



Association between extreme temperature and kidney disease in South Korea, 2003–2013: Stratified by sex and age groups

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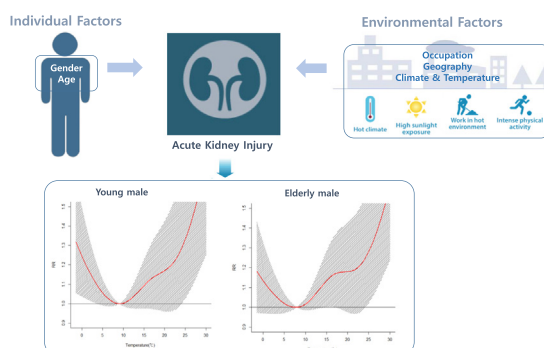
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HIGHLIGHTS

- We observed an association between high temperature and hospital admissions of kidney diseases in South Korea.
- The effect on acute kidney injury hospitalization was significant, but the effect on chronic kidney disease was not.
- We found interactions between gender and age in the association between kidney morbidity and high temperature.

GRAPHICAL ABSTRACT



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ABSTRACT

Weather conditions due to climate change affect the health directly and indirectly. Previous studies have shown associations with temperature, heat wave, and cold spell, and these do not only result in mortality from cardiovascular disease, respiratory disease, etc., but also in morbidity. This study aimed to quantify the relative risk for hospital admissions related to ambient temperature for genitourinary system diseases, which are representative of metabolic disease. We conducted a nationwide retrospective cohort study using claims data generated by medical services for diseases of the urinary system. The data was based on medical claims data from 16 districts in South Korea, to the nationwide level between 2003 and 2013. A total of 1,255,671 hospital admissions through the emergency department because of diseases of the genitourinary system were reported within the study period. The overall cumulative relative risk at the 99th percentile vs. the minimum morbidity percentile for renal diseases was 1.252 (95% confidence interval 1.211 to 1.294) in Seoul, 1.252 (1.21 to 1.296) in Busan, 1.236 (1.196 to 1.276) in Daegu, 1.237 (1.197 to 1.279) in Gwangju, and 1.258 (1.218 to 1.299) in Gyeonggi-do, 1.278 (1.211 to 1.349) in Chungcheongbuk-do, 1.291 (1.235 to 1.35) in Gyeongsangnam-do. In the group of men over 65 years, the overall cumulative RR was high and statistically significant in acute kidney injury (AKI). But we could not find the effect of high temperature for chronic kidney disease (CKD). The association were rather opposite, but not statistically significant. Our nationwide study not only demonstrates relative risk considering lag effects associated with ambient temperature and trends in hospital admissions through the emergency department for genitourinary disorders but also observed differences among disease groups.

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1. Introduction

As temperature increases, patients with baseline diseases may face increased risk due to various disease pathways, with an associated increased use of medical services. 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 this progression to overt disease. This study focused on diseases occurring in organs of the urinary system, which are representative of metabolic disease. Exposure to high temperature and environmental heat is accompanied by perspiration and fluid loss (dehydration), followed by volume depletion and hypovolemia. These can cause hypotension, and could lead to shock, coma, and sudden death thereafter. Dehydration, volume depletion, and hypovolemia can also lead to the formation of kidney stones and, thus, renal colic. Hypovolemia can result in serum electrolyte imbalance, which can cause arrhythmias, coma, and sudden death, as well as acute renal failure (Harlan et al., 2014). Heat stress leads to volume depletion, and, if it becomes serious, volume depletion may cause acute kidney injury even in healthy individuals (Semenza et al., 1999; Kovats et al., 2004; Knowlton et al., 2009). In the absence of functional recovery from the initial injury, acute kidney injury leads to chronic kidney disease (CKD) (Chawla and Kimmel, 2012). Recent studies have shown that subclinical damage also increases the risk of kidney disease, in countries such as Central America, Sri Lanka and India, male labors in the rural area are concerned about an increase in CKD (Glaser et al., 2016). Hyperthermia-induced volume depletion is one of the subclinical injuries to the kidney that may progress to kidney disease (Levin et al., 2008; Venkatachalam et al., 2010).

Many previous studies have been conducted on heat waves and various heat-related illnesses (Knowlton et al., 2009; Green et al., 2010; Lin et al., 2013; Wang et al., 2013; Condemi et al., 2015), and have examined heat stress and related renal dysfunction (Patnala et al., 2014; Moyce et al., 2017). These studies were conducted only in a limited study area, which included only several regions or cities in the country. Moreover, most of these studies were conducted in Western countries. In Australia, based on studies on the relationship between heat threshold and temperature, renal health outcomes have been associated with temperature (Williams et al., 2012) similar to the findings for other regions (Green et al., 2010; Basu et al., 2012; Condemi et al., 2015).

Impact assessments of association between extreme temperature and mortality and morbidity were conducted, but the vulnerable groups varied and were still controversial depending health outcome, regions and type of diseases. Most studies suggest that the very old and the very young are most vulnerable on the effects of extreme heat (Kravchenko et al., 2013; Gronlund et al., 2016). Vulnerability may vary according to sex; during the California heat wave of 2006, the mortality rate among women was higher than among men. Heat-associated hospitalizations for renal diseases were significantly higher people aged 25–44 years in a New York study (Fletcher et al., 2012). In general, the association between temperature and morbidity was analyzed as a whole, male, female, younger and older group. Because these age and sex are a vulnerable determinant of the temperature rise due to climate change and can also be a risk factor for the pathogenesis of the disease.

This study was conducted to evaluate the effects of a specific disease to nationwide level and examined the effects of high temperature on the quantification and characteristics of sex by age.

In order to investigate the effects and patterns of high-temperature on kidney disease with medical utilization data from Korea National Health Insurance Service (NHIS) included patients diagnosed with diseases of the genitourinary system on a national scale.

2. Materials and methods

2.1. Study population and data sources

We obtained the health insurance claims data from the National Health Insurance Services between 2003 and 2013. The distribution and daily number of hospital admissions varied because access to medical services depended on the day of week or on scheduled admissions. Therefore, we included only hospital admissions through the emergency department. Diseases for these admissions were classified based on the International Classification of Diseases, 10th revision. The daily number of admissions with a principal discharge diagnosis of renal disease (N00–N39) was assessed. We included acute renal failure (N17), chronic kidney disease (N18) as being representative of acute and chronic disease etiologies (Nitschke et al., 2007; Fletcher et al., 2012; Vaneckova and Bambrick, 2013; Harlan et al., 2014; Wang et al., 2014). We included only hospital admissions cases through emergency visit in order to remove regular hospital admissions cases due to characteristics of chronic disease and then explored to effects of extreme temperature. Climate data for the study period were obtained from the Korea Meteorological Administration. Daily mean ambient air temperatures and relative humidity for the 16 districts were accessed from a monitoring station. Daily air pollution monitoring records were obtained from the National Institute of Environmental Research.

2.2. Statistical analysis

Analyses were performed using R software, in particular, packages *dlm* and *mvmeta*. We accounted for the effects of ambient temperature by including the mean daily concentrations of PM_{10} and the influence of relative humidity and day of the week on the effects of temperature and use of medical services. The distributed lag non-linear model (*dlm*) assumes that the bi-dimensional exposure-lag-response association between ambient temperature and morbidity were estimated in each district. We used distributed lag non-linear models (*DLNMs*) to quantify the excess risk associated with ambient temperature on hospital admissions through the emergency department based on the National Health Insurance inpatient billing records. The association between daily average temperature and daily cause-specific hospital admissions was evaluated using *DLNM* with quasi-Poisson distribution. Natural cubic spline *DLNM* models were used to analyze the non-linear and delayed effects of temperature. The cross-basis function contained the dimensions of variables and lag days; we estimated the cumulative relative risk (*RR*) of ambient temperature lag for 7 days. For this study, we equally spaced knots of variables at spaced quantiles of the predictor and the knots of lag at equally spaced values on the log scale of lags. *RR* due to temperature was estimated using the cross-basis function in *DLNM* models. To estimate the effect of ambient temperature, the cumulative *RRs* and 95% confidence intervals of each cause-specific case were estimated by comparing the risk associated with the extreme temperatures of the 90th and 99th percentiles with that at the temperature associated with the lowest cause-specific disease (the centered temperature) (Gasparrini et al., 2010):

$$\log[E(Y_t)] = \alpha + CB(\text{mean temperature} : \text{lag}7) + ns(\text{Time}, 4 \times \text{year}) + \text{covariates}$$

where $E(Y_t)$ is the expected number of daily hospital admissions through the emergency department. Covariates were the day of the week, mean PM_{10} , and relative humidity. Fitted multivariate meta-regression models were used to derive the best linear unbiased district from the overall cumulative exposure-response association of each district. The best linear unbiased district represents a trade-off between the district-specific association provided by the first-stage regression and the pooled association. District-pooled lag-response relationships at the 99th temperature percentile were also derived from the re-centered

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