Tian Huang ORCID iD: 0000-0002-6373-2263

2019 novel coronavirus patients' clinical characteristics, discharge rate and fatality rate of meta-analysis

Li Long-quan[1,2,3,#], Huang Tian[1,2,3,#], Wang Yong-qing[4,#], Wang Zheng-ping[5], Liang Yuan[1,2,3], Huang Tao-bi[1,2,3], Zhang Hui-yun[1,2,3], Sun Wei-ming[6,*], Wang Yu-ping[2,3,*]

[1]The First Clinical Medical School of Lanzhou University, Lanzhou 730000, China;lilongquanii@163.com

[2] Department of Gastroenterology, The First Hospital of Lanzhou University, Lanzhou, 730000, China

[3] Key Laboratory for Gastrointestinal Diseases, Gansu Province, The First Hospital of Lanzhou University, Lanzhou, 730000, China

[4] Gansu people's hospital day diagnostic center, Lanzhou 730000, China

[5] Gansu University of Chinese Medicine, Lanzhou, 730000, China

[6] Department of Endocrinology, The First Hospital of Lanzhou University, Lanzhou, 730000, China

# These authors contributed equally to this work.

* Correspondence to: Professor Yu pingWang, Department of Gastroenterology, The First Hospital of Lanzhou University; Key Laboratory for Gastrointestinal Diseases, Gansu Province, The First Hospital of Lanzhou University. No.1 West Dong gang Road, Lanzhou, Gansu 730000, China. E-mail: wangyuping@lzu.edu.cn; Professor Wei mingSun, Department of Endocrinology, The First Hospital of Lanzhou University. No.1 West Donggang Road, Lanzhou, Gansu 730000, China. E-mail: swm77@163.com.

Received: date; Accepted: date; Published: date

Abstract: (1) Background: To study the clinical data, discharge rate, and fatality rate of COVID-19 patients for clinical help. (2)Methods: The clinical data of COVID-19 patients from December 2019 to February 2020 were retrieved from four databases. We statistically analyzed the clinical symptoms and laboratory results of COVID-19 patients and explained the discharge rate, fatality rate with a single-arm meta-analysis. (3)Results: The available data of 1994 patients in 10 literatures were included in our

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jmv.25757.

study. The main clinical symptoms of COVID-19 patients were fever (88.5%), cough (68.6%), myalgia or fatigue (35.8%), expectoration (28.2%), dyspnea (21.9%). Minor symptoms include headache or dizziness: (12.1%) diarrhea (4.8%), nausea, and vomiting (3.9%). The results of laboratory results showed that the lymphocytopenia (64.5%), increase of CRP (44.3%), increase of LDH (28.3%), and leukocytopenia (29.4%) were more common. (4)Conclusions: The results of single-arm meta-analysis showed that: the male took a larger percentage in the gender distribution of COVID-19 patients 60%[95%CI (0.54,0.65)], the discharge rate of COVID-19 patients was 42%[95%CI (0.29,0.55)], and the fatality rate was 7%[95%CI (0.04,0.10)].

Keywords: COVID-19; 2019-nCoV; clinical characteristics; discharge rate; fatality ra te; meta-analysis.

1. Introduction

Since December 2019, there has been an increasing number of unexplained cases of pneumonia in Wuhan, a city of 11 million people in China's Hubei province, which quickly spread to other cities and has also seen similar cases abroad. The Chinese Health Authorities have carried out very appropriate and prompt response measures including that (1) The Chinese government has been dealing with the epidemic in strict accordance with notice no. 1 of the national health commission that pneumonia caused by the new coronavirus shall be included in the management of categories B infectious disease, and the prevention and control measures of groups A infectious disease shall be taken[1]; (2) The government decided to close down Wuhan, Hubei province, and launched a primary public health emergency response in several provinces and cities across the country. At the same time, the World Health Organization has recently declared the 2019-nCOV a public health emergency of international concern (PHEIC)[2]. On January 3, 2020, the 2019 novel coronavirus (SARS-CoV-2) was identified in samples of bronchoalveolar lavage fluid from a patient in Wuhan[3], which is recognized as typical of a lineage B betacoronavirus. It has an envelope, the particles are round or oval, often polymorphic, and the diameter is 60-140nm. Its genetic characteristics are significantly different from SARS-COV and MERS-COV. Current research showed that it had more than 85% homology with bat SARS-like coronavirus (bat-SL-COVZC45). When isolated and cultured in vitro, the SARS-CoV-2 can be found in human respiratory epithelial cells in about 96 hours, while it took about 6 days in Vero E6 and Huh-7 cell lines[4], and it has been identified as the cause of COVID-19.The study found that SARS-CoV-2 had the characteristics of human-to-human transmission, and the R0 was estimated at 3.77[15], which was significantly higher than the MERS-COV. According to the official report, the virus may have the characteristics of aerosol transmission, that is, the potential for aerosol transmission in a relatively closed environment exposed to high concentrations of aerosols for a long time[16]. The identification and control of suspected COCID-19 patients as early as possible were crucial to controlling the further spread of the epidemic by managing the source of infection and cutting off the transmission route. At present, there is however very limited clinical information of the 2019-nCoV.Therefore, in our study, the clinical data of nearly three months from December 2019 to now were retrieved and collected into a large sample to discover and reveal the clinical symptoms, laboratory test data and epidemiological characteristics of COVID-19 patients, so as to provide help for clinical and epidemic prevention and control of the

disease. The data were analyzed by using Microsoft Excel and STATA 15.0 (STATA Corporation, College Station, SE).

2.Data and Methods

2.1. Literature Search and Selection

We conducted a comprehensive systematic literature search of online databases, including PubMed, Embase, Web of Science, WanFang Data, and CNKI, from December 2019 to February 2020 to identify all case studies. The search terms and relative variants were as follows: COVID-19; Novel Coronavirus–Infected Pneumonia;2019 novel coronavirus; 2019-nCoV; SARS-CoV-2;clinical characteristics; discharge rate; fatality rate; a meta-analysis. We also reviewed the references of included articles to guarantee the comprehensiveness and accuracy of our research. All the search results were evaluated according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The inclusion criterions for the 10 articles are as follows: Study population: patients diagnosed with COVID-19; Study design: case studies; Outcomes measure: at least one outcome reported among clinical symptoms and laboratory results, discharge, and death data.

Abstracts from conferences and commentary articles were excluded.

Table Ⅰ. Demographics of the Included Studies

Study	Year	Country	Number of patients	Age media, y	Sex (male%)	Discharge rate(%)	Fatality rate(%)
Guan.W.J[5]	2020	China	1099	47	58.1%	-	15(1.36%）
Chang.D[6]	2020	China	13	34	77.0%	13(100%)	0(0.0%)
Huang.C.L[7]	2020	China	41	49	73.0%	28(68.3%）	6(14.6%）
Wang.D.W.[8]	2020	China	138	56	54.3%	47(34.1%)	6(4.3%）
Li.Q.[9]	2020	China	425	59	56.0%	-	-
Chen.N.S.[10]	2020	China	99	55.5	68.0%	31(31.0%）	11(11.0%）
Wang.Z.W[11]	2020	China	4	-	75.0%	4(100%)	0(0.0%)
Liu.K.[12]	2020	China	137	57	44.5%	-	16(11.7%)
Chen.L.[13]	2020	China	29	56	72.0%	-	2(6.9%)
Zhang.M.Q.[14]	2020	China	9	36	55.6%	-	-

Discharge (Fatality)Rate=discharged (fatal) patients number/total patients number.

2.2. Data Extraction and Quality Assessment

Data extraction and the evaluation of literature quality were conducted independent ly by 2 investigators (L.Q.L. and T.H.). Microsoft Excel database was used to record all available information, including baseline details, clinic data, discharge rate, and f atality rate. Any disagreement was resolved by another investigator (Y.Q.W.)

2.3. Bias risk assessment

The MINORS (table Ⅱ) [17]was used to assess bias risk.

Table Ⅱ. Bias risk assessment

Study	①	②	③	④	⑤	⑥	⑦	⑧	score
Guan.W.J.	2	2	2	2	2	0	0	0	10
Chang.D.	2	2	2	2	2	1	2	0	13
Huang.C.L	2	2	2	2	2	1	2	0	13
Wang.D.W.	2	2	2	2	2	1	2	0	13
Li.Q.	2	2	2	2	2	0	0	0	10
Chen.N.S.	2	2	2	2	2	1	1	0	12
Wang.Z.W.	2	2	2	2	2	1	2	0	13
Liu.K.	2	2	2	2	2	0	0	0	10
Chen.L.	2	2	2	2	2	1	2	0	13
Zhang. M.Q.	2	2	2	2	2	0	0	0	10

①A clearly stated aim;②Inclusion of consecutive patients;③Prospective collection of data;④ Endpoints appropriate to the aim of the study;⑤Unbiased assessment of the study endpoint;⑥Follow-up period appropriate to the aim of the study;⑦Loss to follow up less than 5%;⑧ Prospective calculation of the study size.The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score being 16 for non-comparative studies.

2.4. Statistical Analysis of Data

Microsoft Excel was used to analyze the clinical symptoms and Laboratory results. Single-arm meta-analysis was performed using Stata 15.0 software. Heterogeneity among studies was tested using the Cochran Chi-square test and I^2, When $I^2 < 50\%$, a fixed-effects model was used, while when $I^2 > 50\%$, a random-effects model was selected. If there was statistical heterogeneity among the results, a further sensitivity analysis was conducted to determine the source of heterogeneity. After the significant clinical heterogeneity was excluded, the randomized effects model was used for meta-analysis. Funnel plot and Egger test were used to detect publication bias. $P < 0.05$ was considered as statistical significance (2-sided).

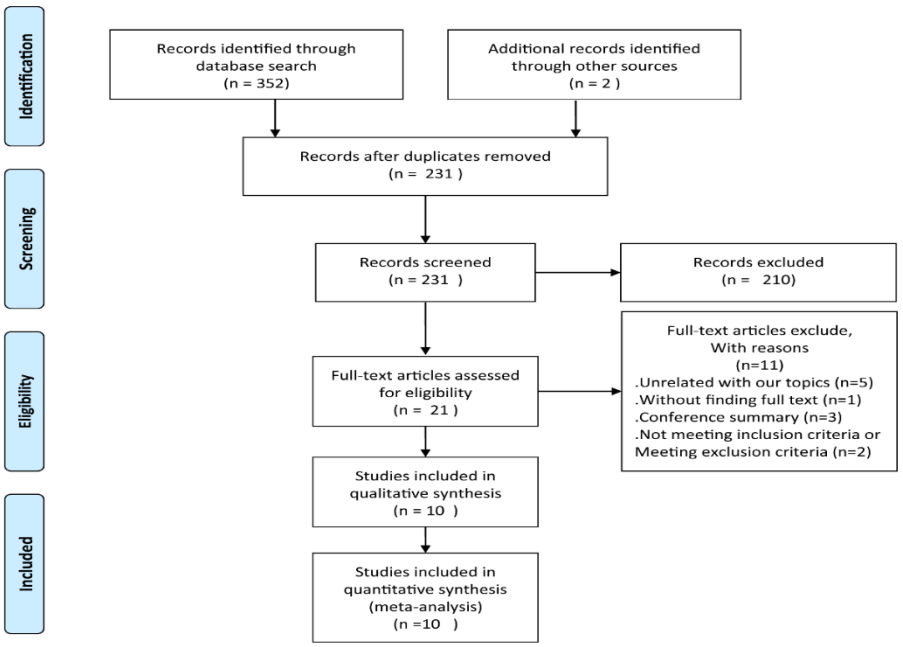

Figure 1. A flow diagram of the inclusion criteria of studies eligible for meta-analysis.

3. Results

3.1. Research Selection and Quality Assessment

Based on the previous search strategy, 354 studies were searched from the online database. After deleting duplicate records, a total of 231 records were retained. Then, 210 articles were excluded by looking at the titles and abstracts, and 11 of the remaining 21 articles were deleted for various reasons. The last 10 articles were included in the meta-analysis (figure 1). The characteristics and demographic data of the included studies are shown in table Ⅰ,table ⅢIand table Ⅳ.

3.2. Clinical Data

The study of clinical data included 10 studies, a total of 1995 cases. Summarizing the clinical data(table ⅢIand tableⅣ), we found that the main clinical symptoms of COVID-19 patients were fever (88.5%), cough (68.6%), myalgia or fatigue (35.8%), expectoration (28.2%), dyspnea (21.9%). Minor symptoms include headache or dizziness: (12.1%) diarrhea (4.8%), nausea, and vomiting (3.9%). The results of the clinical examination showed that the lymphocytopenia (64.5%), increase of CRP (44.3%), increase of LDH (28.3%), and leukocytopenia (29.4%) were more common. The overall performance was consistent with the respiratory virus infection.

TableIII. Clinical Symptoms

Study	fever	cough	expectoration	dyspnoea	haemoptysis	sore throat	nasal congestion	myalgia or fatigue	headache or dizziness	diarrhoea	nausea and vomiting	other symptoms
Guan.W.J.	966(87.9%)	744(67.7%)	367(33.4%)	204(18.6%)	10(0.9%)	153(13.9%)	53(4.8%)	419(38.1%)	150(13.6%)	41(3.7%)	55(5.0%)	134(12.2%)
Chang.D.	12(92.3%)	6(46.2%)	-	-	-	-	1(7.7%)	3(23.1%)	3(23.1%)	1(7.7%)	-	-
Huang.C.L.	40(98.0%)	31(76.0%)	11(28.0%)	22(55.0%)	2(5.0%)	-	-	18(44.0%)	3(8.0%)	1(3.0%)	-	-

Wang.D.W.	136(98.6%)	119(86.2%)	37(26.8%)	43(31.2%)	-	24(17.4%)	-	48(34.8%)	9(6.5%)	14(10.1%)	5(3.6%)	58(42.0%)
Chen.N.S.	82(83.0%)	81(82.0%)	-	31(31.0%)	-	5(5.0%)	4(4.0%)	11(11.0%)	8(8.0%)	2(2.0%)	1(1.0%)	-
Wang.Z.W.	49(100.0%)	3(75.0%)	-	-	-	-	1(25.0%)	2(50.0%)	2(50.0%)	-	-	1(25.0%)
Liu.K.	112(81.8%)	66(48.2%)	6(4.4%)	26(19.0%)	7(5.1%)	-	-	44(32.1%)	13(9.5%)	11(8.0%)	-	10(7.3%)
Chen.L.	28(97.0%)	21(72.0%)	21(72.0%)	17(59.0%)	-	-	-	12(41.0%)	2(7.0%)	4(14.0%)	-	-
Zhang.M.Q.	8(88.9%)	5(55.6%)	-	-	-	4(44.4%)	1(11.1%)	4(44.4%)	-	1(11.1%)	-	1(11.1%)

Data were described as n, and (n/N %), where n is the total number of patients with related symptom, N is the total number of patients with available data.Other symptoms:chill;conjunctival congestion;anorexia;abdominal pain;constipation;heart palpitations,etc.

TableⅣ. The results of clinical examination

Study	Leucocytes		Lymphocytes decreased	PLT decreased	CRP increased	PCT increased	LDH increased	ALT increased	AST increased	TB increased	CK increased	Crea increased	D-dimer increased
	increased	decreased											
Guan.W.J.	58(5.9%)	330(33.7%)	731(82.1%)	315(36.2%)	481(60.7%)	35(5.5%)	277(41.0%)	158(21.3%)	168(22.2%)	76(10.5%)	90(13.7%)	12(1.6%)	260(46.4%)

Huang .C.L.	12(30 .0%)	10(25. 0%)	26(63.0 %)	2(5.0 %）	-	-	29(73. 0%)	-	15(37. 0%)	-	13(33 .0%)	4(10. 0%)	-
Chen. N.S.	24(24 .0%)	9(9.0 %)	35(35.0 %)	12(12. 0%)	-	-	75(76. 0%)	28(28. 0%)	35(35. 0%)	18(18 .0%)	13(13 .0%)	3(3.0 %)	36(36. 0%)
Wang. Z.W.	1(25. 0%)	0(0.0 %)	1(25.0 %)	-	-	-	-	-	-	-	-	-	-
Liu.K.	26(19 .0%)	51(37. 2%)	99(72.3 %)	-	115(8 3.9%)	-	-	-	-	-	-	-	-
Chen. L.	6(21 %)	17(58 %)	20(69.0 %)	5(17.0 %)	27(93. 0%)	-	20(69. 0%)	5(17.0 %)	7(24.0 %)	1(3.0 %)	-	2(7.0 %)	-
Zhang .M.Q	1(11. 1%)	-	2(22.2 %)	-	2(22.2 %)	-	-	-	-	-	-	-	-

Note：Data were described as n, and (n/N %), where n is the total number of patients with related abnormal laboratory results, N is the total number of patients with available data.PLT,Platelets;CRP,C-reactive protein;PCT,Procalcitonin;ALT,Alanine aminotransferase;AST,Aspartate aminotransferase;TB,Total bilirubin;CK,Creatinine kinase;Crea,Creatinine.

3.3. Sex Distribution

A total of 9 studies were included[5-14]. The results of the randomized effects model meta-analysis showed that in the sex distribution of this disease men accounted for 60%[95%CI (0.54,0.65)] of COVID-19 patients(figure 2.1.),which was higher than women. The sensitivity analysis (in supplementary materials) showed that there was no study that greatly interfered with the results of this meta-analysis, suggesting that the study was stable. Funnel plot was drawn to test publication bias (figure. 2.2.).Publication bias test results: Egger's test (P=0.312>0.1) indicated that there was no publication bias.

3.4. Fatality Rate

A total of 7 studies were included[6-8,10-13], with 61 cases. The results of the fixed effects model meta-analysis showed that the fatality rate of the COVID-19 patients was 7% [95%CI (0.04, 0.10)] (figure. 2.3.). The sensitivity analysis (in supplementary materials.) showed that none of the studies had a significant impact on the results of this meta-analysis.

A funnel plot was drawn to test publication bias (figure. 2.4.). Publication bias test results: Egger's test (P=0.614>0.1) indicated that there was no publication bias.

3.5 Discharge Rate

A total of 5 studies were included[7-8,10-12], with 412 cases. The results of the randomized effects model meta-analysis showed that the discharge rate of the COVID-19 patients was 42% [95%CI (0.29, 0.55)](figure.2.5.). The sensitivity analysis (in supplementary materials) showed that none of the literature had significantly interfered with the results of this meta-analysis. A funnel plot was drawn to test publication bias (figure. 2.6.). Publication bias test results: Egger's test (P=0.180>0.1) indicated that there was no publication bias.

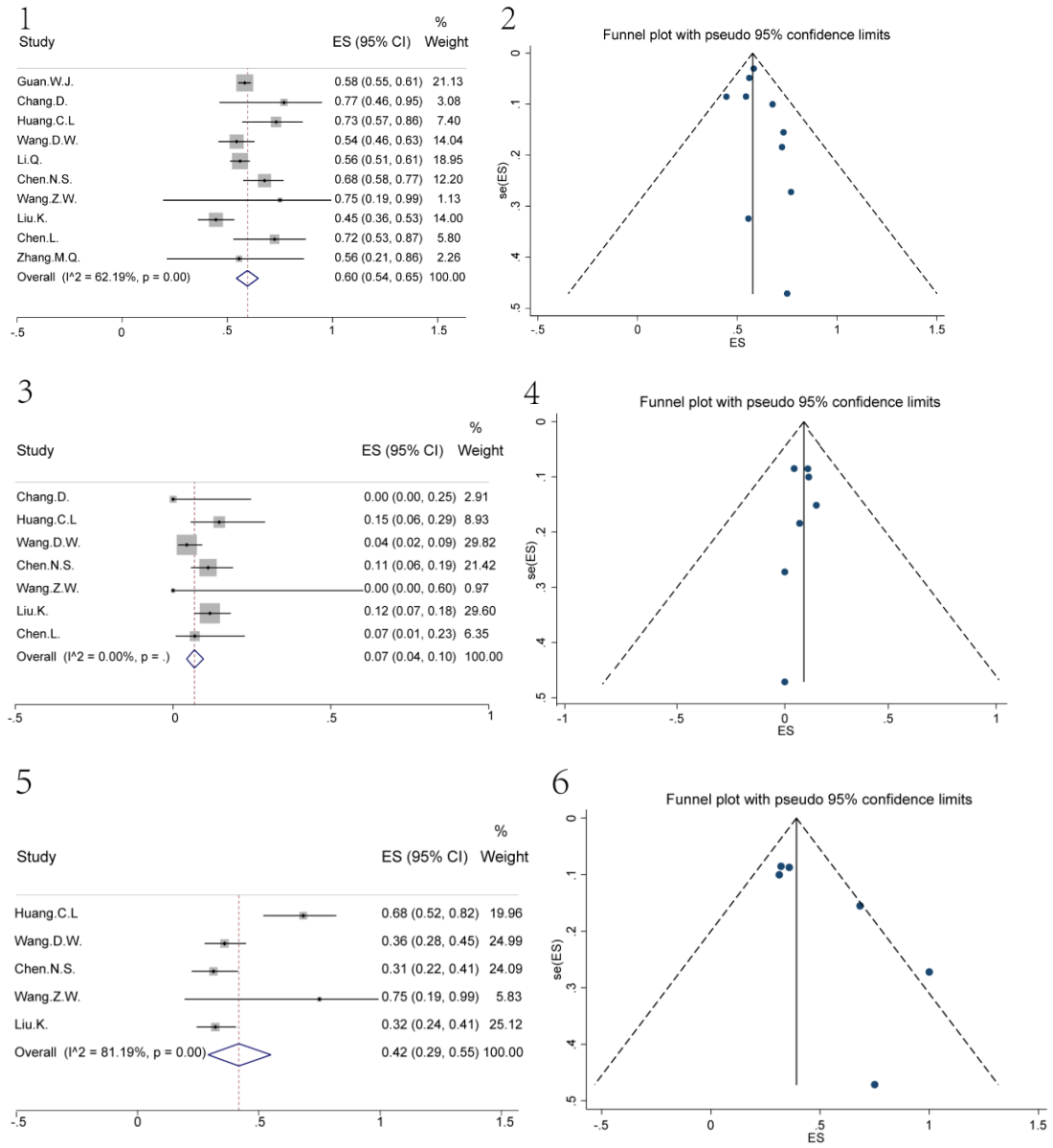

Figure2: Forest plot of all the outcomes. (1, 3, 5.): sex distribution; fatality rate; discharge rate; Funnel plot (2, 4, 6.): sex distribution; fatality rate; discharge rate.

4. Discussion

This meta-analysis included the latest studies from December 2019 to March 2019 to analyze the clinical characteristics of the novel coronavirus. Our study, which included 1,994 patients, reflects the most recent data since the emergence of novel coronaviruses. Although all the studies were case studies and data of randomized controlled studies were lacking, most of our results had relatively low heterogeneity in terms of single-arm meta-analysis, and the sensitivity analysis also showed that the results were not affected by individual studies and there was no publication bias. Meta-analyses of randomized controlled trials are not necessarily superior to non-randomized controlled trials in terms of the level of evidence [18].

The main clinical symptoms of COVID-19 patients were fever (88.5%), cough (68.6%), myalgia or fatigue (35.8%), expectoration (28.2%), dyspnea (21.9%). In addition to common respiratory symptoms, the symptoms of headache or dizziness (12.1%) diarrhea (4.8%), nausea, and vomiting (3.9%) were also obvious in some patients. Up to 30% of patients with Middle East respiratory syndrome coronavirus (MERS-COV) also have diarrhea[19]. Moreover, MERS-COV was shown to survive in simulated fed gastrointestinal juice and the ability to infect intestinal organoid models[20]. A recent study showed that nCOV was detected in stool samples of patients with abdominal symptoms[21]. Therefore, while paying great attention to patients with the respiratory system as the primary symptom, more attention should also be paid to patients with headaches, dizziness, diarrhea, anorexia, nausea, and vomiting. Fecal samples should be tested to exclude a potential alternative route of transmission that is unknown at this stage[7]， in order to minimize false negatives in the diagnosis.

Laboratory results showed that lymphocytopenia (64.5%), increase of CRP (44.3%), increase of LDH (28.3%), and leukocytopenia (29.4%), were more common. Overall, all of which were consistent with respiratory virus infection. The lymphocytopenia could be used as a reference index in the diagnosis of new coronavirus infections in the clinic. Studies have shown that levels of inflammatory cytokines may be related to the severity of the disease [7, 13], which is expected to be an indicator of the severity of the disease. For the data provided are not comprehensive enough, and the Laboratory result values in different studies are not uniform, more studies are needed to confirm whether relevant indicators can provide clinical help.

The study suggests that males account for a more significant percentage in the gender distribution of COVID-19 patients 60% [95%CI (0.54, 0.65)]. And the certain reasons for it remains to be further explored. There are some studies showed MERS-COV, and SARS-COV patients have also been found to infect more males than females[22,23]. The reduced susceptibility of females to viral infections could be attributed to the protection from X chromosome and sex hormones, which play an essential role in innate and adaptive immunity[24]. But men should pay more attention to protective measures.

The included cases period was January 1 to February 7, and our study suggested that the discharge rate of CIVID-19 patients during this period was 42%, with a fatality rate of 7%. The fatality rate of SARS-COV and MERS-COV is reported to be over 10% and 35%[25,26], respectively. In comparison, COVID-19 has a lower fatality rate. Notably, 43% of the dead patients had one or more of the following cases: advanced age (> 60 years),

cancer, more underlying diseases, or major infections. Guo et al.[12, 27] found that the fatality rate of patients with viral pneumonia increased when they had a basic disease and mixed bacterial infection, which was consistent with the results of our study.

Due to the lack of awareness of the virus in the early stage of this disease, inadequate medical protection, and treatment measures, the high infectivity of the virus led to a dramatic increase in the number of patients, a lack of medical resources. As a result, the patient discharge rate is relatively low. Recently reported that Remdesivir clinical effect is visible, clinical Ⅲ trials are ongoing in the domestic, and survivors plasma treatment for heavy, severe cases has shown definite curative effect[16]. We should believe that these treatments will significantly reduce the mortality of such patients soon. Limited by the number and quality of included studies, more extensive and large-scale studies are required to identify the clinical features of the disease.

Author Contributions: Methodology, Sun.wei-ming.; validation, Zhang.hui-yun.; formal analysis, Liang.yuan.; investigation, Huang.tao-bi.; data curation, Wang. Zhen-ping.; writing—original draft preparation, Li.long-quan.; Hunag.tian. and Wang.yong-qing.; writing—review and editing, Wang.yu-ping.

Funding: This study was supported by the Gansu Provincial COVID-19 Science and Technology Major Project, China, the Key Program of the Natural Science Foundation of Gansu Province, China (18JR3RA366).

Acknowledgments: No.

Conflicts of Interest: None of the authors have any conflicts of interest related to this study.

References

1. National Health Commission of the People's Republic of China main website. https: //www.nhc.gov.cn(accessed January 20th, 2020)

2. WHO main website. https://www.who.int (accessed February 5th, 2020)

3. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. The New England journal of medicine. 2020;382(8):727-733.

4. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020.

5. Guan W-j, Ni Z-y, Hu Y, et al. Clinical characteristics of 2019 novel coronavirus infection in China. medRxiv. 2020:2020.2002.2006.20020974.

6. Chang, Lin M, Wei L, et al. Epidemiologic and Clinical Characteristics of Novel Coronavirus Infections Involving 13 Patients Outside Wuhan, China. Jama. 2020.

7. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet (London, England). 2020;395(10223):497-506.

8. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. Jama. 2020.

9. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020.

10. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet (London, England). 2020;395(10223):507-513.

11. Wang Z, Chen X, Lu Y, Chen F, Zhang W. Clinical characteristics and therapeutic procedure for four cases with 2019 novel coronavirus pneumonia receiving combined Chinese and Western medicine treatment. Biosci Trends. 2020.

12. Kui L, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chinese medical journal. 2020.

13. Lei C, Huiguo L, Wei L, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. Chinese Journal of Tuberculosis and Respiratory Diseases. 2020;43(00):E013-E013.

14. Mingqiang Z, Xiaohui W, Kaili C, et al. Clinical features of 2019 novel coronavirus pneumonia in the early stage from a fever clinic in Beijing. Chinese medical journal. 2020.

15. Yang Y, Lu Q, Liu M, et al. Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China. 2020.

16. National Health Commission of the People's Republic of China main website. https: //www.nhc.gov.cn(accessed February 18th, 2020)

17. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (minors): development and validation of a new instrument. ANZ journal of surgery. 2003;73(9):712-716.

18. Abraham NS, Byrne CJ, Young JM, Solomon MJ. Meta-analysis of well-designed nonrandomized comparative studies of surgical procedures is as good as randomized controlled trials. Journal of clinical epidemiology. 2010;63(3):238-245.

19. Chan JF, Lau SK, To KK, Cheng VC, Woo PC, Yuen KY. Middle East respiratory syndrome coronavirus: another zoonotic betacoronavirus causing SARS-like disease. Clinical microbiology reviews. 2015;28(2):465-522.

20. Zhou J, Li C, Zhao G, et al. Human intestinal tract serves as an alternative infection route for Middle East respiratory syndrome coronavirus. Science advances.

2017;3(11):eaao4966.

21. Zhang H, Kang Z, Gong H, et al. The digestive system is a potential route of 2019-nCov infection: a bioinformatics analysis based on single-cell transcriptomes. 2020.

22. Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. International journal of infectious diseases: IJID: official publication of the International Society for Infectious Diseases. 2016;49:129-133.

23. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-Based Differences in Susceptibility to Severe Acute Respiratory Syndrome Coronavirus Infection. Journal of immunology (Baltimore, Md: 1950). 2017;198(10):4046-4053.

24. Jaillon S, Berthenet K, Garlanda C. Sexual Dimorphism in Innate Immunity. Clinical reviews in allergy & immunology. 2019;56(3):308-321.

25. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. Respirology (Carlton, Vic). 2018;23(2):130-137.

26. Song Z, Xu Y, Bao L, et al. From SARS to MERS, Thrusting Coronaviruses into the Spotlight. Viruses. 2019;11(1).

27. Wang XF, Shi GC, Wan HY, et al. Clinical features of three avian influenza H7N9 virus-infected patients in Shanghai. The clinical respiratory journal. 2014;8(4):410-416.