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Research Article

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 in 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 January2011 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 filteration 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 40^0C 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 factor 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/1.73m^2 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 m^2), stage 2 (GFR 60 to 89 ml/min/1.73 m^2), stage 3(GFR 30 to 59 ml/min/1.73 m^2), stage 4 (GFR 15 to 29 ml/min/1.73 m^2) and stage 5 (GFR less than 15 ml/min/1.73 m^2) [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 prevail 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 January2011 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 with0.85 if female) [16] CG formula is adjusted to body surface area (BSA) by using DuBois, DuBois method. BSA = ($W^{0.425}$ x $H^{0.725}$) x 0.007184 [17], [18].

MDRD Creatinine Clearance (ml/min/1.73m^2) = 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 1: Cases registered in Renal Insufficiency and CKD during the period of January 2011 to December 2012

Months	2011		2012	
	Renal Insufficiency (n=322)	CKD Patients (n=98)	Renal Insufficiency (n=334)	CKD Patients (n=100)
January	22	6	24	5
February	20	5	26	6
March	34	12	38	13
April	36	14	40	15
May	42	19	42	18
June	31	7	30	8
July	29	7	26	7
August	22	6	21	6
September	20	5	20	7
October	24	6	23	5
November	20	6	24	6
December	22	5	20	4

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.

The table 2: Shows blood urea and serum creatinine were significantly higher (p<0.001) in CKD patients when compared to control.

Table 2: Demographic features and diagnostic parameters in controls and CKD Patients

	Control (n=123) (mean±SD)	CKD Patients (n=198) (mean±SD)
Age in years	44.02±13.76	46.64±11.63
Sex (Males %)	69%	63%
(Females %)	31%	37%
Body weight(kgs)	66.72±6.64	62.24±6.95
Height (cm)	172.67±5.17	171.96±5.87
Blood urea (mg/dl)	28.55±8.16	98.77±36.77**
Serum Creatinine (mg/dl)	0.90±0.13	4.60±2.54**

Table 3: Creatinine clearance in controls and CKD Patients

	Control (n=123) (mean±SD)	CKD Patients (n=198) (mean±SD)	P value comparison between control vs. CKD
CG (ml/min/1.73m^2)	92.12±20.41	23.06±14.51	<0.001
MDRD (ml/min/1.73m^2)	92.61±20.52	20.82±15.08	<0.001
MCQE (ml/min/1.73m^2)	114.94±19.11	22.47±17.18	<0.001

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.

The table 4: Shows most of the people registered in agriculture workers and labor, who are continuously exposed to heat weather.

Table 4: Distribution of CKD patients based on occupation

Occupation	CKD patients (198)
Agriculture workers	47 (24%)
Construction workers/ Labor	45 (23%)
Industrial workers	38 (19%)
Official job holders	24 (12%)
House holders	22 (11%)
Others	22 (11%)

Table 5: Calculated GFR by CG, MDRD and MCQE versus age in control group

	20-29 years	30-39 years	40-49 years	50-59 years	60-70 years
CG (ml/min)	113.89	103.44	89.36	79.08	72.93
MDRD (ml/min)	108.46	99.5	87.25	84.75	83.28
MCQE (ml/min)	133.56	124.27	110.23	105.58	99.77

The table 5: Shows creatinine clearance was compared age wise in control group, it was noticed that there was marked difference in the values of GFR as age advanced.

DISCUSSION

Climatic parameters such as temperature, humidity, wind, evaporation and sunshine influence the human health [21], [22]. Alteration of theses parameters, particularly raised temperature will causes health complications. Body gains heat from two sources that is the environment and the metabolic sources. This gained heat will be regulated to 37^0C by hypothalamic thermoregulatory center, and regulates even the rise of less than 1^0c. The main regulatary 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 aspect, 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 40^0c. In such regions, if the day temperature exceeds by 3-4^0c above the normal, it is said to be affected by a heat wave. If greater than 5^0c or more than the normal, it is severe heat wave. The second category considers the regions where the normal maximum is 40^0c or less. In these areas, if day temperature is 5-6^0c 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 6^0c.

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 these 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 in sufficiency [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. 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, the thermoregulatory physiological and circulatory mechanisms are necessary to overcome extreme heat conditions. These may cause mild to moderate renal hypoperfusion following hypohydration and peripheral vasodialation 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 psycotropic 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 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

1. McMichael AJ, Woodruff R, Whetton P, Hennessy K, Nicholls N, Hales S, et al. Human Health and Climate Change in Oceania: A Risk Assessment 2002. Canberra: Commonwealth of Australia, 2003.
2. Semenza JC, McCullough JE, Flanders WD, McGeehin MA, Lumpkin JR. Excess Hospital Admissions during the July 1995 Heat Wave in Chicago. Am J Prev Med. 1999; 16: 269–277.
3. Ellis FP, Prince HP, Lovatt G, Whittington RM. Mortality and Morbidity in Birmingham During the 1976 Heat wave. Quart J Med. 1980; 49: 1– 8.
4. Marzuk PM, Tardiff K, Leon AC, Hirsch CS, Portera L, Iqbal MI et al. Ambient Temperature and Mortality from Unintentional Cocaine Overdose. JAMA. 1998; 279: 1795–800.
5. Easterling DR, Meehl GA, Parmesan C, Changnon SA, Karl TR, Mearns LO. Climate Extremes: Observations, Modeling, and Impacts. Science 2000; 298: 2068-2074.
6. Nakai S, Itoh T, Morimoto T. Deaths from Heat Stroke in Japan. 1968- 1994. Int J Biometeorol. 1999; 43: 124-127.
7. Venkatachalam MA, Griffin KA, Lan R, Geng H, Saikumar P, Bidani AK. Acute Kidney Injury: A Springboard for Progression in Chronic Kidney Disease. Am J Physiol Renal Physiol. 2010; 298(5): 1078–1094.
8. Levin A, Kellum JA, Mehta RL. Acute Kidney Injury: Toward an Integrated Understanding through Development of a Research Agenda. Clin J Am Soc Nephrol. 2008; 3(3): 862-863.
9. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, and Coresh J. Definition and classification of chronic kidney disease: A position Statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int. 2005; 67: 2089–2100.
10. Graham RD Jones, Ee-Mun Lim. The National Kidney Foundation Guideline on Estimation of the Glomerular Filtration Rate. Clin Biochem Rev. 2003; 24: 95-97.
11. National Kidney Foundation: K/DOQI Clinical Practice Guideline to Define Chronic Kidney Disease: Evaluation, Classification and Stratification. Am J Kidney Dis. 2002; 39(1): 1–266.
12. Athuraliya NT, Abeysekera TD, Amerasinghe PH, Kumarasiri R, Bandara P, Karunaratne U, et al. Uncertain Etiologies of Proteinuric-Chronic Kidney Disease in Rural Sri Lanka. Kidney Int. 2011; 80(11): 1212-1221.
13. Kamel EG, El-Minshawy O. Environmental Factors in the Development of End Stage Renal Disease in EI-Minia Governorate, Upper Egypt. Int J Nephrol Urol. 2010; 2(3): 431-437.
14. Tiffany, T.O. Jansen J, Burtis C.A. Overton J.B. and Scott C.D. Urea Assay. Clin. Chem. 1972; 18: 829.
15. Bowers LD (1980) Kinetic serum creatinine assays. The Role of Various Factors in Determining Specificity. Clin. Chem. 26: 551-554.
16. Cockcroft DW, Gault MH. Prediction of Creatinine Clearance from Serum Creatinine. Nephron. 1976; 16: 31-41.
17. DuBois D, DuBois EF. A Formula to Estimate the Approximate Surface Area if Height and Weight be known. Arch Intern Medicine. 1916; 17: 863-71.
18. Wang Y, Moss J and Thisted R. Predictors of Body Surface Area. J Clin Anesth. 1992; 4(1): 4-10.
19. Levey AS, Greene T, Kusek JW, Beck GJ. MDRD Study Group: A Simplified Equation to Predict Glomerular Filtration Rate from Serum Creatinine. J Am Soc Nephrol. 2000; 11: 155.
20. Rule AD, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Cosio FG, et al. Using Serum Creatinine to Estimate Glomerular Filtration Rate: Accuracy in Good Health and in Chronic Kidney Disease. Ann Intern Med. 2004; 141: 929-937.
21. Park K, meteorological environment. In: Park's Text Book of Preventive and Social Medicine 19th ed. Jabalpur: Bansida Bhanot; 2007; 602-606.
22. Stephan F, Ghiglione S, Decailliot F, Yakhou L, Duvaldestin P and Legrand P. Effect of Excessive Environmental Heat on Core Temperature in Critically Ill Patients. An Observation Study during the 2003. European heat wave. Br J Anaesth. 2005; 94: 39-45
23. Buono MJ, Sjoholm NT. Effect of Physical Training on Peripheral Sweat Production. J Appl Physiol. 1988; 65: 811-814.
24. Nelson N, Eichna LW, Horvath SM, Shelley WB, Hatch TF. Thermal Exchanges of Man at High Temperatures. Am J Physiol. 1947; 151: 626-652.
25. Alana LH, Peng Bi, Philip R, Monika N, Dino Pan d Grame T. The Effect of Heat Waves on Hospital Admissions for Renal Disease in a Temperate City of Australia. International Journal of Epidemology. 2008; 1-7.
26. Knochel JP. Exertional Heat Stroke-Pathophysiology of Heat Stroke In: Hyperthermic and Hypermetabolic Disorders. Cambridge: Cambridge university press. 1996; 42-62.
27. Dematte JE, O Mara K, Buescher J, Whitney CG, Forsythe S, McNamee T, et al. Near-Fatal Heat Stroke During the 1995 Heat Wave in Chicago. Ann Intern Med. 1998; 129: 173-181.
28. Kumaresan R, Giri P. A Comparison between Serum Creatinine and Cystatin-C based Formulae: Estimating Glomerular Filtration Rate in Chronic Kidney Disease Patients. Asian Journal of Pharmaceutical and Clinical Research 2012; 5(1): 42-44.
29. Raju DSSK, Lalitha DL, Kiranmayi. Observation of Estimated GFR in the Assessment of Chronic Kidney Disease: Application and Practice. Asian Journal of Pharmaceutical and Clinical Research 2012; 5(4): 201-206.
30. Rowell LB. Measurement of Hepatic Splanchnic Blood Flow in Man by Dye Techniques. In: The Theory and practice of Indicator Dilution. Baltimore: University Park Press, 1974; 209–229.
31. Rowell LB. Human Circulation: Regulation during Physical Stress. New York: Oxford University Press, 1986.
32. Orantes CM, Herrera R, Almaguer M, Brizuela EG, Hernandez CE, Bayarre H, et al. Chronic Kidney Disease and Associated Risk Factors in the Bajo Lempa region of El Salvador: Nefrolempa Study, 2009. MEDICC Rev. 2011; 13(4):14-22.
33. Donnell JK, Tobey M, Weiner DE, Stevens LA, Johnson S, Stringham P, et al. Prevalence of and Risk Factors for Chronic Kidney Disease in Rural Nicaragua. Nephrol Dial Transplant. 2011; 26(9):2798-2805.
34. Torres C, Aragon A, Gonzalez M, Lopez I, Jakobsson K, Elindre CG, et al. Decreased Kidney Function of Unknown Cause in Nicaragua: A Community-Based Survey. Am J Kidney Dis. 2010; 55(3):485-496.

35. Delgado Cortez O: Heat Stress Assessment among Workers in a Nicaraguan Sugarcane Farm. Glob Health Action. 2009; 11: 2.
36. Laux TS, Bert PJ, Barreto Ruiz GM, Gonzalez M, Unruh M, Aragon A, et al. Nicaragua Revisited Evidence of Lower Prevalence of Chronic Kidney Disease in a High-Altitude, Coffee-Growing. J Nephrol. 2011; 22: 3.
37. Chaudary SK, Gore Jm, Sinha Ray KC. Impact of Heat Waves over India. Curr Sci. 2000; 79: 153-155.
38. Reid CE, Oneil MS, Gronlund CJ, Brines SJ, Brown DG, Diez-Roux AV, et al. Mapping Community Determinants of Heat Vulnerability. Environ Health Perspect. 2009; 117: 1730-1736.
39. Flynn A, McGreevy C, Mulkerrin EC. Why do Older Patients Die in a Heat wave? Q J Med 2005; 98:227–229.
40. Faunt JD, Wilkinson TJ, Aplin P, Henschke P, Webb M, Penhall RK, et al. The Effete in the Heat: Heat-Related Hospital Presentations during a Ten Day Heat Wave. Aust N Z J Med. 1995; 25:117–121.
41. Lindeman RD, Tobin JD, Shock NW. Longitudinal studies on the rate of decline of renal function with age. J Am Geriatr Soc. 1985; 33:278–285.
42. Shannon RP, Minaker KL, Rowe JW. Ageing and Water Balance in Humans. Semin Nephrol. 1984; 4: 346–353.
43. Conti S, Masocco M, Meli P, Minelli G, Palummeri E, Solimini R, et al. General and Specific Mortality Among the Elderly During the 2003 Heat Wave in Genoa (Italy). Environ Res. 2007; 103: 267–274.
44. Kuan-Che Lu, MD; Tzong-Luen Wang, Heat Stroke. Ann Disaster Med. 2004; 2: 97-109
45. Medina-Ramon M, Zanobetti A, Cavanagh DP, Schwartz J. Extreme Temperatures and Mortality: Assessing Effect Modification by Personal Characteristics and Specific Cause of Death in a Multi-City Case-Only Analysis. Environ Health Perspect. 2006; 114: 1331–36.
46. Semenza JC. Acute Renal Failure during Heat Waves. Am J Prev Med. 1999; 17: 97.
47. Al-Tawheed AR, Al-Awadi KA, Kehinde EO, Abdul-Halim H, Al-Hunayan A, Ali Y, et al. Anuria Secondary to Hot Weather-Induced Hyperuricaemia: Diagnosis and Management. Ann Saudi Med. 2003; 23: 283–287.
48. Mogensen CE, Christensen CK, Vittinghus E. The Stages in Diabetic Renal Disease. With Emphasis on the Stage of Incipient Diabetic Nephropathy. Diabetes. 1983; 32 (2): 64–78.
49. Martin-Latry K, Goumy MP, Latry P, Gabinski C, Begaud B, Faure, I, et al. Psychotropic Drugs Use and Risk of Heat-Related Hospitalization. Eur Psychiatry. 2007; 22: 335–338.
50. BedfordM, Farmer C, Levin A, Ali T, Stevens P: Acute Kidney Injury and CKD: Chicken or Egg? Am J Kidney Dis. 2012; 59: 485–491.