Heat strain, volume depletion, and incident acute kidney injury in a cohort of agricultural workers in California

by

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DEDICATION

I dedicate this work to Pati, a migrant farm worker, whose diagnosis of chronic kidney disease was the catalyst for my career.

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ABSTRACT

BACKGROUND

Agricultural work exposes workers to many occupational risks and poor health outcomes. Working long hours during summer harvests puts may result in heat strain and volume depletion, which can cause acute damage to the kidneys. Acute kidney injury (AKI) is a potential occupational risk factor of agricultural work, and has been identified in workers in Central America after a single day in the fields. To date, no study has examined AKI in agricultural workers in California.

PURPOSE

This doctoral study was conducted to estimate the cumulative incidence of AKI after a single day of agricultural work and to test the associations of heat strain and volume depletion on incident AKI.

METHODS

In a convenience sample of 295 agricultural workers, we collected a capillary blood sample and estimated incident AKI based on elevations of serum creatinine between pre-and post-shift blood samples. Heat strain was assessed based on changes in core body temperature and heart rate. Volume depletion was assessed using changes in body mass over the work shift. Logistic regression models were used to estimate the associations of AKI with traditional risk factors (age, diabetes, hypertension and history of kidney disease) as well as with occupational risk factors (years in farm work, method of payment and farm task).

RESULTS

We found incident AKI in 35 participants (11.8%) after a single work shift. Workers who experienced heat strain had increased adjusted odds of AKI (adjusted odds ratio [AOR] 1.34, 95% CI 1.04 - 1.74). Workers who were paid by the piece had AKI AOR of 4.24 (95% CI 1.56 - 11.52). Volume depletion was not associated with AKI.

CONCLUSION

The cumulative incidence of AKI after a single day of working in the fields suggests that kidney damage is a previously unrecognized occupational risk factor of agricultural work. Modifications to the payment structure and measures to prevent heat strain in may protect the kidneys from AKI. Nurses play a pivotal role in advocating for occupational safeguards to protect the renal health of California's agricultural workers.

CHAPTER 1: INTRODUCTION

Statement of the Problem

The majority of agricultural work is seasonal, and during California's summer harvest, workers typically perform arduous physical labor for 10-12 hours a day under direct sun.[1,2] These occupational conditions put workers at risk for developing heat related illness, such as heat stress or hyperthermia,[3] due to the rise in body temperature in response to ambient conditions and increased workload in extreme temperatures.[4] When heat stored in the body exceeds the body's ability to release it, a person experiences hyperthermia and heat stress.[5] The body's natural mechanism for reducing core body temperature is to sweat, creating an evaporative effect, which can result in transient volume depletion, further increasing the risk of heat stress and of decreased blood flow to the kidneys.[6,7] If inadequately compensated, heat stress can cause damage to vital organs, including the kidneys, or even death.[8]

From studies of military personnel and athletes, there is evidence that renal hypoperfusion may lead to acute kidney injury (AKI). However, to date, little research has examined the effect of heat exposure and volume depletion on kidney function among agricultural workers in the United States, yet this population of immigrants is vulnerable and their risks for poor health outcomes related to agricultural work conditions are often underreported.[9] Due to this population's limited access to medical care for a chronic condition,[10,11] including virtually no access to dialysis, understanding the magnitude of occupational heat-related kidney dysfunction is important to plan occupational interventions for its prevention.

Agricultural Workers

Agricultural workers are a vulnerable population due to their social and economic position in the United States. In California, most agricultural workers are immigrants from Mexico and Central America; 95% are foreign-born and the remaining 5% are children of immigrants.[10] It is estimated that at least half of the 450,000+ agricultural workers in California are “not authorized” to legally work.[11] While occupational protections for agricultural work exist, immigration status limits access to legal recourse if these regulations are violated, putting workers at risk for workplace injuries. Agricultural work has been termed “sweatshops in the field”[1] and is notorious for giving workers low wages, few breaks, no health benefits, and no job security. In 2012, the median annual wage for an agricultural worker in the United States was $18,910.[12] Approximately 58-70% of workers lack health insurance.[10]

In the Central Valley of California, where daily summer temperatures regularly exceed 95^{O}F, agricultural workers are at particular risk for developing a heat-related illness or of dying from heat exposure. An analysis of occupational heat-related deaths in the United States between 1992 and 2006 revealed that the heat-related fatality rate among agricultural workers was 20 times higher than the rate of 0.2 per one million for civilian workers overall.[2] Almost 80% of these deaths were of men between the ages of 20 and 54 years.[13] Heat-related illnesses in the agricultural sector are far more common than deaths, however. It is estimated that agricultural workers in the United States are four times as likely to have a heat-related illness than workers in other industries.[14] Over half of a sample of 405 farmworkers in one study reported experiencing at least one symptom of heat-illness in the previous year.[15] Due to fear of losing their jobs or fear of immigration action, agricultural workers likely underreport these illnesses, and actual rates of injury and mortality may be higher.[2]

Heat Protection Regulations in California

In response to multiple deaths in the agricultural sector, in 2005 California became the first state to adopt occupational heat protection regulation.[2] Farmers and employers are required to provide 2 gallons of water per employee for an 8-hour work shift and shade for breaks, to allow for breaks when a worker is experiencing heat-related symptoms, to have an emergency plan for heat illness, and to train workers and supervisors in prevention and treatment of heat related-illness (Cal/OSHA Heat Illness Regulation 3395). While the regulation is directed toward the employer, the actual enactment of these standards tends to place the responsibility on the worker rather than the employer. Effective prevention of heat stress requires the worker to stop his or her activities to rest or drink water.[16] Fear of employment repercussions may cause many workers who experience heat-related symptoms to self-treat and not report these events.[2] Additionally, regulations apply to farms with 11 or more employees, but approximately 95% of farms in California employ less than 11 people and so are exempt from these regulations.[17] Further, the regulations that do apply are poorly enforced.[16] Despite the progressive standards in California, studies show that agricultural workers do not have adequate protection from heat exposure or volume depletion and significant numbers of heat-related illnesses continue to occur.[2]

Beliefs and Behaviors of Agricultural Workers

A recent study of agricultural workers' knowledge of heat illness in California's Central Valley found that over 90% of workers reported receiving training on heat illness prevention, but only 30% of surveyed workers correctly answered questions about heat illness.[18] Additionally, a study of workers in Washington state found that despite having the knowledge of heat exposure prevention, workers often did not follow recommendations. For example, despite knowing that wearing loose, light-colored clothing protects against heat illness, women in that study told researchers they often wear multiple layers of dark clothing in order to increase sweating and lose weight.[19] Additionally, workers are reluctant to take recommended breaks due to a fear of a negative reaction from coworkers and supervisors, the Latino notion of *machismo*, or from a fear of losing wages when being paid for piece-work.[2,18,19] Workers often work as part of a team, and breaks undercut the earning potential for all members of the team, so workers are often reluctant to stop for even short breaks.[18]

Estimates of water or fluid intake among agricultural workers during work hours have been difficult to obtain, but it is believed that very few drink the recommended amount.[2,18] A recent analysis found that, on average, workers consume 11 drinks during a work shift (the volume was not recorded). According to Cal/OSHA standards (Cal/OSHA Heat Illness Regulation 3395), employers are required to encourage workers to drink an 8-ounce cup of water every 15 minutes to maintain hydration during conditions when the weather exceeds 95^{O}F. We can assume, therefore, that 11 drinks during a typical work shift is not adequate for rehydration.[18] Actual estimates of fluid intake suggest that what workers drink is not sufficient to replace fluids and electrolytes lost during the work shift,[9] as many do not believe they are at risk for injury and do not rehydrate.[20] In addition, agricultural workers often have a distrust of water supplied by employers, and do not bring enough of their own water to adequately hydrate during the day.[19] In a qualitative analysis of workers' hydration behaviors, women reported a reluctance to drink employer-supplied water because of its location near the bathroom facilities where men often urinated in the dirt, and the women believed the water to be contaminated.[19] Further, women limit their fluid intake because of lack of available bathroom facilities or poor sanitation of facilities.[18] Despite knowing that caffeine and alcohol can increase the risk of heat illness, workers report drinking caffeinated beverages to increase alertness in the fields or drinking beer to quench thirst during the day.[9,19] In focus groups (Wadsworth, unpublished), workers stated that water does not satisfy their thirst, preferring beer or soda instead. Workers also reported that they only drink water because their employers tell them to, not because they feel it will benefit them or prevent heat-related illness. Finally, cultural beliefs may prevent some agricultural workers from drinking cold water, believing, for example, that drinking cold water in the heat leads to mouth ulcers.[19]

Heat, Volume Depletion and the Kidneys in Healthy Populations

One of the primary health hazards among the potential risks to a worker's health from repeated exposure to heat and volume depletion is damage to the kidneys. Working in temperatures in excess of 95°F (or 35°C) puts a strain on the body's ability to thermoregulate.[5] The body's heat load is influenced by environmental factors such as ambient temperature, humidity, and air movement,[21,22] causing a rise in the internal temperature and requiring additional adjustments to maintain homeostasis.[2] Performing work in high temperatures leads to a further rise in the metabolic heat load as the increased heart rate and working muscles generate internal heat.[23] While the amount of metabolic heat generated is dependent on factors such as age, physical conditioning, acclimatization, and hydration status,[4,21] studies from the military suggest that heat from increased work load is one of the most influential factors on heat stress[23] and can cause heat strain even during periods of cooler ambient temperatures.[2]

In high ambient temperatures, the body has four mechanisms of cooling itself: convection, conduction, radiation, and evaporation. These result in an elevated heart rate and vasodilation to increase circulation at the skin.[22,24] When air temperatures exceed 95°F, evaporation—or sweating—is the only mechanism which can effectively lower body temperature.[24] Although essential for cooling, prolonged sweating may lower blood volume and deplete the body's stores of water and electrolytes, resulting in decreased blood flow to the kidneys.[25,26] Intake of water and electrolytes is necessary to replace such losses during sweating and to prevent volume depletion. Unfortunately, thirst is a late signal of volume depletion – usually occurring after a person has already lost 1-2 liters of fluid. If that person is working hard, thirst may not appear until after the loss of 3-4 liters of fluid, and the decreased blood volume is therefore even more difficult to correct.[20] Voluntary hydration – that is, drinking in response to the thirst mechanism – during periods of exercise is not sufficient to replace fluids lost, and decreased renal perfusion results.[27]

At rest, blood flow through two healthy kidneys is approximately 1200ml/min.[28] The combination of the body's physiological response to heat, potential volume depletion, and shunting of blood away from the kidneys during exercise in the heat may lead to decreased renal perfusion,[29] which remains low even after a period of rest.[30] This decrease is intensified when combined with heat stress and volume depletion, as demonstrated in studies of healthy populations such as athletes and military personnel.[31–33] Smith, Robinson and Pearcy found that exertion in cool temperatures decreased renal blood flow 22%, in hot conditions 31%, and when combined with volume depletion, renal blood flow decreased 56%.[26] When blood flow is already shunted to working muscles, the decrease in renal perfusion can drop to 250ml/min during maximum work load.[28] Kidney injury, then, can result from ischemia due to the decreased blood flow to the kidneys.[34]

A further mechanism of injury to the kidneys may result from rhabdomyolysis,[31] the process whereby muscle cells, damaged from exertion, release myoglobin into the body's circulation which concentrate along renal tubules, causing obstruction.[6] Even during moderate exercise, muscle damage can lead to the release of myoglobin, which leads to kidney damage.[35]

In studies of athletes and military personnel, those who experienced rhabdomyolysis from exercise in the heat were more likely to be diagnosed with acute kidney injury (AKI).[32, 33]

The effect of exercise on renal function is exacerbated by high ambient temperatures – likely due to the combination of rhabdomyolysis and volume depletion. Clarkson, in a study of marathon runners, noted that AKI is an uncommon event due to the conditioning of the athletes and the usually cooler temperatures of early-morning race start times. However, from case reports, those who developed AKI were found to have rhabdomyolysis exacerbated by heat stress.[31] This was also found to be the case in military recruits during summer training drills. Those performing exercises in the heat while dehydrated were more likely to develop AKI.[37] During periods of physical exertion in the heat, changes in hemodynamics to cool the body and supply working muscles as well as potential volume depletion may lead to decreased renal perfusion, which may be one mechanism leading to AKI.[38]

Acute Kidney Injury

Previously known as acute renal failure, acute kidney injury (AKI) is a response to an acute event, such as volume depletion or drug exposure, with a rapid decrease in kidney function, usually resolving within 2-4 weeks. Due to the decrease in the kidneys' excretory functions, AKI is characterized by a rise in metabolic waste products, such as creatinine or urea, and a decreased urine output. Estimates of the incidence of AKI are hard to determine, based on incomplete criteria for characterizing and diagnosing the injury.[39] However, in a study of members of Kaiser Permanente of Northern California, the incidence of AKI not requiring dialysis treatment was estimated to account for more than 500 cases per 100,000 people per year in 2003.[40]

The very limited studies of AKI acquired in the community have found pre-renal causes to contribute to its etiology,[41] such as volume depletion related to infectious disease[42] or diarrhea and vomiting.[43] A study in Australia found there to be a 10% increase in hospital admissions for renal disease during heat waves versus non-heat wave periods – almost 4% of those were for AKI.[3] These results are echoed in a study of nine counties in California which found that with an increase in ambient temperature of 10˚F, there was an 11% increase in hospital admissions for dehydration and a 7.4% increase in admissions for AKI.[44]

Most AKI is reversible, particularly if fluid replacement is timely.[45] However, there is increasing evidence that AKI can lead to chronic kidney disease (CKD) with repeated exposure and damage to the kidneys without adequate time to recover.[6,46] The rate of CKD after an episode of AKI was found to be 7.8 per 100 person years in one study.[47] Animal studies show that AKI causes permanent damage to renal vasculature, resulting in subsequent lasting abnormalities in kidney function,[48] periodically leading to CKD.[47] Additionally, AKI leads to changes in fluid balance, electrolytes, and hormonal regulation, which all play a role in the potential development of CKD.[49]

Global Context of Heat Exposure and Kidney Disease Among Agricultural Workers

While the relationship between heat exposure and volume depletion on acute kidney injury has not been expressly studied in agricultural workers, there is a disquieting literature suggesting that chronic kidney disease is increasingly recognized in agricultural workers exposed to heat. In areas of Central America, an epidemic of chronic kidney disease, termed Mesoamerican Nephropathy, has emerged in the previous two decades. While it is unclear whether there is a growing trend in the occurrence of the disease or if there is improved ascertainment of the disease, Mesoamerican Endemic Nephropathy (MeN) is estimated to have been the cause of 20,000 deaths in Central America in the last two decades.[50] Although chronic kidney disease is typically a disease affecting men and women older than 60 years of age with a previous history of diabetes or hypertension,[51] MeN disproportionately affects young men more than women at a 5-to-1 ratio,[52] and these men are typically in their 30s-40s, work in agricultural jobs and lack a previous history of associated risk factors.[50,53] The exact etiology of MeN is unknown; however, based on a consensus of researchers, heat exposure and recurrent volume depletion were identified as the likely primary risk factors.[53] In multiple studies of the condition, an association between heat exposure and elevated creatinine levels in otherwise healthy individual was identified.[52,54] One study examined renal biopsies of patients with MeN and found tubulointerstitial disease with tubular atrophy, interstitial fibrosis, and glomerulosclerosis. These results are consistent with decreased renal blood flow from repeated volume depletion.[55]

Acute Kidney Injury in California's Agricultural Workers

Available evidence supports the hypothesis that California's agricultural workers are at increased risk of AKI. This is based on research among athletes, military personnel, and of agricultural workers in Central America. Repeated work in high ambient temperatures increases the risk of volume depletion, and returning to the fields day after day may exacerbate dehydration, not allowing the kidneys adequate time to recover from the previous day's damage before returning to the fields.[18] Further, limited enforcement of California heat regulations suggests that workers are continually exposed to high levels of physical exertion in extreme temperatures in the Central Valley. Therefore, investigating heat exposure, volume depletion, and kidney function in agricultural workers, repeatedly exposed to heat and volume depletion, is an important priority.

Agricultural work in high temperatures without adequate shade, rest, and hydration likely puts workers at increased risk for kidney damage. While evidence is emerging from Central America on the prevalence and associated risk factors for MeN and the relationship of heat exposure and volume depletion to AKI is well established in other populations, no research to date has examined the association between heat exposure, volume depletion, and kidney function in agricultural workers in California. The Central Valley of California, with summer temperatures consistently above 95°F is an ideal place to study this relationship. Understanding risks inherent in agricultural work is important to protect the health of workers, many of whom have limited access to health services or a voice to advocate for themselves.

Doctoral Research

The California Heat Illness Prevention Study (CHIPS), conducted by a research team at the University of California, Davis, investigates heat illness among agricultural workers in California. The goal of CHIPS is to understand physiological responses to ambient heat and physical work and the socio-cultural influences that affect workers' behavior and risk of heat-related illness. Nested within CHIPS, this doctoral research sought to identify evidence of early kidney insufficiency associated with increased heat exposure among California agricultural workers. Understanding risks inherent in agricultural work is important to protect their health, as many lack access to health services or a voice to advocate for themselves. Results from this study may provide additional information about the environmental impact of working in extreme temperatures and may inform future studies on the link between heat exposure and kidney function.

Additionally, it is imperative that we understand the impact of working in hot, dry conditions on kidney function so that we may advocate for effective safety measures, such as improving hydration and availability of shade, thereby preventing kidney function loss and resulting morbidity or mortality. The prevalence of AKI in this population may indicate a need for more stringent Cal/OSHA regulations and better regulatory oversight. Finally, results from this dissertation study will be used to plan future interventions and to advocate for further occupational health protections for agricultural workers.

CHAPTER 2: CUMULATIVE INCIDENCE OF ACUTE KIDNEY INJURY IN CALIFORNIA'S AGRICULTURAL WORKERS

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Abstract

Objective: Chronic kidney disease in Central America suggests agricultural work is potentially harmful to the kidneys. We investigated the cumulative incidence of acute kidney injury (AKI) over one work shift during the summer among agricultural workers in California.

Methods: Serum creatinine was measured both before and after a work shift to estimate AKI. Associations of incident AKI with traditional and occupational risk factors were tested using chi-square and trend tests and logistic regression.

Results: In 295 agricultural workers, AKI after a summer work shift was detected in 35 participants (11.8%). Piece-rate work was associated with 4.52 adjusted odds of AKI (95% confidence interval 1.61-12.70).

Conclusions: The cumulative incidence of AKI after a single day of summer agricultural work is alarming due to increased risk of long-term kidney damage and mortality.

Cumulative Incidence of Acute Kidney Injury in California's Agricultural Workers

Background

In areas of Central America, an epidemic of chronic kidney disease, termed Mesoamerican Nephropathy, has been identified in the last two decades. Mesoamerican Nephropathy (MeN) is estimated to be the cause of 20,000 deaths in Central America.[50] While chronic kidney disease (CKD) typically affects men and women older than 60 years old with previous history of diabetes or hypertension,[51] MeN disproportionately affects young men typically in their 30s-40s who work in agricultural jobs and lack a previous history of traditional risk factors, such as obesity, diabetes, or hypertension.[50,53] Men are affected more than women at a 3 or 4-to-1 ratio.[56] Research suggests that the etiology of the disease may be found in an occupational hazard of agricultural work.[53,57]

A risk factor for the development of CKD is the closely related condition, acute kidney injury (AKI).[58,59] AKI, formerly termed acute renal failure, is characterized by a rapid decrease in kidney function causing a rise in metabolic waste products, such as creatinine.[60] In 2012, the Kidney Disease Improving Global Outcomes (KDIGO) Working Group created a new working definition of the stages of AKI, based on elevations in serum creatinine and/or decreased urine output.[14] In field studies, detection of CKD is difficult due to the need for consistent monitoring over a number of months; however, incident AKI can be detected based on elevations in serum creatinine that occur rapidly and are detectable within hours.[61] Common risk factors for the development of AKI are the same as those for CKD, such as obesity, diabetes, and hypertension. Additional risk factors include dehydration from acute diarrhea or other causes, infectious diseases, venom from animal bites, and "natural" medicines.[42,62–64] The occupational and environmental hazards of agricultural work expose workers to conditions which may increase their risk for AKI via dehydration or exposure to unknown kidney toxins.

Few studies have examined the incidence of AKI among agricultural workers, despite the relationship between AKI and CKD and the apparently increasing prevalence of CKD among agricultural workers in Central America. Santos and colleagues examined changes in serum creatinine after a day working in the sugarcane harvest in Brazil and found incident AKI in 18.5% of their sample.[65] Garcia-Trabanino and colleagues studied renal function among sugarcane cutters in El Salvador. They found a high prevalence reduced renal function in pre-shift samples: 14% of men met the criteria for chronic kidney disease based on decreased estimated glomerular filtration rate and 20% had elevated serum creatinine. After the work shift, they found the prevalence of elevated serum creatinine had increased to 25% of their sample.[66]

California employs between 350,000 and 700,000 agricultural workers each year,[67] yet very little is known about their renal health. Studies of renal function and MeN suggest that AKI among agricultural workers could be an important but under-recognized problem, and may be a precursor to further kidney damage. Despite occupational regulations on California's farms to protect the health of workers, many factors influence the ability of the worker to take advantage of these regulations. For example, variations in pay structure or in field tasks may put workers at increased risk for AKI, as those paid by the piece may perceive that earnings are reduced when they take breaks. We conducted an exploratory study to investigate the cumulative incidence of AKI over a work shift in a sample of agricultural workers in California and to evaluate the association of both traditional and occupational risk factors with AKI in this population.

Methods

Population

A convenience sample of 300 field workers was recruited from 15 farms throughout the prime agricultural region of the Central Valley of California during the summer of 2014 as part of the California Heat Illness Prevention Study (CHIPS). After receiving permission from the farm owner or the farm labor contractor, recruitment was conducted the day before data collection began. Bilingual, bicultural field staff explained the purpose and protocol of the study in Spanish to potential participants. If interested, participants were enrolled in the study after consent was obtained and field staff reviewed consent documents. Workers were included if they were 18 years of age or older, worked in the fields for at least six hours per day, and understood Spanish. They were excluded if they were pregnant, had experienced a recent illness or fever, or if they spent the majority of their work day in a tractor cab or other vehicle rather than working in the field. Each volunteer participated in the study for one work day only, and was given a small monetary compensation for their participation in the study.

Due to time constraints at enrollment sessions and the dispersion of workers on the farms, we were unable to document exact rates of refusal. Overall, we estimate the refusal rate to be between 40-50%. Of those who agreed to participate, 295/300 had complete serum creatinine data and were included in the current analysis.

Data Collection

Pre-Shift Measures. A brief, pre-shift questionnaire was administered orally in Spanish to assess participant eligibility and to collect demographic information. A capillary blood sample was taken and analyzed using the handheld i-STAT point of care test (Abbot Point of Care, Inc., Princeton, NJ) to measure serum creatinine (traceable to isotope dilution mass spectrometry through the standard reference material SRM967).[68] Hemoglobin A1c (Hgb A1c) was measured using a Siemens DCA Vantage Analyzer (Siemens Healthcare Diagnostics Inc., Tarrytown, NY).

Weight was measured in a base layer of clothing using a Seca 874 medical scale, and height was measured without shoes using a Seca model 213 stadiometer (Seca GMBH, Hamburg, Germany). All staff involved in data collection were trained and supervised, and all equipment was regularly calibrated to ensure accuracy.

Post-Shift Measures. Following the work shift, approximately 7 to 12 hours later, a post-shift questionnaire was orally administered in Spanish to obtain information on health history and possible social and behavioral risk factors, including a personal or family history of kidney disease, work history, method by which they are paid, primary task on the farm, and general health rating. A second capillary blood sample was obtained to document serum creatinine, and a single blood pressure was obtained in the seated position using an automated blood pressure cuff (Omron blood pressure monitor, Lake Forest, IL).

Participants' BMI, blood pressure, diabetes risk status and blood creatinine level were shared with them at the conclusion of the day, and participants who had abnormal results were referred to local health clinics for follow-up care.

All study procedures were approved by the University of California, Davis Institutional Review Board.

Acute Kidney Injury

The primary outcome of interest was cumulative incident AKI during the work shift, defined by a specified increase in serum creatinine from the pre-shift to the post-shift measure. The KDIGO[49] definition and stages of injury were used to ascertain and classify changes in serum creatinine between the pre- and post-shift measures. AKI was defined as an increase of the post-shift serum creatinine by $\geq$ 0.3mg/dl or $\geq$ 1.5 times the pre-shift creatinine. AKI staging was based on the following: stage 1 (≥ 0.3mg/dl or 1.5-1.9 times pre-shift serum creatinine); stage 2 (2.0-2.9 times pre-shift serum creatinine); and stage 3 (≥3.0 times pre-shift serum creatinine).

Predictor Variables

Demographic variables thought to be associated with incident AKI were selected *a priori* based on a review of the literature and feasibility of collecting data in the field. Demographic variables included sex (male v. female), and age (continuous). Occupational variables collected were years in agricultural work (continuous), type of farm task performed the majority of the day (picking, hoeing, irrigation, packing/sorting/planting, pruning/weeding, or other task such as machine maintenance or supervision of workers), and how the worker was paid (by the piece, hourly, or salary). Clinical data were also obtained. Body mass index (BMI) was calculated from pre-shift height and weight measurements in a base layer of clothing (BMI=(weight in kg)/(height in meters)^2, and classified based on WHO recommendations[69] as normal weight (BMI<25), overweight (BMI 25<30), or obese (BMI≥30). Diabetes status was defined by standard categories of hemoglobin A1c (Hgb A1c):[70] no diabetes (Hgb A1c<5.7%), pre-diabetes (Hgb A1c 5.7-6.4%), or diabetes (Hbg A1c ≥6.5%). Blood pressure was based on a single reading taken on the left arm and categorized as recommended by the Joint Commission:[71] normal blood pressure (<120/80 and no self-reported anti-hypertensives), pre-hypertension (120-139/80-89), or hypertension (≥140/90 or taking anti-hypertensives). Estimated glomerular filtration rate (eGFR) was calculated using pre-shift serum creatinine based on the CKD-EPI equation[72] and categorized as ≥90ml/min/1.73^2, 60-89 ml/min/1.73^2, or <60 ml/min/1.73^2. Self-reported information on personal or family history of kidney disease (yes v. no) and self-reported health status (excellent/good versus fair/poor) were also collected.

Statistical Analysis

Descriptive statistics were calculated for the outcome and potential risk factors stratified by sex. Subjects were classified based on development of AKI and the unadjusted cumulative incidence of AKI was estimated with respect to candidate risk factors. Data were categorized, and unadjusted associations between incident AKI and candidate risk factors were tested for statistical significance using trend tests for ordinal variables[73] (via the Stata command nptrend) and chi-square tests for nominal variables. Simple logistic regression was used to estimate the crude odds ratio of incident AKI for each of the worker characteristics. Variables for multiple logistic regression were chosen using a multi-step process. We first used a directed acyclic graph to encode investigator beliefs about the causal relationships among variables. We then screened variables for variation and dropped those without sufficient variation. In some cases, categories were collapsed to increase the number of observations in each cell and to improve the precision of the corresponding estimates. The resulting variables were included in a multiple logistic regression model to test adjusted associations for candidate risk factors. Data were analyzed both stratified by sex and pooled. Observations with intermittently missing values (n=6) were dropped (i.e. we performed a complete case analysis). All analyses were conducted using STATA12 (StataCorp LP, College Station, Tex).

Results

Characteristics of Sample

Most participants were male (64.7%), from Mexico (93.6%), with more than a decade of work in agriculture (mean 13.6 years, standard deviation (SD) 11.6) (Table 1). Most of the sample had normal eGFR at the morning sample (92.2%) and reported no history of kidney disease (75.6%). The sample tended to be overweight (42%) or obese (39.3%), without significant differences between the sexes. Male participants had significantly more pre-hypertension or hypertension than women (48.9% versus 38.5% and 38.4% versus 23.1%, respectively). Males were also more often employed in picking than females (31.1% versus 22.9%). The majority of participants were paid hourly (71.2%), which did not differ between males and females. Three persons had elevated serum creatinine at baseline (pre-shift), with values of 1.39 mg/dl, 1.3 mg/dl, and 1.2 mg/dl. These three men were aged 31, 69, and 39 years old, respectively.

Post-Shift Data

Incident AKI occurred in 35 participants (11.8%); 13 (37.1%) females and 22 (35%) males (Table 2). Using the criterion of 1.5-1.9 times baseline, 17 participants were classified as stage 1 AKI. An additional 14 individuals met the criterion of an absolute increase of ≥ 0.3mg/dl, yielding a total of 31 persons classified as stage 1 AKI (10.5%, 95% CI 0.07-0.14). There were 4 participants who had an elevation of 2-2.9 times baseline and were classified as stage 2 AKI (1.3%, 95% confidence interval (CI) 0.01-0.03), and no one exhibited an elevation in serum creatinine that classified him/her as stage 3 AKI. Differences in the incidence of AKI between male and female participants were not statistically significant based on chi-square tests ($p=0.83$).

For the group as a whole, mean pre-shift serum creatinine was 0.72 mg/dl (standard deviation [SD] 0.18mg/dl) and increased to the mean post-shift serum creatinine of 0.82mg/dl (SD 0.21mg/dl). Mean change in creatinine over the work shift was an increase of 0.09 mg/dl (SD 0.15 mg/dl), though creatinine values did not increase in all participants. Among those without AKI, mean pre-shift creatinine was 0.73 mg/dl (SD 0.17 mg/dl) and increased to a mean post-shift creatinine of 0.79 mg/dl (SD 0.19mg/dl). Mean change in those without AKI was 0.06 mg/dl (SD 0.11 mg/dl). Among those classified as AKI, mean pre-shift creatinine was 0.65 mg/dl (SD 0.20 mg/dl) and increased to 1.01 mg/dl. Mean change in serum creatinine for those with AKI was +0.36 mg/dl (SD 0.13mg/dl).

For simplicity, final unadjusted, bivariate analyses were run on models combining males and females (Table 3). Based on trend tests or chi-square, the association between incident AKI and payment method was statistically significant ($p<0.01$), with those being paid by the piece having higher proportions of AKI (24.7%). Unadjusted odds ratios were significant for weight classification and payment method. Obese participants had lower crude odds than healthy weight participants in developing AKI (OR 0.38, 95% CI 0.25-0.95). Those paid by the piece had higher crude odds of developing AKI (OR 3.97, 95% CI 1.92-8.22) when compared to those paid hourly. In models adjusting for all of the following: sex, age group, BMI, diabetes status, blood pressure, history of kidney disease, level of education, years in agricultural work, payment method, and farm task, the association between obesity and AKI was no longer significant (adjusted odds ratio (AOR) 0.42, 95% CI 0.15-1.19). (Table 4.) However, the adjusted odds ratio (4.52, 95% CI 1.61-12.70) for payment method remained significant. No other associations were statistically significant in the final model.

Discussion

In a study of 295 agricultural workers in the Central Valley of California, we found the cumulative incidence of AKI (stage 1 or stage 2) to be 11.8%, as defined by KDIGO classification based on elevations in serum creatinine over a single work shift. We also found that being paid by the piece was associated with 4 ½ times the odds of incident AKI in our sample.

No other traditional risk factor, including age, BMI, diabetes, or hypertension were associated with incident AKI.

We are aware of only two studies that have described AKI in a sample of agricultural workers, despite the potential link between kidney disease and agricultural work suggested by studies of MeN.[50,56,74] Our estimate of AKI cumulative incidence are somewhat lower than the study of sugarcane harvesters in Brazil which detected incident AKI in 5 of 27 workers (18.5%) after a work-shift. Overall, the mean changes in serum creatinine in our sample were lower than estimates from Brazil. We found a mean change of 0.36 mg/dl in those with AKI, while Santos and colleagues found a mean change of 0.48 mg/dl. Additionally, in participants without AKI, we found a mean change of 0.06 mg/dl while Santos and colleagues found a mean change of 0.15 mg/dl. There are many reasons these estimates may differ, including sampling size and variability, assessment method, underlying population health, work and ambient conditions, and differences in hydration. On the other hand, our results of a 10% increase in mean creatinine over the shift are similar to those of Garcia-Trabanino and colleagues who also found a 10% increase in serum creatinine over a similar time period.[66] Their results differ from ours, however, in their finding of elevated serum creatinine before the work shift in 20% of their sample. We found elevated creatinine in only 1% of our sample prior to the work shift, which makes the elevations in serum creatinine over a work shift in our study more pronounced. However, comparisons between our study and the above mentioned studies are limited because those studies were performed among sugarcane cutters, and sugarcane harvesting is recognized as a particularly demanding crop with high levels of heat stress.[20,75,76] California agriculture (including fruits, olives, wine grapes, and melons) does not carry the same risks as harvesting sugarcane. Because of the limited number of studies of AKI in agricultural workers, further studies to obtain additional estimates are warranted.

While years in agricultural work were not significantly associated with incident AKI in our sample, the increased odds of AKI among those being paid by the piece is a significant finding. Those who are paid by the piece may be more reluctant to take recommended breaks to rest in the shade or drink water because stopping work cuts into time that could be spent picking and may result in lower wages.[15] Therefore, those paid by the piece may inadvertently expose themselves to greater levels of occupational hazards, including heat illness and dehydration,[19] which may prove damaging to the kidneys. Fortunately, the method of paying agricultural workers is a modifiable risk factor and could be an approach to reducing incident AKI over a work-shift.

Not everyone in our sample who met criteria for AKI had serum creatinine levels above normal limits. In fact, only 18 of the 22 males (81%) had post-shift creatinine levels greater than 1.2 mg/dl, and 2 of the 13 females (15%) had post-shift creatinine levels greater than 1.1 mg/dl. KDIGO classification uses changes in serum creatinine to estimate AKI, which does not always imply that the second measure will be above normal limits. Changes in serum creatinine in themselves can be damaging to health. In fact, one study estimates a serum creatinine rise of 0.5 mg/dl increases the odds of mortality 6.5-fold among hospitalized patients.[77] Those in our sample with decreased kidney function at baseline (eGFR<89ml/min/1.73m^2) did not develop AKI over the course of a work-shift. Our results, then, suggest that baseline kidney function is not predictive of incident AKI.

The lack of association of AKI to other traditional risk factors including age, obesity, diabetes, and hypertension strengthens the impression that the development of AKI in our sample may be related to occupational hazards rather than physiological disposition. Studies investigating the etiology of MeN have found significant associations between agricultural work and development of CKD. Our finding of the association of piece-rate work corroborates the association of kidney damage, albeit acute and transitory, to work circumstances, though further elucidation into the mechanisms of AKI in piece-rate workers is needed.

Injury to the kidneys after a single agricultural shift is disquieting, and there are several reasons that early detection of AKI is important in agricultural workers. First, after acute injury, serum creatinine often returns to normal limits, and the kidney injury may be unrecognized or remain subclinical.[60,78] This sub-clinical injury may precipitate further damage to the kidneys because elevations in serum creatinine are associated with increased risk of long-term kidney damage and mortality.[77,79] Specifically, agricultural workers who develop AKI are at risk for the development of chronic kidney disease.[6,46,49] Second, agricultural workers in California are a vulnerable population, typically lacking insurance coverage and regular health care and may not have access to the care they need should the AKI not resolve and require further medical intervention. Although a majority of agricultural workers in California are undocumented immigrants from Mexico, California is one of the states which provide hemodialysis to undocumented immigrants with end-stage renal disease. In 2009, there were more than 61,000 hemodialysis patients in California, and costs of their treatment were estimated to be $51 million. Of these patients, 1,350 were undocumented immigrants.[80]

Limitations

This study has multiple limitations that need to be recognized. First and importantly, the classification of AKI based on KDIGO ideally includes a measure of urine output over 6-24 hours in the staging of AKI. Because our data were collected in the field setting, documenting urine output was not feasible. Second, serum creatinine levels after a day of physical labor in agricultural fields must be interpreted with caution as muscle injury causes release of creatinine, and it is possible that the physical exertion of field work results in muscle injury which, in turn, results in elevated creatinine. Third, it would be ideal to follow participants over a longer period of time to detect consistent elevations of serum creatinine over a number of days of work or to assess other risk factors. However, longitudinal participation over many days or months would be difficult in this population. Fourth, the use of a convenience population may limit generalizability of the findings, but we believe this was not significant because we have no reason to suspect that participation was based on factors related to kidney health. Finally, while the current study was designed in response to recent research on MeN, our results do not provide evidence that there is a definitive link to cases of MeN. We were only able to include a limited number of variables related to occupational risks, which limits our contribution to the investigation of the etiology of MeN. MeN is an unexplained CKD, not AKI. While there is a link between the two conditions, we did not assess CKD in our study. Our results do, however, point to a previously unrecognized and under-studied health outcome of agricultural work.

Strengths of the study include use of direct clinical measurements to estimate kidney injury in a difficult to study population. Additionally, the comparison of pre- and post-work measurements allows us to estimate injury that occurs in a single day of work.

Conclusion

To our knowledge, this is the first study to examine the incidence of AKI in a population of agricultural workers in the United States. The cumulative incidence of AKI is alarming due to the recognized association between AKI and chronic kidney disease, particularly in light of the growing prevalence of MeN in Central America. The association between piece-rate work and incident AKI should be studied further, and may point to the need for modifications to methods of payment for agricultural workers to protect their health. Due to the vulnerability of this often undocumented population, early detection and prevention of AKI should be an important public health objective to prevent the potential development of chronic kidney disease and the need for hemodialysis in this population.

Table 1. Characteristic of Study Participants							
	Total Sample (n=295)		Male (n=191)		Female (n=104)		
	n	%	n	%	n	%	p-value
Age (mean, SD)	38.5	12.4	38.2	13.0	38.9	11.6	0.64
Years in Agricultural Work (mean, SD)	13.6	11.6	14.8	12.6	11.3	9.6	<0.01
Country of Origin							0.15
United States	16	5.4	13	6.8	3	2.9	
Mexico	276	93.6	175	91.6	101	97.1	
El Salvador	3	1.0	3	1.6	0	NA	
Level of Education							<0.01
No Education/Don't Know	9	3.0	8	4.2	1	0.9	
Less than High School	198	67.1	115	60.2	83	80.0	
Some High School	45	15.3	34	17.8	11	10.6	
Graduated High School	43	14.6	43	17.8	10	8.7	
Health Status							<0.01
Excellent/Good	160	54.2	116	60.7	44	42.3	
Fair/Poor	135	45.7	75	39.3	60	57.7	
BMI[1]							0.24
Normal Weight (<25 kg/m^2)	55	18.6	41	21.5	14	13.5	
Overweight (25-30 kg/m^2)	124	42.0	78	40.8	46	44.2	
Obese (>30 kg/m^2)	116	39.3	72	37.7	44	42.3	
HgbA1c[2]							0.76
HgbA1c <5.7% (No diabetes)	227	79.1	148	80.4	79	76.7	
HgbA1c 5.7-6.4% (Pre-diabetes)	40	13.9	24	13.0	16	15.5	
HgbA1c ≥6.5% (Diabetes)	20	7.0	12	6.5	8	7.8	
Blood Pressure[3]							<0.01
Normal blood pressure (<120/80)	65	21.7	24	12.6	40	38.5	
Pre-hypertensive (120-139/80-89)	135	45.0	93	48.9	40	38.5	
Hypertension (≥140/90)	99	33.0	73	38.4	24	23.1	
eGFR at morning sample[4]							0.32
≥90ml/min/1.73m^2	272	92.2	171	90.5	99	95.2	
60-89ml/min/1.73m^2	22	7.5	17	9.0	5	4.8	
<60ml/min/1.73m^2	1	0.3	1	0.5	0	NA	
History of Kidney Disease							0.51
None	223	75.6	147	77.0	76	73.1	
Personal History	14	4.7	10	5.2	4	3.8	
Family History	60	20.0	34	17.8	24	23.1	

Differences based on chi-square tests between males and females

[1] BMI=Body Mass Index (kg/m^2)

[2] HgbA1c=Hemoglobin A1c, from capillary blood sample

[3] Blood pressure based on JNC7 categories

[4] Categorized based on KDIGO guidelines

Table 2. Stages of Acute Kidney Injury Stratified by Sex

KDIGO[1] Stage	Increase SeCr[2]	Male (n=191)			Female (n=104)			Total (n=295)			
		n	%	(95% CI[3])	n	%	(95% CI[3])	n	%	(95% CI[3])	p-value[4]
											0.83
No injury	<1.5 times baseline	168	88.4	(0.84-0.93)	91	87.5	(0.81-0.94)	260	88.1	(0.84-0.92)	
Stage 1[4]	1.5-1.9 times baseline or ≥0.3mg/dl increase	20	10.5	(0.06-0.15)	11	10.6	(0.05-0.17)	31	10.5	(0.07-0.14)	
Stage 2	2.0-2.9 times baseline	2	1.1	(-0.01-0.03)	2	1.9	(-0.01-0.05)	4	1.3	(0.01-0.03)	
Stage 3	3.0 times baseline	0	NA	NA	0	NA	NA	0	NA	NA	

[1] Kidney Disease Improving Global Outcomes

[2] Serum Creatinine measured via capillary sample before and after work shift

[3] CI = confidence interval

[4] P-value based on chi-square tests of differences between males and females

[4] Stage 1 classified based on meeting at least one of the criteria

Table 3. Proportion and Crude Odds Ratio of Incident AKI among Common Risk Factors							
	Total Sample	Proportion of AKI			Odds of AKI		
	n=295	n=35			n=295		
Sample Characteristic	n	n	%	p-value[4]	OR	95% CI	p-value
Gender				0.80			
Male	191	22	35.0		reference	--	--
Female	104	13	37.1		1.10	(0.53-2.28)	0.81
Age				0.46			
18-25 years	48	9	18.8		0.50	(0.20-1.27)	0.15
26-40 years	125	13	10.4		0.38	(0.31-1.09)	0.07
41-55 years	87	7	8.0		0.90	(0.29-2.80)	0.85
>55 years	35	6	17.1		reference	--	--
BMI[1]				0.052			
Normal Weight (<25)	55	11	20.0		reference	--	--
Overweight (25-30)	124	14	11.3		0.51	(0.21-1.21)	0.125
Obese (>30)	116	10	8.6		0.38	(0.25-0.95)	0.04
Diabetes Status [2]				0.15			
No diabetes (HgbA1c <5.7%)	227	24	10.6		reference	--	--
Pre-diabetes (HgbA1c 5.7-6.4%)	40	5	12.5		1.20	(0.43-3.34)	0.73
Diabetes (HgbA1c ≥6.5%)	20	5	25.0		2.80	(0.94-8.36)	0.06
Blood Pressure[3]				0.37			
Normal blood pressure (<120/80)	65	11	17.2		reference	--	--
Pre-hypertensive (120-139/80-89)	135	13	9.8		0.53	(0.22-1.26)	0.15
Hypertension (≤140/90)	99	11	11.3		0.63	(0.25-1.55)	0.31
eGFR at morning sample[4]				0.07			
≥90ml/min/1.73m^2	272	35	12.9		reference	--	--
60-89ml/min/1.73m^2	22	0	N/A		N/A	N/A	N/A
<60ml/min/1.73m^2	1	0	N/A		N/A	N/A	N/A
History of Kidney Disease				0.55			
None	223	25	11.2		reference	--	--
Personal history	14	2	14.3		1.32	(0.28-6.24)	0.73
Family history	60	8	13.8		1.27	(0.54-2.98)	0.59
Years in Agricultural Work				0.64			
Five years or less	98	2	7.4		reference	--	--
6-10 years	51	5	10.2		0.83	(0.30-2.32)	0.73
11-20 years	82	11	12.8		1.23	(0.50-3.00)	0.65
More than 20 years	64	8	12.7		1.06	(0.45-2.53)	0.89
Country of Origin				0.75			
United States	16	2	12.5		1.05	(0.23-4.84)	0.95
Mexico	276	33	12.0		reference	--	--
El Salvador	3	0	N/A		N/A	N/A	
Level of Education				0.99			
No Education/Don't Know	9	1	11.1		0.91	(0.11-7.57)	0.93
Less than High School	198	24	11.8		reference	--	--
Some High School	45	3	12.5		0.71	(0.23-2.15)	0.54
Graduated High School	43	7	11.9		1.18	(0.45-3.08)	0.33

[1] p-value based on trend tests for ordinal variables or chi-square tests for nominal variables

[2] BMI=Body Mass Index (kg/m^2)

[3] HgbA1c=Hemoglobin A1c, from capillary blood sample

[4] Blood pressure based on JNC7 categories

[5] Categorized based on KDIGO guidelines

Table 4. Adjusted Odds of Incident AKI among Select Risk Factors			
	Odds of AKI		
	n=295		
Sample Characteristic	AOR	(95% CI)	p-value
Gender			
Male	reference	--	--
Female	0.96	(0.42-2.21)	0.93
Age (mean, SD)			
18-25 years	0.59	(0.21-1.64)	0.31
26-40 years	0.37	(0.11-1.30)	0.12
41-55 years			
>55 years	reference	--	--
BMI[1]			
Normal Weight (<25)	reference	--	--
Overweight (25-30)	0.55	(0.21-1.49)	0.24
Obese (>30)	0.42	(0.15-1.19)	0.10
Diabetes Status [2]			
No diabetes (HgbA1c <5.7%)	reference	--	--
Pre-diabetes (HgbA1c 5.7-6.4%)	1.84	(0.58-5.82)	0.30
Diabetes (HgbA1c ≥6.5%)	4.18	(1.12-15.56)	0.03
Blood Pressure[3]			
Normal blood pressure (<120/80)	reference	--	--
Pre-hypertensive (120-139/80-89)	0.56	(0.22-1.44)	0.23
Hypertension (≤140/90)	0.58	(0.19-1.77)	0.34
History of Kidney Disease			
None	reference	--	--
Personal or family history	1.42	(0.61-3.28)	0.42
Years in Agricultural Work			
Ten years or less	reference	--	--
More than 11 years	0.93	(0.41-2.08)	0.86
Level of Education			
Less than High School	0.38	(0.13-1.12)	0.59
High School or Beyond	reference	--	--

[1] p-value based on trend tests for ordinal variables or chi-square tests for nominal variables

[2] BMI=Body Mass Index (kg/m^2)

[3] HgbA1c=Hemoglobin A1c, from capillary blood sample

[4] Blood pressure based on JNC7 categories

[5] Categorized based on KDIGO guidelines

CHAPTER 3: HEAT STRAIN, VOLUME DEPLETION AND KIDNEY FUNCTION IN CALIFORNIA AGRICULTURAL WORKERS

Sally Moyce, Diane Mitchell, Tracey Armitage, Daniel Tancredi, Jill Joseph, Marc Schenker

Abstract

Background: Agricultural work can expose workers to increased risk of heat strain and volume depletion due to repeated exposures to high ambient temperatures, arduous physical exertion and limited rehydration. These risk factors may result in acute kidney injury (AKI).

Methods: We estimated incident AKI in a convenience sample of 283 agricultural workers based on elevations of serum creatinine between pre-and post-shift blood samples. Heat strain was assessed based on changes in core body temperature and heart rate. Volume depletion was assessed using changes in body mass over the work shift. Logistic regression models were used to estimate the associations of AKI with traditional risk factors (age, diabetes, hypertension and history of kidney disease) as well as with occupational risk factors (years in farm work, method of payment and farm task).

Results: Thirty-five participants were characterized with incident AKI over the course of a work-shift (12.3% 95% confidence interval [CI] 8.5% to 16.2%). Workers who experienced heat strain (PSI≥7.5) had increased adjusted odds of AKI (adjusted odds ratio [AOR] 1.34, 95% CI 1.04 - 1.74). Workers who were paid by the piece had AKI AOR of 4.24 (95% CI 1.56 - 11.52).

Discussion: Heat exposure and piece-rate work are associated with incident AKI after a single shift of agricultural work. Modifications to payment structures may help prevent AKI.

Heat Exposure, Volume Depletion and Kidney Function in California Agricultural Workers

Background

Agricultural work exposes laborers to multiple environmental and work hazards that can contribute to adverse personal health outcomes.[81] The work is most commonly seasonal, and during summer harvest, workers often spend long hours under direct sun, in intense heat, performing arduous physical labor.[1,2] In the Central Valley of California, which employs the majority of the estimated 450,000+ agricultural workers, summer temperatures regularly exceed 100 degrees Fahrenheit.[18] California farm work is often labor intensive and exposes workers to high ambient temperatures, varying levels of physical exertion and reliance on the worker to maintain sufficient hydration.[9,20] These conditions may result in high rates of heat strain and volume depletion, but this condition has rarely been studied among U.S. farmworkers. Agricultural workers often report symptoms of heat-related illness,[15,18] and in the U.S. they are estimated to be four times more likely to have a heat-related illness than workers in other industries.[14]

Of particular concern is the effect these working conditions may have on kidney function, particularly acute kidney injury (AKI). AKI is defined as a reduction in kidney function, often as a result of decreased renal blood flow.[49] During periods of increased work load, renal perfusion progressively declines,[29] and when coupled with high ambient temperatures and volume depletion, it may be reduced by over 50%.[26] We are aware of tow other studies in which AKI in agricultural workers has been examined. In an exploratory study, Santos and colleagues estimated the incidence of AKI in agricultural workers in Brazil to be 18% after a single day of work, and to be associated with measures of volume depletion.[65] Garcia-Trabanino and colleagues surveyed sugarcane workers in Nicaragua and found elevated serum creatinine levels in 25% of their sample, which was also significantly associated with high ambient temperature and volume depletion.[66] In previous work, we estimated the cumulative incidence of AKI among agricultural workers in California to be nearly 12% after a single day of work.[82]

To our knowledge, no investigations have examined the association of heat strain and volume depletion with kidney function in agricultural workers in the United States, despite the occupational risks of physical labor in high ambient temperatures. We conducted a study to examine these associations in a sample of California agricultural workers.

Methods

Participants

A convenience sample of 300 field workers was recruited from 15 farms in agricultural regions of California's during the summer of 2014. Bilingual, bicultural field staff explained the purpose and protocol of the study in Spanish and obtained consent. Eligible participants were 18 years of age or older, worked in the fields for at least six hours per day, understood Spanish and were neither pregnant nor had any impediment to swallowing the ingestible sensor (such as current gastrointestinal illness or pacemaker). Participants were enrolled for the study for a single day of data collection and were given a small monetary gift of appreciation.

Data Collection

Pre-Shift Measures

A brief, pre-shift questionnaire was administered orally in Spanish to assess participant eligibility and to collect demographic information. A capillary blood sample was taken and analyzed using the handheld i-STAT point of care test to measure serum creatinine (Abbot Point of Care, Inc., Princeton, NJ). The i-STAT measurements are traceable to isotope dilution mass spectrometry through the standard reference material SRM967.[68] Weight was measured in a base layer of clothing using a Seca 874 medical scale, and height was measured without shoes using a Seca model 213 stadiometer (Seca GMBH, Hamburg, Germany). Participants swallowed a CorTemp HT15002 ingestible wireless temperature transmitter probe (HQInc, Palmetto, Florida, USA). The probe transmitted core temperature at 1-minute intervals.[83] Participants were fitted with a Polar T31 ECG heart rate transmitter around the thorax which transmitted heart rate measurements at 1-minute intervals. Signals from both the probe and the heart rate strap were recorded using a CorTemp HT150016 Data Recorder attached to their belts. All staff involved in data collection were trained and supervised, and all equipment was regularly calibrated to ensure accuracy.

Post-Shift Measures

Following the work shift, approximately 7 to 12 hours after ingestion of the CorTemp, a post-shift questionnaire was orally administered in Spanish to obtain information on health history and possible social and behavioral risk factors, such as a personal or family history of kidney disease, work history, and general health rating. A second capillary blood sample was obtained to document serum creatinine, and hemoglobin A1c (Hgb A1c) was measured using a Siemens DCA Vantage Analyzer (Siemens Healthcare Diagnostics Inc., Tarrytown, NY). Workers were reweighed in the base layer of clothing, and a single blood pressure was obtained in the seated position using an automated blood pressure cuff (Omron blood pressure monitor, Lake Forest, IL).

Participants' BMI, blood pressure, diabetes risk status and blood creatinine level were shared with them at the conclusion of the day, and participants who had abnormal results were referred to local health clinics for follow-up care.

All study procedures were approved by the University of California, Davis Institutional Review Board.

Outcome: Acute Kidney Injury

AKI during the work shift, defined by a specified increase in serum creatinine from the pre-shift to the post-shift measure, was the primary outcome of interest. Using the recommended definition and stages of injury from the Kidney Disease: Improving Global Outcomes group (KDIGO),[49] AKI was defined as an increase of the post-shift serum creatinine by ≥ 0.3mg/dl or ≥ 1.5 times the pre-shift creatinine. AKI staging was based on the following: stage 1 (≥ 0.3mg/dl or 1.5-1.9 times pre-shift serum creatinine); stage 2 (2.0-2.9 times pre-shift serum creatinine); and stage 3 (≥3.0 times pre-shift serum creatinine).

Exposure: Heat Exposure and Volume Depletion

Exposure variables explored were heat strain from a combination of work and environmental exposure and volume depletion. Acute heat strain was estimated by calculating the physiological strain index (PSI),[84] based on readings collected throughout the work shift. Minute-by-minute readings of core body temperature and heart rate were pre-processed to remove physiologically impossible changes and then smoothed using loess estimation procedures in SAS. A validated and reliable estimation of heat strain, PSI indicates the level of physiological strain on a scale from 0-10. The formula uses a combination of heart rate and core temperature (in ^{0}C) to estimate the effect of temperature and workload, as specified in the following equation:

PSI = 5*(peak core temp – base core temp) / (39.5- base core temp) + 5*(peak hr – base hr) / ([220-age] – base hr),[84] with input value derived from the preprocessed, smoothed heart rate and temperature minute-by-minute traces.

Volume depletion was assessed via percent change in body mass by comparing pre- and post-shift body weights and dividing by the pre-shift body weight (([post-shift – pre-shift] / pre-shift) x 100%). In field conditions, body mass change is considered the most accurate method for estimating hydration status,[85,86] and one kilogram of body weight represents one liter of body fluid.[87] Recommendations of the National Institute of Occupational Safety and Health (NIOSH) to prevent heat-related illness among agricultural workers state that workers should not lose more than 1.5% body mass over the course of a work shift.[88]

Covariates

Variables thought to be associated with AKI were selected *a priori* based on a review of the literature and feasibility of collecting data in the field. Demographic variables included sex (male v. female), age (continuous), and level of education (none/don't know, less than high school, some high school, or graduated high school). Clinical data were also obtained. Estimated glomerular filtration rate (eGFR) was calculated using pre-shift serum creatinine based on the CKD-EPI equation[72] and categorized as ≥90ml/min/1.73^2, 60-89 ml/min/1.73^2, or <60 ml/min/1.73^2. Body mass index (BMI) was calculated from pre-shift height and weight measurements (BMI=weight in kg/height in meters squared), and classified based on WHO recommendations[69] as normal weight (BMI<25), overweight (BMI 25.0 - 29.9), or obese (BMI≥30). Diabetes status was defined by standard categories of hemoglobin A1c (Hgb A1c):[89] no diabetes (Hgb A1c<5.7% and no self-reported anti-diabetic medications), pre-diabetes (Hgb

A1c 5.7-6.4%), or diabetes (Hbg A1c ≥6.5% or self-reported diabetes diagnosis or self-reported anti-diabetic medications). Seated blood pressure was measured by a single reading taken on the left arm and categorized as recommended by the Joint Commission:[71] normal blood pressure (<120/80 and no self-reported anti-hypertensives), pre-hypertension (120-139/80-89), or hypertension (≥140/90 or taking anti-hypertensives). Self-reported information on personal or family history of kidney disease (yes v. no) was collected. Variables related to occupation included years in agricultural work (continuous), how the worker was paid (hourly, by the piece [or amount of produce harvested], or salary), and the farm task they engaged in most during that day (picking, hoeing, irrigation, packing/sorting/planting, hand pruning/weeding, or other (e.g. vehicle maintenance or supervising)).

Statistical Analysis

Descriptive statistics were calculated for the outcome and potential risk factors. We determined AKI classification using the three stages of AKI. We then estimated the association of categories of percent change in body mass (no change, gained any weight, lost <1.5%, lost ≥1.5%) and PSI (<7.5 versus ≥7.5) with AKI categories. In regression models, we dichotomized AKI as "any" versus "none". Logistic regression models assessed the associations between AKI and predictor variables. To aid in interpretation of the main effects in models which included interaction terms, we centered the PSI at a selected reference point (PSI=4) and subtracted 4 from each value of PSI. Model 1 estimated the adjusted association of AKI (dependent variable) body mass change and PSI while controlling for traditional risk factors (sex, age, BMI, diabetes, hypertension, history of kidney disease). Model 2 estimated the same associations while adding occupational risk factors (years in farm work, payment method, and farm task). To test for effect modification of heat strain on volume depletion, Model 3 added the interaction term of body mass change*heat strain (PSI). Similarly, Model 4 added the interaction term of body mass change*piece-rate work to test for effect modification of piece-rate work on volume depletion. Model 5 added the interaction term of heat strain (PSI)*obesity to test effect modification of obesity on heat strain. The Akaike and Bayes information criteria are model goodness of fit measures that incorporate a complexity penalty in favor of parsimonious models, with smaller values indicating better model fit. We report these measures for all models and used them to select the final model, with preference going to Akaike in case of conflicting results.

Investigator beliefs about possible causal linkages were encoded using directed acyclic graphs, to develop a parsimonious set of candidate covariates. Covariates were also screened for variation. Those without sufficient variation were dropped. For some categorical variables, levels were combined to increase the precision of estimates involving these factors. Subjects with missing values for critical variables (n=17) were dropped (i.e. we performed a complete case analysis). A total of 300 participants were enrolled in the study. Five participants were missing either pre-shift or post-shift creatinine measures, and an additional 12 were missing variables required for PSI calculation, and the final analyses therefore included 283 participants (94% of enrollees).

All analyses were conducted using STATA12 (Stata Corp LP, College Station, Tex).

Results

The majority of our sample was male (64.3%) from Mexico (93.6%), and had less than a high school education (66.1%). The mean age was 38.6 years (standard deviation 12.4). Most participants were overweight (42%) or obese (39.6%) and were pre-hypertensive (45.7%) or hypertensive (31.9%). Most had normal eGFR (92.2%), were not diabetic or prediabetic (78.2%), and had no personal or family history of kidney disease (75.3%). Mean years in agricultural work was 13.5 (standard deviation 11.6), and most participants were paid by the hour (70.3%). Farm tasks varied among participants; almost a third were engaged in picking (hand harvesting) (29%). (Table 1b)

Using changes in serum creatinine from pre-shift measures to post-shift measures, 31 participants (11.0%) met KDIGO criteria for stage 1 AKI (Table 2b). An additional four participants (1.3%) met criteria for stage 2 AKI. The majority of participants (273/283; 96.5%) did not experience heat strain, as estimated by PSI <7.5. There were no statistically significant unadjusted associations of AKI with either the PSI or the change in body mass classification variables when compared with chi-squared tests (Table 2b). Three persons who had PSI ≥7.5 had stage 1 AKI (30%). No one who had PSI ≥7.5 met criteria for stage 2 AKI. The majority of the sample lost body mass during the work shift: 196 (59.7%) lost <1.5% and 25 (8.8%) lost ≥1.5%. Almost a third of the sample gained weight over the shift (27.9%), and 9 of those developed AKI (11.4%). Of those who lost <1.5% body mass, 16 developed stage 1 AKI (9.5%) and 2 developed stage 2 AKI (1.1%). Of those who lost ≥1.5%, seven developed stage 1 AKI (28%). None developed stage 2 AKI.

In Model 1 (Table 3b), which controlled for demographic and physiological characteristics, heat strain was associated with a statistically significant adjusted odds ratio (AOR) of 1.30 for AKI (95% confidence interval [CI] 1.03-1.65). Obese participants had decreased adjusted odds of AKI (AOR 0.29, 95% CI 0.10-0.82). No other associations were statistically significant.

Model 2 added occupational risk factors. The association of heat strain and AKI remained significant, and the adjusted odds ratio did not appreciably change (AOR 1.34, 95% CO 1.04-1.74). The association of obesity and AKI remained statistically significant (AOR 0.32, 95% CI 0.11-0.96) Participants who were paid by the piece had increased adjusted odds of AKI when compared to those paid by the hour or salary (AOR 4.24, 95% CI 1.56-11.52). Neither years in farm work nor farm task were significantly associated with AKI in these models.

In Model 3, we added the interaction term of volume depletion*heat strain to assess whether either term modified the effects of the other. The interaction term was not statistically associated with AKI, nor did the model-fit statistics improve with the addition of the interaction term. The interaction term attenuated the main effect of heat strain on AKI and the main effect of obesity on AKI. The association of piece-rate work remained statistically significant (AOR 4.46, 95% CI 1.64-12.15).

Model 4 added the interaction term of heat strain*piece-rate work, which was not significantly associated with AKI. The association of obesity to AKI returned to significance (AOR 0.31, 95% CI 0.10-0.94). The adjusted odds of piece-rate work decreased slightly to 3.72 (95% CI 1.28-10.81).

The final model, Model 5, added the interaction term of heat strain*obesity, which was not significantly associated with AKI. The addition of the interaction term did not change the other estimates appreciably, results not shown.

Model fit statistics favored Model 2, which we used as our final model in interpretation. In sensitivity analysis, we found that volume depletion, as estimated by percent loss of body mass over the work shift, occurred more often in workers paid by the piece (OR 1.67, 95% CI

1.09-2.54) results not shown. Heat strain, however, was not statistically different for workers who were paid by the piece. Additionally, obese participants were less often paid by the piece (OR 0.45, 95% CI 0.25-0.80), though there was no statistically significant difference in the PSI or percent change in body mass among obese participants.

Discussion

Incident AKI occurred in 35 participants (12.3%) in our sample of 283 agricultural workers in the summer of 2014. High levels of heat strain, as determined by the PSI, were independently associated with increased odds of incident AKI. Additionally, participants who were paid by the piece had more than four times the odds of incident AKI than those paid by the hour or by a salary. These findings together suggest that incident AKI is an occupational risk factor of heat strain over a work shift, and that those who are paid by the piece are at particular risk.

Given the high ambient temperatures in the Central Valley and the strenuous nature of agricultural work, our estimates of heat strain through the PSI were surprisingly lower than we expected, Other researchers have found agricultural work to be associated with high levels of heat strain both in the United States and in other countries.[2,9,15,75,90–93] The Central Valley has low levels of humidity, which may allow workers to maintain cooler body temperatures than in other agricultural areas with high humidity. In addition, California is progressive in its prevention of heat related illness through regulations of the state Occupational Safety and Health Administration (Cal-OSHA). Under Cal-OSHA requirements, farmers are required to provide heat illness prevention training for workers and offer regular breaks to cool off and rehydrate (Cal-OSHA Heat Illness Regulation 3395). Despite research that suggests workers do not remember the information provided in the trainings and do not take recommended breaks,[18,19] our estimates of PSI indicate that workers in our sample do not experience high levels of heat strain. However, the finding that heat strain was statistically associated with incident AKI suggests that agricultural workers who do experience high levels of heat strain continue to be at risk of adverse renal effects. Heat exposure has been linked to AKI in other studies of otherwise healthy individuals such as althletes[31,35] and military recruits.[33] Additionally, in other studies of agricultural workers, heat strain has been associated with increased risk of renal insufficiency,[52,54] and heat strain has been named as one of the potential risk factors for the development of Mesoamerican Endemic Nephropathy, a chronic kidney disease identified among agricultural workers in Central America.[94–96]

Our finding that workers paid by the piece had higher odds of AKI requires further investigation. Piece-rate work incentivizes the worker to work harder and to take fewer breaks by financially rewarding higher productivity.[97] Piece-rate work is associated with poor health outcomes, including higher rates of accidents,[98] musculoskeletal injury,[99–101] and risk-taking among workers.[102] Agricultural workers drink water during breaks at work and rest in the shade.[19] Piece-rate workers likely take fewer breaks to maximize earning potential, therefore potentially experiencing higher levels of heat strain and less likelihood of maintaining hydration during the day. We found an association between piece-rate work and hydration status, though no association between piece-rate work and heat strain. The independent association of piece-rate work on AKI in our models suggests that piece-rate work is a marker of conditions potentially damaging to kidney function, and that this mechanism is separate from heat strain or hydration status. Alternatively, piece rate work may be a better measure of the factors suspected to be involved in the development of AKI, which could explain the associations found here. In either case, modifications to the pay structure may help prevent AKI in agricultural workers.

The majority of workers in our sample experienced volume depletion after an agricultural work shift as measured by change in body mass. Other estimates of fluid intake among agricultural workers suggest that the amount of water workers drink is not sufficient to replace fluids and electrolytes lost during the work shift,[9] as many do not believe they are at risk for injury and do not adequately rehydrate.[20] In addition, agricultural workers often distrust water supplied by employers, and do not bring enough of their own water to adequately hydrate during the day.[19] However, the lack of association of volume depletion to AKI was surprising, given the above findings. Volume depletion has been posited as a mechanism for AKI and potentially further damage.[40,60,103] Recent research suggests that chronic volume depletion leads to sustained release of vasopressin and increased uric acid levels, which may precipitate long-term damage to the kidneys.[104,105] Our findings suggest that heat strain, not volume depletion, is a more dangerous risk factor in this population.

Surprisingly, we found a dose-response inverse relationship of weight classification and AKI, wherein those classified as obese had lower odds of developing AKI than those classified as normal weight. Obesity is generally accepted as a risk factor for the development of AKI,[106] however, one study found that increased BMI is associated with decreased mortality from AKI in elderly surgical patients.[107] The inverse relationship of obesity to AKI in our results is puzzling. If AKI is a result of agricultural work, it is conceivable that obese participants modified or reduced their work load, thus reducing their risk of AKI.

Limitations

Limitations of our study include our sampling method of recruiting participants at their work sites. Farms that were willing to allow a team of researchers to measure hydration and heat strain may be more likely to protect their workers, for example stopping work earlier in the day under conditions of extreme heat, and adhering to state regulations for high heat protection. Recruitment of agricultural workers in California is difficult, due to their mobile lifestyle and concerns regarding documentation status. A second limitation is the calculation of the PSI variable. Due to limitations of our equipment, some of the measurements of heart rate and core body temperature were missing, which may have affected our estimates of PSI and heat strain. We were able to account for this by working with a team of exercise physiologists, clinicians, and statisticians to provide robust and accurate estimations. Finally, estimates of AKI based on KDIGO guidelines use a 24-hour measure of urine output, which is not feasible in the field setting. Additionally, elevations in serum creatinine in our sample are potentially related to muscle injury (rhabdomyolysis), which we were unable to assess in our study. Despite these limitations, we were able to estimate the incidence of AKI over the course of a work shift and test associations between traditional and occupational risk factors.

Agricultural workers are a vulnerable population, often undocumented, living in poverty, culturally and linguistically isolated, with reduced worker protections.[100,108] The development of AKI over the course of a work-shift in this population may lead to further kidney damage, including chronic kidney disease, particularly because it is unlikely that workers know they are damaging their kidneys while working in the fields. While occupational regulations are in place to protect workers from heat-related illness, we have shown that workers who experience high levels of heat strain and who are paid by the piece are at increased risk. Fortunately, these risk factors are both modifiable, and incident AKI associated with heat strain and piece-rate work may be prevented.

Table 1b. Sample Characteristics (n=283)		
	n	%
Sex		
Male	182	64.3
Female	101	35.7
Age (mean, standard deviation)	38.6	12.4
Country of Origin		
United States	15	5.3
Mexico	265	93.6
El Salvador	3	1.1
Level of Education		
No Education/Don't Know	9	3.2
Less than High School	187	66.1
Some High School	44	15.5
Graduated High School	43	15.2
Baseline eGFR[a]		
≥90 ml/min/1.73^2	261	92.2
60-90 ml/min/1.73^2	21	7.4
<60 ml/min/1.73^2	1	0.4
BMI[b]		
Normal Weight (<25)	52	18.4
Overweight (25-30)	119	42.0
Obese (>30)	112	39.6
Diabetes[c]		
No diabetes (HgbA1c <5.7%)	215	78.2
Pre-diabetes (HgbA1c 5.7-6.4%)	33	12.0
Diabetes (HgbA1c ≥6.5%)	27	9.8
Blood Pressure[d]		
Normal blood pressure (<120/80)	63	22.3
Pre-hypertensive (120-139/80-89)	129	45.7
Hypertension (≤140/90)	90	31.9
History of Kidney Disease		
None	213	75.3
Personal History	14	4.9
Family History	56	19.8
Years in Agricultural Work (mean, standard deviation)	13.5	11.6
Payment Method		
Hourly	199	70.3
Piece-rate	76	26.9
Salary	8	2.8
Farm Task		
Picking	82	29.0
Hoeing	28	9.9
Irrigation	30	10.6
Packing/Sorting/Planting	34	12.0
Hand Pruning/Weeding	55	19.4
Other[e]	54	19.1

[a] eGFR=estimated glomerular filtration rate, based on CKD-EPI equation

[b] BMI=Body Mass Index (kg/m^2)

[c] HgbA1c=Hemoglobin A1c, from capillary blood sample

[d] Blood pressure based on JNC7 categories

[e] "Other" includes supervising staff, machinery repair, shoveling dirt, or fumigating.

Table 2b. Heat Strain[a] and Volume Depletion[b] by Acute Kidney Injury Categories

	KDIGO[c] Stage			p-value[d]			p-value[d]	Total Sample
	No Injury	**Stage 1[e]**	**Stage 2**		**No AKI[f]**	**AKI**		
n (%)	262 (92.6)	31 (11.0)	4 (1.3)		248 (87.6)	35 (12.4)		
Heat Strain				0.14			0.09	
PSI<7.5	241 (88.3)	28 (10.3)	4 (1.5)		241 (88.3)	32 (11.7)		273 (96.5)
PSI≥7.5	7 (70)	3 (30)	0		7 (70)	3 (30)		10 (3.5)
Volume Depletion				0.16			0.1	
No body mass change	9 (90)	1 (10)	0		9 (90)	1 (10)		10 (3.5)
Gained any body mass	70 (88.6)	7 (8.9)	2 (2.5)		70 (88.6)	9 (11.4)		79 (27.9)
Lost <1.5% body mass	151 (89.3)	16 (9.5)	2 (1.1)		151 (89.3)	18 (10.7)		169 (59.7)
Lost ≥1.5% body mass	18 (72)	7 (28)	0		18 (72)	7 (28)		25 (8.8)

[a] Heat strain estimated by physiologic strain index

[b] Volume depletion estimated by percent change in body mass (post-shift weight - pre-shift weight) x 100%/Pre-shift weight

[c] Kidney Disease Improving Global Outcomes

[d] p-value based on chi2 tests

[e] Stage 1 classified based on meeting at least one of the criteria

[f] AKI as dichotomous variable (stage 1 or 2 versus no injury)

Table 3b. Association of Risk Factors with Acute Kidney Injury based on Logistic Regression[a] (n=283)

	Model 1				Model 2				Model 3				Model 4			
	AOR	[95% CI]	p-value		AOR	[95% CI]	p-value		AOR	[95% CI]	p-value		AOR	[95% CI]	p-value	
Loss of Body Mass	0.66	0.41 - 1.06	0.09		0.70	0.42 - 1.17	0.18		0.86	0.48 - 1.53	0.60		0.70	0.42 - 1.16	0.17	
Heat Strain (PSI[b])	1.30	1.03 - 1.65	0.03	*	1.34	1.04 - 1.74	0.02	*	1.16	0.82 - 1.63	0.41		1.25	0.90 - 1.74	0.19	
Loss of Body Mass x Heat Strain									0.81	0.59 - 1.12	0.20					
Heat Strain x Piece-rate Work													1.19	0.72 - 1.98	0.50	
Heat Strain x Obesity																
Gender																
Male (reference)	--	--	--		--	--	--		--	--	--		--	--	--	
Female	1.44	0.60 - 3.44	0.41		2.12	0.80 - 5.63	0.13		2.11	0.80 - 5.59	0.13		2.17	0.81 - 5.80	0.12	
Age	0.99	0.95 - 1.02	0.42		0.98	0.94 - 1.02	0.34		0.98	0.94 - 1.03	0.38		0.98	0.94 - 1.02	0.33	
BMI[c]																
Normal Weight (<25) (reference)	--	--	--		--	--	--		--	--	--		--	--	--	
Overweight (25-30)	0.39	0.15 - 1.00	0.05		0.41	0.15 - 1.09	0.07		0.42	0.16 - 1.11	0.08		0.40	0.15 - 1.07	0.07	
Obese (>30)	0.29	0.10 - 0.82	0.02	*	0.32	0.11 - 0.96	0.04	*	0.33	0.11 - 1.00	0.05		0.31	0.10 - 0.94	0.04	*
Diabetes[d]																
A1c <5.7% (reference)	--	--	--		--	--	--		--	--	--		--	--	--	
A1c≥5.7%	2.45	0.93 - 6.46	0.07		2.63	0.93 - 7.41	0.07		2.45	0.86 - 7.01	0.10		2.65	0.94 - 7.45	0.07	
Blood Pressure[e]																
Normal blood pressure (<120/80) (reference)	--	--	--		--	--	--		--	--	--		--	--	--	
Pre-hypertensive (120-139/80-89)	0.64	0.24 - 1.70	0.37		0.73	0.26 - 2.06	0.56		0.73	0.26 - 2.03	0.55		0.74	0.26 - 2.07	0.56	
Hypertension (≤140/90)	0.74	0.24 - 2.23	0.59		0.94	0.29 - 2.99	0.91		0.86	0.27 - 2.78	0.80		0.93	0.29 - 2.99	0.90	
History of Kidney Disease																
None (reference)																
Personal or Family History	1.35	0.58 - 3.13	0.49		1.64	0.68 - 3.98	0.27		1.66	0.68 - 4.03	0.26		1.68	0.69 - 4.07	0.25	
Years in Agricultural Work					1.03	0.98 - 1.08	0.21		1.03	0.98 - 1.08	0.20		1.03	0.99 - 1.08	0.19	
Payment Method																
Hourly/Salary (reference)					--	--	--		--	--	--		--	--	--	
Piece-rate					4.24	1.56 - 11.52	0.01	*	4.46	1.64 - 12.15	<0.01	*	3.72	1.28 - 10.81	0.02	*
Farm Task																
Picking					1.10	0.41 - 2.92	0.86		1.10	0.41 - 2.94	0.85		1.13	0.42 - 3.04	0.81	
Other (reference)[f]					--	--	--		--	--	--		--	--	--	
Model Fit Statistics																
AIC		214.97				207.84				208.22				209.38		
BIC		255.07				258.88				262.90				264.06		

[a] Acute kidney injury based on KDIGO classification of elevations in serum creatinine

[b] Heat strain estimated by physiologic strain index (PSI); Centered at PSI-4

[c] BMI=Body Mass Index (kg/m^2) categorized based on WHO recommendations

[d] HgbA1c=Hemoglobin A1c, from capillary blood sample

[e] Blood pressure based on JNC7 categories

[f] Other includes all other farm tasks except picking

* significant at α<0.05

CHAPTER 4: CONCLUSION

In a cohort study of 300 agricultural workers in the Central Valley of California, we found incident acute kidney injury (AKI) in nearly 12% of the sample after a single day of work. We also determined that AKI incidence is related both to heat exposure and piece-rate work. To our knowledge, we are the first to examine incidence of AKI over the work shift in the United States, and our findings point to a previously undetected health risk of agricultural work.

Discussion

Prior research of AKI in agricultural workers has been limited, and only two studies to date have examined the incidence of decreased renal function over the course of a work shift. Santos and colleagues studied sugarcane workers in Brazil and found AKI, based on elevations in serum creatinine, in five of the 28 workers sampled (18.5%).[65] The second study of sugarcane harvesters conducted by Garcia-Trabanino and colleagues in El Salvador, found decreased estimated glomerular filtration rate (eGFR) in 23 of the 189 workers sampled (14%).[109] Our estimates of AKI are lower than both of these previous studies, which may reflect some of the differences in crops harvested, humidity, and occupational regulations. Agricultural workers in California are largely an immigrant population,[81] and their relative health may be reflected in the healthy worker effect, which supposes that only workers who are healthy enough to work are part of the sample.[110]

The finding that AKI is associated with heat strain is echoed in other research. Hospital admissions for AKI increase during times of heat waves,[3,44] and studies of exercise-induced AKI show decreased renal perfusion during periods of intense work combined with heat strain and dehydration.[26,111] Additionally, research into the etiology of an unexplained chronic kidney disease in Central America, termed Mesoamerican Endemic Nephropathy (MeN), suggests that kidney damage in agricultural workers is related to occupational risk factors such as heat exposure and volume depletion.[53,56,96] Our findings add to this work by demonstrating an association of heat strain to AKI. Using the physiologic strain index (PSI), ours is the first study among agricultural workers to use a biophysical measure of heat strain that accounts for both core body temperature and workload. Previous research in this population used proxies for heat exposure such as wet-bulb globe temperature[66,76] or elevation.[52,54,112] The empirical data presented herein further support the hypothesis that heat strain is associated with AKI.

Our results do not support the etiological hypothesis that kidney injury in agricultural workers is related to volume depletion over the course of a work shift. In the study of sugarcane harvesters in Brazil, Santos and colleagues reported AKI was associated with volume depletion, estimated by urinary sodium and serum hematocrit measurements.[65] Additionally, Garcia-Trabanino and colleagues concluded that the decreased renal function in their sample in El Salvador was related to volume depletion, estimated via self-reported fluid intake, as a result of strenuous work in hot and humid conditions.[66] It is difficult to directly compare our findings with those noted above because of the different measurements used to estimate hydration status. Urinary measures of hydration are not always reliable, particularly due to the role of the kidneys in concentrating the urine.[27] Further, self-reported hydration estimates are subject to recall bias. We used percent change in body mass to estimate hydration status and found that volume depletion was not associated with AKI in our sample. These seemingly contradictory findings are in line with other studies of kidney function in agricultural workers conducted in Nicaragua. Research teams found that decreased renal function was associated with self-reported *increased* fluid intake during a work shift.[113,114] The association of volume depletion and AKI must be further studied to investigate the current hypothesis.

A significant and novel finding of our studies is that AKI in agricultural workers is related to piece-rate work. Compensation based on the amount of produce harvested (piece-rate work) can be a contentious issue in the agricultural industry. On the one hand, piece-rate work can be beneficial to both worker and grower. Growers favor paying workers by the piece because it increases worker productivity. Workers enjoy the increased earnings and increased control they have over the pace of their work.[115] Workers who are efficient and highly skilled at their jobs are rewarded for their productivity and enjoy greater earning potential.[97] Moreover, some workers report preference for piece-rate work because of the feeling of control it gives them.[115]

However, it is generally accepted that piece-rate work leads to greater physical strain on the worker,[97] and it has been associated with increased risk of injury.[116] In a study of agricultural workers in Washington state, researchers found that piece-rate work was associated with increased odds of heat related illness.[117] The nature of piece-rate work may be in direct conflict with occupational regulations that require workers to take breaks, putting workers in a position to choose between earning potential and recommended breaks.[16] For a working population earning approximately $20,000 annually, recommended breaks may be interpreted by those paid by the piece as too costly to their bottom line.[18] In our study, piece-rate work was associated with markedly increased odds of incident AKI, adding to the evidence of the health risks of this payment method.

Implications

The implications of our findings are clear. Acute damage to the kidneys after a single day of agricultural work adds to the list of potential hazards inherent in the occupation. Regulations to the agricultural industry from Cal/OSHA provide workers with guidelines for protecting themselves from heat strain and potential death. Incident AKI provides another rationale for improved efforts aimed at enforcing existing regulations. These findings indicate a need for more stringent Cal/OSHA regulations and better regulatory oversight. Targeted dissemination of these results should be aimed at policy makers, farmers, labor contractors, and workers.

These results will inform future research efforts to determine the scope of incident AKI after a day of agricultural work. Prior to this work, incident AKI was unexplored in agricultural workers in the United States. Our findings suggest that the true incidence is not fully recognized and likely occurs in other agricultural workers in other parts of the United States. Future studies aimed at estimating the incidence of AKI in other locations will help define the magnitude of the problem.

Finally, research into potential interventions aimed at reducing heat strain in this population may help mitigate this environmental risk factor. Despite regulations at the state and national level, workers continue to experience heat strain during a work shift, putting their health in jeopardy. Modifications to pay structure, agricultural practices, and worker education need to be developed and tested to protect the health of workers.

Implications for Nursing Science and Healthcare Leadership

Advocating for a vulnerable population, such as agricultural workers in California, is not only the mission of the Betty Irene Moore School of Nursing, but is also essential to a nurse's scope of practice. Understanding risks inherent in agricultural work, therefore, is important to protect the health of workers, many of whom have limited access to health services or opportunities to advocate for themselves. Nurses working in federally qualified health centers are in the unique position to serve agricultural workers who may present to clinics with signs of dehydration or heat strain. Patient education aimed at protecting workers' kidneys may help prevent the progression of AKI to chronic kidney disease.

Results from this study provide additional information about the environmental impact of working in extreme temperatures and the risks inherent in piece-rate payment structures. Nurse advocates working at the policy level or in occupational health have the responsibility to lobby for changes to current agricultural practices that protect the health of the workers. The incidence of AKI after a single agricultural work shift is a public health issue that must be addressed to ensure the health of the workers who harvest the food we eat.

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