Geographical distribution of hyperuricemia in mainland China: a comprehensive systematic review and meta-analysis

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Abstract

Background: Fructose plays an important role in the complex metabolism of uric acid in the human body. However, high blood uric acid concentration, known as hyperuricemia, is the main risk factor for development of gout. Therefore, we conducted an updated meta-analysis on the prevalence and geographical distribution of hyperuricemia among the general population in mainland China using systematic literature search.

Methods: Five electronic databases were used to search for relevant articles published until 2019. All calculations were conducted using the Comprehensive Meta-Analysis (CMA) software. We included 108 eligible articles (172 studies by sex, 95 studies by regions, and 107 studies by study type) and an overall sample size of > 808,505 participants.

Results: The pooled prevalence of hyperuricemia among the general population in mainland China was 17.4\% (95\% CI: 15.8–19.1\%). Our subgroup analysis indicated that the pooled prevalence by regions ranged from 15.5 to 24.6\%. Those living Northeast region and being males had the highest prevalence ($P < 0.001$). In addition, some provinces in South Central, East and Northeast regions reported a high prevalence (> 20\%), particularly in males. An increasing prevalence was reported since 2005–2009 until 2015–2019. No publication of bias was observed as indicated by a symmetrical funnel plot and Begg and Mazumdar rank correlation ($P = 0.392$).

Conclusion: Prevalence of hyperuricemia is increasing in China, and future studies should investigate the association between the prevalence of hyperuricemia and its risk factors in order to tackle the issue, particularly among the vulnerable groups. Also, our study was the first comprehensive study to investigate the overall prevalence of hyperuricemia in mainland China covering the six different regions.

Keywords: Uric acid, Hyperuricemia, Gout, China, Urbanisation

Background

High blood uric acid concentration, known as hyperuricemia, is the main risk factor for development of gout \cite{1, 2}. Uric acid is a terminal metabolite of human purine compounds, which is slightly soluble in water and easy to form crystals \cite{3, 4}. When uric acid increases to a certain threshold level in the human body, it is considered hyperuricemia \cite{5}.

The body has $\sim 1200$ mg and $\sim 600$ mg total body pool of exchangeable uric acid in males and females, respectively \cite{6}. There are about 600 mg uric acid that are produced every day, and another 600 mg uric acid are excreted, resulting in a balanced state \cite{7}. A disturbed state of purine metabolism can cause a variety of disorders, such as hyperuricemia, chronic gout, joint deformation and renal failure \cite{3}. Among them, hyperuricemia has received increasing attention in recent decades.
because of its increasing global trends and risk of associated metabolic diseases. The prevalence of hyperuricemia can be influenced by several factors, including genetics, gender, age, lifestyle, diet, medication and economic development. For example, a higher prevalence is usually reported in the economically developed regions [8].

In addition, higher uric acid concentration is associated with increased risk of hospitalization, chronic kidney disease and cardiovascular disease (CVD), which can result in higher total medical costs and hospitalisation costs per patient. For example, the mean annual healthcare costs in Italy for hyperuricemic patients ranged from €2752 to €4607 [5]. Elderly patients with hyperuricemia in China are at risk of gout attacks caused by iatric problems, which may bring about complications such as deep vein thrombosis (DVT) and a prolonged hospital stay [9]. Therefore, this does not only increase the cost of medical treatment for patients, but also increase the cost of treatment for hospitals.

There are many observational studies on the prevalence of hyperuricemia, however most of them were focused on specific populations such as children from a region of mainland China. In addition, there are only two meta-analyses in the past that have examined the prevalence of hyperuricemia in mainland China; both with limitations [10, 11]. The first meta-analysis was conducted in 2011 with 59 articles [10] and the second one was in 2015 with 44 articles [11]; both did not have comprehensive coverage of the whole of China (for example, the former one did not include Inner Mongolia, while the latter one did not include Ningxia and Qinghai). Since China is the world’s most populous country with about 1.4 billion (i.e. 18.4% of the world population), updating the epidemiology of hyperuricemia can help to fill the gap in public health research and policy. To date, there have been no published English articles that have extensively reviewed the prevalence of hyperuricemia in mainland China until December 2019. Therefore, the aim of our study was to conduct a comprehensive review and quantitative meta-analysis on the prevalence of hyperuricemia in mainland China over the past two decades. In addition, analyses were also performed to provide a more detailed and updated epidemiological distribution of hyperuricemia by comparing different regions in mainland China.

Methods

Search strategy
A systematic literature search from January 1995 to December 2019 was conducted for articles published in Chinese language from the following electronic databases: Wanfang Data, Shanghai Science and Technology Innovation Resources Center (SSTIR), China National Knowledge Infrastructure (CNKI) and Chinese Scientific Journals Fulltext Database (CQVIP). Keywords used in the database search included: “hyperuricemia” OR “high uric acid” OR “uric acid” OR “gout” AND “Chinese” OR “China” OR the name of the provinces in China. Database search results were entered into EndNote X8.2 file (Clarivate Analytics, New York, USA). The current systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [12] (Fig. 1). The protocol of the systematic review and meta-analysis was registered at PROSPERO, as CRD42019141243, which is an international database of prospectively registered systematic reviews in health and social care. Since our systematic review and meta-analysis used data from published articles, there are no requirements for us to apply for the ethics approval. However, all human studies included in our systematic review and meta-analysis have been reviewed by the appropriate ethics committee in their institutions and have therefore been performed in accordance with the ethical standards laid down in an appropriate version of the WMA Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subject.

Study selection
Studies were deemed to be eligible if they met the following criteria: (1) cross-sectional, cohort or case-control studies that were conducted in non-pregnant adults living in mainland China; (2) prevalence of hyperuricemia and sample size were reported; (3) detailed diagnostic criteria were included; and (4) full text of the article was able to be retrieved. Studies were excluded if they were: review articles and/or meta-analyses and inclusion of terminally ill or pregnant adults as participants.

Quality assessment
The quality of eligible studies was independently assessed by two authors (J. H. and Z. F. M.) using a modified version of Newcastle-Ottawa Scale (NOS). When there were disagreements between the authors, they were resolved by discussion.

Data extraction
For all eligible studies, the information about the authors, publication year, study design, age, sex, province, cases of hyperuricemia, total sample size, prevalence of hyperuricemia and cut-offs used for the determination of hyperuricemia was extracted. The corresponding authors of eligible studies were also contacted for obtaining the missing data in their articles.
Statistical analysis
Meta-analysis was performed using the Comprehensive Meta-Analysis (CMA) software (V2.0, Biostat, Englewood, New Jersey). Random-effects models were used to estimate the pooled prevalence of hyperuricemia and 95% confidence intervals (CI) due to the large variation of study design among the included studies. Subgroup analyses were performed by province, study design, sex and study period. Heterogeneity tests were determined using the Q-test ($P < 0.10$) and $I^2$ statistic ($> 75\%$) [13]. Potential publication bias was assessed by the funnel plots and Begg and Mazumdar rank correlation ($P < 0.05$). The one-study-removed sensitivity analysis was performed to determine the possible causes of heterogeneity between the studies.

Results
Characteristics of the included studies
A total of 108 articles were identified after screening for relevancy and duplicates (Fig. 1). Table 1 shows a detailed description of the included studies in the systematic review and meta-analysis [10–12, 14–123]. All included studies were published between 1999 and 2019 and together comprised > 808,505 participants. Of the 108 articles, there were 172 studies by sex, 95 studies by regions, and 107 studies by study type (Table 2).

Pooled prevalence of hyperuricemia
The pooled estimate of prevalence in the general population was 0.174 (95%CI: 0.158–0.191) (Fig. 2), which suggested that 17.4% of the population in mainland China had hyperuricemia.

Subgroup analysis
The prevalence of hyperuricemia was analysed in subgroups, which were categorised according to the following categories: provinces/municipalities/autonomous regions, regions (northeast, northwest, north, southwest, south central and east), sex, study type and year.

The pooled prevalence of hyperuricemia by regions ranged from 15.5 to 24.6%. The pooled prevalence in Northeast region was the highest (24.6%), followed by South Central (20.7%), East (17.3%), North (17.4%), Southwest (15.8%), and Northwest (15.5%) (Table 2). In terms of gender distribution, the pooled prevalence of hyperuricemia in males was significantly higher than
| No. | Study | Study type | Provinces (cities)/municipalities/autonomous regions | Region | Age (years) | Case | Sample size | Prevalence (%) | Diagnostic cut-offs | Gender |
|-----|--------|------------|-------------------------------------------------|--------|------------|------|-------------|-----------------|---------------------|--------|
| 1   | Ma, Chen & Li (1999) [14] | CS | Guangdong | South Central | 55–82 | 452 | 2041 | 22.1 | >420 μmol/L. | Both |
|     |        |            |        |              |       | 364  | 1696 | 21.5 | >420 μmol/L. | Male |
|     |        |            |        |              |       | 88   | 345  | 25.5 | >420 μmol/L. | Female |
| 2   | Shao et al. (2003) [15] | CS | Nanjing | East | ≥18 | 1038 | 7778 | 13.3 | NS | Both |
|     |        |            |        |              |       | 688  | 3790 | 17.6 | ≥417 μmol/L. | Male |
|     |        |            |        |              |       | 370  | 3988 | 9.3  | ≥357 μmol/L. | Female |
| 3   | Chen et al. (2004) [16] | CC | Anhui | East | 45 ± 12 | 105  | 430  | 24.4 | NS | Both |
|     |        |            |        |              |       | 70   | 227  | 30.8 | >420 μmol/L. | Male |
|     |        |            |        |              |       | 35   | 203  | 17.2 | >360 μmol/L. | Female |
| 4   | Wu et al. (2005) [17] | CS | Guangzhou, Guangdong | South Central | > 55 | 197 | 642  | 30.7 | NS | Both |
|     |        |            |        |              |       | 46   | 152  | 30.3 | >420 μmol/L. | Male |
|     |        |            |        |              |       | 151  | 490  | 30.8 | >350 μmol/L. | Female |
| 5   | Yang et al. (2005) [18] | CS | Shandong | East | 18–54 | 537 | 8640 | 6.2 | NS | Both |
|     |        |            |        |              |       | 459 | 6289 | 7.3 | ≥416 μmol/L. | Male |
|     |        |            |        |              |       | 78   | 2351 | 3.3  | ≥357 μmol/L. | Female |
| 6   | Wang et al. (2006) [19] | CS | Shandong | East | 20–80 | 269 | 2605 | 10.3 | > 350 μmol/L. | Female |
| 7   | Li et al. (2008) [20] | CH | Chinaa | NAa | 45–54 | 10 | 274 | 3.6 | NS | Both |
|     |        |            |        |              |       | 5   | 90   | 5.6 | ≥416 μmol/L. | Male |
|     |        |            |        |              |       | 5   | 184  | 2.7 | ≥356 μmol/L. | Female |
|     |        |            |        |              | 55–64 | 18  | 307  | 5.9 | NS | Both |
|     |        |            |        |              |       | 13  | 138  | 9.4 | >416 μmol/L. | Male |
|     |        |            |        |              |       | 5   | 169  | 3.0 | ≥356 μmol/L. | Female |
|     |        |            |        |              | 65–74 | 21  | 229  | 9.2 | NS | Both |
|     |        |            |        |              |       | 12  | 116  | 10.3 | ≥416 μmol/L. | Male |
|     |        |            |        |              |       | 9   | 113  | 8.0 | ≥356 μmol/L. | Female |
| 8   | Fan et al. (2009) [118] | CS | Xinyang, Henan | South Central | 40–75 | 738 | 5235 | 14.1 | NS | Both |
|     |        |            |        |              |       | 379 | 1763 | 21.5 | ≥420 μmol/L. | Male |
|     |        |            |        |              |       | 354 | 3472 | 10.2 | ≥360 μmol/L. | Female |
| 9   | Lu et al. (2010) [21] | CS | Tianjin | North | 22–53 | 19 | 151 | 12.6 | ≥410 μmol/L. | Male |
| 10  | Yu et al. (2010) [22] | CS | Foshan, Guangdong | South Central | 20–88 | 1117 | 7403 | 15.1 | NS | Both |
|     |        |            |        |              |       | 714 | 3581 | 19.9 | ≥417 μmol/L. | Male |
|     |        |            |        |              |       | 403 | 3822 | 10.5 | ≥357 μmol/L. | Female |
| 11  | Yuan et al. (2011) [23] | CS | Guiyang | Southwest | > 60 | 399 | 2600 | 15.3 | ≥420 μmol/L. | Both |
|     |        |            |        |              |       | 227 | 1430 | 15.9 | NS | Male |
|     |        |            |        |              |       | 172 | 1170 | 14.7 | NS | Female |
| 12  | Zhang & Zhang (2011) [24] | CS | Chinaa | NAa | ≥18 | 427 | 5774 | 7.4 | NS | Both |
| 13  | Guo et al. (2012) [25] | CS | Taiyuan, Shanxi | Northwest | 23–87 | 371 | 4228 | 8.8 | NS | Both |
|     |        |            |        |              |       | 249 | 1308 | 19.0 | ≥420 μmol/L. | Male |
|     |        |            |        |              |       | 122 | 2920 | 4.2  | ≥420 μmol/L. | Female |
| 14  | Wang et al. (2012) [26] | CS | Yinchuan, Ningxia | Northwest | ≥18 | 926 | 5921 | 15.6 | NS | Both |
### Table 1

Characteristics of the included studies in the systematic review and meta-analysis (Continued)

| No. | Study | Study type | Provinces (cities)/municipalities/autonomous regions | Region | Age (years) | Case | Sample size | Prevalence (%) | Diagnostic cut-offs | Gender |
|-----|-------|------------|---------------------------------------------------|--------|-------------|------|-------------|-----------------|----------------------|--------|
| 15  | Chen et al. (2013) [27] | CS | Guangxi | South Central | ≥ 18 | 3152 | 7322 | 18.5 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 16  | Duan et al. (2013) [28] | CS | Xinjiang | Northwest | ≥ 18 | 1635 | 8717 | 18.8 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 17  | Li et al. (2013) [29] | CS | Quanzhou, Fujian | East | 40–80 | 1352 | 319 | 927 | 34.4 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 18  | Li & Cao (2013) [30] | CS | Karamay, Xinjiang | Northwest | ≥ 18 | 157 | 8717 | 30.9 | NS | Male |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 19  | Lv et al. (2013) [31] | CS | Yantai, Shandong | East | 31–78 | 162 | 508 | 38.7 | NS | Female |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 20  | Su et al. (2013) [32] | CS | Nanhai, Guangdong | South Central | 45–80 | 157 | 419 | 30.9 | NS | Male |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 21  | Wang et al. (2013) [33] | CS | Shanghai | East | 40–70 | 162 | 508 | 38.7 | NS | Female |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 22  | Zhang, Wu & Lv (2013) [34] | CS | Hebei | North | 21–95 | 162 | 508 | 38.7 | NS | Female |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 23  | Zhou & He (2013) [35] | CH | Shenyang, Liaoning | Northeast | 50–70 | 162 | 508 | 38.7 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 24  | Chen, Dai & Lin (2014) [36] | CS | Guangzhou, Guangdong | South Central | 45–75 | 162 | 508 | 38.7 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 25  | Cui et al. (2014) [37] | CS | Hebei | North | ≥ 20 | 162 | 508 | 38.7 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 26  | Li, Zhao, Gao (2014) [38] | CS | Yunnan | Southwest | 27–89 | 162 | 508 | 38.7 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 27  | Lin et al. (2014) [39] | CS | Guangdong | South Central | > 60 | 162 | 508 | 38.7 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 28  | Liu et al. (2014) [40] | CS | Jilin | Northeast | 38 ± 10 | 162 | 508 | 38.7 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
|     |       |           |         |         |       |      |       |    |       |       |
| 29  | Pan et al. (2014) [41] | CS | Jiangsu | East | 35–70 | 162 | 508 | 38.7 | NS | Both |
|     |       |           |         |         |       |      |       |    |       |       |
Table 1: Characteristics of the included studies in the systematic review and meta-analysis (Continued)

| No. | Study type | Study | Provinces (cities)/municipalities/autonomous regions | Region | Age (years)\(^c\) | Case size | Sample size | Prevalence (%) | Diagnostic cut-offs | Gender |
|-----|------------|-------|------------------------------------------------------|--------|-------------------|-----------|-------------|------------------|---------------------|--------|
| 30  | CS         | Song et al. (2014) [42] | Jiangxi | East | > 40 | 362 | 1349 | 26.8 | ≥420 μmol/L. | Male |
|     |            |       |           | | | 211 | 1773 | 11.9 | ≥380 μmol/L. | Female |
| 31  | CS         | Yong & Ye (2014) [43] | Hebei | North | ≥18–20 | 813 | 5269 | 15.4 | NS | Both |
|     |            |       |           | | | 769 | 2717 | 28.3 | >420 μmol/L. | Male |
|     |            |       |           | | | 44 | 2552 | 1.7 | >350 μmol/L. | Female |
| 32  | CS         | Zhu, Wang, Liu (2014) [44] | Xinjiang | Northwest | 20–93 | 1489 | 10,025 | 14.9 | NS | Both |
| 33  | CS         | Cao, Li & Yi (2015) [45] | Guangzhou, Guangdong | South Central | 20–80 | 290 | 988 | 29.4 | NS | Both |
|     |            |       |           | | | 264 | 601 | 43.9 | >420 μmol/L. | Male |
|     |            |       |           | | | 26 | 387 | 6.7 | >350 μmol/L. | Female |
| 34  | CS         | Li et al. (2015a) [46] | Gansu | Northwest | 48 ± 15 | 392 | 2364 | 16.6 | NS | Both |
|     |            |       |           | | | 256 | 1254 | 20.4 | >420 μmol/L. | Male |
|     |            |       |           | | | 136 | 1110 | 12.3 | >360 μmol/L. | Female |
| 35  | CS         | Li et al. (2015b) [47] | Guangxi | South Central | ≥20 | 14,181 | 51,206 | 27.7 | NS | Both |
|     |            |       |           | | | 10,722 | 27,144 | 39.5 | >417 μmol/L. | Male |
|     |            |       |           | | | 3459 | 24,062 | 14.4 | ≥357 μmol/L. | Female |
| 36  | CS         | Li et al. (2015c) [48] | Dongguan, Guangdong | South Central | ≥18 | 519 | 1375 | 37.6 | NS | Both |
|     |            |       |           | | | 366 | 657 | 26.6 | >420 μmol/L. | Male |
|     |            |       |           | | | 153 | 718 | 11.1 | >350 μmol/L. | Female |
| 37  | CS         | Liu et al. (2015) [11] | Guangzhou, Guangdong | South Central | ≥18 | 1334 | 4237 | 31.5 | NS | Both |
|     |            |       |           | | | 859 | 2257 | 38.1 | >420 μmol/L. | Male |
|     |            |       |           | | | 475 | 1980 | 24.0 | >360 μmol/L. | Female |
| 38  | CS         | Lu (2015) [49] | Shanghai | East | 65–85 | 220 | 1128 | 19.5 | NS | Both |
|     |            |       |           | | | 165 | 607 | 27.2 | >420 μmol/L. | Male |
|     |            |       |           | | | 63 | 511 | 12.3 | >350 μmol/L. | Female |
| 39  | CS         | Zhao (2015) [50] | China\(^a\) | NA\(^b\) | 20–60 | 4616 | 12,650 | 36.5 | NS | Both |
| 40  | CS         | Zhou et al. (2015a) [51] | Sichuan | Southwest | ≥18 | 182 | 972 | 18.7 | NS | Both |
|     |            |       |           | | | 123 | 452 | 27.2 | ≥420 μmol/L. | Male |
|     |            |       |           | | | 59 | 520 | 11.3 | ≥360 μmol/L. | Female |
| 41  | CS         | Zhou et al. (2015b) [52] | Henan | South Central | 20–60 | 1196 | 4916 | 24.3 | NS | Both |
|     |            |       |           | | | 1128 | 4290 | 26.3 | ≥420 μmol/L. | Male |
|     |            |       |           | | | 68 | 626 | 10.9 | ≥357 μmol/L. | Female |
| 42  | CS         | Guli, He & Zhang (2016) [53] | Gansu | Northwest | 20–80 | 780 | 6400 | 12.2 | >420 μmol/L. | Both |
| 43  | CS         | Chen & Xing (2016) [54] | Beijing | North | 25–82 | 151 | 868 | 17.4 | ≥416 μmol/L. | Male |
| 44  | CS         | Chen & Zhou (2016) [55] | Zhejiang | East | > 60 | 691 | 4160 | 16.6 | NS | Both |
|     |            |       |           | | | 393 | 2182 | 18.0 | >420 μmol/L. | Male |
|     |            |       |           | | | 298 | 1978 | 15.1 | >360 μmol/L. | Female |
| 45  | CS         | Fan et al. (2016) | Shanghai | East | ≥18 | 5413 | 27,615 | 19.6 | NS | Both |
| No. | Study | Study type | Provinces (cities)/municipalities/autonomous regions | Region | Age (years) | Case size | Sample size | Prevalence (%) | Diagnostic cut-offs | Gender |
|-----|-------|------------|---------------------------------------------------|--------|------------|-----------|------------|----------------|---------------------|--------|
| 46  | Feng et al. (2016) [57] | CS | Jiangsu East | 18–93 | 3993 | 14,104 | 28.3 | >420 μmol/L | Male |
| 47  | Li (2016) [58] | CS | Tianjin North | ≥18 | 10,344 | 77,787 | 13.3 | NS | Both |
| 48  | Li et al. (2016) [59] | CS | Chongqing Southwest | 39 | 1596 | 9653 | 83.9 | NS | Both |
| 49  | Liu et al. (2016) [60] | CS | Shanghai East | ≥18 | 8100 | 9653 | 81.2 | >420 μmol/L | Male |
| 50  | Liu, Zhou & Yin (2016) [61] | CS | Yunnan Southwest | 32–60 | 131 | 390 | 33.6 | NS | Both |
| 51  | Lu (2016) [62] | CS | Xinjiang Northwest | ≥60 | 233 | 986 | 23.6 | NS | Both |
| 52  | Pu et al. (2016) [63] | CS | Chinaa | 20–91 | 1078 | 11,967 | 9.0 | NS | Both |
| 53  | Wang (2016) [64] | CS | Hubei South Central | 18–22 | 358 | 4333 | 8.3 | NS | Both |
| 54  | Xie et al. (2016) [65] | CS | Beijing; Tangshan and Zhangjiakou, Hebei | North | 18–60 | 632 | 2782 | 22.7 | NS | Both |
| 55  | Yang, Wang & Wang (2016) [66] | CS | Tianjin North | 18–93 | 1165 | 8968 | 13.0 | NS | Both |
| 56  | Zhang (2016) [67] | CS | Chinaa | NAa | 198 | 794 | 24.9 | >420 μmol/L | Male |
| 57  | Zhao et al. (2016a) [68] | CS | Lanzhou, Gansu Northwest | ≥45 | 37 | 175 | 21.1 | NS | Both |
| 58  | Zhao et al. (2016b) [69] | CS | Beijing North | 20 ± 3 | 1716 | 6400 | 26.8 | NS | Both |
| 59  | Zhao et al. (2016c) [70] | CS | Beijing North | 20–89 | 1086 | 6690 | 16.2 | NS | Both |
| 60  | Feng et al. (2017) [71] | CS | Beijing North range | >18 | 2257 | 12,335 | 18.3 | NS | Both |
| 61  | Guo et al. (2017) [72] | CS | Heilongjiang Northeast | 20–59 | 419 | 1477 | 28.4 | >420 μmol/L | Male |
| 62  | He (2017) [73] | CS | Dalian, Liaoning Northeast | 22–91 | 358 | 2002 | 17.9 | NS | Both |
| No. | Study | Study type | Provinces (cities)/municipalities/autonomous regions | Region | Age (years)* | Case size | Sample size | Prevalence (%) | Diagnostic cut-offs | Gender |
|-----|-------|------------|--------------------------------------------------|--------|--------------|----------|-------------|-----------------|---------------------|--------|
| 63  | Li et al. (2017) [74] | CC | Urumqi, Xinjiang | Northwest | 18–78 | 221 | 1644 | 24.1 | >420 μmol/L | Male |
| 64  | Li, Zhou & Pan (2017) [75] | CS | Guangdong | South Central | 22–90 | 314 | 3071 | 10.2 | NS | Both |
| 65  | Lin et al. (2017) [76] | CS | Yunnan | South Central | 18–84 | 196 | 1682 | 11.7 | ≥417 μmol/L | Male |
| 66  | Liu et al. (2017a) [77] | CS | Shanghai | East | ≥18 | 148 | 908 | 16.3 | NS | Both |
| 67  | Liu et al. (2017b) [78] | CS | Shanghai | East | 20–80 | 1444 | 9294 | 15.5 | NS | Both |
| 68  | Liu et al. (2017c) [79] | CS | Hunan | South Central | 20–80 | 1435 | 5356 | 26.8 | >420 μmol/L | Female |
| 69  | Liu, Yan & Li (2017) [80] | CS | Hebei | North | ≥18 | 698 | 6045 | 11.5 | >416 μmol/L | Male |
| 70  | Liu & Yang (2017) [81] | CC | Beijing | North | 21–67 | 204 | 1799 | 11.3 | >357 μmol/L | Female |
| 71  | Min (2017) | CS | Shenyang, Liaoning | Northeast | | | | | | Both |
| 72  | Pan & Jiang (2017) [82] | CS | Fuzhou, Fujian | East | 75 | 210 | 744 | 28.2 | >420 μmol/L | Male |
| 73  | Wang & Bai (2017) [83] | CS | Ningxia | Northwest | 22–60 | 121 | 1012 | 12.0 | >420 μmol/L | Female |
| 74  | Wang & Bao (2017) [84] | CS | Shanghai | East | 60–93 | 454 | 2426 | 18.7 | >420 μmol/L | Male |
| 75  | Xie et al. (2017) [85] | CS | Guangdong | South Central | 35–75 | 279 | 2587 | 10.8 | >417 μmol/L | Male |
| 76  | Yu & Jie (2017) [86] | CS | Shandong | East | 21–76 | 1191 | 10,743 | 11.1 | ≥430 μmol/L | Male |
| 77  | Zhang (2017a) [87] | CS | Liaoning | Northeast | 21–50 | 121 | 500 | 24.2 | NS | Both |
| 78  | Zhang (2017b) [88] | CS | Anhui | East | 25–87 | 19 | 230 | 8.3 | >420 μmol/L | Both |
| No. | Study | Study type | Provinces (cities)/municipalities/autonomous regions | Region | Age (years) | Case Sample size | Prevalence (%) | Diagnostic cut-offs | Gender |
|-----|--------|------------|------------------------------------------------------|--------|-------------|-----------------|----------------|---------------------|--------|
| 79  | Zhang, Chen & Liu (2017) [89] | CS         | Zhuhai, Guangdong South Central | 18–75 | 590 1834 290 679 300 1155 | NS | Both |
| 80  | Zheng (2017) [90] | CS         | Chinaa NAa | 24 ± 6 | 432 1721 | >420 μmol/L | Male |
| 81  | Chen et al. (2018a) [91] | CS         | Liaoning, Heilonjiang, Shandong, Henan, Hunan, Jiangsu, Guizhou, Guangxi | NAa | 1435 8785 886 4110 549 4675 | 16.3 | Both |
| 82  | Chen et al. (2018b) [92] | CS         | Guangxi South Central | > 60 | 161 817 | >420 μmol/L | Both |
| 83  | Chen et al. (2018c) [93] | CS         | Guangdong South Central | ⩾ 18 | 328 981 | >420 μmol/L | Male |
| 84  | Chen et al. (2018d) [94] | CS         | Guangxi South Central | 65–96 | 241 1223 163 629 78 594 | 19.7 | Both |
| 85  | Fan, Mao & Chen (2018) [95] | CS         | Ningbo, Zhejiang East | ⩾45 | 750 3395 | >420 μmol/L | Both |
| 86  | He (2018) [96] | CS         | Henan South Central | 25–89 | 410 2193 305 1156 105 1037 | 18.7 | Both |
| 87  | Hu et al. (2018) [97] | CS         | Guangxi South Central | 20–70 | 1035 6241 755 3271 280 2970 | 16.6 | Both |
| 88  | Huang & Huang (2018) [98] | CS         | Guangzhou, Guangdong South Central | 51–82 | 55 338 49 289 6 49 | 16.3 | Both |
| 89  | Huang et al. (2018) [99] | CS         | Guizhou Southwest | 18–75 | 26, 341 143,687 280, 954 68,323 15, 387 20, 954 | 18.3 | Both |
| 90  | Li, Wang & Xu (2018) [100] | CS         | Beijing North | 18–80 | 255 1700 116 620 139 1080 | 15.0 | Both |
| 91  | Lin et al. (2018a) [101] | CS         | Fujian East | 18–63 | 666 2666 411 1251 255 1415 | 25.0 | Both |
| 92  | Lin et al. (2018b) [102] | CS         | Guangzhou, Guangdong South Central | ⩾18 | 1642 5603 1590 5281 53 322 | 29.3 | Both |
| 93  | Lu (2018a) [103] | CS         | Zhejiang East | 55 | 147 1200 93 597 54 603 | 12.3 | Both |
| 94  | Lu (2018b) [104] | CH         | Inner Mongolia North | ⩾35 | 383 2554 | >350 μmol/L | Both |
Table 1 Characteristics of the included studies in the systematic review and meta-analysis (Continued)

| No. | Study                        | Study type | Provinces (cities)/municipalities/autonomous regions | Region          | Age (years)$^a$ | Case   | Sample size | Prevalence (%) | Diagnostic cut-offs | Gender |
|-----|------------------------------|------------|------------------------------------------------------|----------------|-----------------|--------|-------------|-------------------|----------------------|--------|
| 95  | Su et al. (2018) [105]       | CS         | Zhejiang East range ≥18                              |                |                 | 694    | 3905        | 17.8              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 364    | 1797        | 20.3              | NS                   | Male   |
|     |                              |            |                                                      |                |                 | 330    | 2108        | 15.7              | NS                   | Female |
| 96  | Tuo et al. (2018) [106]      | CS         | Gansu Northwest 20–80                               |                |                 | 768    | 4263        | 18.0              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 432    | 1783        | 24.2              | ≥420 μmol/L          | Male   |
|     |                              |            |                                                      |                |                 | 336    | 2480        | 13.6              | ≥350 μmol/L          | Female |
| 97  | Wang et al. (2018a) [107]    | CS         | Beijing; Xi’an, Shaanxi; Harbin, Heilongjiang; Chengdu, Sichuan; Chongqing, Changsha, Hunan; Shanghai | NA$^b$         | ≥60              | 754    | 5351        | 14.1              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 304    | 2304        | 13.2              | ≥420 μmol/L          | Male   |
|     |                              |            |                                                      |                |                 | 450    | 3047        | 14.8              | ≥360 μmol/L          | Female |
| 98  | Wang et al. (2018b) [108]    | CS         | Liaoning; Heilongjiang; Jiangsu; Shandong; Henan; Hunan; Guangxi | NA$^b$         | ≥18              | 555    | 4111        | 13.5              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 361    | 1871        | 19.3              | >418 μmol/L          | Male   |
|     |                              |            |                                                      |                |                 | 194    | 2240        | 8.7               | >357 μmol/L          | Female |
| 99  | Wang & Ma (2018) [109]       | CS         | Liaoning Northeast 22–65                             |                |                 | 432    | 1481        | 29.2              | ≥420 μmol/L          | Male   |
| 100 | Yang et al. (2018) [110]     | CS         | China$^a$                                             | NA$^a$         | ≥18              | 3855   | 24,095      | 16.0              | NS                   | Both   |
| 101 | Yu et al. (2018) [111]       | CS         | Xinjiang Northwest 30–81                             |                |                 | 2648   | 14,426      | 18.4              | NS                   | Both   |
| 102 | Zhang et al. (2018) [112]    | CS         | Ningxia Northwest ≥18                                |                |                 | 3880   | 19,356      | 20.0              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 3180   | 12,115      | 26.2              | >420 μmol/L          | Male   |
|     |                              |            |                                                      |                |                 | 700    | 7241        | 9.7               | ≥350 μmol/L          | Female |
| 103 | Zhou et al. (2018) [113]     | CS         | Ningxia                                              |                | ≥35              | 279    | 1743        | 16.0              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 193    | 1044        | 18.5              | NS                   | Male   |
|     |                              |            |                                                      |                |                 | 86     | 699         | 12.3              | NS                   | Female |
| 104 | Hu, Zhao & Shang (2019) [114]| CS         | Tibet North 20–49                                   |                |                 | 170    | 1669        | 10.2              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 114    | 952         | 12.0              | NS                   | Male   |
|     |                              |            |                                                      |                |                 | 56     | 717         | 7.8               | NS                   | Female |
| 105 | Tian et al. (2019) [115]     | CS         | Beijing North 18–97                                  |                |                 | 10,795 | 52,673      | 20.5              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 8524   | 27,419      | 31.1              | NS                   | Male   |
|     |                              |            |                                                      |                |                 | 2271   | 25,254      | 9.0               | NS                   | Female |
| 106 | Wang et al. (2019) [123]     | CC         | China$^a$                                             | NA$^a$         | ≥18              | 2977   | 22,983      | 13.0              | NS                   | Both   |
|     |                              |            |                                                      |                |                 | 1999   | 10,787      | 18.5              | NS                   | Male   |
females (22.7% (95% CI: 20.2–25.4%) vs. 11.0% (95% CI: 9.6–12.6%)) (P < 0.001) (Table 2). For the study types, there was no difference in prevalence (P = 0.062) and the range of prevalence of hyperuricemia was from 11.9 to 18.1%.

Figure 3 shows the prevalence of hyperuricemia in mainland China by different provinces, municipalities and autonomous regions. Shanghai, Jiangxi, Jilin, Liaoning, Fujian, Guangdong and Guangxi reported a high prevalence of hyperuricemia ≥20%, while Hubei, Shanxi and Shanxi had a low prevalence of hyperuricemia < 10%. The remaining provinces, municipalities and autonomous regions had a moderate prevalence of hyperuricemia (10–19%). For males, five provinces (i.e. Anhui, Guangdong, Guangxi, Jilin, and Fujian) reported a very high prevalence of hyperuricemia ≥30% and the remaining provinces, municipalities and autonomous regions reported a moderate-to-high prevalence of hyperuricemia ≥10–29%. For females, majority of the provinces, municipalities and autonomous regions reported a low-to-moderate prevalence of hyperuricemia (0–19%), while Guizhou was the only province with high prevalence of hyperuricemia (≥20%).

In the general population, there was a downward trend in the prevalence of hyperuricemia from 1995 to 1999 (22.1%) to 2015–2019 (18.6%). Similar downwards trends in the prevalence of hyperuricemia for males and females were also observed.

Analysis of heterogeneity and publication bias
There was a significant heterogeneity in the included studies (I^2 = 99.735%, P < 0.001). However, no indications of publication bias were observed as indicated by a symmetrical funnel plot (Fig. 4) and Begg and

| Table 1 | Characteristics of the included studies in the systematic review and meta-analysis (Continued) |
| --- | --- |
| No. | Study | Study type | Provinces (cities)/municipalities/autonomous regions | Region | Age (years) | Case | Sample size | Prevalence (%) | Diagnostic cut-offs | Gender |
| 107 | Yang (2019) [116] | CH | Guilin, Guangxi | South Central | 20–68 | 160 | 1545 | 10.4 | NS | Female |
| 108 | Yu et al. (2019) [117] | CS | Shenyang, Liaoning | Northeast | ≥18 | 7705 | 14,323 | 53.7 | NS | Both |

CS Cross-sectional, CC Case control, CH Cohort study, NA Not applicable, NS Not stated

No specific provinces were reported

More than one region was involved

Mean used unless range reported

| Table 2 | Prevalence of hyperuricemia by subgroups in mainland China |
| --- | --- |
| Subgroups | No. of studies | Pooled | 95% CI | I² (%) | P-value |
| Region | | | | | |
| East | 23 | 0.173 | 0.139–0.213 | 99.844 | < 0.001 |
| North | 16 | 0.174 | 0.134–0.222 | 99.241 | < 0.001 |
| Northeast | 6 | 0.246 | 0.163–0.353 | 99.873 | < 0.001 |
| Northwest | 18 | 0.155 | 0.121–0.197 | 97.447 | < 0.001 |
| South Central | 26 | 0.207 | 0.170–0.249 | 99.373 | < 0.001 |
| Southwest | 6 | 0.158 | 0.102–0.236 | 99.779 | < 0.001 |
| Overall | 95 | 0.181 | 0.163–0.201 | 99.734 | 0.281 |
| Sex | | | | | |
| Females | 83 | 0.110 | 0.096–0.126 | 99.678 | < 0.001 |
| Males | 89 | 0.227 | 0.202–0.254 | 99.447 | < 0.001 |
| Overall | 172 | 0.163 | 0.149–0.178 | 99.613 | < 0.001 |
| Study type | | | | | |
| Cross-sectional | 94 | 0.181 | 0.164–0.200 | 99.261 | < 0.001 |
| Cohort | 9 | 0.119 | 0.082–0.169 | 95.073 | < 0.001 |
| Case control | 4 | 0.149 | 0.088–0.240 | 94.186 | < 0.001 |
| Overall | 107 | 0.174 | 0.158–0.191 | 99.735 | 0.062 |
Fig. 2 Forest plot of the pooled prevalence and 95% CI of hyperuricemia among the general population in mainland China
Mazumdar rank correlation ($P = 0.392$). The overall results remained unchanged as well after we performed a trim and fill method. Similarly, no publication bias was also reported for the subgroups analysis (Begg and Mazumdar rank correlation with a $P$-value > 0.05) and all funnel plots were symmetrical.

**Discussion**

We performed a comprehensive meta-analysis of 108 observational studies over two decades and covered 27 provinces, autonomous regions and municipalities in the mainland China. In our meta-analysis, the prevalence of hyperuricemia in the general population of mainland China was 17.4% (22.7% in males and 11.0% in females), which was within the range of reported global prevalence (ranging from 1 to 85%) [8].

Our pooled prevalence was higher than a meta-analysis reported by Liu et al. i.e. 13.3% (19.4% in males and 7.9% in females) [11]. Our prevalence was similar to some developing countries in Asia. In Thailand, the overall prevalence of hyperuricemia was 10.6% in the general population with 18.4 and 7.8% in males and females, respectively [124]. In Turkey, the overall prevalence of hyperuricemia was 12.1% and males had a higher prevalence than females (i.e. 19.0% vs. 5.8%) [125].

However, our results were lower than that reported in developed countries [122, 126]. In the United States, the prevalence of hyperuricemia was 21.2 and 21.6% in males and females, respectively [126]. In Japan, the prevalence of hyperuricemia in the general population was 25.8% (34.5 and 11.6% in males and females, respectively) [122]. The higher prevalence reported in developed countries was most likely due to rapid aging and urbanisation [126]. In addition, the prevalence of non-communicable disease and obesity has also increased in these developed countries [122, 126], which might have contributed to the higher prevalence of hyperuricemia. Therefore, we strongly recommend that the Chinese health authorities should introduce more effective public health policies measures including prevention of obesity.

![Fig. 3 Prevalence of hyperuricemia in mainland China according to different provinces, municipalities and autonomous regions](image-url)
programme and promotion of health lifestyles to reduce the prevalence of hyperuricemia in Chinese population.

Since China is a vast country characterised by distinct regions, the prevalence of hyperuricemia varies largely in different provinces and regions. Our results reported that the prevalence of hyperuricemia ranged from 15.8 to 24.6%, with the highest prevalence in the Northeast region. We postulated that the large variability in the prevalence might be caused by the difference in the economic development and sedentary lifestyle adopted in these regions and provinces. For example, those living in Guangxi, Guangdong, Fujian and Jiangxi, people would consume more meat, alcohol and seafood. These foods are rich in purine which can cause an increase in the production of uric acid in the body [127]. Shanghai is one of the most economically developed areas in China. Rapid economic growth has led to unhealthy lifestyles and dietary patterns in the Shanghai population. In addition, an increased inactivity at work has also contributed to a higher prevalence of hyperuricemia [128]. In Jilin and Liaoning, we also reported a high prevalence of hyperuricemia (20–29%), which could be due to the high consumption of alcohol intake, particularly beer and liquor [129]. However, the specific reasons why these regions had a high prevalence require further research. In addition, with these results, the management of hyperuricemia (including routine health check-ups and serum uric acid screening tests) in these regions can be better implemented and improved by the health authorities. Nutrition education and lifestyle interventions can also be developed and specifically targeted to the high risk regions with proper healthcare resources by the health authorities. This is because if hyperuricemia is not well managed and prevented especially in regions with high prevalence, it can induce several medical complication including chronic failure and gout, which increases the cost of medical care [2].

In addition, we reported that males had a significantly higher prevalence of hyperuricemia than females (22.7% vs. 11.0%). Such a difference might be due to the sex hormones [130]. Serum uric acid level is generally higher in males than females. This is because there is an increase renal urate clearance by estrogen in women [129]. Our findings were consistent with the results reported in several countries from Asia and the Asia Pacific region including Nepal [131], Thailand [132], Turkey [125], Saudi Arabia [133], Seychelles [134], Japan [122] and New Zealand [135].

Our study also reported an increasing prevalence of hyperuricemia over time in males and females. We speculated that factors including aging population and obesity have contributed to the increase [126]. However, we also noticed different diagnostic cut-offs were used to diagnose hyperuricemia. It will be helpful to compare these different cut-offs in the same population in order to understand their validity in diagnosing hyperuricemia.

Our meta-analysis has several strengths. Firstly, to our knowledge, our study is the most comprehensive study among the general population in mainland China. Unlike the previous two meta-analyses [10, 11], our sample size (> 808,505 participants) and number of eligible articles (n = 108) were larger; and we included analyses on differences across regions, provinces, sex and study periods. Secondly, our pooled data covered all the six regions in China. In addition, all the provinces, municipalities and autonomous regions were also included, except for Qinghai, Chongqing, Hong Kong, Macao and Hainan. Thirdly, the authors who were involved in the data extraction and interpretation were proficient in the Chinese language. However, our study also suffered from a
few limitations. Most of the included articles were cross-sectional studies. Since the definition of hyperuricemia varied according to the diagnostic cut-offs used by different studies, this factor should also be taken into consideration when interpreting these results. There was also a large heterogeneity in the quality of the articles, although no indications of publication bias were reported. We also did not make a clear distinction between urban and rural areas. Therefore, future studies with larger populations should consider investigating if health literacy, health status, sociodemographics and physical activity level play an important factor in the prevention and management of hyperuricemia, especially in adolescents, pregnant women and older adults with lower socioeconomic status [136].

Conclusions

Hyperuricemia has become an important public health problem in mainland China, particularly among males. Special attention should be paid to the residents in geographical regions with high prevalence of hyperuricemia. In addition, our study was the first comprehensive study to investigate the overall prevalence of hyperuricemia in mainland China covering the six regions. Our study also underline the importance of having more large population-based intervention studies to tackle the increasing problem of hyperuricemia, particularly the vulnerable groups in mainland China. Future studies should investigate the association between the prevalence of hyperuricemia and its risk factors such as geographical region, economic level and sex in order to develop public health policies for tackling the issue.

Abbreviations

CMA: Comprehensive Meta-Analysis; CVD: Cardiovascular disease; SSTI: Skin and Soft Tissue Infection; SUTI: Sexually Transmitted Infection; NOS: Newcastle-Ottawa Scale; CI: Confidence intervals

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Authors’ contributions

Conceptualization: ZFM & JH. Methodology: JH, ZFM, YZ, ZW, YL, HZ, AC & YYL. Formal analysis: JH, ZFM, YZ, YL, HZ & AC. Roles/Writing - original draft: JH & ZFM. Writing - review & editing: JH, ZFM, YZ, ZW, YL, HZ, AC & YYL. All authors read and approved the final manuscript.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

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Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interest.

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