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| RESEARCH ARTICLE

Occupational Heat Stress and Chronic Kidney Disease of Uncertain Etiology: An Emerging Public Health Crisis in the Outdoor Workforce

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| ABSTRACT

Chronic kidney disease of unknown cause (CKDu) is now considered an important occupational and public health problem. It affects predominantly outdoor workers in agriculture, construction, and industries. Whereas typical cases of CKD are usually caused by diabetes and/or hypertension, recent studies have linked CKDu to repeated occupational heat stress, dehydration, and nephrotoxicity in hot work environments. This review incorporates relevant literature on the subject to demonstrate the possible pathways through which chronic heat exposure can lead to renal damage. These pathways include repetitive acute subclinical injury to the kidneys from dehydration and hyperthermia; fructokinase pathway activation from dehydration; oxidative stress pathways; and nephrotoxic effects due to co-exposure to agrochemicals and heavy metals. Considerations regarding occupational health practice are discussed. The rising temperatures due to climate change make heat-related disorders common not just in outdoor occupations but in most industries. Thus, CKDu is a preventable occupational disorder that warrants the attention of environmental health experts, policymakers, and employers.

| KEYWORDS

Chronic kidney disease of uncertain etiology (CKDu); occupational heat stress; outdoor workers; renal injury; heat illness prevention; climate change; environmental health

| ARTICLE INFORMATION

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1. Introduction

An emerging occupational health epidemic that has not yet garnered equal attention from governmental workplace regulators, employers, and public health officials is the increasing burden of chronic kidney disease in outdoor workers without traditional risk factors. The disorder, in contrast to CKD that is clearly secondary to diabetes mellitus, hypertension, and glomerulonephritis, appears to be most strongly related to occupational and environmental exposures, specifically heat stress and inadequate hydration in the setting of high workload and too few rest breaks in hot environments. Initially reported in high numbers in Central American sugarcane workers, the disorder has now been described among rice workers in South Asia, brick kiln workers, salt pan workers, and construction workers in many different tropical settings. It is not limited to low and middle income countries; there is increasing evidence that some U.S. agricultural workers (particularly in California, Florida, and the Southeast) also are at increased risk (Riefkohl et al., 2020; Glaser et al., 2016). Climate change can only be expected to worsen the problem, with increased maximum temperatures making heat exposure more intense and more widespread geographically. CKDu can be expected to increase in sectors such as agricultural work, construction work, transportation, and utility work where high heat exposure has been and will be more prevalent (IPCC, 2022). This review will discuss the evidence for the association between occupational heat and CKDu, the pathophysiology of

the disorder, and occupational risk factors. The implications for occupational health practice and policy in the context of this large body of evidence for a severe emerging health threat are discussed.

2. Epidemiology of CKDu in Outdoor Workers

There exists clear-cut evidence in epidemiology of CKDu showing a marked prevalence and incidence of CKDu in male workers performing strenuous activities in hot climates without presenting risk factors common in chronic kidney diseases among other patients in the community. The prevalence rate of CKDu in the affected populations ranges between 15% and 30%, compared with less than 5% in the general populace (Levin et al., 2019; Jayasumana et al., 2014).

The occupational exposure risk factor depends entirely on the type of occupation. Most at risk in the field are individuals performing tasks such as sugarcane harvesting, rice transplanting, concrete mixing, as well as using heavy machinery under the hot sun during daylight. Based on the evidence provided in the literature, risk exposure increases as a result of; (a) number of years working in hot environments; (b) duration of work under the hot weather; (c) lack of potable water in the workplace; and (d) failure to take adequate breaks away from hot areas (Weiss et al., 2021).

In an example of cross-sectional research performed on agricultural workers in North Carolina, results showed higher rates of serum creatinine levels and lower eGFR in comparison to the non-agricultural workforce after controlling for the confounding effects of age, hypertension, and diabetes (Moyce et al., 2017). Similar results have been documented in studies conducted in Florida among agricultural fieldworkers, who had experienced more than one heat stress incident in a season. This was confirmed through longitudinal analysis of their renal function.

There exist marked sex disparities in terms of CKDu in the affected communities. Males have a higher representation in this category, possibly due to assignment of different tasks, long-term heat exposure and differential fluid intake habits during the workday. However, increasing reports of CKDu among women in the same profession show that a major portion of the sex disparity might be attributed to different periods of heat exposure.

3. Biological Mechanisms of Heat-Induced Renal Injury

Pathological processes involved in the development of CKDu can be attributed to multiple interacting biological mechanisms in which heat stress plays a causative role in initiating renal injury. The study of the biology of this process is of critical importance when developing occupational health and safety strategies, as well as biomonitoring standards for workers exposed to hot environments.

3.1 Repeated Episodes of Subclinical Acute Kidney Injury

The currently best-understood biological mechanism leading to CKDu is recurrent episodes of subclinical acute kidney injury caused by hemodynamic alterations in heat stress. Heat exposure results in redistribution of blood flow from internal organs to the periphery, including kidneys, and sweating causes extracellular dehydration, which increases serum osmolality, reduces plasma volume, and consequently renal perfusion. Thus, each episode of heat-related dehydration can induce an episode of subclinical AKI marked by elevation in serum creatinine levels and other biomarkers, resolving as a result of rehydration but leaving behind renal damage manifested in tubular atrophy, interstitial fibrosis, and glomerulosclerosis without evidence of inflammation characteristic of glomerulonephritis.

3.2 Fructokinase Pathway Activation

Another separate pathway involved in development of CKDu is the induction of endogenous uric acid production through activation of the fructokinase (KHK) cascade as a response to dehydration. With increased serum osmolality, fructose production in the body is stimulated via the polyol pathway, which converts sorbitol to fructose. Further fructose metabolism via KHK results in generation of uric acid, depletion of ATP in cells and oxidative stress within tubular epithelial cells. The cellular cascade described above produces inflammatory damage to the organ without involvement of any toxins and has been shown experimentally to cause histopathological lesions indistinguishable from those found in CKDu patients (Roncal-Jimenez et al., 2016).

This mechanism is especially relevant in relation to workplace hazards, as it clearly shows that repeated episodes of heat stress and dehydration without any nephrotoxic exposures lead to renal damage. Thus, measures aimed exclusively at reducing toxic chemical exposure would not protect against CKDu.

3.3 Oxidative Stress and Inflammatory Pathways

Heat stress also independently causes systemic oxidative stress mediated by mitochondrial dysfunction, ischemia-reperfusion injury due to recurrent periods of renal hypoperfusion and activation of the renin angiotensin aldosterone system. Hyperthermia also induces the expression of heat shock proteins and a pro-inflammatory cytokine profile that with repetitive activation lead to apoptotic death of renal tubular epithelial cells and renal interstitial inflammation. Increased urinary excretion of IL-18, N-acetyl-beta-D-glucosaminidase and kidney injury molecule-1 (KIM-1) all established markers of tubular epithelial injury has been demonstrated in heat exposed agricultural workers despite absence of clinical AKI (Moyce et al., 2017). These findings confirm subclinical kidney injury occurring with heat stress alone.

3.4 Nephrotoxic Co-Exposures

In addition to dehydration and heat stress being independently sufficient to cause CKDu there are numerous co-exposures commonly encountered in agricultural and industrial workplaces that have additive or synergistic effects on renal injury. Pesticides containing organophosphates or carbamates, heavy metals such as cadmium and arsenic from irrigation water or soil contaminants as well as non-steroidal anti-inflammatory drugs (NSAIDs) used to treat musculoskeletal pain are all nephrotoxic. Exposure to these chemicals among workers with pre-existing subclinical kidney damage from heat stress may promote development of clinical CKDu. Chemical hygiene assessments of these potential workplace exposures are therefore important to include along with heat stress interventions.

4. Vulnerable Populations and Occupational Risk Factors

Risk for CKDu does not equally affect the entire population of workers engaged in outdoor occupations. Certain demographic and occupational risk factors lead to substantially increased susceptibility to CKDu, requiring specialized prevention efforts.

Workers engaged in agricultural occupation constitute the most at-risk group. The summer harvesting season increases the exposure to extreme heat and simultaneously adds significant physical strain, and the incentive system involving payment by performance makes workers hesitant to take breaks or drink enough fluids. In addition, lack of appropriate shading facilities and absence of necessary hydrating facilities increase heat and dehydration risks. The additional challenges faced by agricultural migrants include language issues, which limit information flow regarding health matters, poor availability of occupational health services, and fear of reporting symptoms owing to their migration status (Quandt et al., 2013).

Occupations in construction industry with outdoor work include concrete works, roofing, site leveling, heavy equipment driving, among others. They are exposed to the same heat as agricultural workers, but also to silica dust, heavy metals, and other risk factors. Among other groups at substantial risk for developing renal impairment under the effects of heat are utility workers, military personnel undertaking outdoor maneuvers, and salt pan workers.

Certain individual risk factors can significantly influence susceptibility to CKDu and include the following: previous AKI or UTI, NSAID or nephrotoxic drug use, pre-existing hypertension, and heat acclimatization effectiveness. Particularly vulnerable individuals are those that are unacclimatized to heat, especially in the initial stage of acclimatization process in the beginning of the season or returning back to heat-exposed jobs. Unrecognized mild renal impairment is yet another vulnerability factor.

5. Climate Change and the Expanding Risk Landscape

The prevalence of CKDu cannot be explained outside of its broader climate context. The average global temperature has increased by 1.2°C above pre-industrial levels, with heat extremes becoming more common and more widespread both geographically and temporally at a faster rate than increases predicted for average temperatures. These changes translate into extended periods of work under dangerous WBGT conditions, increased frequency of heat extremes beyond physiological limits, and increased geographic distribution of areas at risk of heat stress.

Based on current climate predictions, by mid-century, outdoor workers in tropical and subtropical climates may experience a number of conditions during which prolonged work would become physically impossible without adaptation for parts of each year. In the United States, there is a projected increase in the number of days above the WBGT limit safe for moderate outdoor labor in southern and western U.S. states as well as the agricultural core region. The U.S. Bureau of Labor Statistics shows an increase in the incidence of heat-related illnesses in agriculture and construction sectors; however, the actual numbers are expected to be even higher given the numerous limitations to reporting.

Climate change poses a fundamental planning problem to professionals in occupational health since the past patterns of heat exposure may no longer serve as the base for protection. Heat-stress programs need to account for climate trends and adaptive capacity.

6. Occupational Health and Regulatory Responses

The response of regulatory authorities within the United States and internationally remains insufficient compared to the extent of the risk, despite the considerable amount of scientific literature on heat stress and CKDu. As of 2025, the U.S. Occupational Safety and Health Administration (OSHA) had proposed but not finalized a federal heat illness prevention standard, leaving the issue unresolved by the agency and relying on the general duty clause and various states' regulations. California's heat illness prevention regulation is among the most comprehensive nationally but does not include renal injury endpoints and biomonitoring for CKDu.

The two critical aspects of managing CKDu from the perspective of occupational health involve primary prevention of CKDu, including minimizing the intensity of exposure to heat, and preventing dehydration and secondary prevention, which includes detection of subclinical injuries to the kidneys in workers exposed to heat stress. Table 1 contains the list of the most important interventions in these categories.

Primary prevention methods have varying levels of scientific evidence, but those involving hydration and breaks in the shade are most widely supported. Following the dehydration paradigm of the CKDu pathophysiology, a specific recommendation made by OSHA, one cup of water approximately every 15 to 20 minutes while being exposed to heat, should be seen as particularly relevant for CKDu prevention. One of the most common problems with managing exposure to heat, and especially related to CKDu, is seeing hydration as an administrative requirement.

One of the most important protective factors against CKDu associated with heat stress involves heat acclimatization, which takes 7 to 14 days. The benefits associated with it include increased cardiorespiratory efficiency, increased sweating ability, and improvement of thermoregulation. This results in reduced pressure on the kidneys when heat-acclimated individuals perform heavy work. By assigning workers to perform their duties in conditions requiring maximal efforts from their bodies in terms of heat acclimation, agricultural employers increase CKDu risk.

Occupational medical monitoring provides an additional opportunity to catch the earliest stages of the disease and apply preventive measures. Regular annual or seasonal screening tests, including measurement of serum creatinine and eGFR along with urinary biomarkers of tubular damage, like KIM-1, provide an opportunity to catch CKDu early enough to prevent permanent damage. The lack of biomonitoring requirement for heat-exposed workers in the U.S. is one of the major regulatory gaps in this area.

Table 1: *Occupational Health Intervention Framework for CKDu Prevention*

Intervention Domain	Strategy	Target Population	Evidence Level
Primary Prevention – Hydration	1 cup of water every 15–20 min; employer hydration stations	All outdoor workers	Strong
Primary Prevention – Heat Engineering	Shade, cooling stations, rest breaks, WBGT monitoring	Agricultural, construction	Strong
Primary Prevention – Acclimatization	Structured 7–14 day protocol for new and returning workers	Seasonal workers	Strong
Secondary Prevention – Biomonitoring	Pre/post-season creatinine, eGFR, urinary KIM-1, and NGAL	High-risk workers	Moderate
Secondary Prevention – Surveillance	Annual occupational medical surveillance with renal function testing	Agricultural, construction	Moderate
Regulatory Compliance	OSHA heat illness prevention; state heat standard compliance	All employers	Standard of practice
Education and Training	Heat illness training in the worker's primary language; symptom reporting	All outdoor workers	Strong

7. Discussion

This body of evidence demonstrates that CKDu is a credible, serious, and preventable occupational disease, caused by heat stress and dehydration via a clearly characterized mechanism of renal damage. It is deemed a priority problem in occupational health because it has arisen as a public health emergency in multiple nations under similar conditions of occupational exposure, has shown persistent increases in prevalence, and will see exacerbation of the causal factors due to climate change.

The practice of environmental health and safety has far-reaching consequences. Professionals working in occupational health within the agriculture, construction, utilities, and other heat-heavy industries need to incorporate renal endpoints into their risk assessment protocols. Although current approaches to preventing heat illnesses focus on preventing heat stroke and heat exhaustion, these approaches should be extended to include the body of knowledge around CKDu and the idea that there is a history of accumulated damage occurring silently throughout one's life.

Economically, the case can be made quite easily for preventative action. The total cost of CKDu, including the dialysis itself and the loss of productivity, disability claims, and workforce attrition, adds up to a significant amount of money that is probably being understated in current occupational health cost accounting. Dialysis for end-stage renal failure costs upwards of $90,000 annually per person in the US, most of which is covered by the workers' comp system, Medicaid, and the patients themselves. The cost of implementing preventative programs for heat stress pales in comparison to that of treating diagnosed CKDu.

A final, crucial point has to do with equity. Due to the lack of a federal heat illness prevention regulation with adequate specificity, such as a requirement for biomonitoring thresholds, renal surveillance, etc., many outdoor workers find themselves reliant upon voluntarily provided safeguards from their employers. Translation of CKDu research into policy recommendations for regulatory agencies has become a top advocacy priority for occupational and environmental health specialists.

8. Conclusions

Chronic kidney disease of uncertain etiology (CKDu) is an under-recognized but growing occupational disease. The combination of epidemiological, physiological, and clinical evidence suggest that heat stress and dehydration dominate the etiological factors for most impacted workforces, with nephrotoxic co-exposures as amplifying drivers. The impact of climate change is likely to broaden the scope of work and locations exposed to this disease. The need for proactive occupational health measures in this area will become critical.

Environmental health and safety professionals are uniquely positioned to raise awareness and adopt novel prevention measures, enforce regulations, and promote the development of CKDu surveillance frameworks. Critical first steps include: (1) embedding renal health outcomes into occupational heat illness prevention frameworks; (2) instituting renal function biomonitoring for heat-exposed workers at the beginning and end of work seasons; (3) implementing heat acclimatization for all seasonal and new outdoor workers; and (4) supporting federal legislation on heat illness prevention that will treat CKDu as a compensable occupational illness and require renal biomonitoring for heat-exposed workers.

Agricultural and construction workers, among other outdoor workers, are among the most vulnerable and occupationally underserved workforce populations. Protecting their renal health is an occupational justice imperative.

8.1 Study Limitations and Areas for Further Study

This review has several limitations. Many relevant data and experience may have been excluded due to this review being based on published literature, which may underestimate CKDu in regions where there is minimal occupational health care or research attention, or in population groups where there is a lack of access to occupational health care. Much of this review focused on the Central American and South Asian regions where epidemiological studies on CKDu have been conducted; these epidemiological findings may not be generalizable to other regions, such as the United States. Also, the majority of these cited studies are cross-sectional, limiting inferences about causality. Overall, epidemiological and biomonitoring data on heat-exposed workers in the U.S. are insufficient. Studies that would advance the understanding of CKDu and heat illness in occupational settings should include (1) large prospective cohort studies assessing renal function endpoints in outdoor workers in the U.S., (2) intervention studies in occupational settings aimed at reducing heat illness and assessing CKDu biomarkers, and (3) identification and evaluation of CKDu surveillance case definitions in occupational health care settings.

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