CLIMATE CHANGE AND CHRONIC KIDNEY DISEASE

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ABSTRACT

Background: The adverse effects of climate change are detrimental to health, wealth and economy of mostly the poor and low-income communities around the world. These climate changes have bearing on human health evidenced by increase in heat-related illnesses and deaths. It is well documented that acute renal failure is one of the complication of heat stress. All these factors eventually develop repeated subclinical renal dysfunction, which may further develop into chronic kidney disease (CKD). In India CKD is an increasing public health concern with poor outcome.

Methods: Renal insufficiency patients who are admitted during January 2011 to December 2012 are selected; in this 198 patients with evidence of CKD were taken as cases. These CKD patients were admitted into Nephrology unit of MIMS hospital, Nellimarla.

Results and Conclusion: In our study, most of the CKD (48.4%) cases are registered relatively high between the months of March and May. In the present study, creatinine clearance values using CG, MDRD and MCQE in CKD patients are significantly lowered when compared with control (p<0.001). In our study, most of the people registered are agricultural workers (24%), construction workers or laborers (23%) and industrial labor workers (19%) who belong to low income group. In the present investigation, it was observed that there was a progressive decline in GFR as the age advanced; these are more at risk of developing renal disease when exposed to heat stress.

Keywords: climate change, chronic kidney disease, glomerular filtration rate

INTRODUCTION

Increasing frequency and intensity of heat waves is one of the consequences of global warming. As there is progressive global warming, the adverse affect of heat wave on human health is increasing day by day. Exposure to hot weather causes heat related illnesses [1], [2]. Heat related illness depends not only on weather condition at any given time, but also on previously existing health conditions and also socioeconomic status [3]. Most of the people affected by this type of stress are elder people and urban dwellers [4].

The temperature is on rise for the past few years and continues in to the future pertaining to the present scenario. In India majority of the population depends on agriculture and industries. Thus continuous exposure to constant hot and humid weather is inevitable. Also, the low income groups survive in poor living conditions with meagre facilities. Heat stroke is a life threatening illness characterized by elevated core temperature that rises above 40°C leading to abnormal organ function and death if not treated. The incidence of such deaths may increase with global warming [5], [6].

Heat stress causes volume depletion, if severe; it may cause acute kidney injury even in healthy individuals. It is a known fact that acute kidney injury leads to chronic kidney disease in general, in the absence of functional recovery from the initial injury and recent studies have shown that sub-clinical damage also increases the risk of CKD. Hyperthermia induced volume depletion leads to repeated sub-clinical damage to the kidney, and further progresses to CKD [7], [8].

Chronic kidney disease manifests as a result of either structural damage or decreased kidney glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m² for 3 or more months [9]. Classification is a major step in CKD which is done by quantifying the glomerular filtration. GFR will assess the filtering capacity of nephrons in the kidney [10]. GFR is helpful for not only for early detection of renal impairment but also a good indicator for the need of dialysis. CKD patients are classified based on GFR under five stages. These are stage 1 (GFR ≥ 90 ml/min/1.73 m²), stage 2 (GFR 60 to 89 ml/min/1.73 m²), stage 3 (GFR 30 to 59 ml/min/1.73 m²), stage 4 (GFR 15 to 29 ml/min/1.73 m²) and stage 5 (GFR less than 15 ml/min/1.73 m²) [11].

Diabetes mellitus, hypertension, glomerulonephritis, renal vascular disease and many other nephrotoxic factors cause progressive damage to kidney function and the effect of heat stress speeds up the progression to overt disease. Prevalence of CKD with characteristics similar to the Indian epidemic has been reported in specific regions in Sri Lanka, Egypt and Central America [12], [13]. Many epidemiological studies have been carried out on hot weather condition and various heat related illnesses. But very few studies were carried out on heat stress and related renal dysfunction. Besides, most of the studies are carried out in well developed countries of west, where the living conditions and facilities are relatively better than those of India, still a developing country. Thus the present study is chosen to study the effect of heat on the development of CKD where poor living conditions and enormous exposure to heat prevails in most of the parts of India.

MATERIALS AND METHODS

Control group comprised of 123 healthy individuals who were free of features of kidney disease and were having a normal blood urea and serum creatinine level. The upper limit for serum creatinine levels was 1.2 mg/dl and the corresponding value for blood urea was 45 mg/dl. Individuals suffering from diseases that are likely to alter these parameters were excluded from the study. Likewise, persons with history of drug intake which cause changes in these parameters were also excluded. Renal insufficiency patients who are admitted during January 2011 to December 2012 are selected; in this 198 patients with evidence of CKD were taken as cases. These CKD patients were admitted into Nephrology unit of MIMS hospital, Nellimarla. The CKD cases included both non dialysis group and hemodialysis group. They were included in the study on the basis of clinical signs and symptoms of kidney disease along with elevated blood urea and serum creatinine levels. The hemodialysis patients
were undergoing hemodialysis in Nephrology department, but non
dialysis patients were under conservative medical therapy.

Informed consent was taken from the patients and controls who
participated in the present study. Ethical committee approval has
also been obtained.

In all these groups blood urea and serum creatinine were measured.
The blood urea was estimated by GLDH – Urease method [14].
Serum creatinine was estimated by Jaffes method [15]. The eGFR
was computed by the following methods:

Cockcroft-Gault Creatinine Clearance (ml/min) = (140 – age) x
(weight in kg) / Serum Creatinine (mg/dl) x 72 (Multiply with 0.85 if
female) [16] CG formula is adjusted to body surface area (BSA) by

BSA = (W^{0.425} x H^{0.725}) x 0.007184 [17], [18].

MDRD Creatinine Clearance (ml/min/1.73m²) = 186 x (Serum
Creatinine (mg/dl))^{1.154} x (age in years)^{0.203} x 0.742 (Multiply with 0.742 if female) [19].

The MCQE estimated GFR (ml/min/1.73 m²) = \exp[1.911 + 5.249 / SCr – 2.114 / SCr^2 – (0.00686 x age [years]) - 0.205 if female] [20].

SCr is Serum Creatinine in mg/dl. Values <0.8 mg/dl set to 0.8 mg/dl,
as per the reported method.

**Statistical analysis:** All the data is expressed in Mean and Standard
deviation. For the statistical significance, Z test was performed

**RESULTS**

<table>
<thead>
<tr>
<th>Table 1: Cases registered in Renal Insufficiency and CKD during the period of January 2011 to December 2012</th>
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<tbody>
<tr>
<td>Months</td>
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<td>December</td>
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The table 1: Shows the number of cases registered as Renal
Insufficiency and CKD are much higher in the month of March to May
then compare to other months.

<table>
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<th>Table 2: Demographic features and diagnostic parameters in controls and CKD Patients</th>
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<tr>
<td>Age in years</td>
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<tr>
<td>Sex (Males %)</td>
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<tr>
<td>(Females %)</td>
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<tr>
<td>Body weight(kgs)</td>
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<td>Height (cm)</td>
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<tr>
<td>Blood urea(mg/dl)</td>
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<td>Serum Creatinine (mg/dl)</td>
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The table 2: Shows blood urea and serum creatinine were
significantly higher (p<0.001) in CKD patients when compared to
control.

<table>
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<th>Table 3: Creatinine clearance in controls and CKD Patients</th>
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<tr>
<td>Control (n=123)</td>
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<td>CG (ml/min/1.73m²)</td>
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<td>MDRD (ml/min/1.73m²)</td>
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<td>MCQE (ml/min/1.73m²)</td>
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The table 3: Shows When the creatinine clearance values between
control and CKD cases were compared on the basis of CG, MDRD and
MCQE equation it was observed that the values were significantly
decreased (p<0.001) in the CKD cases as per all the three equations.

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<th>Table 4: Distribution of CKD patients based on occupation</th>
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<tr>
<td>Occupation</td>
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<tr>
<td>Agriculture workers</td>
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<tr>
<td>Construction workers / Labor</td>
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<td>Industrial workers</td>
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<td>Official job holders</td>
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<td>House holders</td>
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<tr>
<td>Others</td>
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The table 4: Shows most of the people registered in agriculture
workers and labor, who are continuously exposed to heat weather.
A physiological phenomenon, resulting in initiating thermal sweating. The sweat evaporates and sunshine influence the human health [21], [22]. Alteration of these parameters, particularly raised temperature will cause heat complications. Body gains heat from two sources that is the environment and the metabolic sources. This gained heat will be regulated to 37°C by hypothalamic thermoregulatory center, and regulates even the rise of less than 1°C. The main regulatory process is cutaneous vasodilation which increases the flow of warm blood in the skin thus initiating thermal sweating. The sweat evaporates and cools the body surface, but humid climate restricts the evaporation process leading to discomfort. In heat dissipation, there is more cutaneous circulation and lesser visceral circulation, particularly in the intestine and kidneys and causes organic dysfunction. Continuous sweating without adequate water intake causes dehydration and further leads to hypovolemia and salt depletion which impair thermoregulation [23], [24].

The environmental conditions of India are different from western regions and the rest of the world as well. Considering these aspects, Indian meteorological department (IMD) has categorized heat waves differently in to two. The first category includes places where the normal maximum temperature is greater than 40°C. In such regions, if the day temperature exceeds by 3-4°C above the normal, it is said to be affected by a heat wave. If greater than 5°C or more than the normal, it is severe heat wave. The second category considers the regions where the normal maximum is 40°C or less. In these areas, if day temperature is 5-6°C above the normal, then the place is said to be affected by moderate heat waves. A severe heat wave condition exists when the day temperature exceeds the normal maximum temperature by 6°C. In our study, most of the CKD (48.4%) cases are registered between the months of March and May. The renal insufficiency cases are also registered more between months of March and May (Table-1). In these months there is a rise in temperature. At same time there is also increased humidity in the areas which can lead to hyperthermia. Alana et al. [2008] reported that there is a renal function marker i.e. serum creatinine that rises, in about 67% of patients who are affected by heat stress. And they also reported that during summer season there is an increased hospital admission for renal disease during heat waves when compared to non heat wave period [25]. Knochel et al. [1996] reported that incidence of acute renal failure is 30% due to extreme heat, which may cause a pre renal disease of volume depletion [26]. Dematte et al. [1998] reported in their study 53% of patients affected with classical heat stroke developed moderate to severe renal insufficiency [27].

In the present study, Blood urea and serum creatinine register an increase in their levels in patients with CKD when compared to those of controls (p<0.001, Table-2). The reason attributed to raised blood urea and serum creatinine in patients with CKD is the declining of glomerular filtration rate. Evaluation of renal function by estimating GFR is one of the most important aspects in the management of CKD. Serum creatinine acts as a marker for GFR [28]. In the present study, creatinine clearance values using CG, MDRD and MCQE in CKD patients are significantly lowered when compared with control (p<0.001) (Table-3). This is evident by raised serum creatinine in CKD group. We chose three formulas because each formula as their own limitation [29] so that we compared with three formulae for evaluates CKD.

There is evidence that consequence of heat exposure is renal dysfunction resulting from dehydration and hyperthermia [2]. In hyperthermia, thermoregulatory physiological and circulatory mechanisms are necessary to overcome extreme heat conditions. These may cause mild to moderate renal hydropufusion following hypohydration and peripheral vasodilation and lead to stress on the kidneys. Acute renal failure is one of the complications of heat stress [30], [31]. Direct thermal injury may cause kidney tissue damage and leads to renal impairment. All these factors eventually develop repeated subclinical renal dysfunction, which may further develop in to chronic kidney disease (CKD). It is also registered that people living in lower altitudes are more likely to develop CKD than those living at higher altitude because of higher temperature at lower altitudes [32], [33], [34]. CKD finally ends in end stage renal failure and requires dialysis for survival, further exposure to heat leads to adverse effects.

In the present study, most of the people registered are agriculture workers (24%), construction workers or laborers (23%) and industrial labor workers (19%) (Table-4) and belong to low income group. Such workers are engaged in strenuous physical activity in extreme hot environmental condition during summer. It causes hyperthermia, leading to volume depletion based on the type of hydration practices outside the work. Also, the nature of work caused muscle damage consequently leading to subclinical kidney damage and further more CKD. Besides this if these are any other causative factors for CKD, the heat stress makes the disease status overt. The other major issue is most of these workers engaged in hot weather and lesser water intake suffer from volume depletion which further causes changes in the blood perfusion affecting kidney, a sensitive organ and leads to ischemic injury of the kidney [35].

Some of the studies show that workers in the agriculture, mining, fishing and shipping industries have higher prevalence rate of CKD [36]. Chaudary et al. and Reid et al. noted that loss of human lives was more in regions of poor socioeconomic condition than the regions of better conditions [37], [38].

In our study of control subjects, it was observed that there was a progressive decline in GFR as the age advances and it is true by all the three methods of estimation of GFR (Table-5). In elderly healthy individuals also both anatomical and functional changes occur in kidney. Renal mass is lost, mainly due to progressive atrophy of renal cortex and decreased of renal blood flow [39], [40]. The glomerular filtration rate (GFR) reduced at an average of 8ml/min/1.73m2/ decade in normal healthy individuals without renal impairment starting at the age of 40 years [41], [42]. Increasing age results in a decline in lean body mass and water content in the body this can cause greater strain in elderly people exposed to hot weather due to loss water in the form of sweat. Besides this, the elderly are more at risk of developing heat related renal disease due to lowered thermotolerance, impaired thirst sensation and diminished conservation of sodium and water during dehydration [43]. Elderly people with poor left ventricular function face difficulty to overcome this physiological phenomenon, resulting in hypoperfusion of the kidney [30], [31]. In one of the studies they found that elderly age group people admitted more during heat waves with renal disease [25].

Besides this, obese people contain more adipose tissue which acts as a less effective surface area and can cause insufficient heat loss and also there is less water content due to more adipose tissue. All these factors result in ineffective heat loss and promote to heat stress [44]. Some of the studies reported that people suffering from diabetes mellitus have an increased susceptibility to extreme heat and heat related renal dysfunction [45], [46] possibly due to pre existing renal conditions resulting in unfavorable kidney damage in heat stress [47], [48]. Many therapeutic drugs like psychotropic drugs, antihypertensive drugs and anti-histamines can inhibit thermoregulation in various ways. Patients using the above drugs and also exposed to heat undergo more heat stress [49].
Accordingly, we hypothesize that repeated exposure to hot weather causes hyperthermia further leading to volume depletion which may cause impaired renal function. Heat stress precipitates overt renal dysfunction if there is already a pre-existing renal compromise due to other factors. There is evidence that acute kidney injury follows heat stress. But such repeated sub-clinical renal insults eventually progress to CKD. However, repeated acute kidney injury, though silent, produces self-perpetuating cycle of inflammation and repair, resulting in kidney fibrosis that has more adverse effect and finally presents clinically as CKD [50].

Our study has certain limitation that the sample size is small and influence of regional factors where the patients are mostly from north east part of Andhra Pradesh. In our study, the factors accentuating CKD are poor socioeconomic and physical labor of agricultural and industrial workers where there is continuous intense exposure heat. However, this requires further more detailed study that might also throw light on the present havoc of global warming.

CONCLUSION

In accordance with global warming trends reported worldwide, temperatures are gradually increasing. Along with raised both heat and humidity adversely affects people living in the poor facilities and working in hot climatic conditions. Our data suggest that burden of renal diseases may increase as period of hot weather becomes more frequent. This is further aggravated if age advanced and people with chronic diseases like diabetes and hypertension. Long term treatment of end stage renal disease is costly and increases mortality. Health education programs need to awareness the climate changes and heat related illness.

REFERENCES


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