Association between heat exposure and urolithiasis in workers

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Abstract. Heat exposure can trigger stone formation in persons more susceptible to urolithiasis, due to concentrated urine causing crystal precipitation. The risk also is increased in people who are significantly exposed to heat in their jobs or who have a sedentary lifestyle. We determined the relationship between heat exposure and urolithiasis in workers. A search of PubMed and Google Scholar databases ultimately yielded only one study describing the most relevant appropriate approach to answer the PICO clinical question. The cross-sectional study measured the rate of heat conducted qualitatively. Although there was no follow-up, the data were complete and the study long enough. The odds ratio was 9.97, indicating that workers exposed to high temperatures have an up to nine times greater risk of urolithiasis (95% confidence level [CI], 7.38–13.47, P < 0.0001). The number needed to harm was 14 (i.e., for every 14 workers exposed to heat, one will suffer urolithiasis). Heat exposure in the workplace increased urolithiasis risk in workers. Our review still lacked evidence to answer the clinical question because only one study was considered relevant. A cross-sectional design does not best prove a causal relationship. For etiology, the best design is a cohort study.

1. Introduction
Kidney stone disease is a significant health problem in Indonesia and worldwide, with a prevalence estimated at 13% in men and 7% in women. The prevalence of kidney stones in the United States varies depending on race, sex, and geographic location. In one study, four of five patients were male, whereas peak age was the third to fourth decade [1].

Urinary tract stones can be caused by many factors, one of which is hot temperatures. Urinary tract stones usually arise from concentrated urine leading to precipitation of crystals. In summer, there is increased exposure to sunlight, which contains vitamin D. Vitamin D helps increase the absorption of calcium, so that it can trigger the occurrence of stones. In equatorial areas, the incidence is higher because of increased sweating and high calcium absorption rates. Urinary tract stones can result from calcium concentration, infection, or gout.

Men have a 3–4 times greater risk than women [2]. Generally men have a longer urinary tract, and their urine contains a greater concentration of calcium and oxalate (accumulation can cause stones) and lower citrate concentration (citrate is known to prevent stones). Because of the different hormones between men and women, the composition of the stones formed is different: more calcium stones are formed in men, whereas women have more infection stones. Other risk factors for stone formation are related to work: people who work in the field or are exposed to heat (cooks, laundry, or machine part workers) and those who have a sedentary lifestyle are at increased risk for urinary tract stone formation [3–5].
2. Methods

2.1. Database search
PubMed and Google Scholar databases were obtained for scientific evidence on September 25, 2013, using keywords (urate OR stone* OR nephrolithiasis) AND (occupation* OR outdoor work) AND (heat OR hot) for PubMed and urate and stone, nephrolithiasis, occupation, outdoor work, heat, and hot for Google Scholar, and retrieved 18 and 37 articles, respectively. Inclusion criteria were human species, workers, exposure to hot temperatures, urinary stones, and English text. Exclusion criteria were general discussion, not workers, not exposed to heat, and not urinary stones. After screening according to inclusion and exclusion criteria, six cohort, cross-sectional, and case–control studies were obtained. However, only the study of Atan et al. [6] described the most relevant and appropriate PICO approach and answered the clinical questions.

A research article review using criteria from The Oxford Centre for Evidence-based Medicine, including assessment of validity, importance, and applicability, is shown in Table 1.

2.2. Study design
The selected study designs were cohort, cross-sectional, and case–control studies in workers exposed to a temperature/heat environment. The study outcome was the formation of urinary tract stones. The study protocol was approved by Health Research Ethics Committee, Faculty of Medicine Universitas Indonesia-Cipto Mangunkusumo Hospital.

2.3. Case illustration
A 30-year-old man presented with a 2 month history of left hip pain that disappeared and did not spread. History was positive for hematuria and passing urinary stones and negative for nausea, vomiting, and fever. The patient had undergone extracorporeal shock wave lithotripsy for left kidney stones 3 years previously, with passage of the stones.

The patient worked daily in steel production for 10 years and stated that the working environment temperature is quite hot. Unreported similar ache pain in other co-workers. There was no history of renal or familial stone disease.

Physical examination revealed left costovertebral angle pain but no abnormalities. Laboratory results showed hemoglobin 12.8 g/dL and leukocytes 7700/μL. Urinalysis was positive for blood and urine leukocytes and negative for crystals. Intravenous pyelography showed a 1 cm inferior left kidney calix stone, with no hydronephrosis and normal renal function.

Personal protective equipment used at work included a helmet, goggles, safety shoes, leather gloves, clothes overalls, and earplugs. The body map indicated no complaints. Results of the Brief Survey demonstrated high risk to both hands and wrists, shoulders, back, and both legs.

The clinical diagnosis in these patients was the recalcitrant left renal caliceal calculi, and the “seven steps of occupational diagnosis” established that the disease was aggravated by occupation.

2.4. Clinical question
On the basis of complaints that occur in these patients, the clinical question to be answered was “Does the hot temperature in the work environment affect the formation of urinary tract stones in workers?”

3. Results
The cross-sectional study of Atan et al. [6] found during the database search was quite valid and subjectively measured the heat level, and not objectively, with the wet and spherical temperature index (ISBB). Urinary tract stones were measured objectively through imaging/radiologic studies. Although there was no follow-up, the data were complete and the study duration was long enough (3 years). Before the study, all subjects were confirmed not to be suffering from urinary tract stones. Workers exposed to excessive heat had low urine volume, and concentrated urine is a risk factor for lithogenesis. This finding is comparable with the study of Borghi et al. [7], who reported an 8.5% prevalence (n = 236) of urinary tract stones among workers in the glass industry (P = 0.03; Table 1).

The magnitude of this study is illustrated by the 9.97 odds ratio (OR), indicating that workers exposed to high temperature have an up to nine times greater risk of urinary tract stones than those not exposed to heat (95% confidence level [CI] = 7.38–13.47, P < 0.0001, significant).
The number needed to harm in this study was 14 (i.e., for every 14 workers exposed to heat, one will have urinary tract stones), indicating that heat exposure is quite dangerous.

Overall, the study was considered quite good because the data were significant enough to answer the clinical question regarding the prevalence of urinary tract stones in cases of heat exposure. The validity, importance, and applicability of the studies obtained, and criteria for etiological studies used are shown in Table 1 [8].

| No | Questions | Journal: High kidney stone risk in men working in steel industry at hot temperatures [6] |
|----|-----------|--------------------------------------------------------------------------------------|
| 1  | Were there clearly defined groups of patients, similar in all important aspects other than exposure to the treatment or other cause? | **No**, because it was a cross-sectional study. |
| 2  | Were treatment exposures and clinical outcomes measured the same manner in both groups (e.g., was the assessment of outcomes either objective (e.g., death) or blinded to exposure)? | **No**, heat levels were measured subjectively, and not objectively, with the wet and spherical temperature index (ISBB). Urinary tracts were measured objectively through imaging/radiology, but unknown if blinded. In the second stage, outcomes were assessed based on evaluation of metabolic serum and urine. |
| 3  | Was the follow-up of study patients complete and long enough? | **Yes**. There was no follow up, but the data were complete and study duration long enough, since male workers had been employed for at least 3 years and they previously had no history of urinary tract stones. Study time between March 1999 and December 2002. |

**Do the results satisfy some “diagnostic tests for causation?”**

| 1  | Is it clear that the exposure preceded the onset of the outcome? | **Yes**, before the study, all subjects assessed were determined not to have suffered from urinary tract stones previously. |
| 2  | Is there a dose-response gradient? | **Not analyzed.** |
| 3  | Is there positive evidence from a “dechallenge-rechallenge” study? | **Not applicable.** Because when it is formed, the stone cannot be lost even though it was not exposed to heat again (irreversible) |
| 4  | Is the association consistent from study to study? | **Yes** In accordance with other studies, these findings are comparable to those of Borghi et al. [7], who reported an 8.5% prevalence of urolithiasis among workers in the glass industry. |
| 5  | Does the association make biological sense? | **Yes** Workers exposed to excessive heat have low urine volume. Urine is concentrated, which is a risk factor for lithogenesis. |
Table 1. Continue

| No | Questions                                                                 | Journal: High kidney stone risk in men working in steel industry at hot temperatures [6] |
|----|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|

Are the valid results from this etiology study important?

1. **Relative risk (RR) or OR?**

| Area       | Urolithiasis | No Urolithiasis | Total |
|------------|--------------|-----------------|-------|
| Hot area   | 103          | 1186            | 1289  |
| Non-hot area | 78          | 8959            | 9037  |

OR = 9.975  
95% CI = 7.38–13.47  
P < 0.0001

Should these valid, potentially important results of a critical appraisal about an etiological treatment change the treatment of your patient?

1. **Can the study results be extrapolated to your patient?**  
   - Yes

2. **What are your patient’s risks of the adverse outcome?**
   - **Absolute Risk Increase** = 0.07  
     NNH = 1/0.07 = 14 (of every 14 workers exposed to heat, one will have urinary tract stones)

3. **What are your patient’s preferences, concerns and expectations from this treatment?**
   - The patient’s hope is not to suffer from urinary tract stones and to know what factors can increase the incidence of stones so that precautions can be taken against their formation.

4. **What alternative treatments are available?**
   - Education on the relationship of heat exposure to urinary tract stone formation and other risks, as well as administration of potassium citrate to workers exposed to heat in the workplace.

4. Discussion

The most relevant study found was that of Atan et al. [6] This article was relevant because it fit well in terms of the domain, determinant, and desired outcome and sufficiently answered the clinical question regarding the magnitude of urinary stone prevalence. The significance of this study was illustrated by the 9.97 OR (P < 0.0001).

The cross-sectional study was performed in two stages. Workers were exposed to heat (group 1) or room temperature (group 2) conditions and assessed for urinary tract stone formation. Exposure measurements are assessed qualitatively, not objectively, using the ISBB. The outcome of stones was assessed equally through medical records and radiologic examination. In stage 2, the outcome was assessed through metabolic evaluation of urine within 24 h of collection.

In a cross-sectional study, risk factors for heat exposure and urinary tract output were assessed at one time. There was no follow-up, but the data were complete and the study was long enough (the male workers had worked for at least 3 years, from March 1999 to December 2002). The prevalence of urinary tract stones was compared between the two groups. This cross-sectional study determined
the relationship between risk factors and disease. In this study, researchers could control subject selection. This study may be an early stage of a cohort or analytic study.

The advantages of this cross-sectional study are that the number of samples is quite large among the working population of 10,326 people, the design was relatively inexpensive, and the results were obtained rapidly. The study also evaluated several variables and two outcomes at once, that is, exposure of heat in relation to urinary tract stone formation, low urine volume, and hypocitraturia ($P < 0.05$). There was no loss to follow-up (dropout).

Another advantage of this study is that all workers who participated did not have a prior history of stones based on medical records and radiologic examination. To reduce selection bias, phase 2 of the study was conducted on 59 workers who were exposed to heat and worked at room temperature, but had no previous stone history.

The weakness of this cross-sectional study is that it did not not describe the course of the disease, was unable to assess the dose–response gradient, and it was difficult to determine that heat exposure caused urinary tract stones because the risk and effect data measurements were done at the same time (temporal relationship was not clear). A cross-sectional design is not the best design to prove a causal relationship. For etiology, the best design is a cohort study. However, the relationship between heat exposure and increased risk of urinary tract stones may be justified, because workers exposed to excessive heat have low urine volume and concentrated urine is a risk factor for lithogenesis. This finding is comparable with results reported by Borghi et al. [7], who observed an 8.5% prevalence ($n = 236$) of urinary stones among workers in the glass industry ($P = 0.03$). Similarly, Ng Tze Pin et al. [9] reported on 406 male workers in some outdoor and indoor occupations and found that the prevalence of urinary stones in tropical environments is higher in outdoor than in indoor workers (5.2% vs. 0.85%, $P < 0.05$).

In this study, bias may occur because of improper/insensitive measurement (insensitive measurement bias). Bias can occur when measuring heat exposure levels because the measurements are subjective, and not objective, using the ISBB. This finding is similar to results of two other studies that assessed the level of heat exposure qualitatively on the basis of the type of outdoor work [5,9].

To mitigate this bias, efforts should be made to improve the accuracy of hot pressure level measurements using the ISBB. The ISBB consists of dry temperature, natural wet thermometer, and spherical temperature thermometers. This ISBB tool is installed and placed at the measurement point as high as 1–1.25 m from the floor, approximately 50 cm from the heat source, and then switched on. After 20 min at each point, when the number or location on the monitor is not moving any more, the values of natural wet temperature, dry temperature, spherical temperature, wet temperature, and the wet and spherical temperature index (ISBB) for indoor and outdoor areas are recorded [10,11].

The results obtained from the study can be applied in Indonesia, considering that Indonesia also has a steel mill and some working environments have such hot temperatures. Therefore, hot temperatures in the work environment may similarly increase the risk of urinary tract stones in Indonesian workers. Sufficient fluid intake and administration of potassium citrate can be expected to reduce the incidence of urinary tract stones.

The Evidence-based Case Report (EBCR) for occupational medical practice is greatly beneficial in answering patient clinical questions through valid and relevant research/study results. The EBCR demonstrates how research results can be applied as in this etiological study.

5. Conclusions
Our review demonstrated that heat in the work environment will increase the risk of urinary tract stones in workers, but there still was little evidence to answer this clinical question because only one study was obtained and considered relevant. Cross-sectional studies cannot prove cause-and-effect relationships and demonstrate the dose–response gradient. For etiology, the best study design is the cohort study.

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