



Impact of Heat Stress on Renal Function: A Systematic Literature Review Focusing on Workplace Heat

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Abstract

Background: There is evidence that exposure to heat stress over time may lead to chronic kidney disease. This study aimed to summarize the evidence on the effects of heat stress on renal function among individuals exposed to occupational heat stress.

Materials and Methods: In this systematic review, all papers on the effect of heat stress on kidney function among workers at any workplace and heat level were included. Reviews, case reports, conference proceedings, letters, editorials, abstracts without full text, in-vitro, and animal studies were excluded. Furthermore, studies conducted on children, general populations, and hospitalized patients, as well as those not measuring heat stress, were also excluded. Medline, Scopus, ISI, and Embase databases were searched from 1st January 1991 to 19th October 2021. Search criteria were prepared by combining an 'exposed population' AND 'exposure' AND 'outcome' keywords. Quality assessment was done using the National Institutes of Health Quality Assessment tool.

Results: A total of 24 articles with 14,282 participants were considered for qualitative synthesis. Although most papers indicated a positive association between heat stress and kidney dysfunction, especially regarding dehydration, the present study found heterogeneous evidence. Glomerular filtration rate, serum creatinine level, and albumin-to-creatinine ratio, due to occupational heat stress, were other markers mentioned in primary studies.

Conclusions: This review highlighted the impact of occupational heat stress on renal function. Among the markers investigated in this review, most studies reported a positive association between occupational heat stress and dehydration.

Keywords: COVID-19, Anxiety, Depression, Insomnia, Health Personnel

Introduction

Heat stress (HS) refers to an aggregation of both the heat produced by the body (metabolic heat) and the heat received from the environment

(environmental heat) minus the heat transferred from the body to the environment [1, 2]. Heat exposure can cause a wide range of adverse effects on human health. Heat cramps, heat

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collapse, heat rashes, heat fatigue, heat exhaustion, heat stroke [3, 4], adverse effects on productivity [5, 6], performance impairment [7, 8], and kidney diseases [9] are among the reported consequences of HS.

Chronic Kidney Disease of non-traditional origin (CKDnt) is a condition not related to traditional risk factors such as diabetes or hypertension [10]. CKDnt is initially asymptomatic but later can lead to end-stage renal disease [11]. There is increasing evidence that HS is associated with a risk for kidney damage in populations at risk of CKDnt [10, 12]. HS can lead to high body temperature and dehydration with subsequent volume depletion, which may cause kidney damage [12, 13]. Heat-exposed workers such as miners and industrial and agricultural workers are prone to HS and subsequently develop CKDnt, because of manual work in hot environments, short breaks, and inadequate fluid intake [10, 14].

Timely and appropriate screening can be used to prevent kidney damage in high-risk populations such as workers exposed to occupational heat. The standard screening tests include the assessment of renal biomarkers such as serum creatinine and albuminuria. Further, urine-specific gravity is an inexpensive test that can accurately detect early kidney injury [13].

It is stated that CKDnt is prevalent mainly in young, male agricultural laborers [15]. Occupational HS has been associated with kidney disease in a longitudinal study that revealed a significant decrease in glomerular filtration rate from pre-harvest to late harvest among migrant and seasonal farmworkers [16]. Sugarcane cutters are also a particular group among other agricultural workers who are more susceptible to developing kidney dysfunction because of working in hot and humid conditions and inadequate fluid intake [5, 15, 17, 18]. Moreover, some non-agricultural occupations carry increased risks [15]. For example, miners have been considered a high-risk population for developing CKDnt since ambient temperatures in the mines can be in excess of more than 30°C wet bulb globe temperature [19]. Construction workers also risk developing kidney damage, as indicated in previous studies [20-22].

On the contrary, in some studies, no statistically significant difference has been observed between workers with and without HS in kidney function biomarkers [23-25].

Controversy can be observed between studies investigating the effect of HS on kidney function. The present review aimed to improve understanding of the renal disorders related to occupational heat exposure. . We attempted to describe and summarize any recently reported

evidence of the association between workplace heat and kidney damage. A better understanding of early biomarkers of kidney damage serves to perform preventive and therapeutic interventions and can finally lead to promotion in workers' health.

Materials and Methods

To conduct this systematic review, Preferred Items for Reporting Systematic Reviews and Meta-Analyses (PRISMA) statements were followed [26]. Given the considerable heterogeneity in the included studies, a quantitative meta-analysis was not applicable; hence, a qualitative synthesis was carried out.

Study selection, quality assessment of the included studies, and data extraction were carried out by two independent experts. Disagreements between the two reviewers were resolved through discussion or by the decision of the third expert.

Eligibility Criteria: All papers on the effect of occupational HS on kidney function among workers at any workplace and heat level were included in the research. Study designs included cohort, case-control, cross-sectional, and randomized (trial).

Review articles, case reports, conference proceedings, letters, editorials, abstracts without full text, in-vitro, and animal studies were excluded. Furthermore, studies conducted on children, general populations, and hospitalized patients, as well as those not measuring heat stress, were excluded.

Search Strategy: The Cochrane Library was searched initially to know whether there is any systematic review on the HS effect on renal function. International databases, including Web of Science, Medline (PubMed), EMBASE, and Scopus, were searched by two independent researchers to check any systematic review existence and find the relevant English articles published from 1st January 1991 to the 19th October 2021 without any restriction on study design. The search strategy was based on a combination of free text words (i.e., non-Mesh words or phrases) and medical subject heading (Mesh) such as ("Hot Temperature" [Mesh] OR Heat[Mesh] OR "Extreme Heat" [Mesh] OR "heat stress") AND ("Kidney Diseases" [Mesh] OR hydration OR Dehydration[Mesh] OR "kidney function" OR "kidney function tests" [Mesh] OR "Acute Kidney Injuries" OR "Acute Renal Failure" OR "Chronic kidney disease" OR Urea[Mesh] OR Creatinine[Mesh] OR "Urine specific gravity" OR "Glomerular filtration rate" [Mesh] OR "Blood urea nitrogen" [Mesh]) AND ("occupational exposure"

[Mesh] OR "Occupational group" [Mesh] OR "Occupational groups" [Mesh] OR Workplace [Mesh] OR "Work Site" [Mesh] OR "Job Site" [Mesh] OR "Work Locations" [Mesh] OR Worker OR Employee). To avoid missing any relevant papers, the reference lists of all included articles were also searched manually.

Study Selection: To screen the results of the initial systematic search, all articles were exported to the EndNote software (version X8, for Windows, Thomson Reuters, and Philadelphia, PA, USA). In selecting the relevant articles, the terms related to the exposed population, exposure, and outcome were considered. Initially, the duplicates were excluded, and then the remaining articles were screened by title, abstract, and full text based on the eligibility criteria. In the cases where two similar articles were from a single study, we included the article that best suits our review objectives and eligibility criteria.

Quality Assessment of the Evidence: Quality assessment of the included studies was done using the National Institutes of Health (NIH) Quality Assessment tool for observational and interventional studies [27]. This tool includes items for evaluating the potential sources of bias (e.g., patient selection, performance, attrition, and detection), confounding factors, study power, the strength of causality in the association between interventions and outcomes, and other factors. The tool items were evaluated as "yes," "no," "cannot determine," "not applicable," or "not reported." Later, studies were categorized (good, fair, or poor) in terms of their quality. In this regard, a study with 'good' quality has the least risk of bias. A fair-quality study is susceptible to some bias. A study with poor quality indicates a significant risk of bias. Arbitrary cut-off points were used to determine 'good' and 'fair' quality studies; articles that gained 60% of items as "yes" were defined to have good quality, and the others reached less than 60% of "yes" were evaluated as acceptable quality.

Data Collection Process: In order to extract the relevant data from each included primary study, a data extraction sheet was prepared in Excel software containing the variables of the first author's name, year of publication, country of study, study design, outcome, and exposure, sample size, age, gender, and occupation.

In the cases where some of the required information was missing, the corresponding author of that article was contacted via e-mail.

Results

Study Selection: The initial search retrieved 5,105 articles. After removing the duplicates, 4,906 papers remained. After screening the titles and abstracts, 4,805 articles were excluded due to a lack of relevance. As a result, 101 full-text articles were assessed for eligibility criteria. Subsequently, 77 articles were excluded due to not meeting the inclusion criteria. The manual reference checking of the searched articles yielded 16 papers. Finally, 24 articles were retained in the systematic review. The study selection flow diagram is represented in Figure 1.

Study Characteristics: Overall, 24 studies with 14,282 participants were investigated in this review. The selected studies included one non-randomized intervention, one prospective cohort study, one longitudinal study, and the rest were cross-sectional. Table 1 represents the characteristics of the included studies. Regarding the participants' gender, eight studies were conducted on both male and female workers, one study was performed only on women, and the remaining studies were carried out only on men.

In the studied research, exposure to HS was evaluated based on the temperature measurement and calculating thermal or physiological parameters; for example, core and skin temperature and heart rate were used to calculate the PSI index. Also, atmospheric parameters were required for calculating the WBGT and TWL indicators (dry bulb temperature, wet bulb temperature, radiant temperature, air velocity or wind speed, and atmospheric pressure).

Different studies evaluated various biomarkers as indicators of renal dysfunction. The most-reported biomarkers were urinary specific gravity (USG), estimated glomerular filtration rate (eGFR), serum creatinine (SCr), serum uric acid (SUA), blood urea nitrogen (BUN), and albumin-to-creatinine ratio (ACR), respectively.

Risk of Bias within Studies: According to the NIH Quality Assessment tool, 19 studies had good quality, three were fair in quality, and two had poor quality.

Table 1. Characteristics of the included studies

First author (publication date) ^[reference]	Country	Sample size	Occupation	Gender	Age (mean±sd)	Definition of exposure	Exposure (heat)	Outcome	Quality rating
Cross-sectional studies									
Atan (2005) ^[23]	Brazil	10,326	Steel industry workers	M	35.02±6.43	Air temperature	Indoor	SUA, SCr	Good
Nerbass (2019) ^[24]	Brazil	31	Metallurgical workers	M	31 (26–39) [†]	WBGT	Indoor	eGFR, SUA, SCr, ACR	Good
Moyce (2017) ^[29]	USA	283	Agricultural workers	Both	38.6±12.4	PSI	Outdoor	eGFR, SCr	Good
Mix (2017) ^[28]	USA	192	Agricultural workers	Both	38.0±8.2	HI	Outdoor	eGFR, SCr, USG, BUN	Good
Brake (2003) ^[30]	Australia	39	Mine workers	M	35.0±8.0	WBGT and TWL	Indoor	USG	Good
Garcia- Trabanino (2015) ^[17]	El Salvador	189	Sugarcane cutters	Both	30±7.33	WBGT and HI	Outdoor	eGFR, SUA, SCr, USG, BUN	Good
Meade (2015) ^[40]	USA	32	Electrical utility workers	M	36.0±10.0	PSI	Outdoor and indoor	USG	Fair
Spector (2018) ^[36]	USA	46	Agricultural workers	Both	39.1±14.1	WBGT	Outdoor	USG	Good
Peiffer (2012) ^[19]	Australia	77	Mine workers	M	34.88±10.97	TWL	Outdoor	USG	Good
Piil (2018) ^[35]	Denmark, Cyprus, Greece and Spain	139	Manufacturing, agricultural, tourism, and construction workers; police officers	M	30.0±2.0	WBGT	Outdoor and indoor	USG	Good
Paula Santos (2014) ^[39]	Brazil	28	Sugarcane workers	M	24.9±5.6	Air temperature	Outdoor	eGFR, SCr	Fair
Brearley (2016) ^[25]	Australia	20	Electric utility workers	M	31.5±10.0	WBGT and PSI	Outdoor	USG	Good

Farshad (2014) ^[22]	Iran	60	Construction workers	M	30.8±6.59	WBGT and TWL	Outdoor	USG	Good
Ueno (2018) ^[21]	Japan	23	Construction workers	M	41.0±15.0	WBGT	Outdoor and indoor	USG	Fair
Hunt (2014) ^[34]	Australia	15	Mine workers	Both	36.7±9.7	WBGT	Outdoor	USG	Poor
Dang (2014) ^[33]	USA	60	Aluminum potroom workers	Both	32*	WBGT	Indoor	USG, BUN, SCr	Good
Wagoner (2020) ^[37]	Mexico	28	Agricultural workers	M	NR	WBGT	Outdoor	USG	Good
Al-Bouwarthan (2020) ^[31]	Saudi Arabia	23	Construction workers	M	42.7±8.8	WBGT	Outdoor and indoor	USG	Good
Venugopal (2020) ^[12]	India	1842	8 work sectors	Both	36.8±12.6	WBGT	Outdoor and indoor	USG, eGFR	Good
Nainggolan (2021) ^[13]	Indonesia	119	Shoe factory workers	F	38 (31–50) [†]	WBGT	Indoor	eGFR, USG	Good
Butler-Dawson (2021) ^[14]	Guatemala	107	Sugarcane cutters	M	28 (9)[†]	WBGT	Outdoor	USG, SCr	Good
Longitudinal studies									
Sorensen (2019) ^[18]	Guatemala	105	Sugarcane workers	M	30.1±9.1	WBGT	Outdoor	eGFR, ACR	Good
Prospective cohort studies									
Butler-Dawson (2019) ^[32]	Guatemala	418	Sugarcane cutters	M	28 (24-35) [†]	WBGT	Outdoor	eGFR, SCr, USG	Good
Non-randomized interventional									
Wegman (2018) ^[38]	El Salvador	80	Sugarcane cutters	Both	45*	WBGT	Outdoor	eGFR	Poor

* M: male, F: female. WBGT: wet bulb globe temperature, PSI: physiological strain index, HI: heat index, TWL: thermal work limit, BUN: blood urea nitrogen, ACR: albumin-to-creatinine ratio, SUA: serum uric acid, SCr: serum creatinine, eGFR: estimated glomerular filtration rate, USG: urinary specific gravity. *mean only. † median (interquartile range). NR: Not Reported.

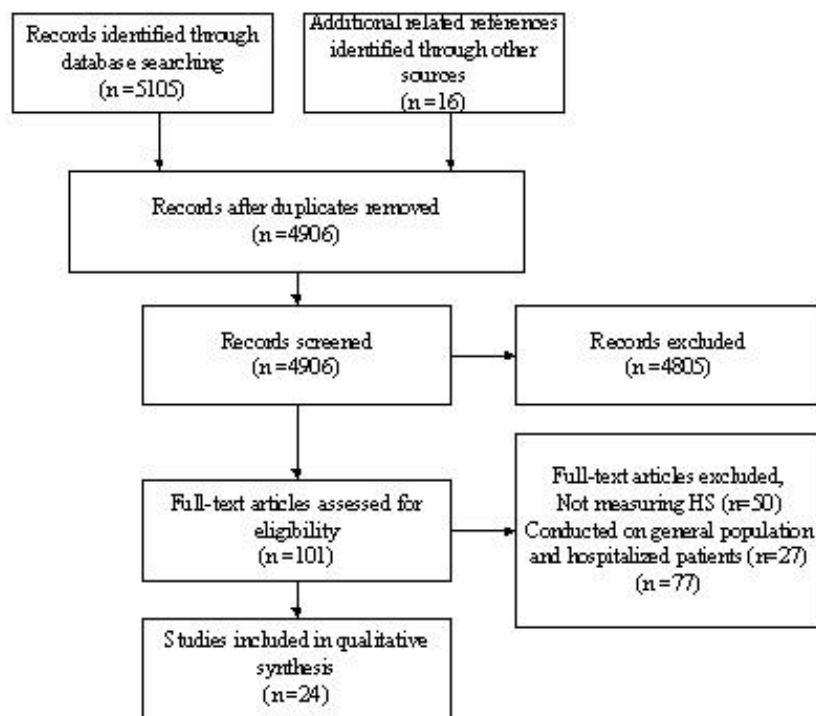


Fig. 1. PRISMA flow diagram showing the different phases in searching relevant publications

Exposure Assessment: Regarding the exposure assessment methods, two studies calculated heat index (HI) using an OSHA chart [17, 28]; one of the two studies measured the temperature and relative humidity needed to calculate the HI during the study [17]. The other research calculated HI by the National Weather Service algorithm using the temperature and relative humidity data obtained from Florida Automated Weather Network [28].

In two studies, the core body temperature and heart rate were measured using an ingestible wireless temperature transmitter probe, a heart rate transmitter, and a physiological strain index (PSI) [25, 29]. In three studies, the thermal work limit (TWL) index was calculated [19, 22, 30]; one of these studies obtained the daily data from the Australian Bureau of Meteorology [19]. In two studies, data were measured by researchers [19, 22]; one of these studies considered barometric pressure as 110 kilopascals [30].

In 18 studies, wet bulb globe temperature (WBGT) index was calculated [12-14, 17, 18, 21, 22, 24, 25, 30-38]; 15 of these articles used the WBGT meter [12, 14, 17, 18, 21, 22, 25, 30-33, 35-38]. In two of these studies, the index values were obtained from the safety engineering department [13, 24], and in another study, the temperature and relative humidity were measured using a digital weather meter [34]. Furthermore, two studies measured the environmental temperature and did not calculate the heat indices [23, 39]. In four studies that assessed heat exposure, two types of indices were used [17, 22, 25, 30].

Results of Individual Studies: Search results revealed considerable population heterogeneity and outcomes among individual studies. Workers with a variety of occupations at various workplaces were studied in the searched articles. Moreover, a considerable diversity was observed in terms of indicators of renal function. For these reasons, a quantitative meta-analysis was not possible. Thus, the findings were qualitatively synthesized, as mentioned in the following sections.

Serum Creatinine and eGFR: The eGFR is considered the best measure of overall renal function. An eGFR level below 60 mL per minute per 1.73 m² represents a loss of one-half or more of the adult level of normal kidney function [40]. Elevated SCr has also been used as a traditional endogenous biomarker for renal function [41].

Agricultural Workers: Reduced eGFR and increased SCr were reported in eight studies of agricultural workers. In this regard, an interventional study showed implementing water, rest, and shade (WRS) programs decreased HS and kidney damage. The study included one group that worked in a cool climate while the other group worked in a hotter climate. Decreased cross-shift eGFR was observed in both groups: -10.5 mL/min per 1.73m² (95%CI: -11.8, -9.1). However, this rate was lower for the intervention group after receiving the WRS. Moreover, decreased eGFR was observed in both groups during the harvest season so that the eGFR was -3.4 mL/min per 1.73m² (95% CI: -5.5, -1.3) in the intervention group and -5.3 (95% CI: -7.9, -2.7) in the control group [38].

Another study reported that 12.3% of the participants had acute kidney injury (AKI) throughout a work shift. This study showed that HS was associated with developing AKI after a single shift of agricultural activity. The authors defined AKI as an increase of the post-shift SCr by ≥ 0.3 mg/dL or ≥ 1.5 times the pre-shift creatinine. Workers with $PSI \geq 7.5$ were also classified as experiencing HS. In addition, HS was associated with a 1.29 adjusted odds ratio (OR) of AKI (95% CI: 1.03, 1.61) based on the age and gender-adjusted logistic regression model. In addition to the elevated SCr, most participants (92.2%) had $eGFR \geq 90$ mL/min per 1.73 m^2 [29]. Similarly, another research showed that 78% of all workers had at least one episode of AKI over the three work shifts. At the baseline, the median eGFR was 116 mL/min per 1.73 m^2 , and the median pre-shift eGFR was approximately 130 at all three-time points (February, March, and April). Almost all workers (92, 93, and 94% in February, March, and April, respectively) had a normal eGFR at the start of the work shift (≥ 90). Based on the findings, one worker had an $eGFR < 60$ at all three-time points, and two workers had < 60 at two-time points [32]. Additionally, in a survey, AKI was observed in 33% of the participants, and a significant association was observed between HI and developing AKI (OR=1.37, 95%CI: 1.11, 1.97). A statistically significant increase was also observed in the mean and standard error of SCr (mg/dL) (0.70 (0.01) to 0.81 (0.01)) from the pre- to post-shift measures ($P < 0.001$). The mean and standard error of eGFR (mL/min per 1.73 m^2) also decreased from 112.8 (1.22) to 102.5 (1.21) ($P < 0.001$) [28].

Working in hot temperatures significantly predicted reduced eGFR (OR=3.50, 95%CI: 1.30, 9.40). A significant cross-shift increase (about 10%) was also observed in SCr. The prevalence of elevated SCr increased from 20% pre-shift to 25% post-shift, indicating a drop in eGFR [17].

Moreover, the findings of a study indicated that SCr after the work shift was significantly higher than before (1.06 ± 0.20 vs. 0.84 ± 0.10 , $P < 0.001$). The eGFR after the work shift was significantly lower than before the work shift (100 ± 15.0 vs. 120 ± 9.00 mL/min per 1.73 m^2 , $P < 0.001$). No significant difference was found between workers with and without AKI considering the post-pre shift difference of SCr ($P = 0.070$). In other words, the median and interquartile range (IQR) of the post-pre shift difference of SCr was 0.45 (0.36, 0.58) and 0.13 (0.10, 0.21) among the AKI and non-AKI workers, respectively. The eGFR was significantly higher among individuals without AKI than those with AKI ($P < 0.001$). The median and IQR of post-pre shift difference of eGFR among non-AKI and

AKI workers was -14.60 (-18.60, -8.25) and -43.10 (-52.30, -34.88), respectively [39].

An investigation across seven consecutive work shifts found that increased WBGT was associated with increased SCr across the shift on all seven workdays (regression coefficient= 2.5%, p-value= 0.02) [14].

In another study, a high prevalence of acute cross-shift decrease was reported in eGFR so that the eGFR declined significantly from pre- to post-shift in February, March, and April ($P < 0.01$) [18].

Metal Industries: Four studies examined eGFR and SCr in metal industry workers. A study of metallurgical industry workers showed a reduced eGFR at the beginning of the working day among workers exposed to HS compared to the control group (106 ± 13 vs. 119 ± 15 mL/min per 1.73 m^2 , $P < 0.05$). Although the reduced eGFR was observed in both exposed and unexposed workers after a working shift, the decrease was more significant in the heat-exposed group by 12% [24]. Moreover, a study conducted in eight industrial sectors found that workers exposed to higher WBGT had a 2.9 times higher risk of decreased kidney function, as indicated by their eGFR values (OR=2.9, $P = 0.05$) [12].

An investigation among aluminum potroom workers indicated a statistically significant increase in SCr from pre- to post-shift measurements. The mean and standard deviation of SCr in pre- and post-shift were 1.06 ± 0.18 and 1.34 ± 0.32 , respectively ($P < 0.01$) [33]. On the contrary, a study among steel industry workers found no statistically significant difference between people who worked in the hot areas and those who worked in the non-hot areas in terms of the SCr level ($P > 0.05$) [23].

Other Industries: In an investigation of 119 indoor heat-exposed individuals working at a shoe-making factory, decreased eGFR (i.e., $< 90 \text{ mL/min/1.73 m}^2$) was observed among 12.6% of the workers [13].

ACR: ACR was used by two eligible studies. In one of these studies, one group of individuals with exposure to occupational heat and a control group without exposure to heat participated. In both exposed and unexposed groups, there was no statistically significant difference in the mean of ACR between pre- and post-shift. Moreover, no statistically significant difference was observed in the mean of ACR between the exposed and non-exposed workers ($P > 0.05$) [24]. Findings of another study showed that ACR, measured in three-time points (February, March, and April), ranged from 9-22 $\mu\text{g/mg}$ pre-shift to 18-30 $\mu\text{g/mg}$ post-shift and only increased significantly across the work shift in March [18].

Markers of Hydration Status

Agricultural Workers: Hydration status was investigated in 11 studies of agricultural workers. It was shown that the mean of USG and prevalence of dehydration at the pre-and post-shift assessment increased from 1.020 to 1.024 ($P<0.001$) and 53% to 81%, respectively [28]. In addition, an investigation of two groups found $USG>1.020$ to be lower at pre-shift than post-shift among the production workers. However, the hydration status of the cane cutters did not change from pre- to post-shift. According to the univariate regression model results, pre-and post-shift USG was significantly associated with developing AKI in sugarcane workers. In other words, the ORs were 1.41 (95%CI: 1.19, 1.67) and 1.48 (95%CI: 1.27, 1.72) for the pre-and post-shift USG, respectively. Moreover, in the multivariable regression model, post-shift USG was significantly associated with the developing AKI (OR=1.24, 95%CI: 1.02, 1.52). However, no statistically significant association was observed in terms of pre-shift USG (OR=1.21, 95% CI: 0.99, 1.45) [32].

Another study showed that most workers were dehydrated post-shift across the different seasons. Moreover, clinical dehydration, which was $USG\geq 1.030$, was at the highest level during the harvest season [37].

In a study of sugarcane workers, USG increased across shifts so that the mean of USG was 1.016 in the pre-shift and 1.020 in the post-shift samples ($P<0.001$) [17]. Additionally, in another study of sugarcane workers, 46% of workers had USG lower than 1.005 pre-shift, which increased to 67% post-shift across the monthly time points in February, March, and April. About 47% and 25% of the workers had normal USG pre-shift and post-shift, respectively. Nearly 6% of the workers were dehydrated pre-shift, which increased to 9% post-shift [18]. Nevertheless, in a group of agricultural workers, no significant change was found in the USG values comparing pre- and post-shift ($P=0.40$) [36].

On the other hand, an elevated level of SUA was observed among the sugarcane cutters exposed to HS. Elevated SUA (>7 mg/dL in men and >6 mg/dL in women) was observed in 26% and 43% of workers at pre- and post- shifts, respectively. A significant cross-shift increase (about 10%) was also found in BUN among sugarcane cutters [17]. Furthermore, a value of urine protein > 30 mg/dL was reported in a sample of agricultural workers from 2% to 10% in the pre- to post-shift measure, respectively ($P<0.001$). Concerning the BUN, a statistically significant increase was observed in the mean and standard error of BUN (mg/dL)

(14.5 ± 0.32 to 15.8 ± 0.32) from the pre- to post-shift ($P<0.001$), respectively [28].

Metal Industries: A study of the aluminum pot room workers showed that USG increased significantly from pre- to post-shift. The mean and standard deviation of the USG were 1.023 ± 0.01 and 1.028 ± 0.01 for pre- and post-shift measures, respectively ($P<0.01$). Another study found a significant elevation in the BUN level of workers at an aluminum smelter. The mean and standard deviation of BUN were 14.47 ± 3.98 and 16.23 ± 4.31 for the pre-and post-shift measures, respectively ($P<0.01$) [33]. Moreover, in a study among metallurgical industry workers exposed to indoor HS, SUA was higher in the exposed group than in those without exposure to heat ($P<0.05$) [24]. Conversely, a study performed among steel industry workers found no statistically significant difference between exposed and non-exposed workers in terms of SUA (572.6 ± 185.5 and 543.0 ± 178.0 , respectively, $P=0.54$) [23].

Mining: One study compared the hydration status of iron ore mining workers working at the open-cut iron ore mining/processing site1 and iron ore processing/shipping site2. The mean ambient temperature was greater at Site1 ($35.3\pm 1.9^{\circ}\text{C}$) compared with Site2 ($31.5\pm 2.1^{\circ}\text{C}$). The mean and standard deviation of USG was found to be greater among workers at Site1 (1.029 ± 0.006) compared with those at Site2 (1.021 ± 0.007) [19]. A study on miners showed that many of them were dehydrated at the beginning and during the work shift. Considering $USG\geq 1.020$ as the dehydration indicator, 78.6% of workers were dehydrated (83.3% and 87.5 % in pre- and post-shift, respectively). The mean of pre- and post-shift USG was not significantly different (1.023 ± 0.007 and 1.025 ± 0.007 pre- and post-shift, respectively, $P=0.068$) [34]. However, in a study among male underground mine workers, no statistically significant difference was observed in the USG at the start compared to the midpoint and end of shift, as well as midpoint compared to the end of shift ($P>0.05$) [30].

Electric Power Industry: Among the electrical utility workers who worked in heat-stressed conditions, the frequency of dehydration ($USG\geq 1.020$) was found to be 62 and 75% before and after the work period [42]. On the other hand, in an investigation of electric power workers, no significant change was found in the USG from pre- to post-shifts. The mean and standard deviation of USG at the pre-shift was 1.022 ± 0.006 and at the post-shift was 1.022 ± 0.007 ($P=0.372$) [25].

Construction Industry: A study conducted among construction workers exposed to the sun heat and

those working in shadow (controls) revealed a statistically significant difference in the mean of USG between the exposed and control groups (1.0259 ± 0.0050 vs. 1.0213 ± 0.0054 , respectively, $P=0.001$). Regarding the three time points (beginning, middle, and end of the work), a statistically significant difference was observed in the USG level in the exposure group ($P=0.024$). In addition, a high and significant correlation was found between USG and WBGT ($r=0.89$, $P=0.001$). However, a high negative and significant correlation was observed between USG and TWL ($r=-0.93$, $P=0.001$) [22].

In another study, USG was measured six times: at the start of the work shift (SW), morning break (MB), before lunch (BL), after lunch (AL), afternoon break (AB), and at the end of the work shift (EW). According to the results, the USG of AB was significantly higher than SW, MB, and BL ($P<0.05$), and the USG of EW was larger than those of SW and BL ($P<0.05$). The ratio of workers with USG above the clinically dehydrated level of 1.030 was 5, 16, 11, 21, 26, and 21% at SW, MB, BL, AL, AB, and EW, respectively [21].

In another study conducted among construction workers in an indoor situation, a USG level of ≥ 1.020 was observed among 76% and 63% of workers at pre- and post-shift, respectively. In addition, the mean and standard deviation of USG were 1.025 ± 0.008 and 1.023 ± 0.007 at pre- and post-shift, respectively ($P>0.05$). An increased level of USG in the outdoor situation also was observed among 85% and 81% of workers at pre- and post-shift with the mean \pm standard deviation of 1.024 ± 0.009 and 1.025 ± 0.008 , respectively ($P<0.05$) [31].

Other Industries: A study conducted in eight industrial sectors found that workers with a very high heat exposure combined with physical exertion had 3.6 times higher odds of increased USG ($OR=3.6$, $P<0.001$) [12]. Moreover, a study conducted on 119 indoor heat-exposed individuals working in a shoe-making factory showed that 64.7% of the workers had an abnormal USG level (i.e., USG of ≥ 1.020) [13].

In one study conducted among manufacturing workers, agricultural workers, police officers, tourism workers, and construction workers, no significant difference was reported in the mean of USG. In other words, the mean and standard deviation of USG was 1.023 ± 0.001 at the start of a work shift and 1.023 ± 0.001 at the end of a shift across all industries. Furthermore, 70% and 69% of the participants had $USG \geq 1.020$ at the beginning and end of the work shift, respectively [35].

According to the evidence, HS may play an important role in dehydration and consequently develop kidney damage. However, some studies have shown no statistically significant difference between heat-exposed and non-exposed workers in terms of kidney dysfunction. Therefore, controversy exists about the HS effect on changes in dehydration markers.

Discussion

The association between occupational HS and renal dysfunction has been reported in many investigations, but it is still unclear in other studies. This systematic review presented some evidence regarding the potential effects of occupational HS on developing kidney dysfunction. Our results demonstrated that most markers of kidney function were affected by HS in workers. This review investigated a wide range of occupational groups in diverse climatic conditions, presenting a rich source of evidence.

Studies among agricultural workers reported a high prevalence of kidney dysfunction related to occupational HS. Agriculture is one of the several occupations with a high risk of heat-related disease and damage [43]. It is a seasonal occupation, and workers are required to do heavy physical activities for long periods in summer under direct sunlight without any occupational health and safety programs [29, 43]. For example, Dawson et al. reported that workers harvest an average of more than five tons of sugarcane per day [32]. Heavy physical activity in heat can lead to mild muscle injury with increased creatine kinase blood level (features related to subclinical rhabdomyolysis), which is associated with biomarkers of kidney damage and decreased renal function. However, subclinical rhabdomyolysis has a relatively small risk of impaired renal function because nucleic acids released from damaged muscles can increase the production of uric acid [44]. Garcia-Trabanino et al. reported an elevation in SUA during the work shifts [17]. Although some sugarcane workers drink one to two liters of water per hour, a decrease in urine volume and an increase in USG are observed in the people, which is associated with dehydration. Sodium and water loss are probable among workers; however, since sweat is hypotonic, losing water is dominant, and farmers experience daily dehydration [45]. Heat exposure, physical work, and dehydration are the real challenges for the cardiovascular system and transferring oxygen to active muscles of vital organs, such as kidneys [46]. Under these conditions, especially along with dehydration,

muscles release myoglobin, which can lead to acute kidney injury [47]. When urine becomes concentrated and acidified, the performance of water and electrolyte balance systems is impaired [44, 45]. Thus, repeated subclinical kidney injuries can cause chronic kidney disease (CKD) [48]. In addition to the separated and combined effects of heat and physical activity on kidney function, exposure to agrochemicals, with the potential to damage this organ, must be considered. Based on the evidence, a number of pesticides used in many areas of the world are identified as human nephrotoxins [49, 50]. However, a systematic review presented little evidence regarding the association between pesticides and CKD. On the contrary, given the poor evaluation of pesticide exposure in most of the investigated studies, the potential impact of nephrotoxic agrochemicals cannot be certainly ruled out [51]. Therefore, more studies are needed to reach a definitive conclusion.

All reviewed studies on construction workers investigated the USG, and their results indicated a high frequency of dehydration in the participants. Construction workers are among the vulnerable occupational groups working in unorganized sectors [52]. Among these people, direct sunlight, building radiation, poor air velocity, work overload, high thermal insulation, and clothing evaporative resistance increase heat strain. At a construction site, the ambient temperature can be higher than the measured temperature at 1.5 meters above the ground, where airflow is not disturbed [38]. When the ambient temperature exceeds the skin surface temperature, the convective temperature is transferred from the environment to the body. To maintain body temperature, construction workers sweat heavily, which increases the number of sweat drops, prevents the evaporation of sweat on skin and body cooling, and results in the loss of body water and minerals, increasing the body's central temperature and dehydration. Physical activity also increases the body's metabolism and heat production, which can increase the risk of health problems [53, 54].

In this regard, three cross-sectional studies on the hydration status of miners provided conflicting results, which can be due to the study design, low sample size, and the type of mine (since hot working conditions vary greatly in different types of mine). The heat exposure in open-cut mines is similar to other outdoor workplaces. However, more HS-related complications were reported in underground mines [55]. In this vein, some researchers studied some health problems in underground miners [56, 57] and found that more than half of the miners were dehydrated before

and after their shift [58]. Since the temperature increases in deeper soil horizons of the mines and due to the auto-compression of air for ventilation, the high humidity of the water used for controlling dust and the heat generated by the equipment increase the thermal load significantly [30, 55, 57]. Of the three investigated studies conducted in the metallurgical industry, the results of two studies showed a significant relationship between heat exposure and kidney biomarkers [24, 33]. Although the study by Atan et al. had a large sample size, the evidence did not indicate such an association [23]. However, based on the results of these studies, the health effects of exposure to occupational HS cannot be ruled out. In such industries, workers' health status is tested before recruitment, and a "healthy worker effect" is expected. Moreover, large industries usually provide engineering and management control principles to prevent exposure to occupational risk factors. However, workers in the manufacturing industry with an indoor working environment with little or no direct sunlight are also exposed to heat-related illnesses. The HS around hot machines, furnaces, ovens, and molten metal can be very severe. Even in winter, the temperature near furnaces in a steel plant ranges from 35.5 to 46.5°C, while the outdoor temperature is only 14 to 18°C [59]. An increased number of hot days due to climate change can worsen the conditions for people who work near a heat source [55]. Studies conducted on electrical utility workers did not show conflicting results regarding the association between HS and dehydration [25, 42].

Given that the tasks of these workers are often completed outdoors, radiation heat sources such as the sun, vehicles, and mechanized workplace equipment can play a significant role in producing HS. Even in temperate environments, high work rates, the subsequently metabolic heat load, and restriction of body heat excretion due to the protective clothing can severely impair the workers' ability to regulate body temperature, thus increasing the risk of heat-related diseases [60]. In addition, working at high temperatures is not only associated with an increase in central temperature but also causes considerable changes in dehydration and cardiovascular stability [42]. Due to the working conditions of this group of workers, the relationship between HS and dehydration cannot be ignored.

In addition to occupational risk factors, there are other risk factors associated with an increased risk of kidney disease in workers. Aging, male gender, ethnicity, family history of kidney disease, socioeconomic status, metabolic syndrome, urological disorders (obstruction, recurrent urinary

tract infections), medications (nonsteroidal anticoagulants, antibiotics), cardiovascular disease, diabetes mellitus, and hypertension are predisposing factors of kidney dysfunction [61]. In order to prevent kidney damage, it may be necessary to consider the interaction between such risk factors and occupation-related risk factors.

The findings suggested an association between dehydration and exposure to HS in different occupational workers; thus, keeping workers hydrated may be the most important intervention in managing the health of workers exposed to HS [62]. However, if adequate amounts of liquids are available to people working in the heat, their sweating is more than the water they take. According to some studies, some workers may start their workday with dehydration [2, 34]. Some others may tolerate thirst for a long time since water resources are far away or unavailable; in such cases, portable water supplies can be helpful. Furthermore, weight monitoring and fluid replacement (250ml every 20 minutes or by lost body weight) are recommended during exposure to heat [63]. In the case of severe perspiration, water alone is insufficient to compensate for dehydration; thus, lost electrolytes should also be replaced [64]. To our knowledge, this study is the first systematic review on the association between occupational HS and renal biomarkers. However, the impossibility of searching for gray literature is the limitation of this study.

Conclusion

The results suggested heterogeneous evidence regarding the HS effects on renal function among workers. However, most evidence showed a positive relationship between occupational HS and kidney dysfunction. Among the markers investigated in this review, many studies reported a positive association between occupational HS and dehydration. At present, the frequency of exposure to HS is not well studied in various occupations and regions. Workers should be trained to know the symptoms of heat-related illnesses and prevent dehydration by regular drinking during and after working hours. In addition, employers should be aware that the establishment of hydration results in an elevation in workers' productivity and can compensate for the small productivity decline due to rest breaks. Moreover, engineers, health officials, researchers, and policymakers can play a key role in preventing occupational HS.

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