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- Peer Review Report -

Reviewer #1: The authors present data from an instrument to three cohorts of VA subjects: IC, other pelvic pain versus healthy subjects. They showed generally increased prevalence of many food comestibles among IC subjects versus the other cohorts.

In my opinion, this paper would be enhanced if the authors were to consider the following revisions:

1) I read your paper several times and may have missed a basic demographic point, but please clarify for me: what were the mean/median ages of each cohort? Was there any statistical difference in ages?

2) I am not familiar with the instrument used. You indicate that it has been validated. I suggest you add the instrument as an Appendix and clarify which foods were grouped together. Further, I am fuzzy how a subject might interpret the language of the instrument: "(1) I don't know, (2) Worsens symptoms, (3) No effect, and (4) Improves symptoms." If a subject feels a specific comestible worsens symptoms by 5%, their answer would be (2), the same as a subject feels that same comestible worsens their symptoms 90%. Arguably, a subject may be confused between daily variability of a few percent versus interpreting the question that any degree of worse food trigger is a positive. How did your validation of the instrument control for this possibility?

3) Did you control for subjects who use Prelief or any similar compounds to reduce their food triggers? Again, an IC subject using Prelief to advantage might respond to your question that they do not have food triggers (as long as they take calcium glycerophosphate) which would reduce the number of food triggers "worsens symptoms" responses in your IC cohort. (Presumably subjects in the other two cohorts would be far less likely to ingest Prelief.)

4) Why did you stratify blacks versus whites? Is there evidence of ethnicity as a food trigger variable? What about subjects of color in general (Asian Americans, Latinos or Hispanic Americans)? If skin pigmentation has any impact on food triggers (above and beyond cultural differences in specific comestibles one culture might consume), one would anticipate a gradation of food trigger sensitivity. I would anticipate a VA population to have a large representation by Hispanic Americans and African Americans, but that is just a guess.

5) There is a potential bias in this database particularly given the slight male preponderance among the IC cohort. Presumably, the majority of VA patients are male and very few women are in VA care (compared to the non-VA population). With most IC studies showing a 8:1 to 10:1 female:male ratio, it seems obvious that your nearly 50:50 ratio represents the outsized male population of the VA. To my knowledge, male IC patients generally are less likely to have non-urologic pelvic pain syndromes compared to women IC patients in most studies that have looked at enough subjects, i.e., women IC patients have greater prevalence of IBS and fibromyalgia compared to male IC patients. These differences could potentially bias your IC cohort results either way (too few food triggers, too many food triggers).

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6) You comment on potential mechanisms for food triggers: infection, inflammation and GAG layer issues. I would also reference papers by Klumpp, Schaeffer and colleagues for their elucidation of pelvic cross talk and hindgut von Frey receptors as a food trigger mechanism.

Reviewer #2: The authors used the validated Shorter Moldwin Food Sensitivity Questionnaire (SMQ) to determine diet sensitivities in a heterogeneous population of male and female veterans diagnosed with IC/BPS and examine differences between those diagnosed with other pelvic pain conditions, and healthy controls (HC).
They found that IC/BPS patients had significantly more food sensitivities than those without IC/BPS. The authors concluded that food sensitives could be indicative of IC/BPS, which could make the SMQ a helpful diagnostic tool and aid in distinguishing IC/BPS from conditions often confused with IC/BPS.

This is an interesting paper, but some points need to be cleared.

Q1. The authors should provide the biochemical rationales to stand their points on special food stimulation for IC/BPS patients.

Q2. In IC/BPS patients combined with IBS, did foods sensitive to both bladder and bowel, or any food with organ specific sensitivity?

Q3. How can the sensitive food component come to sensitize bladder? Any detectable molecular identified from urine related to sensitive food?

Q4. Tomato products have been known to have anti-inflammatory effects, why it became sensitive food for IC/BPS?

Q5. How to identify or recruit healthy control cohorts in the current study?

Q6. If SMQ is a must-be tool for IC/BPS patients, will it cause psychological burden in daily life to avoid any potential sensitive food?

Reviewer #3:

1) The authors describe food sensitivities (citrus, spicy foods, alcoholic beverages, etc.) of IC/BPS patients are more severe than other pelvic pain and HC. Systematic examination regarding food sensitivities might be important for more appropriate diagnosis of IC/BPS.

2) These findings are extremely important and should be examined more deeply.

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3) At first glance, food sensitivities of IC/BPS patients are natural, but detailed examinations might improve the diagnostic accuracy of IC/BPS.

4) Please describe without abbreviation (FFQ; food frequency questionnaire).

Reviewer #4: This is a survey based study of self-reported food sensitivities between patients with IC/BPS, pelvic pain, and healthy controls within the VA system. A standardized, validated inventory of food-related provocation of bladder symptoms was mailed. The overall nature of this descriptive study seems to mirror prior work and it's not clear it would change clinical practice or bring new knowledge to the IC/BPS scientific field,.

Introduction
- As presented, not a very compelling justification for why this study needed to be done, as the authors indicate prior studies have found what they anticipated finding, but they had a larger sample.

Methods
- Appropriate analysis strategy presented.
- While the diagnostic criteria for identifying IC/BPS seem reasonable, it is not clear these are validated.
- No formal power analysis.
- Appropriate su analysis for IBS and food sensitivities, and FM+ vs. FM- patients within the IC/BPS group.

Results
- Generally well written.
- Unclear how many individuals completely filled out the food sensitivity questionnaire.
- Were there were null findings? Was there a power calculation to ensure these are in fact nonsignificant (IBS subanalyses)?
- Equal probably should be described by generic chemical compound composition (artificial sweetener, aspartame based [aspartame, acesulfame potassium, dextrose and maltodextrin ingredients].

Discussion
- It seems like your conclusion that food sensitivity is indicative of IC/BPS is a reach, as the analysis did not look at the frequency of bladder symptoms in food sensitive individuals in general.
- No discussion about why you had such findings. What is the biology behind sensory issues, bladder dysfunction and food sensitivities? For that matter, what is the underlying biology of food sensitivities?
- Seems essential - the finding of higher bladder irritation from foods in black patients seems worth further contemplation.
- The statements about the value of the food questionnaire related to treatment planning are unrelated to the current study's findings. This is also not a "less invasive tool" for managing symptoms.

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Tables
- For Table 3, the exact value of showing the % response to so many individual food items does not seem to be essential to the presentation of your dataset. Maybe group and simplify?

Editorial commentary: In addition to the comments from external reviewers, we would ask for authors to pay careful attention to reporting guidelines for statistics (Assel et al, (https://www.auajournals.org/doi/10.1097/JU.0000000000000001) and figures/tables (Vickers et al, (https://www.auajournals.org/doi/full/10.1097/JU.0000000000001096) to ensure appropriate reporting overall and please pay special attention to guideline 2.4, 3.6, 4.2.

Consultants and Editors contributing to the peer review process for this article were Toby C. Chai, Hitoshi Oh-Oka, D. Robert Siemens, and three anonymous reviewers.