

Heat-related illness—Clinical profile and predictors of outcome from a healthcare center in South India

George Abraham Ninan¹, Karthik Gunasekaran¹,
Jonathan Arul Jeevan Jayakaran¹, Jacob Johnson¹, Abhilash KPP²,
Kishore Pichamuthu³, Ramya Iyadurai¹

¹Department of General Medicine Unit V, Christian Medical College, ²Department of Emergency Medicine, Christian Medical College, Vellore, Tamil Nadu, ³Division of Critical Care, Christian Medical College, Vellore, Tamil Nadu, India

ABSTRACT

Background: Heat-related illness is a common medical emergency. There is failure of thermoregulatory mechanisms of the body resulting in multiple organ dysfunction syndrome which if not identified and treated urgently can result in high mortality rate and permanent neurological damage. This study provides description of clinical profile patients presenting with heat-related illness and identifies clinical and laboratory variables resulting in poor outcome. **Methods:** This retrospective study was done identifying adult patients admitted with a diagnosis of heat-related illness from April to August 2019 in tertiary care center. Their clinical profile, laboratory investigations and outcome were extracted from medical records and variables associated with poor outcome were analyzed for statistical significance. **Results:** Mean age of the patients in the study was 61 years with mean heat index of the localities being 39.6-degree C. 66% of patients had multiple organ dysfunction with central nervous system dysfunction (77%) followed by respiratory distress syndrome (61%) as the most common organ derangement. Evaporative cooling measures were incorporated in management of all patients, followed by cold saline infusion in 60%. Higher J-ERATO score at admission was found to be a predictor for underlying multiple organ dysfunction syndrome (P value < 0.029). The mortality rate associated with heat-related illness in this study was 11.1%. **Conclusions:** Multiple organ dysfunction is seen in majority of the patients and calculation of simple admission J-ERATO score helps in predicting the same. Declining mortality rate observed in our study as compared to the earlier studies could be attributed to increased awareness, prompt diagnosis and initiation of rapid cooling measures.

Keywords: Air-conditioned heat stroke units, heat-related illness, J-ERATO score, outcome

Introduction

Heat-related illness is a common medical emergency with life threatening consequences. Thermoregulatory mechanisms of the body fail in maintaining homeostasis during heat waves of summer resulting in multiple organ dysfunction syndrome (MODS) with

significant neurological deterioration.^[1] Heat accumulation within the body is a combination of environmental exposure, increased metabolic requirements, and restricted or obtunded cooling mechanisms.^[2] The clinical spectrum of heat-related illness varies from early signs of dehydration, which could present as lethargy and generalized weakness. This could progress to heat cramps, where the patient could experience painful involuntary contraction of muscles, which usually resolves in a few hours with hydration and stretching of the muscles. Heat exhaustion is a mild version of a heat stroke with minimal neurological

Address for correspondence: Dr. Jonathan Arul Jeevan Jayakaran, Department of General Medicine Unit V, Christian Medical College, Vellore, Tamil Nadu, India.
E-mail: jonathan.ajj@gmail.com

Received: 23-04-2020

Revised: 10-06-2020

Accepted: 25-06-2020

Published: 25-08-2020

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_690_20

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How to cite this article: Ninan GA, Gunasekaran K, Jayakaran JA, Johnson J, Abhilash KP, Pichamuthu K, et al. Heat-related illness—Clinical profile and predictors of outcome from a healthcare center in South India. J Family Med Prim Care 2020;9:4210-5.

involvement, along with temperatures between 37° and 40°C. Aggressive cooling measures are imperative at this stage sans which could progress to heat stroke.^[3]

Earliest used definition of heat stroke worldwide was devised by Bouchama,^[4] wherein he defined heat stroke as core body temperature above 40°C, accompanied by hot dry skin along with central nervous system dysfunction, such as delirium, convulsions, or coma. The relevance of core temperature was challenged in the following years as the core temperatures of these patients would have already begun to decrease in response to pre-hospital treatment or transfer to hospital.^[5,6] Innovative classification systems have been developed without reference to core body temperature and estimating the severity of heat-related illnesses based on the grade of organ dysfunction caused.^[7] Classic heat-related illness or non-exertional heat-related illness affects elderly individuals with underlying medical co-morbidities that impair thermoregulation, avert removal from hot environment, or restrict attempted access to hydration or cooling.^[8] These conditions include cardiovascular disease, neurologic or psychiatric disorders, obesity and physical disability among many others.^[9] Pathophysiology of heat-related illness lies in dysregulation of thermoregulatory mechanism. As the body temperature rises, cutaneous vasodilation allows increased blood flow to the skin^[10] causing relative reduction in intravascular volume, decrease in visceral perfusion resulting in organ failure.^[4,11] In addition, heat stress releases inflammatory cytokines causing activation of leukocytes and endothelial cells leading to systemic inflammatory response syndrome.^[12]

In India, following establishment of Indian Meteorological Department, recording deaths due to heat wave was initiated in 1979 and in the annual reports on “Disastrous Events,” 505 deaths were reported from all over India in 2001. In 2015 deaths from heat stroke were recorded as 2040, 5 times as compared to 2001.^[13] Over the years, heatwaves have inclined to begin earlier and temperatures rise to 40–43°C in various parts of India.^[14]

Most common complications arising from heat stroke include acute respiratory distress syndrome, renal failure, shock, disseminated intravascular coagulation (DIC), rhabdomyolysis, hepatic dysfunction, and cerebral oedema.^[15] Several assessment tools have been developed for predicting clinical outcome in patients with heat-related illness. Hayashida *et al.*^[16] developed J-ERATO score in 2018 and validated the scoring through multiple independent cohorts in Japan. J-ERATO score was defined as the sum of the six binary components (systolic blood pressure <100 mmHg, respiratory rate >22/min, body temperature >38°C, heart rate >100 beats per minute, age >65 years, and Glasgow coma scale <15), for a total score of 6. Multivariate analyses performed at validation of J-ERATO score reported it to be independent positive predictor for in-hospital mortality, hospital admission, intensive care unit admission. This allows high alertness and early initiation of rapid cooling measures to contain the mortality and morbidity of heat-related illness.

Patients and Methods

Patients and setting

This retrospective study was conducted in tertiary care center in South India where in adult patients admitted with a diagnosis of heat-related illness during the summer months of April to July of 2019 were included. Patient search was initiated with assistance from medical records division and all consecutive in-patients who were admitted under Department of Medicine between April 1st 2019 and August 31st 2019 with a diagnosis of heat-related illness were identified and included in the study. Medical records of patients were reviewed and demographic details, comorbidities, symptomatology and duration illness prior to presentation, temperature at arrival, vitals, Glasgow coma scale, clinical examination findings, course of hospital stay, condition at discharge, outcome, radiological and blood investigations were recorded. The location of dwelling of patients were plotted on map and heat index was obtained through historical search from meteorological database.^[17,18] Patients with proven central nervous system infection, sepsis with identifiable source and malaria were excluded.

Patient management and outcome parameters

All patients were managed with supportive therapy including fluid resuscitation, correction of dyselectrolytaemia, hemodynamic support, mechanical ventilation, renal replacement therapy as indicated. Dedicated air-conditioned heat stroke ward was used for sicker patients. Organ system dysfunction was quantified using SOFA score (sequential organ failure assessment score) with variables being entered using clinical and laboratory parameters available and a score of 2 or more was considered to have MODS. J-ERATO score was also calculated based on vitals at presentation as assessment of early risk predictor and severity of heat-related illness was graded into low risk (score 1–4) and high risk (score 5–6) based on the same. The outcome of interest was mortality, need for ventilation, need for intensive care unit, and duration of hospital duration. Using the presence of MODS as high mortality indicator, various initial parameters were compared for assistance in prediction of poor outcome.

Ethical approval and funding

This retrospective study protocol was approved by the Institutional Ethics Review Board (IRB NO: 12260), Christian Medical College, Vellore, India. In this study, data was collected from the hospital inpatient electronic medical records, the information collected was anonymized.

Statistical analysis

Data was entered into a Microsoft Excel worksheet and results obtained were subjected to statistical analysis. Descriptive statistics were employed for all the variables in the study. Categorical and continuous variables were compared for outcome using the Fisher’s exact test and student t-test, respectively. All continuous data were expressed as mean with standard deviation (SD) unless the data was not normally distributed. A *P* value of < 0.05 was

considered statistically significant. Statistical analysis was done using Statistical Package for Social Sciences for Windows (SPSS Inc. Released 2007, version 16.0. Chicago).

Results

Data of 27 patients were included in analysis. 55% of the patients included in the study were females. Mean (SD) age of the patients included was 61 (13.5) years. The mean heat index of the localities where the patients were dwelling prior to presentation was 39.6°C, ranging from 37°C to 42°C. Baseline evaluation revealed that 48% of the patients had diabetes, 67% had hypertension, and 30% had underlying cardiovascular disease.

Medications which predispose patients to heat-related illness were reviewed and one third of them were found to be on beta blockers. Only 2 (7%) and 3 (11%) of the patients were on diuretics and antipsychotic medications, respectively. Baseline characteristics are described in Table 1.

The location of residence of the patients were plotted on geographical map as shown in Figure 1 which provides pictorial representation of distribution of cases and clustered cases indicates areas of higher case incidence. Contrary to the idea that dehydration in patients presenting with heat-related illness would result in hypernatremia and elevated lactate, 60% of the patients presented with hyponatremia with none having hypernatremia at presentation and only 25% had lactate elevation more than 2 mmol/L.

Patients with SOFA score >2 were considered to have MODS, which was the case with 66% of the admissions. Among the patients with organ dysfunction most common involvement was CNS dysfunction (77%), followed by respiratory distress syndrome (61%), acute kidney injury (50%), and hepatic dysfunction (22%) [Figure 2]. 16% of the patients with MODS required intensive care unit admission with ventilatory and vasopressor support and only one in three survived in spite of the same. Overall mortality of heat-related illness among in-patients was 11.1% and one among them had a SOFA score of 11 which was predictive of high risk of mortality. The treatment and outcome variables are described in Table 2.

Using statistical analysis, correlation of variables in predicting MODS and subsequently mortality was studied. Higher J-ERATO score at presentation was found to be an independent predictor for underlying MODS with significant *P* value of 0.029. However, none of the variables were found to predict mortality [Table 3].

Discussion

Heat-related illness encompasses a spectrum of illness which ranges from heat exhaustion to heat stroke. The aim of this retrospective study was to profile patients admitted with heat-related illness, identify risk factors which predisposes them

Table 1: Baseline characteristics of patients with heat-related illness (n-27)

Variable	Value
Age, mean±SD, years	61.67±13.53
Gender ratio (Male: Female)	12:15
Heat index, mean±SD, degree Celsius	39.63±1.62
Duration of illness, median (IQR), days	2 (2-3)
Hypertension	18 (67)
Diabetes mellitus	13 (48)
Cardiovascular disease	8 (30)
Parkinsons disease	2 (7.4)
Cerebrovascular accident	1 (3.7)
Predisposing medications	
Beta blockers	9 (33.3)
Diuretics	2 (7.4)
Anti-cholinergic	3 (11.1)
Anti-psychotics	1 (3.7)
Core body temperature, mean±SD, degree Fahrenheit	103.51±1.79
Total counts, mean±SD cmm	11540.74±4709.26
Creatinine, mean±SD mg%	1.38±0.77
Sodium, mean±SD, m mol/L	129.70±10.37
Bicarbonate mean±SD, m mol/L	19.22±2.64
AST median (IQR),	35 (25-86)
ALT median (IQR),	24 (14-53)
SOFA score, median (IQR),	3.33 (1-3)
J-ERATO score, mean±SD	3.41±0.97

SD=Standard deviation, IQR=Inter quartile range, AST=Serum aspartate aminotransferase, ALT=Serum alanine transaminase, SOFA=Sequential Organ Failure Assessment

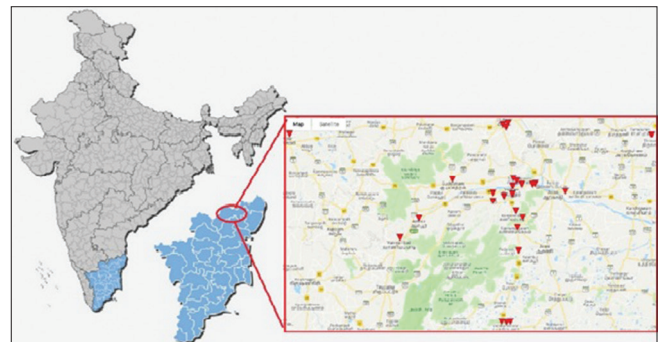


Figure 1: Figure depicting distribution of cases as red triangles in district of Vellore

to heat-related illness and identify predictors for MODS. This study was conducted in a tertiary care center in Vellore district of Tamil Nadu where heat waves are common in summer months and ambient temperatures recorded reach more than 40°C.

The overall mortality rate associated with heat-related illness in this study was 11.1%. Similar studies done by contemporaries in the same center had reported mortality rate of 50% in 2005^[19] and as high as 92.8% in 1998 [Figure 3]. These trends are welcome especially in the setting of climate change and global warming resulting in hotter summers. Reasons for this significant decrease in mortality could be attributed to early recognition due to increased awareness among healthcare workers, rapid cooling assisted by advancement in air conditioning facilities which

have extended to include emergency department and dedicated heat-related illness wards in summer months.

Demographic details of the patients reveal that elderly (age more than 60 years) were most commonly affected and high proportion of them have underlying co-morbidities which have been implicated in non-exertional heat-related illness for decades. High prevalence of hypertension combined with anti-hypertensive medications such as beta blockers and diuretics further put them at risk for developing heat-related illness. Topographical distribution reveals clustering of cases within the urban sector of the city. This data could be biased as the healthcare center was in close proximity to the affected patients. However, being a referral center, it also received cases from other districts. However, spreading awareness among population within these neighborhoods would be a daunting yet rewarding venture in preventing heat-related illness.

Most patients presented within 2 days of illness with a core temperature at arrival of above 103°Fahrenheit. Assessing the vitals at presentation and looking for source of infection along with organ dysfunction is of prime importance but does not surpass the need for initiation of aggressive cooling methods. A simple binary pre-hospital score for risk assessment of patients with heat-related illness was validated in Japan^[16] and is a composite of vitals at presentation of illness along with age and core temperature. J-ERATO score was found to be an independent predictor of MODS (P value 0.029) in this study and using initial assessment with calculated of J-ERATO score, patients could be categorizing into those more susceptible for

MODS; hence, identifying those needing prompt intensive care unit admission. A previous similar study done in same center had concluded that high levels of CPK (1000 IU/l), metabolic acidosis, and elevated liver enzymes were associated with MODS.^[19] Electrolyte abnormality, in particular sodium, has also been studied as a predictor for mortality in heat-related illness. Study conducted by Haufaster *et al.*^[20] concluded serum sodium abnormalities were frequently seen in patients with non-exertional heat-related illness; however, only hypernatremia was found to be an independent risk factor of death. Most of the patients in this series had presented with hyponatremia, which were similar to studies conducted by Lakhotia *et al.*^[21] and Mohanaselvan *et al.*^[22], and no predictive potential for mortality or development of organ dysfunction could be delineated statistically.

Among patients with MODS, neurological obtundation as depicted by GCS score of less than 15 was most common, followed by acute respiratory dysfunction. Higher intensive care admissions were seen in patient with MODS with only one in three surviving the same. Statistical analysis was not able to conclude with significance any predictor for mortality. However, this finding should be considered with caution in view of low mortality rates in this series. Assessment of severity using simple at admission J-ERATO score at primary care level and initiation of cooling measures and triage of patients with MODS to higher centers by primary care physician can improve morbidity and mortality.

Being a retrospective study, there are limitations. Variation in diagnostic investigations and therapeutic practice could have

Table 2: Treatment and outcome variables of patients with heat-related illness (n=27)

Variable	Values
Evaporative cooling method	27 (100)
Cold saline infusion	16 (59.3)
Presence of MODS	18 (66.7)
Use of vasopressors	3 (11.1)
Need for ICU care	2 (7.4)
Need for mechanical ventilation	3 (11.1)
Duration of hospital stay, mean±SD, days	7.44±3.21
Mortality	3 (11.1)

MODS=Multi organ dysfunction syndrome, ICU=Intensive care unit

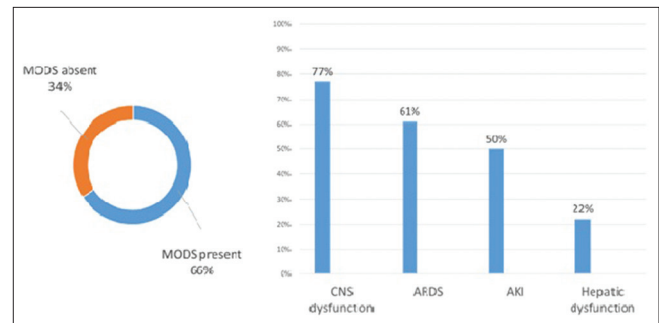


Figure 2: Figure showing proportion of patients with multiple organ dysfunction syndrome and relative percentage of organs involved

Table 3: Comparing patients with heat-related illness with and without multi-organ dysfunction

Characteristics	MODS present (n=18)	MODS absent (n=9)	P
Age, mean±SD, years	64.5±11	56±16.9	0.12
Duration of illness, mean±SD, days	2.3±1.1	2.3±1.3	0.71
Temperature at presentation, mean±SD, degree Fahrenheit	103.6±1.9	103.2±1.4	0.65
J-ERATO score	3.7±0.9	2.7±0.8	0.01*
Leukocytes, mean±SD, cmm	11,455±4762	11,711±4880	0.89
Sodium, mean±SD, m mol/l	131±10.1	127±10.8	0.37
Metabolic acidosis (HCO ₃ <18 mEq/L)	9 (50.0)	2 (22.2)	0.17
CPK >1000 U/L	7 (38.9)	3 (33.3)	0.78
Mortality	2 (11.1)	1 (11.1)	1.00

MODS=Multi organ dysfunction syndrome, CPK=creatin phosphokinase, *significant value

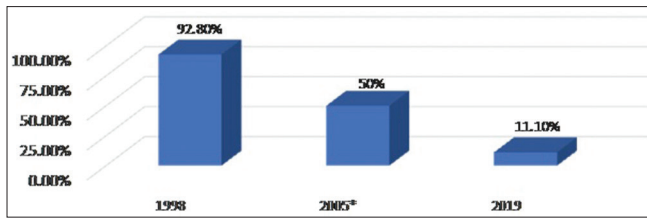


Figure 3: Graph showing mortality of patients admitted with heat-related illness in same center over 2 decades

influenced the outcome. The small number of patients included and low mortality rate limited statistical analysis with multiple logistic regressions. These limitations could be overcome with a prospective study with sufficiently large sample size.

Identification of similar clinical syndrome complex along with supportive risk factor evaluation and laboratory investigations could help primary physician in earlier diagnosis of heat-related illness. Application of J-ERATO score for prognostication of multiple organ dysfunction syndrome could assist decision making in early referral or intensive care admission after prompt cooling measures have been initiated.

Conclusion

MODS is seen in majority of the patients with heat-related illness and calculation of simple at admission J-ERATO score helps in predicting the same, warranting intensive care unit admission and close monitoring. The overall mortality rate associated with heat-related illness in this study was 11.1% which has significantly declined over last few decades. This could be attributed to increased awareness, prompt diagnosis and rapid cooling measures coupled with air-conditioned emergency department and dedicated heat-related illness wards during heat waves.

Research quality and ethics statement

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting and reproducibility guidelines set forth by the EQUATOR Network. The authors also attest that this clinical investigation was determined to require Institutional Review Board/Ethics Committee review, and the corresponding protocol/approval number is IRB Min. No. 12260. We also certify that we have not plagiarized the contents in this submission and have done a Plagiarism Check.

Financial support and sponsorship

The authors received no financial support for the research, authorship and/or publication of this article.

Conflicts of interest

There are no conflicts of interest.

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