PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Prevalence of hyperuricemia in an eastern Chinese population: a cross-sectional study
AUTHORS	Han, Bing; Wang, Ningjian; Chen, Yi; Li, Qin; Zhu, Chunfang; Chen, Yingchao; Lu, Yingli

VERSION 1 - REVIEW

REVIEWER	Sheyu Li West China Hospital, Sichuan University
REVIEW RETURNED	22-Nov-2019

GENERAL COMMENTS	This is a timely report for the prevalence of hyperuricemia in China. The study was generally well prepared with meaningful data. The major concern of the study is that patients are prone to be older in the study (average age: ~55 yrs old) compared to the general population, and may not be fully representative in the study region. May the authors please standardize the prevalence based on the demographic data of the region (open data provided by the Chinese government)? Some minor concerns: 1. Although the protocol has been published previously, a brief description of eligibility criteria is necessary. 2. The BMI cutoffs for overweight and obesity are 24kg/m2 and 28kg/m2 in eastern Asia including In China, respectively, which are preferred in use in the presentation of the study. 3. I did not see parameters which were we usually call "biomarkers" throughout the manuscript. May the authors please revise and shorten the associated paragraph in the Method section? 4. Please be aware that some typos could be found in the manuscript. For example, "FPS" in table 1 should be "FPG" if understanding correctly. 5. P-value should be presented as P<0.001 rather than P=0.000, which is not possible in theory. 6. The English language can be improved if edited by senior authors.

REVIEWER	Yilun Wang Xiangya Hospital, Central South University
REVIEW RETURNED	05-Dec-2019

GENERAL COMMENTS	The authors performed a large-scale cross-sectional study to investigate the prevalence of hyperuricemia (HUA) in the eastern Chinese population. It is obvious that the authors have dedicated significant time and effort to complete this study. However, there are some limitations which could not be ignored. First, the present manuscript needs to be further polished. The current version is hard to read because there exists lots of typos. For example, the authors stated “The prevalence of HUA was decreased in men and increased in women (Page 4, Line 56)” in the Abstract section which is confusing; interpretation of abbreviations is absent (Page 4, Line 46, 50, 53, 57, 58, etc.); data presentation in table 2-4 is confusing which should be rearranged, and relevant footnotes should be added. Second, as the main exposure in the manuscript, the assessment of serum uric acid needs to be clarified further. Data of validity/accuracy should be presented in the Methods section. Moreover, the effects of urban residency and high economic status on HUA seem to be on the opposite direction (2.208, 95%CI 1.674 to 2.913 vs. 0.693, 95%CI 0.543 to 0.886), which should be discussed.

REVIEWER	Masayuki Hakoda Yasuda Women's University, Department of nutritional sciences, Japan
REVIEW RETURNED	19-Dec-2019

GENERAL COMMENTS	The manuscript added a new data to the prevalence of hyperuricemia in China. I have the following comments. Major comments #1. Since there have been many reports describing the prevalence of hyperuricemia in China, it should be shortly reviewed with several (or a number of) references and the position of this manuscript among such reports should be described in Introduction. #2. Although the serum urate level of >6.0 mg/dL (357 μM) may have been used as the criteria of hyperuricemia for women in many reports, >7.0 mg/dL (416 μM) is usually the level for the development of gout in both men and women. Therefore, the data of hyperuricemia >7.0 mg/dL had also better be presented for women, for example, in Table 4, and in Table 5. The criteria of hyperuricemia should be described in the Abstract. #3. Since many of the readers may not be familiar with the geography of China, a concise map showing the position of the 5 provinces and 22 sites where the study population lived will help readers to understand the manuscript. #4. Figure 1 is not necessary. #5. English should be revised by a native English speaker.

	Minor comments #1. “incidence”, “ratio” and “proportion” are used in several sites where “prevalence” should be used. #2. “The prevalence HUA was decreased in men and increased in women” in Abstract should be for example, “The prevalence of HUA associated negatively and positively with age in men and women, respectively”. #3. A reference should be attached to the sentence “The inclusion criteria were described previously” in page 8. #4. Line 151, “Levels” should be “Mean levels” #5. Line 153, “significant differences between” should probably be “significant sex differences in”. #6. Line 170, the sentence should be rewritten correctly. #7. Table 2. There are two subheadings “% (95% CI)” and “Mean (95% CI)”. #8. Where the Tables extend more than 1 page, some announcement such as (Table * continues) may be added.

VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Sheyu Li

Institution and Country: West China Hospital, Sichuan University

Please state any competing interests or state ‘None declared’: None declared.

Please leave your comments for the authors below

This is a timely report for the prevalence of hyperuricemia in China. The study was generally well prepared with meaningful data. The major concern of the study is that patients are prone to be older in the study (average age: ~55 yrs old) compared to the general population, and may not be fully representative in the study region. May the authors please standardize the prevalence based on the demographic data of the region (open data provided by the Chinese government)?

Answer: Thank you for your advice. We have added a standardized prevalence in Table 4. According to the 6th national population census data, the proportions of the population in the different age groups (<40, 40-60, ≥60) are 57.39%, 29.29%, and 13.31% (total); 58.10%, 29.13%, and 12.76% (male); and 56.61%, 29.46%, and 13.91% (female), respectively (http://www.stats.gov.cn/tjsj/pcsj/rkpc/6rp/indexce.htm). Thus, we adjusted the prevalence by these proportions. Finally, the prevalence of HUA in this eastern Chinese population was 11.3% overall and 20.7% and 5.6% in men and women, respectively.

Some minor concerns:

1. Although the protocol has been published previously, a brief description of eligibility criteria is necessary.

Answer: Thank you for your advice. We have added a brief description of the eligibility criteria in the method.

2. The BMI cutoffs for overweight and obesity are 24kg/m2 and 28kg/m2 in eastern Asia including In China, respectively, which are preferred in use in the presentation of the study.

Answer: Thank you for your advice. We have changed the BMI cutoff value and content in Tables 2 and 3.

3. I did not see parameters which were we usually call "biomarkers" throughout the manuscript. May the authors please revise and shorten the associated paragraph in the Method section?

Answer: Thank you for your advice. Biomarker was changed to biochemical index. We also shortened the “Assessment of biochemical indexes” section.

4. Please be aware that some typos could be found in the manuscript. For example, "FPS" in table 1 should be "FPG" if understanding correctly.

Answer: Thank you for your advice. We have changed it in the article.

5. P-value should be presented as P<0.001 rather than P=0.000, which is not possible in theory.

Answer: Thank you for your advice. We have revised them in the article.

6. The English language can be improved if edited by senior authors.

Answer: Thank you for your advice. We have had our article revised by the editors of American Journal Experts (AJE).

Reviewer: 2

Reviewer Name: Yilun Wang

Institution and Country: Xiangya Hospital, Central South University

Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below

The authors performed a large-scale cross-sectional study to investigate the prevalence of hyperuricemia (HUA) in the eastern Chinese population. It is obvious that the authors have dedicated significant time and effort to complete this study. However, there are some limitations which could not be ignored.

First, the present manuscript needs to be further polished. The current version is hard to read because there exists lots of typos. For example, the authors stated “The prevalence of HUA was decreased in men and increased in women (Page 4, Line 56)” in the Abstract section which is confusing; interpretation of abbreviations is absent (Page 4, Line 46, 50, 53, 57, 58, etc.); data presentation in table 2-4 is confusing which should be rearranged, and relevant footnotes should be added.

Answer: Thank you for your advice. We have changed that sentence and added an interpretation of the abbreviations in the abstract. We have revised Tables 2-4 to make them understandable. Finally, we have also had our article revised by the editors of American Journal Experts (AJE).

Second, as the main exposure in the manuscript, the assessment of serum uric acid needs to be clarified further. Data of validity/accuracy should be presented in the Methods section. Moreover, the effects of urban residency and high economic status on HUA seem to be on the opposite direction (2.208, 95%CI 1.674 to 2.913 vs. 0.693, 95%CI 0.543 to 0.886), which should be discussed.

Answer: Thank you for your advice. We have added uric acid measurements as well as validity/accuracy data to the article. We also added a discussion about the effects of urban residency and high economic status on HUA.

Reviewer: 3

Reviewer Name: Masayuki Hakoda

Institution and Country: Yasuda Women's University, Department of nutritional sciences, Japan

Please state any competing interests or state ‘None declared’: None

Please leave your comments for the authors below

The manuscript added a new data to the prevalence of hyperuricemia in China. I have the following comments.

Major comments

#1. Since there have been many reports describing the prevalence of hyperuricemia in China, it should be shortly reviewed with several (or a number of) references and the position of this manuscript among such reports should be described in Introduction.

Answer: Thank you for your advice. We have added new references in the introduction.

#2. Although the serum urate level of >6.0 mg/dL (357 μM) may have been used as the criteria of hyperuricemia for women in many reports, >7.0 mg/dL (416 μM) is usually the level for the development of gout in both men and women. Therefore, the data of hyperuricemia >7.0 mg/dL had also better be presented for women, for example, in Table 4, and in Table 5. The criteria of hyperuricemia should be described in the Abstract.

Answer: Thank you for your advice. We have added this content as Supplemental Tables 1 and 2.

#3. Since many of the readers may not be familiar with the geography of China, a concise map showing the position of the 5 provinces and 22 sites where the study population lived will help readers to understand the manuscript.

Answer: Thank you for your advice. We have added the map in Supplemental Figure 1.

#4. Figure 1 is not necessary.

Answer: Thank you for your advice. We have deleted figure 1.

#5. English should be revised by a native English speaker.

Answer: Thank you for your advice. We have had our article revised by the editors of American Journal Experts (AJE).

Minor comments

#1. “incidence”, “ratio” and “proportion” are used in several sites where “prevalence” should be used.

Answer: Thank you for your advice. We have changed them in the article.

#2. “The prevalence HUA was decreased in men and increased in women” in Abstract should be for example, “The prevalence of HUA associated negatively and positively with age in men and women, respectively”.

Answer: Thank you for your advice. We have changed it in the abstract.

#3. A reference should be attached to the sentence “The inclusion criteria were described previously” in page 8.

Answer: Thank you for your advice. We have added references in the article.

#4. Line 151, “Levels” should be “Mean levels”

Answer: Thank you for your advice. We have changed it in the article.

#5. Line 153, “significant differences between” should probably be “significant sex differences in”.

Answer: Thank you for your advice. We have changed it in the article.

#6. Line 170, the sentence should be rewritten correctly.

Answer: Thank you for your advice. We have changed it in the article.

#7. Table 2. There are two subheadings “% (95% CI)” and “Mean (95% CI)”.

Answer: Thank you for your advice. Diabetes, hypertension, smoking and drinking are categorical variables that are represented as percentages (95%CI). WC, SBP and BMI are continuous variables that are represented as the mean ± SD.

#8. Where the Tables extend more than 1 page, some announcement such as (Table * continues) may be added.

Answer: Thank you for your advice. We have shortened the table to one page.

VERSION 2 – REVIEW

REVIEWER	Sheyu Li West China Hospital, Sichuan University
REVIEW RETURNED	16-Feb-2020

GENERAL COMMENTS	Thanks for the revise from the authors. My comments are technically solved, but could the authors move the Introduction section in front of the Method section, please, which may help read the manuscript. Meanwhile, the 6th national population census data can be used as a citation rather than a linkage in brackets. Cheers,

REVIEWER	Masayuki Hakoda Yasuda Women's University, Japan
REVIEW RETURNED	24-Feb-2020

GENERAL COMMENTS	Although the authors responded to most of the comments, there still be several parts needing responses. Major comments #1. The authors just added one reference of 2018 describing the prevalence of hyperuricemia in elderly people and one that reviewed articles that were published before 2014. There should have been so many studies on the hyperuricemia prevalence in China after 2014. I also commented that the authors should describe the position of this manuscript among such numerous reports.

	#2. A description about the prevalence of hyperuricemia defined by >7.0 mg/dL (416 μM) may be restricted to women and total population. The prevalence in men >7.0 mg/dL (416 μM) has already been described. Repeated description of the same data in the manuscript and in the Tables causes confusion. Although I pointed out that the criteria for hyperuricemia should be described in the Abstract it was not described in the revised manuscript. #3. A map provided in the revised manuscript helps readers. It may be better if the authors add lines connecting the names of provinces and the map of East China. #4. The authors responded to the comment. #5. See below. Minor comments #6. The sentence of lines 186-187 is still hard to be understood. The prevalence increased as compared to what? Was English really revised by a native English speaker?

VERSION 2 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Sheyu Li

Institution and Country: West China Hospital, Sichuan University

Please state any competing interests or state ‘None declared’: None to declare.

Please leave your comments for the authors below

Thanks for the revise from the authors. My comments are technically solved, but could the authors move the Introduction section in front of the Method section, please, which may help read the manuscript. Meanwhile, the 6th national population census data can be used as a citation rather than a linkage in brackets.

Answer : Thank you for your advice. The 6th national population census data has been used as a reference.

Reviewer: 3

Reviewer Name: Masayuki Hakoda

Institution and Country: Yasuda Women's University, Japan

Please state any competing interests or state ‘None declared’: None

Please leave your comments for the authors below

Although the authors responded to most of the comments, there still be several parts needing responses.

Major comments

#1. The authors just added one reference of 2018 describing the prevalence of hyperuricemia in elderly people and one that reviewed articles that were published before 2014. There should have been so many studies on the hyperuricemia prevalence in China after 2014. I also commented that the authors should describe the position of this manuscript among such numerous reports.

Answer : Thank you for your advice. We have added new references in the introduction. Besides, these studies can be divided into regional and national investigations.

#2. A description about the prevalence of hyperuricemia defined by >7.0 mg/dL (416 μM) may be restricted to women and total population. The prevalence in men >7.0 mg/dL (416 μM) has already been described. Repeated description of the same data in the manuscript and in the Tables causes confusion. Although I pointed out that the criteria for hyperuricemia should be described in the Abstract it was not described in the revised manuscript.

Answer : Thank you for your advice. When HUA was defined as serum UA >420 μmol/L both in men and women, we got the similar results as HUA defined by serum UA >420 μmol/L for men and >360 μmol/L for women. However, the latter was wildly used in Chinese population. So we deleted supplemental table 1 & 2 and added criteria for HUA in the abstract.

#3. A map provided in the revised manuscript helps readers. It may be better if the authors add lines connecting the names of provinces and the map of East China.

Answer: Thank you for your advice. We have added arrows in the map to show the names of provinces.

#4. The authors responded to the comment.

Answer: Thank you.

#5. See below.

Minor comments

#6. The sentence of lines 186-187 is still hard to be understood. The prevalence increased as compared to what? Was English really revised by a native English speaker?

Answer: Thank you for your advice. We have revised our manuscript. The prevalence of HUA in normal, prediabetic and diabetic women were 5.7% (4.9, 6.5), 11.6% (10.0, 13.2) and 15.2% (12.5, 17.9) respectively (Table 4). So there was an increased trend of prevalence of HUA in women with different glucose status. Besides, our article was revised by the editors of American Journal Experts (AJE). Editing certificate was issued on February 3, 2020 and may be verified on the AJE website

using the verification code 998D-0A2B-55BD-B431-55C0. We also provide editing certificate in attachment.

VERSION 3 - REVIEW

REVIEWER	Masayuki Hakoda Yasuda Women's University, Japan
REVIEW RETURNED	08-Mar-2020

GENERAL COMMENTS	Although the authors responded to the comments, there still be some parts needing responses. Major comments #1. Although the authors added several reports of hyperuricemia prevalence in China, the order of the studies may be changed. Thus, the nation-wide studies may come first, one of which was the earliest among the studies newly described in the revised manuscript. Further, there should be some comments comparing the prevalence of China with that of other countries described (only the data of USA was described). The authors just described the previous studies in the revised manuscript. Introduction is not just a list of previous works. One of the nation-wide studies (ref. 18) was published in 2020. Some comments should be made on this new data comparing the present study. This may not necessarily be made in Introduction, may be in Discussion. #2. I said that the data of men in the supplementary Table 1 is not necessary because it is already shown in Table 4. The supplementary Table 1 with data for women >7.0 mg/dL (416 μM) is necessary. It should not be deleted. Also, supplementary Table 2 should not be deleted.

VERSION 3 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 3

Reviewer Name: Masayuki Hakoda

Institution and Country: Yasuda Women's University, Japan

Please state any competing interests or state ‘None declared’: None

Please leave your comments for the authors below

Although the authors responded to the comments, there still be some parts needing responses.

Major comments

#1. Although the authors added several reports of hyperuricemia prevalence in China, the order of the studies may be changed. Thus, the nation-wide studies may come first, one of which was the earliest among the studies newly described in the revised manuscript. Further, there should be some

comments comparing the prevalence of China with that of other countries described (only the data of USA was described). The authors just described the previous studies in the revised manuscript. Introduction is not just a list of previous works. One of the nation-wide studies (ref. 18) was published in 2020. Some comments should be made on this new data comparing the present study. This may not necessarily be made in Introduction, may be in Discussion.

Answer: Thank you for your advice. Very good opinion! We have adjusted the order of studies in introduction and added some comments in the discussion.

#2. I said that the data of men in the supplementary Table 1 is not necessary because it is already shown in Table 4. The supplementary Table 1 with data for women >7.0 mg/dL (416 μM) is necessary. It should not be deleted. Also, supplementary Table 2 should not be deleted.

Answer: Thank you for your advice. We have revised supplementary Tables.

VERSION 4 - REVIEW

REVIEWER	Masayuki Hakoda Yasuda Women's University, Japan
REVIEW RETURNED	22-Mar-2020

GENERAL COMMENTS	The authors responded to the most of my comments.