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DIAGNOSTIC AND PROGNOSTIC IMPORTANCE OF CREATININE PHOSPHOKINASE IN HEAT STROKE

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Abstract:

Objective: *To assess the diagnostic and prognostic importance of Creatinine Phosphokinase in patients suffering from heat stroke.*

Methodology: *47 patients diagnosed with heat stroke in May and June 2018 were included in this study. All patients were observed for 24 hours from the time of admission. Patients were divided into three groups according to the prognosis: Group I (survived and discharged), group II (survived by remained unconscious until the study duration) and group III (Died within the study duration). Blood samples of all patients were collected at 0,6,12 and 24 hours from the time of admission to assess plasma levels of creatinine phosphokinase.*

Results: *Out of the 47 patients, 29 (61.7%) were male and 18 (38.3%) were female. A steady rise in plasma Creatinine Phosphokinase levels was observed in patients of all three groups. Statistically significant differences between all three groups were observed through multiple comparisons by ANOVA. Post hoc analysis revealed that serum CPK levels were significantly high ($p = \leq 0.05$) in Group III patients compared to Group II and I. However, difference in levels of serum CPK between group I and II was not significant ($p = > 0.05$).*

Conclusion: *Creatinine phosphokinase can be an important diagnostic and prognostic tool in patients suffering from heat stroke.*

Key Words: *Creatinine phosphokinase, heat stroke, hyperpyrexia, anhidrosis*

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INTRODUCTION:

Heat stroke also known as sunstroke is an acute medical emergency, which comprises of symptoms such as decreased or absent sweating (anhidrosis), high grade fever (hyperpyrexia, increased body temperature > 106.7°F or 41.5°C) and altered state of mentation.[1] It is caused due to highly elevated environmental temperature which leads to heat storage due to decreased heat loss by radiation or convection as well as decreased sweating due to humidity.[2] It is a serious medical condition with reported mortality rates ranging from 17% to 70%.[3] Owing to industrialization, heat stroke has been a major environmental health problem in urban cities.[4]

Historically, heat stroke has been divided into Classic heat stroke or non-exertional heat stroke (NEHS) and exertional heat stroke (EHS). The former is more common in elderly and children especially during environmental heat waves whereas the latter is more common in young population, who engage in vigorous physical activities in a hot environment.[5] However, no universally accepted definition of heat stroke exists to date. Bouchama's definition, the most commonly used definition worldwide, describes heat stroke as core body temperature > 40 °C along with dry skin and altered mental status (disorientation, delusions and/or coma).[6] However, Misset et al. didn't use the term 'core body temperature' and defined heat stroke as hyperthermia >40.5°C.[7]

In Japan, Using data of patients diagnosed with heat related illnesses (regardless of the core body temperature) the Japanese Association for Acute Medicine (JAAM) established and published the criteria for heat-related illnesses, including heat stroke, in 2014 (Fig. 1).[8]

Elevated body temperature (≥40° C) disrupts the homeostatic mechanisms leading to early symptoms such as nausea, vomiting, headache and bradypnea followed by tachycardia and flushed skin. Eventually, the patient develops high-grade fever and altered mental status exhibiting unusual behavior, seizures or coma. [9] In addition, heat stroke (EHS & NEHS) is the most common cause of rhabdomyolysis – a condition characterized by rapid muscle breakdown and leakage of muscle enzymes into the bloodstream. [10] The severity of illness ranges from asymptomatic elevations of the serum levels of muscle enzymes to life-threatening cases associated with extreme elevations of creatinine phosphokinase (CPK) and liver enzymes (ALT, AST), electrolyte imbalances, and acute kidney injury (AKI).

Apart from the conventional diagnostic investigation (rectal temperature, blood complete picture, serum electrolytes, renal and liver function tests, CPK levels have shown to have prognostic implications.[11] In heat stroke, raised serum CPK levels indicate muscle injury, serum levels more than 5 times indicate rhabdomyolysis and serum CPK levels more than 5000 – 10000 U/L indicate AKI.[12]

The aim of this study was to highlight the diagnostic and prognostic importance of CPK in patients suffering from heat stroke.

MATERIALS AND METHODS:

Current prospective study was carried out at the "Heat Stroke Centre (HSC)" of Shah Bhittai Hospital, Hyderabad, Pakistan, during the period of May and June 2018. Present study was conducted on 47 consecutive patients brought in the HSC with Heat stroke (HS). At the time of admission to the HSC, all patients that fulfilled the criteria of HS i.e. Body temperature 41.5ºC, rectal temperature 40.6 °C associated with dry and hot skin and deterioration of consciousness level after exposure to temperate conditions were included in the study. All patients were observed for 24 hours from the time of admission. Vital information including respiratory rate, mean arterial pressure and neurological examination assisted by Glasgow coma scale of the patient was recorded immediately after their admission. Patients' cooling was started instantaneously by evaporation method as mentioned by Weiner and Khogali. [13] Cooling time, defined as the time required in reducing rectal temperature to 38.9°C, of all the patients was also estimated. Patients were divided into three groups according to the prognosis: Group I (survived and discharged), group II (survived by remained unconscious until the study duration) and group III (Died within the study duration). Blood samples of all patients were collected at 0,6,12 and 24 hours from the time of admission. Samples were analyzed for Creatinine Phosphokinase (CPK) enzyme. Data was analyzed using SPSS ver. 22. ANOVA was used for the analysis of continuous variables and Post hoc tukey's analysis was used to assess the statistical differences between the groups. P-value of 0.05 was considered statistically significant.

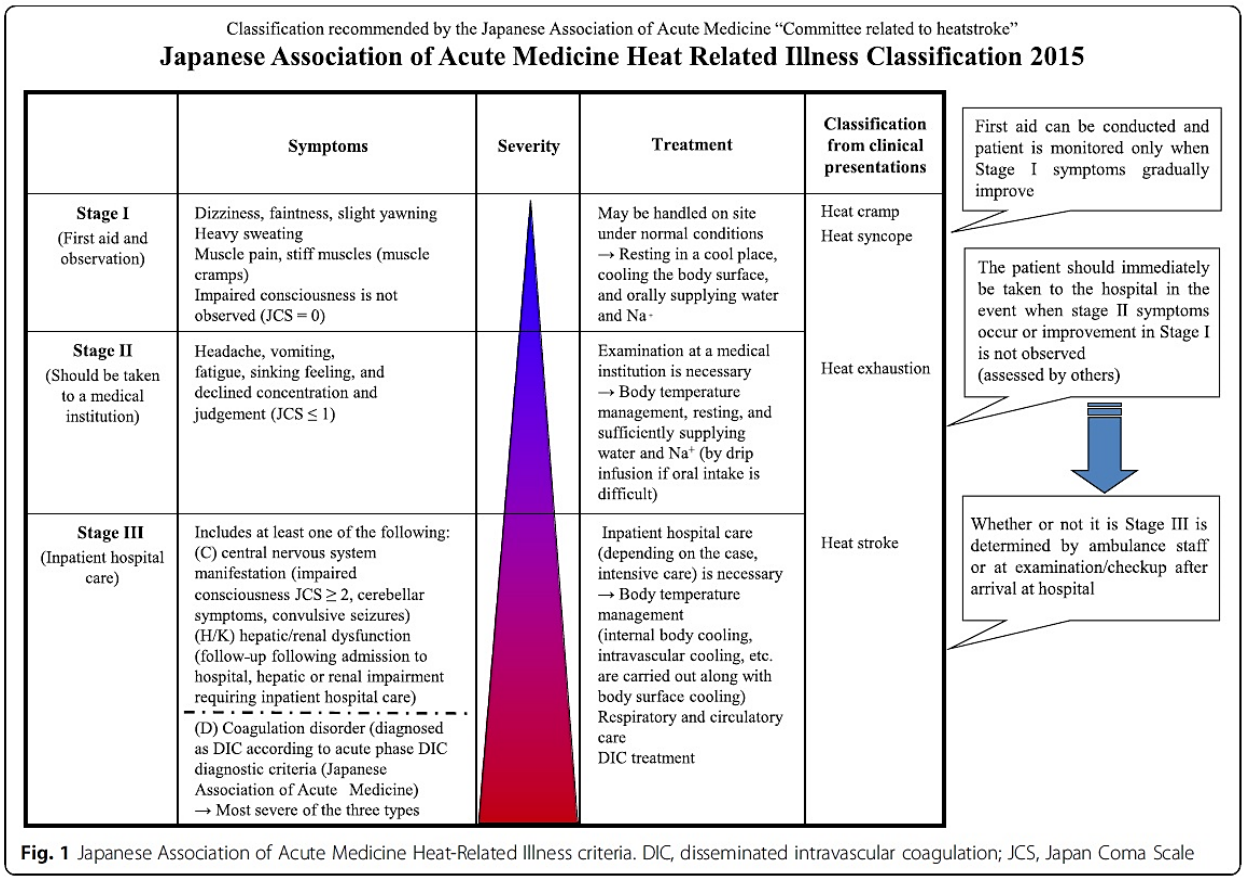

Fig. 1 Japanese Association of Acute Medicine Heat-Related Illness criteria. DIC, disseminated intravascular coagulation; JCS, Japan Coma Scale

RESULTS:

Total 47 patients were included in the study with an age range of 39 to 71 years. Out of them, majority were male. Data regarding mean body and rectal temperature, respiratory rate, mean arterial pressure, cooling time and Glasgow Coma Scale of all patients at the time of admission is presented in Table-1.

Table-1. General characteristics of patients of Heat stroke At the time of admission (n= 47)

Variables (Mean ± SD)	Patients (n=47)
Sex	
- **Male**	29 (61.7%)
- **Female**	18 (38.3%)
Age in years	52.5 ± 8.3
Mean Body Temperature, °C	41.27 ± 0.8
Mean Rectal Temperature, °C	42.34 ± 0.6
Respiratory Rate, breaths/min	33.2 ± 10
Mean Arterial Pressure, mmHg	79.5 ± 22.6
Cooling Time, Min	103 ± 28
GCS	6.4 ± 2.9

GCS = Glasgow Coma Scale

Based on prognosis over the course of 24 hours from the time of admission, 17 patients were included in Group I (discharged), 6 patients in Group II (remained unconscious) and 24 patients in Group III (Died). Data regarding age and gender distribution, mean body and rectal temperature as well as cooling time in all three groups is presented in Table-2.

Table-2: Group wise presentation of general characteristics of Heat stroke patients at the time of admission (n= 47)

	Group I (Quick Recovery)	Group II (Critically ill)	Group III (Died)
Male	9	3	17
Female	8	3	7
Age in years (Mean ± SD)	52.8±5.11	51±6.81	49.4 ± 4.31
Mean Body Temperature (Mean ± SD)	39.77 ± 0.8	40.21± 0.5	41.56± 0.8
Mean Rectal Temperature (Mean ± SD)	41.5 ±0.9	42.2 ± 0.6	42.1 ± 0.5
Cooling time (min) (Mean ± SD)	87 ± 31	104±23	140±28

Fig. 2. shows the plasma values of CPK in all three groups at 0, 6, 12 and 24 hours from the time of admission. A steady rise in plasma CPK levels was observed in patients of all three groups. In group I, the mean plasma CPK levels at 0,6,12 and 24 hours were 438±27, 617±34, 818±51 and 895±73 U/L respectively. Similarly, in group II, the mean plasma CPK levels at 0,6,12 and 24 hours were 531±37, 938±44, 1008±59 and 1081±82 U/L respectively. However, the greatest rise in plasma levels of CPK was seen in group III where plasma levels at 0,6,12 and 24 hours were found to be 830±69, 1859±94, 2967±107 and 3467±135 U/L respectively.

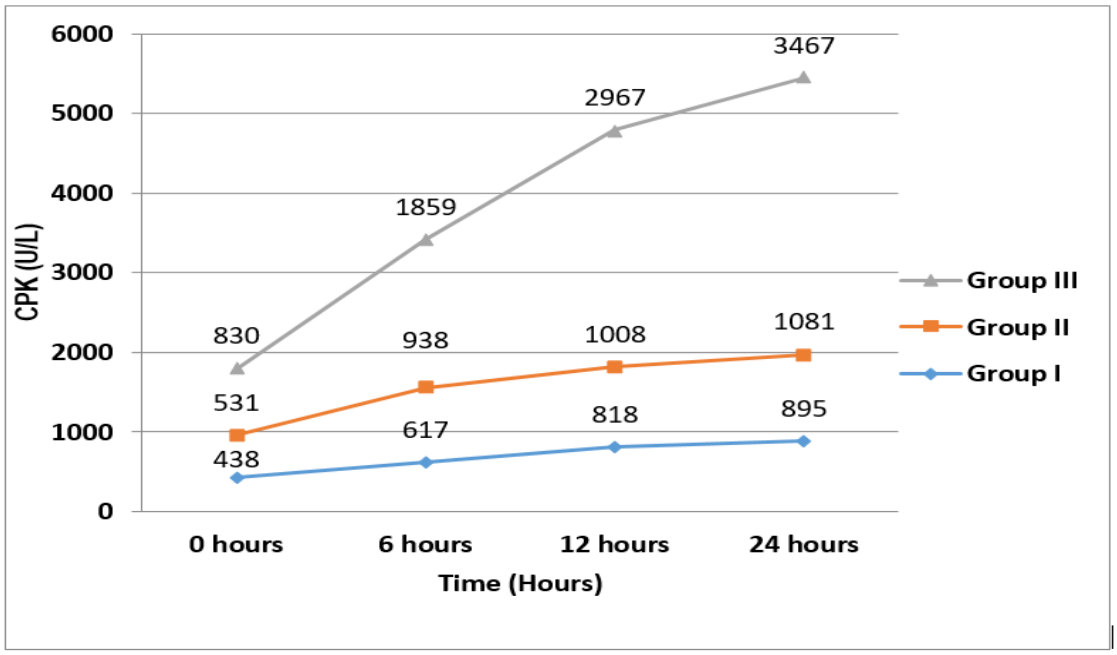

Fig. 2. Level of CPK at different time intervals in all groups.

Statistically significant differences between all three groups were observed through multiple comparisons by ANOVA. Post hoc analysis revealed that serum CPK levels were significantly high ($p = \leq 0.05$) in Group III patients compared to Group II and I. However, difference in levels of serum CPK between group I and II was not significant ($p = >0.05$). The details of differences in CPK levels between groups are given in Table-3.

Table-3. Multiple comparison of Serum CPK levels between groups by Post-hoc Tukey Test (n= 47)

CPK in different time interval	Group I (Quick Recovery)	Group II (Critically ill)	Group III (Died)	P-value
0 Hours	438±27*Ω	531±37†Ω	830±69*†	0.02**
6 Hours	617±34*Ω	938±44†Ω	1859±94*†	
12 Hours	818±51*Ω	1008±59†Ω	2967±107*†	
24 Hours	895±73*Ω	1081±82†Ω	3467±135*†	

DISCUSSION:

Both classic and exertional heat stroke are caused because of compromised thermo-regulation under conditions of high heat exposure. This study was conducted during the intense heatwave of 2018 in which temperatures soaring to 45°C (113°F) coinciding with electrical power cuts and Ramadan claimed the lives of dozens of people across the country. In our study, 61.7% of the patients were males as they are exposed more to the temperate environment. Hypotension was a problem observed in majority (69%) of the heat stroke patients. Sprung et al. demonstrated that hypotension is a predicting factor for poor outcome in heat stroke patients, as circulatory failure is known to precede the demise of many heat stroke victims. [14] Previous research studies have also shown that heat stroke patients may either present with hyper-dynamic state (increased cardiac index, decreased systemic and pulmonary vascular resistance) or hypo-dynamic state (decreased cardiac index, increased systemic and pulmonary vascular resistance) with the latter associated with circulatory failure and poorer prognosis. [14] Out of the 24 patients who died during our study duration, 17 (71%) died of circulatory failure.

In our patients, CPK levels were raised significantly and were markedly segregated among those patients who recovered and those who died. Changes in serum CPK levels in heat stroke patients have been studied and well documented in previous studies, and the enzyme is thought to originate mainly from skeletal muscles and possibly from the liver as well. [15, 16] CPK has been established as a vital test in cases of heat stroke serving as an important marker of muscle damage. [17] Serum levels of lactate dehydrogenase (LDH) and Aldolase are also elevated but CPK levels are raised in both EHS and NEHS cases. Alzeer et al. observed the plasma levels of CPK in heat stroke patients during the annual Hajj pilgrimage and found that the mean plasma CPK levels continued to rise and were significantly higher in non-surviving patients throughout their study duration, with serum CPK and LDH showing the highest prognostic accuracy for patients who survived as compared with those who died. [18] Similarly, Rajesh et al. observed the biochemical effects of EHS among Paratroopers in Agra, India and noted that serum CPK levels were significantly raised. [19]

As mentioned earlier, heat stroke is one of the most common causes of rhabdomyolysis. Significant rhabdomyolysis has been observed in both types of heat stroke especially the exertional type. [10, 20] However, the time of CPK release into and clearance from plasma depends primarily on the type, intensity, and duration of physical exertion as well as on the conditioning state of the subjects. [19] Similar to these findings, Fowler et al. noted high total serum CPK concentrations after muscular exercise in poorly conditioned men as compared with conditioned subjects.[21] de Meijer et al. studied the role of CPK as a predictor of clinical course in rhabdomyolysis and identified CPK levels as an important risk factor for the development of Acute Renal Failure (ARF) as patients with ARF had higher admission rates and peak CPK levels. [22]

In conclusion, this study highlights the diagnostic as well as prognostic importance of serum CPK levels in patients suffering from heat stroke. In this study, the patients were studied prospectively and compared with controls who were under the same environmental conditions and shows that plasma CPK levels can be a useful indicator of the prognosis of heat stroke.

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