 144-149.

Prathep, S.; Sharma, D.; Hallman, M.; et al. (2014): "Preliminary report on cardiac dysfunction after isolated traumatic brain injury". Crit. Care Med., 42 (1): 142-147.

Salim, A.; Hadjizacharia, P.; Brown, C.; et al. (2008): "Significance of troponin elevation after severe traumatic brain injury". J. Trauma Acute Care Surg., 64 (1): 46-52.

Sesso, H.D.; Buring, J.E.; Rifai, N.; et al. (2003): "C-reactive protein and the risk of developing hypertension". JAMA, 290(22): 2945-2951.

Shahin, M.M.; Fathy, A.S.A. and Shadad, M.N. (2016): "Clinical and forensic importance of s100β protein for prediction of outcome and evaluation of medical care in mild to moderate head injuries". Mansoura J. Forensic Med. Clin. Toxicol., XXIV(1): 57-72.

Singer, J.M.; Plotz, C.M.; Pader, E. and Elster, S.K. (1957): "The latex-fixation test. III. Agglutination test for C-reactive protein and comparison with the capillary precipitin method". Am. J. Clin. Pathol., 28(6)**:** 611-617.

Sogut, O.; Guloglu, C.; Orak, M.; et al. (2010): "Trauma scores and neuron-specific enolase, cytokine and C-reactive protein levels as predictors of mortality in patients with blunt head trauma". J. Int. Med. Res., 38(5)**:** 1708-1720.

Sun, R.Q.; Shi, X.Y.; Yang, H.F.; et al. (2013): "An investigation on correlation of severity of brain injury with the expression of activin A and C-reactive protein". Zhonghua wei zhong bing ji jiu yi xue, 25(11)**:** 681-685.

Vázquez, M.; Sánchez-Rodriguez, F.; Osuna, E.; et al. (1995): "Creatine kinase BB and neuron-specific enolase in cerebrospinal fluid in the diagnosis of brain insult". Am. J. Forensic Med. Pathol., 16(3)**:** 210-214.

Wells, S.M. and Sleeper, M. (2008): "Cardiac troponins". J. Vet. Emerg. Crit. Care, 18(3)**:** 235-245.

Zaki, M.K.; Abdel Gawad, S.M.; Tolba, N.H. and Abdel Rahman, A.E.-S. (2011): "Correlation between timing of trauma in living individuals and plasma level of soluble intercellular adhesion molecule type-1 (sICAM-1)". Egypt J. Forensic Sci., 1(2)**:** 87-92.

دراسة طبيه شرعية لبروتين سي التفاعلي و تروبونين I في ضحايا إصابات الرأس

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تمثل إصابات الرأس مصدرا كبيرا لاهتمام جراحى المخ و الأعصاب وخبراء الطب الشرعي. وكان الهدف من هذه الدراسة هو أولا تحديد نمط اصابات الرأس والعوامل المساهمة فيها ، وثانيا لبحث الأهمية السريرية والطبيه الشرعية للبروتين سي التفاعلي و تروبونين القلب I كمؤشرات تشخيصية وتنبؤية واعدة في ضحايا إصابات الرأس. تم تقسيم ستين مصابا وفقا لمقياس جلاسجو للغيبوبة إلى مجموعتين: خفيفة الشدة (١٣-١٥) ومتوسطة الى شديدة (٣-١٢). ثم تم قياس مستويات كلا من بروتين سي التفاعلي و تروبونين القلب I بمصل الدم عند دخول المستشفي وبعد ٢٤ ساعة. لوحظ ارتفاع ذودلالة احصائية لكلا من بروتين سي التفاعلي وتروبونين القلب بمصل الدم في المجموعة المتوسطة الى شديدة (مقارنة بالمجموعة خفيفة الشدة) مع وجود تغيرات ذات دلالة بعد ٢٤ ساعة. تبين ارتباط مستوى بروتين سي التفاعلي بمصل دم فوق ١٢ مجم / لتر بعد ٢٤ ساعة مع المصيرالسيىء لضحايا إصابات الرأس . وقد وجد ارتباط ذو دلالة احصائية لكلا من مستويات بروتين سي التفاعلي وتروبونين القلبI مع فترة البقاء في المستشفى - سواء عند الدخول أو بعد ٢٤ ساعة . وختاما فإنه يمكن استخدام كلا من بروتين سي التفاعلي و تروبونين القلب I كمؤشرات لتحديد شدة ونتائج ضحايا إصابات الرأس.