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REVIEW ARTICLE

HEAT STROKE: A REVIEW ON STRIKING HEALTH RISK OF GLOBAL WARMING

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ABSTRACT

Global climate change is the most challenging and chronic natural calamity that continuously increases the number of intense heat waves and heat events. Earth's temperature is rising at a rate of 2℃ per century, whereas according to Economic Survey of Pakistan global temperature will rise by 1.5℃ till 2050. This continuous increase in temperature and extreme heat causes the most weather related deaths each year and also poses serious health problems such as heat exhaustion or heat stroke. Heat stroke is non infective form of hyperthermia characterized by higher core body temperature up to 40℃ due to failure of thermoregulation that leads to neurological dysfunction that range from modest alteration in mental activity to coma. The present study summarizes current knowledge about heatstroke and determines its worse effects on human body, also highlights its symptoms, causes and possible treatments that can be given immediately to its victims. Data of heat stroke cases from different areas of Asia and Europe was collected and summarized. Tall buildings, deforestation, failure of thermoregulation, greenhouse gases, removal of green belt and pollution are found to be the main causes of heat stroke. Techniques for rapid cooling of patients include hydration, immersion in cold water, immediate removal from heat source and the use of cold packs. Severity of the conditions demands rapid and solid action planning by the governments to mitigate this global warming issue that poses serious health issues like heat stroke. General public awareness may prove beneficial in this regard.

INTRODUCTION

Earth's temperature is increasing gradually day by day by the phenomenon that is called global warming and ultimately it is the main cause of many heat-related illnesses. By the burning of fossil fuels, greenhouse gases are emitted that cause increase in global warming consequently the average temperature of the earth has been raised. Until the 1950s only CO_2 and H_2O were considered as GHG's but from 1971 CH_4, N_2O, and CFC's are also recognized in GHG's. Scientific researchers have shown that global warming is increasing at the rate of 2°C per century (Leon and Baryan, 2010). Heatstroke is a striking feature of global warming that leads towards multi-organ failure and body temperature elevates up to 40°C or above this (Canel *et al*., 2016).

There are usually two types of heat strokes, exertional and non-exertional heat strokes. A comprehensive table 1 shows different parameters that can differ between non-exertional and exertional heatstroke. Exertional heat stroke is due to very high temperature and heatwaves while non-exertional heatstroke is caused due to heat produced by muscular activity during heavy exercise or continued work in hot days (Ali *et al*., 2016; Haded *et al*., 2005; Jardine, 2007).

According to Economics Survey of Pakistan 2006, the total population of the world is nearly 6.5 billion with the addition of 80 million people each year (Sajjad *et al*., 2009). Pakistan is at the 6th number in the world on the basis of population. The main cities like Lahore, Faisalabad, Rawalpindi, Multan, Gujranwala, Sargodha and Sialkot are highly populated and are very hotter as compared to rural areas due to worse effects of heatwaves and urban heat island effect. The increase in heatwave events is due to the ever-increasing population in Punjab, Sindh, and other regions of Pakistan. Baluchistan and Sindh are likely to experience increased heatwave events but the most striking increase is expected in Punjab plains.

Table 1: Factors that can differentiate exertional and non-exertional heatstroke.

Factors	Non Exertional heat illness	Exertional heat illness
Age group	Mostly in very young or elderly people	Young people mostly sports man and military personnel
Heat factor	External heat mostly due to heat waves	Intrinsic heat due to muscular activity
Cause	Inefficient thermoregulatory mechanism	Inability to dissipate excess heat production
Time of occurrence	Mostly in summer season due to extremely hot environment	In any time of year

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Since the start of the 20th-century earth's average temperature has become warmer and particularly at a fast rate during the last 50 years. Figure 1 exhibits the number of deaths due to high temperature in different areas of the world 2003 to 2015 (Ali *et al*., 2016; Blois *et al*., 2015; Kilbourne, 1982).

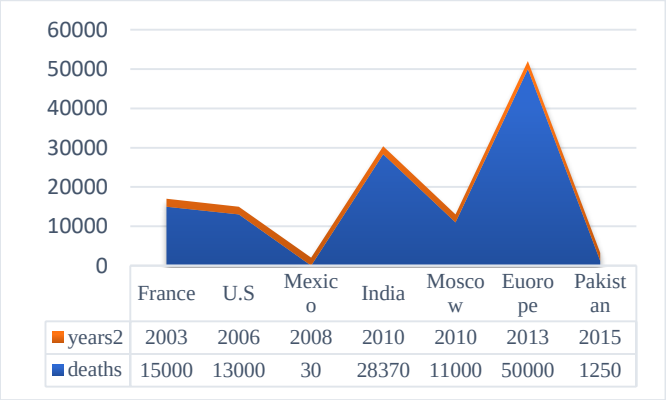

Fig 1: An area graph that is showing no. of deaths in different countries at different times

It is predicted that 3 heatwave events are increasing per year and till the last of the 21st century more than 75 events will achieve in Punjab. (Kilbourne, 1982). The third-largest ice mass in Pakistan, the Himalaya-Karakoram Hindukush region, has warmed up more than 1.5ºC, and an increase in 5ºC is expected by the end of the 21st century (Sajjad *et al*., 2009).

In Western Europe, June 2017 was exceptionally very hot and this heatwave returned to Spain in July and the consequence was a massive forest fire. These heat episodes remained till august and extended to many areas of southern Europe (Kew *et al*., 1970; Meehla *et al*., 2016). Table 2 shows different parameters such as deaths, age, sex and symptoms related to high temperature in different years (Kilbourne, 1982; Bounchama, *et al*., 2007; Khan *et al*., 2012; Blois *et al*., 2015; Carpio, 2015; Ali *et al*., 2016).

On 28th June 2019 in the southern town of Veraguas, the highest temperature was recorded which was 46◦C beating 44.1◦C in 2003. It is estimated by WMO that By keeping in view the adverse effects of increasing temperature following study aims to discuss worse effects on body, risk factors, possible solutions and medication of heat stroke.

METHODOLOGY

A comprehensive online search was conducted with publications including original articles, reviews, weather reports, case reports and news items. A number of keywords and search topics were used to retrieve published documents on heat stress and human health. Data was collected by using keywords 'heatstroke' OR 'stroke heat' OR 'heat hyperpyrexia' OR 'hyperthermia' probably 2019 will be among the top five hottest years and five years ranges from 2015-2019 will be the five hottest years ever recorded (Taleb, 2010 ; Martin, 2013 ; Masters and Henson, 2016 ; Masters, 2016; Myint, 2016; Samenow, 2016; Masters, 2017; Watts, 2018; Depois and Galey, 2019).

In Pakistan climate is becoming severe in last decades. The most worsen conditions were experienced in Karachi where 1200 people died in June 2015 due to extreme heat and shortage of water. During that time the highest recorded temperature was 44.8°C. In 2010 in Mohenjo-Daro heat stroke kill 18 people and the highest temperature was recorded 53.5ºC (Figure 2 indicating highest temperature records in different countries). 4000 cases of heatstroke were reported in Pakistan in 2015 and in India, 1400 people lost their lives due to heatstroke, in the same year in Iran heat index broke all world records (Sajjad *et al*., 2009).

Table 2: Different parameters related to extreme temperature

Year	Area	T°C	Deaths	Age	Sex	Symptoms
Aug 2003	Europe	>40°C	14800	Mostly 40-65yrs Old	Mostly Males	Dehydration Neurological Abnormalities
July 2012	USA	>40°C	23	Average 65	Both Male/ Female	Renal And Hepatic Failure
June 2015	Pakistan	41.2-44.8°C	1200	Median Group	Mostly Males	Abnormal Pulse And Respiratory Rate And Low Blood Pressure
2016	Maricopa	47.8°C	130	50-64(41%)	Males (72%)	Increase In Body Temperature And Renal Failure

OR 'pyrogenic or non-pyrogenic hyperthermia'. Table 3 depicting different terminologies related to heat stroke. The retrieved documents contained necessary information such as, authors, keywords, titles, abstracts, countries, journals, cited references and others.

Causes of heatstroke:

Failure of Thermoregulation: Heat stroke can be caused by continued contact with sunlight (Shah and Najib, 2016) when the thermoregulatory system fails and the internal body temperature gets higher and causes heat stroke (Grogan and Hopkins, 2002). Outdoor

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temperature, humidity, UV rays, clothing, wind strength, and heat repellent material are the main impacts that can cause the rise in internal body temperature (Miyake, 2013).

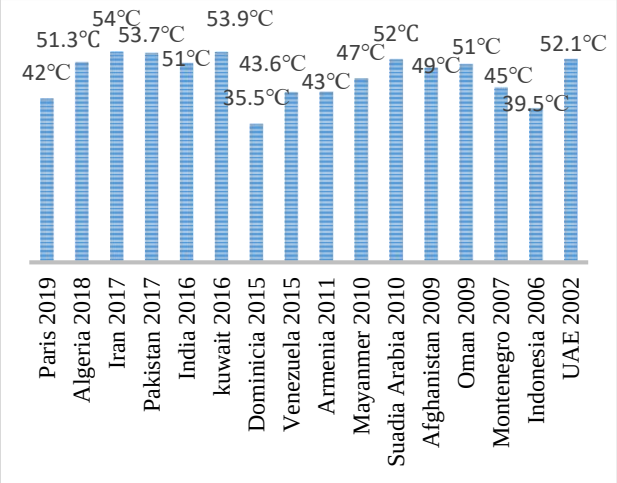

Fig 2: Graph showing highest temperatures recorded in different countries in different years.

Table 3: Different terms related to heat illness.

Heatwave	According to the World Meteorological Organization (WMO) heat-wave occurs when the daily maximum temperature of more than five successive days overshoots the maximum temperature by 5°C, from the regular temperature of a particular area.
Heat stress	The discomfort and physical stress of being exposed to a hot environment, especially during physical activity
Heat exhaustion	A condition of dehydration and salt depletion due to high temperature. Tiredness, weakness, headache, nausea, and vomiting are symptoms of heat exhaustion.
Heat syncope	Due to high ambient temperature, a condition of fainting, blood flow reduces to the brain
Heat cramps	A condition of electrolyte deficiency in muscles due to hard exercise
Hyperthermia	Increased body temperature above the hypothalamic set point when heat-dissipating mechanisms become impaired (by drugs or disease) or stunned by external (induced or environmental) or internal (metabolic) heat
Multiorgan-dysfunction syndrome	Continuation of changes in more than one organ system that occur after trauma such as trauma sepsis, or heat stroke

Summer season in Pakistan: During the year 1996-2007, there is an increase in 3ºC temperature in Pakistan because of this the summer season gets long and due to this, Pakistan is at threat of heatstroke. This heat index increasingly spreads from the south to the north half. In the summer due to an increase in heat index the heat-related death rate increases (Rasul and Zahid, 2010). At the end of the 21st-century future climate projections show that at least 5 °C temperature will increase over the Indus Delta (Khan *et al*., 2012).

Dehydration: Dehydration results in decreased blood volume due to which the capacity of heat transport in the blood gets decreases and increases the chance of heat retention which affects thermoregulation and may cause heat illness (Miyake, 2013). Heatstroke can be caused by hyperventilation due to the excretion of more water and salt (Shah and Najib, 2016).

CO_2 Emission: Each time the CO_2 emission produces 1.9-4.5ºC of heat, according to new discoveries 5% chance of producing 7.1 ºC heat on each emission increases. All the natural gasses like methane, burning of fossil fuels, deforestation, combustion, and rotting of wood release increases CO_2 the global warming, the earth's temperature rises, which could affect mankind and may cause an extreme rise in temperature during summer and increase the risk of heatstroke (Sherwood and Huberb, 2010; Ajay 2012).

Symptoms of heatstroke: Symptoms of heat stroke can sometimes mimic a heart attack or other conditions. Change in physiological response such as hyperthermia and neurological dysfunction are the common symptoms of heat stroke (Bouchama and khonhel, 2002). These dysfunctions may include nervous excitement, cognitive dysfunctions or disturbances of consciousness (Bouchama and khonhel, 2002; Zahid and Rasul, 2004; Bounchama and Chaves, 2007; Walter and Carraretto, 2016).

Pathophysiology

Heatstroke, when severe, results in multi-organ dysfunction. When the ambient temperature rises the efficiency of heat radiation becomes reduced, in a humid environment the efficiency of the body to lose the heat through evaporation reduces as the sweat does not dry and the body surface temperature rise (Ahmed, 2005; Miyake, 2013). Figure 3 showing Multi-organ system effects during heat stroke.

In one study due to heatstroke, 20 percent of cases show injury of the Central nervous system, 23 percent of the cases show muscle destruction causes the release of myoglobin into the bloodstream and risk of renal injury, 9 percent of the cases shows Hepatocytes damaged causing inability of the blood to coagulate and hepatitis. Myocardial muscle damage results in abnormal heart rhythm or even abnormal beating and abnormal contraction of the heart (Grogan and Hopkins, 2002; Hemmelgarn, 2013). During hyperthermia, a decrease in

perfusion to the skin, neurologic impairment, or intracranial disease impairs the heat loss via radiation and convection and also impairs the physiological cooling mechanism (Farrell *et al.*, 2015).

Effects of heat stroke

Besides the body has an efficient system to reimburse heat injury but each individual has different set points so sometimes the body cannot recompense and critical heatstroke assure. The gastrointestinal tract, kidney, heart, lungs, and central nervous systems are the most common organs that are affected due to heatstroke (Grogan and Hopkins, 2002).

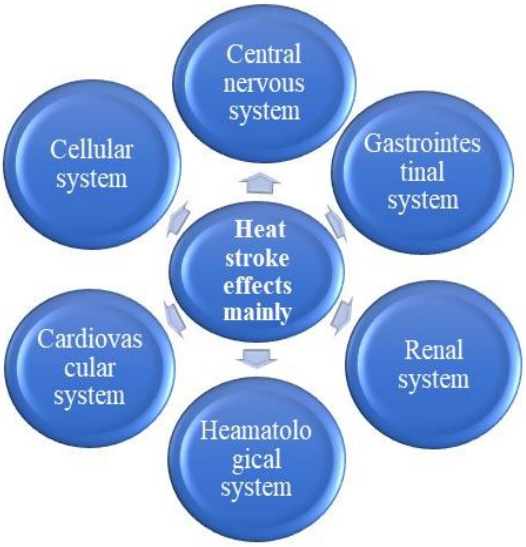

Fig 3: Multi-organ system effects during heat stroke

Numerous inflammatory cytokines produce at a higher rate due to heat which contributes to neuronal injury, low blood pressure, formation of blood clots due to increase in platelet count, endothelial cell injury, increase the level of RBCs and neutrophils, increase in blood viscosity, greater capacity of blood vessel walls to allow for the flow of molecules, all resulting in circulatory collapse and multisystem organ failure (Leon and Baryan, 2010; Carpio, 2015. Hyperthermia even during gestation may cause critical conditions like embryonic death, miscarriage, growth retardation, and other developmental defects (Ali *et al*., 2016).

Central nervous system effects

CNS damage is among the most common consequences of hyperthermia (Ali *et al*., 2016). Brain regions, the anterior and posterior cingulate cortices, ventromedial prefrontal cortex, premotor and motor areas, visual cortex, thalamus and cerebellum shows sweating related activation. The failure in function of these controlling centers can impairs heat loss (Farooqi *et al*., 2005). Cerebellar Purkinje cells are selectively vulnerable to heat injury (Leon and Baryan, 2010).

Heat stroke can cause cellular injury, circulatory changes, tissue abrasion to the heart, liver, kidney, and blood coagulation system, degradation of Purkinje cells, and depression of all cerebral functions (Ali *et al*., 2016). It was also revealed that the ability to memorize things, short-term memory as well as working memory has been decreased by abnormal activity of frontal lobe due to hyperthermia (Sun *et al.*, 2013). The synthesis, release, and function of cholinergic enzymes disturb during heat stress which causes disability in the development of neurons, oligodendrocytes, and tissues of the CNS (Ali *et al.*, 2016).

Cellular effects

Heat causes apoptosis (Ali *et al*., 2016). Regulation of apoptosis and other regulatory processes of the cells is dependent on the activity of Cysteine proteases. Protein denaturing is considered a closely related factor to cell death. Interruption of electrochemical depolarization, ionic transport through trans-membrane proteins, and disturbance of cellular signaling mechanism and mitochondrial function are all causes due to excess heat (Walter and Carraretto, 2016). The functioning of neurotransmitters such as norepinephrine and serotonin is also affected during heat stress (Ali *et al.*, 2016).

Neurological and cognitive effects

Neurological dysfunction is a fundamental feature of heatstroke and is considered the first organ to be affected in HS as Purkinje fibers are sensitive to the toxic effects of heat. Neurological damage may lead to disorganized metabolism, central edema and reduction of blood and oxygen supply to tissues, anxiety, dizziness, and coma (Haded *et al.*, 2005). Mental abilities and activities are referred to as Cognition and Hyperthermia can severely affect attention, memory, and processing of information. Hyperthermia disturbs the pathways and connections involved in cognitive pathways (Walter and Carraretto, 2016).

Gastrointestinal effects

The Systemic inflammatory response syndrome (SIRS) is involved in multiorgan dysfunction. In heat stress, SIRS is a response to bacterial infection that harms the gut and other organs by prolonged reductions in gastrointestinal blood flow, and this blood flow foster nitrosative and oxidative stress that causes tight junctions of the gut to become “leaky” (Leon and Baryan, 2010). Thus, Heat and decreased blood flow impairs the permeability of GI tract due to which intestinal bacteria, Gram-negative and Gram-positive bacteria that are natural flora of the gut lumen and when their toxins pass through the intestinal wall they enter the portal vein blood flow and circulate throughout the body via the liver. Moreover, blood flow to GI tract reduces, denaturation of proteins and production of free radicals increases and GI barrier integrity loses (Miyake, 2013; Walter and Carraretto, 2016).

Renal effects

Almost 30% of the patients died due to renal failure in heatstroke (Haded *et al.*, 2005). Renal injury in heatstroke

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is multifactorial, hypovolaemia, rhabdomyolysis disseminated intravascular coagulation are contributing factors (Wang *et al*., 1995). The clinical findings point out that due to lack of adequate blood flow to each kidney, nitrogen compounds increase in the bloodstream (khan *et al*., 2012). Figure 4 represents a schematic diagram that shows events that lead to heatstroke.

In exertional heatstroke patients, rhabdomyolysis occurs and myoglobin level increases myoglobin which has toxic effects on the kidney nephrons as a result of which uric acid is produced in large amounts in the body. Therefore Rhabdomyolysis exacerbates renal dysfunctioning, it can also lead to coagulopathy (Leon and Baryan, 2010).

Hematological effects

Heatstroke causes direct tissue damage, proteins denaturing, membrane fluidity changes,uncoupled oxidative phosphorylation, high blood glucose, and increased aldosterone level which lowers the level of potassium (Casa *et al*., 2010; Ramos *et al., 2012*). Synthesis of neurons, function of oligodendrocytes and tissues of CNS also disturbs due to heatstroke (Ali *et al*., 2016). When body temperature reaches 40°C enzyme denaturation starts at cellular level and when the temperature reaches up to 41°C, oxidative phosphorylation disturbs due to decrease in mitochondrial function which can lead to organ impairment (Miyake, 2013).

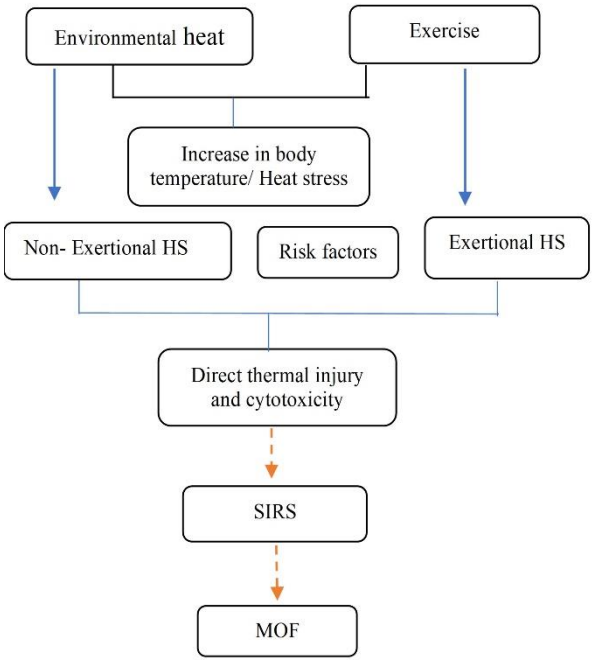

Fig 4: Schematic diagram that shows events that lead to heatstroke. EHS (Exertional heat stroke), NEHS (non-exertional heat stroke), SIRS (Systemic inflammatory response syndrome), MOF (Multi organ failure).

In response to the inflammatory process in heatstroke, hematological failure starts with reactive leukocytosis, later on, alterations in platelet aggregation exist (Casa *et al*., 2010).

Cardiovascular system effects

The main system that is highly disrupted by extremely high temperatures is cardiac system (Buxa *et al.*, 2008). When thermoregulatory mechanism to dissipate heat fails, heat released from the body core is obstructed and body temperature starts to rise and causing heat illness. When body is exposed to an increased temperature for a longer time, then dehydration occurs, blood volume reduces and blood is possessed at the peripheral blood vessels that are dilated. Increased viscosity of the blood causes burden on the heart. To enhance the reduced blood volume the heart contract fast and heart rate increases. But the blood flow to the cardiac muscles is already diminished because heart is itself exposed to a higher temperature so the heart becomes further overloaded. Thus heatstroke can cause an increase in heart rate, low blood pressure, sinus tach, and prolongation of the QT interval (Miyake, 2013). One human study reported that 78% of patients with requite of heart failure developed manifest heart failure in as little as 2 hours after exposure to temperatures of 32.2°C and 75% relative humidity (Farrell, 2015).

Treatment

The effective treatment requires immediate removal from the heat source and if the symptoms do not seems to be resolved within20-30 minutes then heat stroke should be considered strongly. The therapeutic techniques like immediate cooling and support of organ system are very helpful in transferring of heat from body to environment without disturbance of flow of blood to the body (Bouchama and khonhel, 2002; Glazer, 2005).

Immersion in iced water is the most commonly used and efficient technique in which patient is placed in a tub filled with iced water and continued massaging is done to promote vasodilation and heat loss (Bounchama and Chaves, 2007). Evaporative plus convective cooling may also be effective by crushed ice applied diffusely to the body. Figure 5 showing different treatment methods of heat stroke (Smith and Wallis, 2005).

During extreme temperatures, it is essential to maintain the hydration and electrolyte balance of the body. When the level of sweat is not replaced, hypervolemia occurs which can lead to further decreased sweating and in severe conditions can cause hypotension (Gaudio and Grissom, 2016; Li *et al*., 2013).

Dantrolene is a medicine that acts on elements of muscles that are unable to release the Ca+ amount from the sarcoplasmic reticulum of skeletal muscles to the cystol. Due to which excitation-contraction coupling that is dependent on Ca+ may inhibited so involved in the controlling process (Haded *et al.*, 2005). Several other medicines like metaxalone and curare act as skeletal

muscle relaxants and reduce heat production during abnormal muscle contraction (Bounchama and Chaves, 2007). Table 5 indicates different defensive measures against heat stroke.

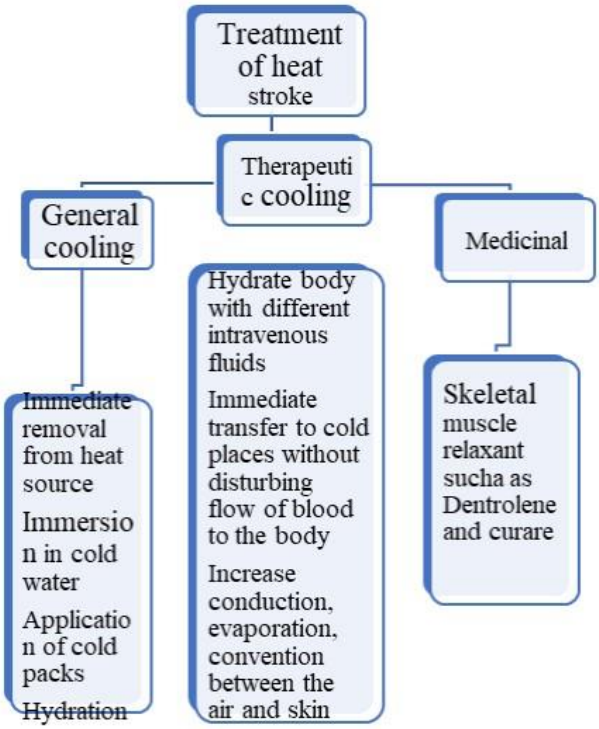

Fig 5: Schematic diagram describing different methods to treat heat stroke.

General awareness

Through social media, education and training, awareness in public regarding hazardous effects of heat illness can be created. To prevent the heat absorption, people should wear light colored dresses that help in sweat evaporation, maintains hydration by drinking different healthy fluids that can also replace the deficiency of electrolytes during the hot weather (Gaudio and Grissom,2016). Enough lowering of body temperature can be lethal, and those who survive, despite of given strong medications or treatments may become permanently neurological patient (Smith and Wallis, 2005).

Conclusion

Heat stroke is continuously becoming one of the main causes of significant morbidity and mortality, world widely. Global warming continues to increase earth's temperature. Rise in temperature every year increases the events of heat related illnesses. Heat stroke is a preventable disease, however, people who spend extensive periods of times in hot temperatures especially elderly people, are more at risk of severe symptoms and, delayed diagnosis can result in death in the most severe cases. Impaired regulation of inflammatory and stress responses and failure of thermoregulation aids the progression from heat stress to heat stroke and contribute to the severity of tissue injury and multi-organ dysfunction. Treatment should be comprehensive, including body temperature management, body cooling, using all available cooling methods along with respiratory, circulatory, hepatic, and renal function support. Awareness to public and knowledge about giving immediate treatments to heat stroke patients can minimize the chances of multiorgan injury and deaths caused by heat stroke.

Table 5: Defensive measures that should adopt during heat stroke.

Preventive measures	**Avoid strenuous exercise, Avoid sun exposure, Avoid the use of caffeine or alcohol**	**(Grogan and Hopkins, 2002), (Gaudio, and Grissom ,2016), (Leon and Baryan, 2010)**
Protective measures	Wear light clothes, Drink plenty of water, Road side plantation	(Smith and Wallis, 2005), (Gaudio and Grissom, 2016)

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