A meta-analysis of clinical characteristics and mortality COVID-19 pneumonia

Shangxia Jiang

Lishui people's hospital

Yueming Wu (✉ yueming_wu@126.com)

Lishui people's Hospital

Tianzheng Lou

Lishui people's Hospital

Junlong Xu

Lishui people's Hospital

Yu Zhang

Lishui people's Hospital

Hu Chen

Lishui people's hospital

Hwei Xu

Lishui People's Hospital

Research article

Keywords: Novel coronavirus pneumonia, COVID-19, mortality, mechanical ventilation, clinical symptom, meta-analysis

Posted Date: April 3rd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-18723/v2>

License: This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Abstract: Objective To investigate the Corona Virus Disease 2019(COVID-19) clinical characteristics and mortality risk by pooling the open published data. Methods Studies relevant to COVID-19 published in Pubmed, China Wanfang database, ChinaXiv and medRxiv were systematic screened by using the text word of "COVID-19", 2019-nCoV, "SARS-CoV-2", "NCP". The mortality and clinical characteristic of the COVID-19 cases such as male/female ratio, mechanical ventilation ratio and top clinical symptom rate of the COVID-19 cases were pooled.

Results Ten clinical studies relevant to COVID-19 were identified by electronic searching the related databases. The combined mortality was 0.03(95%CI: 0.01-0.04) for COVID-19 cases by random effect model. The pooled female ratio of the COVID-19 cases from 10 published data was 0.41(95%CI:0.37-0.46). The pooled invasive and non-invasive ventilation ratio were 0.03(95%CI:0.01-0.05) and 0.06(95%CI:0.02-0.09) respectively for patients with COVID-19 pneumonia. The pooled clinical symptom rate of fever, cough, headache and fatigue were 0.80(95%CI:0.60-1.01), 0.12(95%CI:0.08-0.17), 0.68(95%CI:0.57-0.73) and 0.51(95%CI:0.36-0.67) respectively under random effect model.

Conclusion According to the present published data, male was more cline to susceptible to COVID-19 compared to female. The fever, cough and fatigue were the most common symptom of COVID-19 cases. About 10% of patients received invasive or noninvasive mechanical ventilation with the overall crude mortality of 3%.

Introduction

A novel coronavirus infection (COVID-19) was outbreak in Wuhan China at the end of 2019[1, 2]. Since 8 March, according to the reports of 31 provinces (autonomous regions, municipalities directly under the central government) and Xinjiang production and Construction Corps, there are 16145 confirmed cases in hospital (including 4492 severe cases), 61475 cumulative discharged cases, 3158 deaths, 80778 cumulative confirmed cases in China (<http://www.nhc.gov.cn/>). Furthermore, COVID-19 seems to have been outbreak all over the world with more than 100 countries had been discovered of COVID-19 cases[3, 4], Figure 1. Numerous studies about the clinical features of COVID-19 had been reported in the literature[5-7]. Most of the studies are retrospective clinical epidemiological analysis. However, the sample size of each individual study was small and the statistical power was limited. According to the individual study, the patients characteristics such as sex ratio, the proportion of severe patients requiring mechanical ventilation and the mortality were quite different in different studies. In order to further evaluate the clinical characteristics and mortality of COVID-19, we searched and summarized the published literature, and made the meta-analysis.

Materials And Methods

Publication searching

Studies relevant to COVID-19 were systematic electronic searched in Pubmed, China Wanfang database, ChinaXiv and medRxiv by using the text word of "COVID-19/ Corona Virus Disease 2019", 2019-nCoV, "SARS-CoV-2" and "NCP/Novel Coronavirus Pneumonia ". The references of the included studies were also screened in order to find the potential suitable publication.

Publication inclusion and exclusion criteria

For the initial identified studies, the publications were further screened for inclusion or exclusion by two reviewers (Shangxia Jiang and Yueming Wu) independently. The publication inclusion criteria were: 1) Studies relevant to human beings; 2) COVID-19 was diagnosed by nucleic acid assay; 3) The mortality, male/female ratio, cases received mechanical ventilation and cases of the typical clinical symptom were present in the original publications; 4) Studies were published in English or Chinese; Publication exclusion criteria were: 1) Studies about COVID-19 suspected case; 2) Not enough data such as mortality, symptom and et c can be extracted from the original publications; 3) Studies published in other language neither English nor Chinese.

Data extraction

The data of each included publication was extracted by two reviewers (Tianzheng Lou and Junlong Xu) independently and made cross check. In case of disagreement, the corresponding author was consulted for final decision. The extracted data and information were as follows: 1) The first author's name; 2) publication time; 3) source of literature; 4) number of patients in the original study; 5) source of patients (region); 6) sex ratio COVID-2019; 8) number of deaths; 9) number of patients with mechanical ventilation; 10) number of cases in each symptom.

Statistical analysis

STATA16.0 statistical software was applied for data analysis. Before pooling the results, the data was examined for statistical heterogeneity by I^2 test. If statistical heterogeneity existed ($I^2 > 50\%$, $p < 0.05$), the data was combined through random effect model, otherwise, the data was pooled by fixed effect mode. Two tails $p < 0.05$ was considered statistical difference.

Results

General quality of the included 10 studies

After systematic electronic searching the databases, 10 high quality studies relevant to clinical characteristics of COVID-19 pneumonia were finally identified, Figure 2. All of the included studies are from China mainland and mainly in Wuhan Hubei City. The sample size ranged from 13 to 44672. The general characteristics of the included 10 publications were showed in Table 1.

Pooled gender distribution

All the included 10 publications had reported the gender ratio. Due to significant statistical heterogeneity, the data was pooled by random effect model. The combined female ratio of the COVID-19 cases from 10 published data was 0.41(95%CI:0.37-0.46), Figure 3.

Pooled mortality

Eight studies reported the mortality data of the COVID-19 pneumonia patients. Significant statistical heterogeneity was found across the 8 studies ($I^2=76.4\%$, $P=0.001$). The pooled mortality was 0.03(95%CI: 0.01-0.04) under random effect model, Figure 4.

Pooled mechanical ventilation ratio

The mechanical ventilation data, including invasive and non-invasive ventilation, can be extracted in 6 original studies. Significant statistical heterogeneity was also found in both invasive ($I^2=74.5\%$, $P=0.001$) and non-invasive ($I^2=83.0\%$, $P=0.000$) ventilation. The pooled invasive and non-invasive ventilation ratio were 0.03(95%CI:0.01-0.05) and 0.06(95%CI:0.02-0.09) respectively for patients with COVID-19 pneumonia, Figure 5.

Pooled clinical symptom

The top clinical symptoms of COVID-19 pneumonia were fever, cough, headache and fatigue. The pooled clinical symptom rate of fever, cough, headache and fatigue were 0.80(95%CI:0.60-1.01), 0.12(95%CI:0.08-0.17), 0.68(95%CI:0.57-0.73) and 0.51(95%CI:0.36-0.67) respectively under random effect model, Figure 6.

Discussion

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since Dec 2019[15], known as COVID-2019 or 2019-nCoV, has led to a major concern of the potential for not only an epidemic but a pandemic in China and now it seems to be a public health problem all over the world[4, 16]. Sequencing showed that COVID-19 was a new kind of β -coronavirus, which was similar to SARS-CoV[17]. Since then, COVID-19 has spread rapidly in China, especially in Wuhan[18, 19]. At the same time, COVID-19 is also spread all over the world, such as Korea[20, 21], Italy[22, 23], Japan[24, 25], the United States[26] and Iran, etc. As a new infectious disease, the clinical features and prognosis of COVID-19 is not completely clear yet[27-29]. The clinical characteristics, the proportion of severe patients and the mortality of patients with COVID-19 are different according to different individual publications. The main reason for the differences in different studies is that the sample size of each study is small with limited statistical power[30].

Therefore, we performed this meta-analysis by pooling open published data relevant to clinical characteristics of COVID-19. In the present meta-analysis, we included 10 high quality clinical studies which were published recently in the NEJM, Lancet, JAMA and et c. The original studies were all from

China especially in Wuhan. The pooled data indicated that combined mortality was 0.03(95%CI: 0.01-0.04) for COVID-19 cases with random effect model. The pooled female ratio of the COVID-19 cases from 10 published data was 0.41(95%CI:0.37-0.46), which indicated male subjects seemed to be susceptible to SARS-COV-2 compared that of female. The pooled invasive and non-invasive ventilation ratio were 0.03(95%CI:0.01-0.05) and 0.06(95%CI:0.02-0.09) respectively. The combined clinical symptom of fever, cough, headache and fatigue were 0.80(95%CI:0.60-1.01), 0.12(95%CI:0.08-0.17), 0.68(95%CI:0.57-0.73) and 0.51(95%CI:0.36-0.67) respectively under random effect model, which indicating fever, cough and fatigue were the most common symptom of COVID-19 cases.

Conclusion

Therefore, the infection rate of male patients with SARS-COV-2 was higher than that of female patients. Less than 10% patients need invasive or non-invasive mechanical ventilation, and the overall mortality rate relative low. Most of the mortality patients were serious patients who were admitted to ICU[31]. The mortality of patients with mild disease may be even lower. However, there are some limitations in this meta-analysis. First, there is significant statistical heterogeneity across the original study. Each study uses the random effect model to combine data, resulting in increased confidence interval. Second, all patients are from the mainland of China, and most of them are in Wuhan, which may lead to patient selectivity bias. Therefore, whether the conclusion are applicable for patients from other countries remains unclear.

Declarations

Consent for publication, All authors agree to published our manuscript in you journal when it accept

Availability of supporting data, Can be obtained from the corresponding author

Competing interests, No competing interest to report

Funding, no funding

Authors' contributions

Study Design, Yueming Wu

Data Collection, Shangxia Jiang, Hu Chen

Statistical Analysis, Tianzheng Lou, Hewei Xu

Data Interpretation, Yueming Wu

Manuscript Preparation, Junlong Xu

Literature Search, Yu Zhang

References

1. Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. *J Med Virol* 2020.
2. Lee A. Wuhan novel coronavirus (COVID-19): why global control is challenging. *Public Health* 2020;179:A1-A2.
3. Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, Iosifidis C, Agha R. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *Int J Surg* 2020;76:71-76.
4. Lancet T. COVID-19: too little, too late. *Lancet* 2020;395:755.
5. Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, Dai J, Sun Q, Zhao F, Qu J, Yan F. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang, China. *J Infect* 2020.
6. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, Li SB, Wang HY, Zhang S, Gao HN, Sheng JF, Cai HL, Qiu YQ, Li LJ. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* 2020;368:m606.
7. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA* 2020.
8. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui D, Du B, Li LJ, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS, China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020.
9. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y, Li Y, Wang X, Peng Z. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020.
10. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
11. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung K, Lau E, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Li M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam T, Wu J, Gao GF, Cowling BJ, Yang B, Leung GM, Feng Z. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* 2020.

12. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507-513.
13. Chang, Lin M, Wei L, Xie L, Zhu G, Dela Cruz CS, Sharma L. Epidemiologic and Clinical Characteristics of Novel Coronavirus Infections Involving 13 Patients Outside Wuhan, China. *JAMA* 2020.
14. Zhuang YJ, Chen Z, Li J et al. Clinical and epidemiological characteristics of 26 patients diagnosed with novel coronavirus pneumonia. *Chinese Journal of Nosocomiology* 2020;30(6):817-820.
15. Li Q, Feng W, Quan YH. Trend and forecasting of the COVID-19 outbreak in China. *J Infect* 2020.
16. Maxwell DN, Perl TM, Cutrell JB. "The Art of War" in the Era of Coronavirus Disease 2019 (COVID-19). *Clin Infect Dis* 2020.
17. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may be at least partially responsible for the respiratory failure of COVID-19 patients. *J Med Virol* 2020.
18. Xie J, Tong Z, Guan X, Du B, Qiu H, Slutsky AS. Critical care crisis and some recommendations during the COVID-19 epidemic in China. *Intensive Care Med* 2020.
19. Boldog P, Tekeli T, Vizi Z, Dénes A, Bartha FA, Röst G. Risk Assessment of Novel Coronavirus COVID-19 Outbreaks Outside China. *J Clin Med* 2020;9.
20. COVID-19 National Emergency Response Center, Epidemiology & Case Management Team, Prevention KCfDC&. Contact Transmission of COVID-19 in South Korea: Novel Investigation Techniques for Tracing Contacts. *Osong Public Health Res Perspect* 2020;11:60-63.
21. Kim JM, Chung YS, Jo HJ, Lee NJ, Kim MS, Woo SH, Park S, Kim JW, Kim HM, Han MG. Identification of Coronavirus Isolated from a Patient in Korea with COVID-19. *Osong Public Health Res Perspect* 2020;11:3-7.
22. Porcheddu R, Serra C, Kelvin D, Kelvin N, Rubino S. Similarity in Case Fatality Rates (CFR) of COVID-19/SARS-COV-2 in Italy and China. *J Infect Dev Ctries* 2020;14:125-128.
23. Day M. Covid-19: surge in cases in Italy and South Korea makes pandemic look more likely. *BMJ* 2020;368:m751.
24. Imai H. Trust is a key factor in the willingness of health professionals to work during the COVID-19 outbreak: Experience from the H1N1 pandemic in Japan 2009. *Psychiatry Clin Neurosci* 2020.
25. Arashiro T, Furukawa K, Nakamura A. COVID-19 in 2 Persons with Mild Upper Respiratory Symptoms on a Cruise Ship, Japan. *Emerg Infect Dis* 2020;26.
26. Burke RM, Midgley CM, Dratch A, Fenstersheib M, Haupt T, Holshue M, Ghinai I, Jarashow MC, Lo J, McPherson TD, Rudman S, Scott S, Hall AJ, Fry AM, Rolfes MA. Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 - United States, January-February 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:245-246.
27. Zhu Y, Liu YL, Li ZP, Kuang JY, Li XM, Yang YY, Feng ST. Clinical and CT imaging features of 2019 novel coronavirus disease (COVID-19). *J Infect* 2020.

28. Li K, Wu J, Wu F, Guo D, Chen L, Fang Z, Li C. The Clinical and Chest CT Features Associated with Severe and Critical COVID-19 Pneumonia. *Invest Radiol* 2020.
29. Wang Y, Kang H, Liu X, Tong Z. Combination of RT-qPCR Testing and Clinical Features For Diagnosis of COVID-19 facilitates management of SARS-CoV-2 Outbreak. *J Med Virol* 2020.
30. Hickey GL, Grant SW, Dunning J, Siepe M. Statistical primer: sample size and power calculations-why, when and how. *Eur J Cardiothorac Surg* 2018;54:4-9.
31. Xu Z, Li S, Tian S, Li H, Kong LQ. Full spectrum of COVID-19 severity still being depicted. *Lancet* 2020.

Tables

Table 1. General characteristics of the included 10 studies

First author	Year	Region	No. included	No. death	Journal
		31 province,			
Guan WJ[8]	2020	China	1099	15	N Engl J Med
Xu XW[6]	2020	Zhejiang, China	62	1	BMJ
Wang DW[9]	2020	Wuhan, China	138	6	JAMA
Huang CL[10]	2020	Wuhan, China	41	6	Lancet
Li Q[11]	2020	Wuhan, China	425	NA	N Engl J Med
Yang W[5]	2020	Wenzhou, China	149	0	The Journal of infection
Wu Z[7]	2020	China main land	44672	1023	JAMA
Chen N[12]	2020	Wuhan, China	99	11	Lancet
Chang D[13]	2020	Beijing, China	13	0	JAMA
Zhuang YJ[14]	2020	Beijing, China	26	NA	Chinese Journal of Nosocomiology

Figures

Figure 1

Distribution of Patients with Covid-19 all over the world collected according to world health organization on 11, 2020. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

Figure 2

The publication searching flow chart for of the COVID-19

Figure 3

Forrest plot of female distribution for COVID-19

Figure 4

Forrest plot of mortality for COVID-19

Figure 5

Forrest plot of mechanical ventilation ratio for patients with COVID-19

Figure 6

Forrest plot of top clinical symptom rate for patients with COVID-19