Author’s response to reviews

Title: Cross-sectional study of associations between normal body weight with central obesity and hyperuricemia in Japan

Authors:

Takako Shirasawa (shirasawa@med.showa-u.ac.jp)
Hirotaka Ochiai (h-ochiai@med.showa-u.ac.jp)
Takahiko Yoshimoto (yoshimotot@med.showa-u.ac.jp)
Satsue Nagahama (satsue-n@umin.ac.jp)
Akihiro Watanabe (akhee1090@yahoo.co.jp)
Reika Yoshida (reika.y@med.showa-u.ac.jp)
Akatsuki Kokaze (akokaze@med.showa-u.ac.jp)

Version: 2 Date: 04 Dec 2019

Author’s response to reviews:

Dec 4, 2019

BEND-D-19-00376
Cross-sectional study of associations between normal body weight with central obesity and hyperuricemia in Japan
Takako Shirasawa; Hirotaka Ochiai; Takahiko Yoshimoto; Satsue Nagahama; Akihiro Watanabe; Reika Yoshida; Akatsuki Kokaze

Dear Mauro Lombardo
BMC Endocrine Disorders Editorial Office

Thank you for your email of 23-Nov-2019, regarding our manuscript, "Cross-sectional study of associations between normal body weight with central obesity and hyperuricemia in Japan ", and the valuable comments of the reviewers. I attach here our revised manuscript, as well as a point-by-point response to the reviewers’ comments.

We believe that the revised manuscript is a suitable response to the comments, and is significantly improved.
We trust that it is now suitable for publication in BMC Endocrine Disorders.
Thank you in advance for your kind consideration of this paper.

Yours sincerely,
We wish to express our appreciation to reviewers’ comments, which have helped us significantly improve the paper.

In accordance with the reviewers’ comments, we have revised our paper as follows;

Reviewer 3 reports:

1) According to my suggestion, there is a need to define hyperuricemia in relation to increase uric acid level either by overproduction or due to decrease secretion.

In accordance with this comment, we have revised our text “Method/Variables and measurements” (Page 8) and added a literature (reference No.18).

Although there was a need to define hyperuricemia in relation to increase uric acid level either by overproduction or due to decrease secretion, in the present study, hyperuricemia was defined as serum uric acid >7.0 mg/dL in men or ≥6.0 mg/dL in women, or being under medical treatment for hyperuricemia, which was based solely on serum uric acid levels [12-15]. The definition in men was based on Japanese guidelines for the management of hyperuricemia [12]. Serum uric acid levels are lower in women than in men because female hormones decrease them [16, 17]. Thus, we defined hyperuricemia in women as ≥6.0 mg/dL [13-15]. These cutoff values were selected as they are generally used in clinical laboratories and have been proposed in previous studies in relation to metabolic syndrome and CVD outcomes to define hyperuricemia [12-15, 18].

2) Secondly, weight is very important clinical indicator in order to determine hyperuricemia. Either researcher observe these weight variations throughout research in an individual because weight loss is not a simple nor uniform, matter in different person.

In accordance with this comment, we have revised our text “Discussion/limitation” (Page 15).

Another limitation is that the cross-sectional study design caused difficulties with assessing causal relationships. For the nature of the study design, we did not observe these weight variations, although weight was very important clinical indicator in order to determine hyperuricemia throughout research in an individual. Thus, further longitudinal studies will be needed to establish causality and to consider weight variation.

3) These researchers should uncover the relationship between uric acid and obesity by describing in a comprehensive way how pathophysiology of obesity influence the uric acid metabolism (Either production and secretion).

In accordance with this comment, we have revised our text “Discussion” (Page 12-13) and added a literature (reference No.24).

Several epidemiological studies reported that hyperuricemia was associated with diseases including diabetes mellitus, dyslipidemia, hypertension, CVD, and metabolic syndrome [2, 8, 13, 15]. Similarly,
the present study showed that the prevalences of hypertension, dyslipidemia, and diabetes were higher with than without hyperuricemia in both men and women. Moreover, we also found that OBCO significantly increased the OR for hyperuricemia, compared with NW, regardless of sex. Others have positively associated hyperuricemia with obesity in both men and women [15, 23]. Nagahama et al. reported that the adjusted OR (95%CI) for hyperuricemia in men and women with BMI ≥25 kg/m2 were 1.75 (1.56-1.97) and 2.02 (1.62-2.53) [15]. Yu et al. reported that hyperuricemia was related to abdominal obesity and general obesity in both sexes [23]. The present results are in line with these findings. Even after adjustment for age, lifestyle factors, hypertension, dyslipidemia, and diabetes, our results showed that OBCO had an independently increased risk of hyperuricemia and this was statistically significant between OBCO and hyperuricemia. As one of the reasons, obesity may increase hyperuricemia through increased urate production and decreased renal clearance, and that renal excretion of urate was also reduced in the presence of insulin resistance [24]. However, the underlying mechanism by which serum uric acid increased in obese individuals still remains to explore [18]. Thus, more studies need to be conducted in order to elucidate the mechanism of the association between serum uric acid and obesity.

4) In discussion section of your manuscript, you should need to elaborate your result in a summarized form related to other factors that are used for biochemical analysis. 
In accordance with this comment, we have added a sentence in our text “Discussion” (Page 15).

Serum uric acid was measured using a standardized method at a clinical testing laboratory.

Reviewer 4 reports:
1) eGFR should be adjusted in regression analysis.
In accordance with this comment, we have analyzed again, and revised our text “Results” (Page 11-12).

These results persisted even after adjustment for age, lifestyle factors, hypertension, dyslipidemia, diabetes, and the estimated glomerular filtration rate.

2) English written should be improved. Please ensure that your paper has been corrected by a native English speaker.
When we have submitted our manuscript, it has been corrected by a native English speaker. Moreover, we improved English of the revised manuscript as much as possible.