Peer Review File

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Reviewer A

The authors described the relationship between urine specific gravity and the prevalence rate of kidney stone. Although this manuscript was well prepared but had no innovation. And the authors should detail description the data of USG because of the diffident physical situation will affect the result.

Reply:

Thank you for your suggestion. In the PubMed database, we used an advanced search for articles in which urine specific gravity and kidney stones appeared in the Title/Abstract and found only one relevant article. Venugopal et al.[1] investigated 340 steelworkers who performed moderate to heavy labor and had more than 3 years of heat exposure and observed a significant association between heat exposure, increased core body temperature (CBT) ($p = 0.0001$) and urine specific gravity (USG) ($p = 0.018$). Moreover, years of exposure to heat (≥5 vs <5) were significantly associated with the risk of renal anomalies/calculi. In our study, we used the NHANES database, based on a large population-based study, and found a significant association between USG and self-reported kidney stone disease ($p = 0.026$), and the prevalence of kidney stones increased with increasing USG.

We have described the source of the USG data in detail in Materials and Methods and have added “the different physical conditions of the participants could affect the USG measurements” in the limitation paragraph.

[1] Venugopal V, Latha P K, Shanmugam R, et al. Risk of kidney stone among workers exposed to high occupational heat stress - A case study from southern Indian steel industry[J]. Science of The Total Environment, 2020.

Changes in the text: Page 5/Line 92-98 and Page 10/Line 214-215

Reviewer B

This is a cross sectional study of a large adult population correlating urine specific gravity with renal stone formation.

The study is largely well described. I would like the figure 1 legend to be more detailed with what is shown as this is not clear to the non expert.

I am wondering if stats for >1.020 vs 1.008-1.020 can be compared as this comparison is not performed (or P value not given. The p value is only significant for <1.008 vs >1.020.

Reply:

Thank you very much for your recognition of our research. We provide a more detailed description of the legend to Figure 1. In addition, we add figure of statistical information comparing the > 1.020 group with the 1.008-1.020 group (**Figure S1**).

Changes in the text: Page 8/Line 169 and Page 13/Line 311-312.

Reviewer C

In this manuscript in a retrospective study from the National Health and Nutrional Examination Survey between 2007-2008 the author proposed that increasing urinary specific gravity was significantly correlated with self-reported kidney stones. Although urinary supersaturation plays a key role in kidney stone formation and the manuscript has some value but carries several deficiencies that must be addressed:

1. It is not known whether urinary specific gravity was obtained on a fasting state or throughout the day in between meals and following meals.

Reply:

Thank you for your question. Urine specific gravity was collected in the time of the first morning void [1].

1. Heavner D L, Morgan W T, Sears S B, et al. Effect of creatinine and specific gravity normalization techniques on xenobiotic biomarkers in smokers' spot and 24-h urines.[J]. Journal of Pharmaceutical and Biomedical Analysis, 2006, 40(4): 928-942.

Changes in the text: Page 5/Line 93-94.

2. The kidney stone was diagnosed on self reported history and has not been further documented. Given that this is a key factor and the authors depend on proving the hypothesis on that basis making me suspicious of stone episodes. I recommend a through explanation with this regard.

Reply:

The National Health and Nutrition Examination Survey (NHANES) uses a complex probabilistic sampling design to collect information from different populations through standardized interviews, physical examinations, and sample tests to assess the health and nutritional status of non-institutionalized civilians in the United States. NHANES has been widely used in various studies with a high degree of confidence [1-4]. However, we also need to acknowledge the lack of diagnostic test design. We have added this limitation in the limitation section of the article.

1. Shoag J, Patel N, Posada L, et al. Kidney Stones and Risk of Narcotic Use.[J]. The Journal of Urology, 2019, 202(1): 114-117.

2. Reinstatler L, Khaleel S S, Pais V M, et al. Association of Pregnancy with Stone Formation among Women in the United States: A NHANES Analysis 2007 to 2012[J]. The Journal of Urology, 2017, 198(2): 389-393.

3. Antonelli J, Maalouf N M, Pearle M S, et al. Use of the National Health and Nutrition Examination Survey to calculate the impact of obesity and diabetes on cost and prevalence of urolithiasis in 2030.[J]. European Urology, 2014, 66(4): 724-729.

4. Weinberg A E, Patel C J, Chertow G M, et al. Diabetic Severity and Risk of Kidney Stone Disease[J]. European Urology, 2013, 65(1): 242-247.

Changes in the text: Page 10/Line 214-215.

3. One major deficiency in addition to the documentation of kidney stones, kidney stone disease is the lack of availability of urinary biochemical profiles that also is a major weakness in this manuscript.

Reply:

Thank you for your suggestion. We added two variables: urine albumin and urine creatinine.

Changes in the text: Page 2/Line 34, Page 5/Line 107-108, Page 7/Line 147-148 and Line 157.