Bibliometric analysis of researches on traditional Chinese medicine for coronavirus disease 2019 (COVID-19)

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Abstract:

**Background:** The coronavirus disease 2019 (COVID-19) has caused a worldwide pandemic, and traditional Chinese medicine (TCM) has played an important role in response. We aimed to analyze the published literature on TCM for COVID-19, and provide reference for later research.

**Methods:** This study searched the CBM, CNKI, PubMed, and EMBASE from its establishment to March 11, 2020. VOSviewer 1.6.11 and gCLUTO 2.0 software were used to visually analyze the included studies.

**Results:** A total of 309 studies were included, including 61 journals, 1441 authors, 277 institutions, and 27 provinces. Cooperation among regions was closer, but the teamwork of institutions and authors were more likely to be confined to the same region. Among the authors with frequency
greater than two (65 authors), only 19 authors who had connection with others. More than 70% (358/491) of keywords only presented once, and 20 keywords shown more than 10 times. Five research topics were identified: Data mining method based analysis on the medication law of Chinese medicine in prevention and management of COVID-19, exploration of active compounds of Chinese medicine for COVID-19 treatment based on network pharmacology and molecular docking, expert consensus and interpretation of COVID-19 treatment, research on the etiology and pathogenesis of COVID-19, and clinical research of TCM for COVID-19 treatment.

**Conclusion:** The research hotspots were scattered, and the collaboration between authors and institutions needed to be further strengthened. To improve the quality and efficiency of research output, the integration of scientific research and resources, as well as scientific collaboration is needed.

**Keywords:** COVID-19; Traditional Chinese medicine; Bibliometrics; Visual analysis

1. **Introduction**

During the outbreak of the coronavirus disease 2019 (COVID-19) response, the application of traditional Chinese medicine (TCM) in
disease prevention and treatment has achieved profound effects. Integrated traditional Chinese medicine (ITCM) has played a pivotal role in improving and alleviating clinical symptoms. In the Guideline of Diagnosis and Treatment of COVID-19 (7th Edition), a number of TCM prescriptions and proprietary Chinese medicines were recommended for use in patients in clinical observation and severe and critically-ill patients. Researchers have continuously deepened their exploration into the etiology, pathogenesis, treatment principles, and treatment experience as well as published a large number of studies. However, with the increasing demand for comprehensive evidence, it is necessary to comb and summarize the published studies.

In order to analyze the published studies on TCM for COVID-19, bibliometric analysis is used, which is a quantitative analysis combining mathematics and statistics, focusing on the bibliometric characteristics of research in a particular field, and helping investigators grasp the development priorities and trends in the field and guiding their follow-up work. Bibliometric analysis was already used in the field of TCM to explore the research trends and reveal hot topics.

In this study, the published journals, authors, provinces, institutions and keywords of published studies on prevention and treatment of COVID-19 by TCM in China were analyzed, so as to provide intuitive basis and reference for the later research.
2. Methods

2.1 Data source and collection

Search strategies were performed in the Chinese Biomedical Database (CBM), China National Knowledge Infrastructure (CNKI), PubMed, and EMBASE up to 11th March 2020 by using keywords “2019-nCoV”, “SARS-CoV-2”, “NCP”, “COVID-19”, “new coronavirus pneumonia”, “coronavirus disease 2019”, “traditional Chinese medicine”, and “integrated traditional Chinese and Western medicine”.

2.2 Inclusion and exclusion criteria and literature selection

We included studies on TCM for COVID-19, and excluded duplicate publications, conference abstracts, and news reports. Independently, two reviewers evaluated the title and abstract, and a third reviewer evaluated the discrepant results.

2.3 Data analysis and Visualization

VOSviewer 1.6.11 (Leiden University, Leiden, Netherlands) was used to extract the journals, authors, provinces, and institutions of included studies, and generated network maps for them as well as cluster analysis. The nodes in network map represented the number of publications or frequency, and the links between nodes represented relationships such as collaboration or co-occurrence. Different colors of nodes represented different clusters. We also generated a density map of main keywords, in which the brightness of the color was positively correlated with the
frequency of keywords.

Bibliographic information co-occurrence mining system (BICOMS) and gCLUTO 2.0 were used to conduct the cluster analysis of main keywords and design a visual surface graph. In the visual surface graph, the synthesized Gaussian curves were added together to form a visual hill map. Each hill was mainly used as a rough estimate of the internal data distribution of each cluster, where the height of the hill was proportional to the intra-class similarity, the volume was proportional to the number of objects contained in the cluster, the color of the hill is related to the internal standard deviation of the cluster (the darker the color, the smaller the deviation), and only the color of the summit made sense. We also summarized the research topic based on the high-frequency words and source articles.
3. Results

3.1 Search results and journals

A total of 344 publications were retrieved, of which 329 from CNKI and CBM as well as 15 from PubMed and EMBASE. We excluded 35 publications according to the exclusion criteria. Finally, we included 309 studies, published in 61 journals. The proportion of journals that published more than 4 studies and only one study were 34.4% (21/61) and 39.3% (24/61), respectively. There were four journals of the top ten productive journals saved in Chinese Science Citation Database (CSCD) (Table 1), and the top three productive journals were Journal of Traditional Chinese Medicine (29/309, 9.4%), World Chinese Medicine (27/309, 8.7%), and Chinese Traditional and Herbal Drugs (26/309, 8.4%).

3.2 Provinces and institutions

Twenty-seven provinces and municipalities in China were included in studies on TCM for COVID-19 (Fig 1A), and we generated a network map of the included provinces and municipalities (Fig. 1B), except for Chongqing and the Xinjiang on account of no cooperation with other provinces. As shown in Fig. 1B, the map contained 25 nodes and 176 links. The cooperation among the provinces and municipalities was relatively close, and Beijing (104/309, 33.7%) was the biggest nodes which closely linked to Hubei, Tianjin, Hunan, and many other provinces.
Two hundred and seventy-seven institutions contributed to the publications on TCM for COVID-19, and 187 of them participated in only one study respectively. Institutions that published more than six studies were listed in Table 2, containing ten universities, ten hospitals and one pharmaceutical firm. Network map of institutions with frequency greater than two was shown in Fig. 2, which contained 51 nodes and 11 clusters. The three biggest nodes were Beijing University of Chinese Medicine (37/309, 12.0%), China Academy of Chinese Medical Science (30/309, 9.7%), and Tianjin University of Traditional Chinese Medicine (17/309, 5.5%). The largest cluster (#1) was consisted of China Academy of Chinese Medical Science, Beijing Capital Medical University, and hospitals in Hubei provinces, and the second largest cluster (#2) was mainly consisted of hospitals and universities in the Yangtze river delta, such as Jiangsu province hospital, Longhua Hospital, Shanghai University of Traditional Chinese Medicine. The 10 hospitals were all affiliated hospitals of universities and connected tightly with their universities. For example, the link between Dongzhimen hospital of Beijing University of Chinese Medicine and Beijing University of Chinese Medicine was larger than others, and the same went for China Academy of Chinese Medical Science and its affiliated hospital, Xiyuan hospital of China Academy of Chinese Medical Science.

3.3 Authors
In total, 1441 authors have engaged in relevant research on TCM for COVID-19. Of them, 1224 authors (84.9%) published one study, and 13 authors (0.9%) participated in more than four studies. We plotted the network map of authors with frequency greater than two (65 authors). Fig. 3 only contained 19 authors who had connection with others, and four clusters. On the left side of network map was the research team of Longhua Hospital, Shanghai University of Traditional Chinese Medicine (#2, five authors); cluster on the center of the map was the biggest cluster contained six authors from Tianjin University of Traditional Chinese Medicine (#1), and Yu CQ was an important node connected cluster #1 and cluster #2; the blue cluster (#3) was consisted of authors from Beijing, Hubei and Tianjin, and shown close links with research team of Tianjin University of Traditional Chinese Medicine. Wang YG was the vital node who related cluster #3 to cluster #4 which composed of authors from China Academy of Chinese Medical Science and Hubei Provincial Hospital of Traditional Chinese Medicine.

3.4 Keywords

Four hundred and ninety-one keywords were extracted from the included studies. There were 358 keywords only presented once, and 20 keywords shown more than 10 times (Table 3).

3.4.1 Density map of main keywords

Density map was drawn for the keywords with frequency greater than
four (Fig. 4). Forty-three nodes were shown in the map, and the brightest two were COVID-19 and SARS-CoV-2, located in the center of the map as well, and surrounded by TCM, cold dampness pestilence, prevention and control, treatment, pneumonia, severe illness, etc. The edge of the map was relatively dark, containing clinical research, angiotensin converting enzyme 2, data mining, five elements and six pathogens, TCM ancient books, etc.

3.4.2 Cluster analysis of main keywords

We conducted a cluster analysis of keywords with frequency more than six, and generated a visual hill map (Supplement 1) which contained five themes on TCM for COVID-19. Their related parameters were presented in Table 4.

Theme 0 (hill volume: the smallest, hill height: the second, peak color: yellow): Analysis of the law of Chinese medicine in the prevention and treatment of COVID-19 based on data mining. There has been a number of studies, consensus, and guidelines for COVID-19 prevention and control that were published, so it is necessary to use cluster analysis, complex network analysis and other methods to analyze the regularity of TCM prescriptions for the prevention and treatment of COVID-19 15-17.

Theme 1 (hill volume: the fourth, hill height: the highest, peak color: darkest red): Active compounds of TCM in the treatment of COVID-19 based on network pharmacology and molecular docking method. Through
analysis the chemical constituents, action targets, and signal pathways of TCM prescription in the treatment of COVID-19, such as Yupingfeng powder, Qingfeidayuan powder, and Feiduqing powder, combined with molecular docking method connected active compounds with targets, the action mechanism of TCM prescription was explained at a molecular level which provided more evidence for the exploitation and utilization of TCM prescription \(^{18-20}\).

Theme 2 (hill volume: the third, hill height: the fourth, peak color: green): Guidelines, consensus and interpretation for prevention and treatment of COVID-19. Besides the Guideline of Diagnosis and Treatment of COVID-19 (7th Edition) published by State Administration of Traditional Chinese Medicine and National Health Commission, many local health commissions have published corresponding prevention and treatment protocol, and academic societies have developed clinical practice guidelines for front-line clinical staff. A number of experts and scholars have interpreted the guidelines, consensus and protocols in order to better serve for clinic treatment\(^4,5,21\).

Theme 3 (hill volume: the second, hill height: the third, peak color: green): The etiology and pathogenesis of COVID-19. From the perspective of TCM, many experts analyzed and explained the etiology and pathogenesis of covid-19, combined with the understanding of the ancient scholars of plague and typhoid fever, with the aim of gradually
unifying the knowledge of TCM, establishing TCM treatment standards, and improving the level of diagnosis and treatment 6,22,23.

Theme 4 (hill volume: the biggest, hill height: the lowest, peak color: red): Clinical research of TCM in the treatment of COVID-19. There has been 22 registered clinical research of TCM treatment, mainly focusing on TCM syndrome differentiation and the treatment with Chinese patent medicine combined with conventional therapy24. A number of hospitals and research institutions have carried out clinical research on TCM in the treatment of COVID-19 in the daily diagnosis and treatment, and evaluated their clinical value and advantages in the prevention and treatment of infectious diseases, in order to provided more evidence for TCM treatment25-27.
4. Discussion

This study analyzed the journals, authors, provinces, institutions and keywords of published studies on prevention and treatment of COVID-19 by TCM based on bibliometric and visualization methods, thus directly showed the current situation of studies on TCM for COVID-19 in China.

Journals with the number of publications of more than three and journals with only one publication made up about one-third each, which indicates that although there were some differences among journals involved, the publication of studies were relatively concentrated. Nearly half of the top 10 productive journals were included in CSCD which is an important database in China including more than 1,000 core journals in Chinese and English published in the fields of medicine, health engineering, mathematical physics, and so on. As for the provinces involved, more than 60% of provinces published over four studies, and close cooperation between the different provinces was found, which is conducive to accelerating the quantity and quality of scientific and technological achievements. However, the connection between institutions was not confined to the same province, which may greatly improve the efficiency of scientific research by timely sharing of information to other regions, thus promoting researches of COVID-19. However, geographical distance is still the main factor affecting regional scientific research cooperation, and researchers from various provinces
are more inclined to seek cooperation within the region. Authors in the same area were naturally connected closer, and the connection between two research teams was mainly through one or two key authors. Hence, cooperation between provinces still needs to be strengthened. Among the involved institutions, affiliated hospitals of universities occupied a larger quantity and was closely associated with the universities, which showed the unique position of university affiliated hospitals in medical treatment, teaching and scientific researches.

Among all the keywords, more than 70% of keywords only presented once, which indicated that the focuses of the studies were relatively scattered and wide. Keywords located in the center of network map were the core keywords in this field, while keywords on the edge of the map linked to the core keywords were the new hotspots which received more and more attention. New hotspots, such as data mining, clinical research, angiotensin converting enzyme 2, mainly focused on the analysis of active ingredients of TCM and the investigation of clinical effectiveness. Of the five themes from the visual hill map, active compounds of TCM in the treatment of COVID-19 based on network pharmacology and molecular docking method (theme 1) had the highest intra-class similarity, which may be related to the technology and method that are too technical and specialized. Clinical research of TCM in the treatment of COVID-19 (theme 4) had poor internal similarity because
some secondary studies based on clinical studies were also included for analysis which may affect the internal similarity to some extent.

There are several limitations. The included studies were retrieved from four databases only. However, these four databases are the major electronic databases which have met the needs of this study. Another limitation was that most of the included studies were in Chinese and English, so some studies in other language may not be included, which might cause publication bias to some extent.

In conclusion, the research hotspots in this field are still scattered and extensive, however, there will be more concentrated research directions as time goes by. In response to public health emergencies, the integration of scientific researches and resource as well as scientific collaboration should be strengthened in order to improve quality and efficiency of research output.

**Author contributions**

Conceptualization: KLY, JHZ, and JHT. Methodology: KLY, XYJ, JX, and JHT. Software: KLY, YG, and ML. Formal Analysis: KLY, XYJ, and JX. Writing – Original Draft: KLY, XYJ, and JHT. Writing – Review & Editing: KLY, XYJ, JHZ, and JHT. Visualization: KLY and YG. All authors read and approved the final manuscript.
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**Ethical statement**

This work did not require an ethical approval as it does not involve any human or animal research.

**Conflict of interest**

The authors declare no conflicts of interest.

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**Data availability**

The data will be made available upon request.

**Supplementary material**

Supplement 1. Visual hill map of main keywords, can be found in the online version, at _______.
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Figure titles and legends:

Fig. 1 Provinces involved studies on TCM for COVID-19
Legend: A for waterfall plot of provinces, B for network map of provinces

Fig. 2 Network map of 51 institutions with frequency greater than two
Legend: The nodes represent the number of frequency, the links between nodes represented collaboration, and different colors of nodes represent different clusters.

Fig. 3 Network map of 19 authors with frequency greater than two
Legend: The nodes represent the number of frequency, the links between nodes represent collaboration, and different colors of nodes represent different clusters.

Fig. 4 Density map of main keywords
Legend: The brightness of the color is positively correlated with the frequency of keywords.
Table 1 Top 10 productive journal of studies on traditional Chinese medicine for COVID-19

| Rank | Journals                                      | CSCD | IF   | Number of publications [n (%)] |
|------|-----------------------------------------------|------|------|-------------------------------|
| 1    | Journal of Traditional Chinese Medicine       | Yes  | 1.349| 29 (9.4%)                     |
| 2    | World Chinese Medicine                        | No   | 1.158| 27 (8.7%)                     |
| 3    | Chinese Traditional and Herbal Drugs          | Yes  | 2.048| 26 (8.4%)                     |
| 4    | Acta Chinese Medicine                         | No   | 0.820| 24 (7.8%)                     |
| 5    | Shanghai Journal of Traditional Chinese Medicine | No  | 0.821| 15 (4.9%)                     |
| 6    | China Journal of Chinese Materia Medica       | Yes  | 1.924| 14 (4.5%)                     |
| 7    | Beijing Journal of Traditional Chinese Medicine | No  | 0.612| 14 (4.5%)                     |
| 8    | Tianjin Journal of Traditional Chinese Medicine | No  | 0.656| 13 (4.2%)                     |
| 9    | Chinese Journal of Experimental Traditional Medical Formulae | Yes | 1.577| 11 (3.6%)                     |
| 10   | Clinical Journal of Chinese Medicine          | No   | 0.242| 9 (2.9%)                      |
Medicine

\(^a\text{CSCD = Chinese Science Citation Database}\)

\(^b\text{IF = Impact factor, available from https://www.cnki.net/}\)

Table 2 Institutions published more than six studies on traditional Chinese medicine for COVID-19
| Rank | Institutions                                                                                                           | Frequency   |
|------|------------------------------------------------------------------------------------------------------------------------|-------------|
| 1    | Beijing University of Chinese Medicine                                                                               | 37 (12.0%)  |
| 2    | China Academy of Chinese Medical Science                                                                             | 30 (9.7%)   |
| 3    | Tianjin University of Traditional Chinese Medicine                                                                  | 17 (5.5%)   |
| 4    | Beijing's Capital Medical University Traditional Chinese medicine Hospital                                           | 16 (5.2%)   |
| 5    | Henan University of traditional Chinese medicine                                                                    | 14 (4.5%)   |
| 6    | Shanghai University of Chinese Medicine                                                                             | 13 (4.2%)   |
| 7    | Dongzhimen Hospital, Beijing University of Chinese Medicine                                                         | 13 (4.2%)   |
| 8    | Hubei University of Chinese Medicine                                                                               | 12 (3.9%)   |
| 9    | Xiyuan hospital, China Academy of Chinese Medical Sciences                                                          | 11 (3.6%)   |
| 10   | Nanjing University of Chinese Medicine                                                                               | 11 (3.6%)   |
| 11   | Longhua Hospital, Shanghai University of Traditional Chinese Medicine                                                | 9 (2.9%)    |
| 12   | Hunan University of Chinese Medicine                                                                               | 9 (2.9%)    |
| 13   | Guang 'anmen Hospital, China Academy of Chinese Medical Sciences                                                    | 8 (2.6%)    |
| Rank | Keywords                                      | Frequency [n] |
|------|----------------------------------------------|---------------|
| 1    | COVID-19\(^a\)                               | 257(83.2\%)   |
| 2    | SARS-CoV-2\(^b\)                             | 73(23.6\%)    |
| 3    | TCM\(^c\)                                    | 57(18.4\%)    |
| 4    | plague                                       | 37(12.0\%)    |
| 5    | syndrome differentiation and treatment        | 30(9.7\%)     |

Table 3 Keywords with frequency $\geq$ 10
|   | Description                       |   |
|---|-----------------------------------|---|
| 6 | integrated Chinese and western medicines | 26(8.4%) |
| 7 | Chinese medicines                 | 24(7.8%) |
| 8 | prevention/control               | 24(7.8%) |
| 9 | treatment                         | 21(6.8%) |
| 10| pneumonia                         | 21(6.8%) |
| 11| pathogenesis                      | 20(6.5%) |
| 12| TCM prevention/control           | 19(6.1%) |
| 13| TCM syndrome/symptom             | 19(6.1%) |
| 14| TCM treatment                    | 16(5.2%) |
| 15| cold dampness pestilence         | 16(5.2%) |
| 16| network pharmacology             | 15(4.9%) |
| 17| consensus/guideline              | 12(3.9%) |
| 18| TCM theory                       | 11(3.6%) |
| 19| clinical research                | 11(3.6%) |
| 20| molecular docking                | 11(3.6%) |

a COVID-19 = Coronavirus Disease 2019

b SARS-Cov-2 = Severe Acute Respiratory Syndrome Coronavirus 2

c TCM = Traditional Chinese medicine

Table 4 Parameters of clusters
| Theme number | Theme                                                                 | Number of contained objects | Internal similarities | External similarities |
|-------------|----------------------------------------------------------------------|-----------------------------|-----------------------|------------------------|
| 0           | Analysis of the law of TCM in the prevention and treatment of COVID-19 based on data mining | 5                           | 0.678 (0.040)         | 0.443 (0.047)          |
| 1           | Active compounds of TCM in the treatment of COVID-19 based on network pharmacology and molecular docking method | 6                           | 0.688 (0.054)         | 0.453 (0.026)          |
| 2           | Guidelines, consensus and interpretation for prevention and treatment of COVID-19 | 7                           | 0.601 (0.025)         | 0.467 (0.041)          |
| 3           | The etiology and pathogenesis of COVID-19                           | 10                          | 0.602 (0.024)         | 0.473 (0.030)          |
| 4           | Clinical research of TCM in the treatment of COVID-19               | 11                          | 0.591 (0.051)         | 0.483 (0.072)          |

Values are expressed as mean (standard deviations). COVID-19= Coronavirus Disease 2019; TCM= Traditional Chinese medicine