

Hypertension patients infected with COVID- 19 undergo a longer period of negative conversion:A retrospective study

Bing Xiao (✉ xiaodoctor123@yeah.net)

Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Dou Fu

Department of Nephrology, Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Wei Yang

Department of Gastroenterology, Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Can Zou

Department of Respiratory Medicine,Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Bing Zhang

Department of Gastroenterology, Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Xia Li

Department of Gastroenterology, Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Jing Zeng

Department of Respiratory Medicine,Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

YuanFa Li

Department of Gastroenterology, Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Gong Chen

Department of medical management, Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Junping Sha

Department of Radiology, Xiantao first People's Hospital Affiliated to Yangtze University, xiantao,Hubei, China

Keywords: COVID- 19;hypertension;negative conversion

Posted Date: May 15th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-28173/v1>

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

[Read Full License](#)

Abstract

Purpose Previous studies have showed that age,sex and comorbidities might be associated with severity of patients infected with COVID-19 ,which endangers public health worldwide rapidly.The characteristics and length of negative conversion of Non-severe COVID-19 patients with or without hypertension is limited.This study aims to assess whether non-severe COVID-19 patients with hypertension undergone more longer period of negative conversion .

Methods This single-center, retrospective study was performed in Xiantao first People's Hospital Affiliated to Yangtze University(xiantao, hubei,China) by using medical records.Non-severe COVID-19 patients with a history of hypertension From January 23 to February15 were enrolled as group A. A Control group(group B) was matched (1:1) according to age,sex and the admission date.Data on clinical records, laboratory results, and radiological tests was collected. we conducted all analyses with SPSS software(22.0).

Results We enrolled 24 and 24 Non-severe COVID-19 patients with and without hypertension, respectively. The most common symptoms were fever and cough in both groups.The frequency of fatigue is more in patients with hypertension.The levels of AST,ALT and CRP were higher in group A.The mean periods of negative conversion for COVID-19 virus were 17 days(SD:5.5) and 15 days(SD:3.6)for patients with and without hypertension($P=0.021$).The mean hospitalization periods were 16.8 days (SD:5.6) and 13.7 days (SD:3.8) , respectively ($p=0.083$) .

Conclusion Non-severe COVID-19 patients with hypertension undergone a longer negative conversion for COVID-19 virus and spent more time on clearing COVID-19 virus.

Introduction

In December 2019, an outbreak of Coronavirus disease 2019 (COVID-19) occurred in Wuhan, Hubei Province, China [1,2].Since then, infections spread across China.To date, COVID-19 infection cases have been reported by many countries[3,4,5]. COVID-19 has become a international public health event .However, there are no effective antiviral drugs for COVID-19 based on strong evidence.

Previous studies showed the proportion of comorbidities(such as hypertension,Cardiovascular disease,Diabetes) was higher in Severe cases[6,7].Older age(>65 years) was also risk factor of death for Severe patients[7,8].However,it is not known whether these comorbidities pay a role in the period of negative conversion and duration of hospitalization in non-severe COVID-19 patients.

Therefore,in the study, we compare the clinical characteristics between non-severe COVID-19 patients with hypertension and patients without hypertension,and identify whether hypertension is the potential risk factor of the period of negative conversion.

Method

Study design and patients

The retrospective study was approved by the Ethics Committee in Xiantao first People's Hospital Affiliated to Yangtze University(xiantao, hubei,China). Due to the quarantine,oral informed consent was obtained by telephone.We reviewed clinical characteristics, laboratory results, and chest CT findings of patients confirmed with COVID-19 admitted to our hospital from Jan. 23, 2020 to Feb.15, 2020.Patients were assigned into two groups:patients with hypertension(group A) and patients without hypertension(group B).We included only non-severe patients according to the international guidelines for community-acquired pneumonia[9].As previous studies showed the disease severity was related to age,comorbidities(such as hypertension, diabetes,Coronary heart disease) and the admission date,we excluded the patients who had a previous history of chronic obstructive pulmonary disease,coronary heart disease,heart failure,cerebrovascular diseases,cancer ,chronic renal and liver diseases in both groups[6-8,10]. The match(1:1) was conducted according to three variables:age ,sex and the admission date.

Definition

The criteria for hospital discharge were as follows: (1) normal temperature at least longer than three days, (2) resolved respiratory symptoms, (3) substantially improved acute exudative lesions on chest computed tomography (CT) images, and (4) two consecutively negative RT-PCR test results separated by at least one day.The length of *negative conversion* for COVID-19 virus was defined as the duration from illness onset to the first time of two consecutively negative RT-PCR tests through nasopharyngeal swabs.The nasopharyngeal swabs were collected in cases who met the first two criteria for hospital discharge above after admission.If the RT-PCR test was positive during hospitalization,additional two consecutively RT-PCR tests were performed until both results were negative.

Statistical analysis

We summarised continuous variables as either means and standard deviations(SD) or medians with interquartile ranges(IQR)(nonnormal distribution).Categorical variables were described as frequencies and percentages.Comparisons of continuous variables between groups were performed using independent-sample T test or the Mann-Whitney test.Percentages for categorical variables were compared by using the χ^2 test.All tests were 2-tailed, and a P value less than 0.05 was considered statistically significant.All analyses were conducted with SPSS software, version 22.0.

Results

There were 24 patients in group A and 24 patients in group B enrolled for analysis. Demographic characteristics were shown in Table 1. Age, sex, smokers, Respiratory rate(RR) and oxygen saturation by pulse oximetry(SpO₂) did not differ between both groups.The most frequently symptoms fever and cough in both groups(fever:95.8% vs 83.3%;cough:91.7% vs 75%). Fatigue is more frequently in group A(P=0.017).

For laboratory results on admission (Table 2), the blood counts (white blood cell count, neutrophil count, lymphocyte count and platelet count) showed no differences between two groups. 4 (16.7%) patients showed leucopenia (white blood cell count $<4 \times 10^9 /L$) and 3 (12.5%) showed lymphopenia in group A, which were similar to group B (12.5% and 16.7%). Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) were higher in group A. AST was above the normal range in 7 cases (29.2%) and Level Of ALT increased in 8 patients (33.3%) among group A, which were not statistically significant compared with group B (12.5% and 16.7%). The levels of Lactate dehydrogenase (LDH), Creatine kinase (CK), Blood urea nitrogen (BUN) and Creatinine (Cr) and the frequencies of these four tests above the normal range were not statistically significant between group A and group B. No lesion was found in chest CT images in one case of group B. However, the percentage of bilateral involvement among two groups in chest CT images was not statistically significant (Table 2).

20 patients (83%) received antiviral treatment (Arbidol:15; Lopinavir/ritonavir:2; Arbidol+Chloroquine phosphate:2; Arbidol+lopinavir/ritonavir:1), 11 (45.8%) were given empirical antibiotic treatment, and 11 (45.8%) were given intravenous corticosteroid treatment in group A. Compared to group A, 15 patients (83%) received antiviral treatment (Arbidol:12; Lopinavir/ritonavir:3), 9 (37.5%) were given empirical antibiotic treatment, and 6 (25%) were given intravenous corticosteroid treatment in group B (Table 1). Moreover, all patients were given antihypertensive therapy as usual.

Regarding **clinical course**, the medians of period of fever and cough were 8 (IQR 5.25-10, ranging from 4 days to 12 days, $n=23$) and 15 days (IQR 10.25-19.5, ranging from 9 days to 29 days, $n=22$) respectively, and the mean length of negative conversion for COVID-19 virus was 17 days (SD:5.5, ranging from 8 days to 27 days) in group A. Among group B, the medians period of fever and cough were 7 days (IQR 4.25-9.75, ranging from 4 days to 18 days, $n=21$) and 15.5 days (IQR 4.75-23, ranging from 4 days to 24 days, $n=18$) respectively, and the mean length of negative conversion was 15 days (SD:3.6, ranging from 9 days to 23 days). The mean length of negative conversion was longer in group A than that in group B ($p=0.021$). The median times of RT-PCR test for COVID-19 virus were 3 (IQR 2-3.75, ranging from 2 times to 7 times) in group A and 2 (IQR 2-3, ranging from 2 times to 4 times) in group B during hospitalization. The mean durations of hospitalization were 16.8 days in group A and 13.7 days in group B ($P=0.083$) (Table 3).

Discussion

Previous studies showed hypertension is strongly related to severe or ICU Patients infected with COVID-19 and Non-survivor cases [7,8,11].

However, these studies mainly explored the independent risk factors or predictive factors of severe or Non-survivor COVID-19 patients. The clinical course of Non-severe COVID-19 patients with hypertension was reported rarely.

In our study, Non-severe COVID-19 patients with hypertension undergone a longer negative conversion for COVID-19 virus. Although the duration of hospitalization, the medians of fever and times of RT-PCR tests during hospitalization are not statistically significant differences, we think no statistical significance does

not indicate clinically equivalence .For example,the means of systolic blood pressure and diastolic blood pressure in both groups were showed no statistical significance,but hypertension really existed in group A.Therefore,we think the clinical course of Non-severe COVID-19 patients with hypertension is longer than patients without hypertension.It indicates that Non-severe COVID-19 patients with hypertension will spend more time on overcoming COVID-19 virus.Hypertension patients need more protection from COVID-19 virus infection.

Notably,We found that the results of RT-PCR tests were also positive in some patients with clinical symptoms improvement and substantially improved acute exudative lesions on chest CT,especially in group A.Of which,two cases in group A were given chloroquine phosphate for antiviral therapy after using abidol ineffectively.This situation was also reported in asymptomatic infections with COVID-19[12].This may be one reason for longer hospital stay in COVID-19 patients with hypertension.Previous study showed the tests of RT-PCR for COVID-19 of four patients were positive 5-13 days later after hospital discharge[13].Meanwhile,the longest period of negative conversion for SARS-CoV-2 in group A was 27days.These findings may indicate that a longer duration of quarantine after hospital discharge is needed for Non-severe COVID-19 patients with hypertension.But appropriate quarantine period remains unclear.

With respect to laboratory tests and chest CT findings ,the results were similar to published study[6].In our experience,during the clinical course,fever and cough are the most common symptoms,cough lasts longer and abnormal laboratory tests recover firstly.Although there are no specific antiviral therapy for COVID-19 so far,Arbidol,Lopinavir/ritonavir and Chloroquine phosphate may be therapeutic drugs.In addition,whether intravenous corticosteroid and empirical antibiotic treatment are benefit for non-severe COVID-19 patients is not known.Further studies focusing on these aspects are needed.

There were some limitations in this study.Firstly, epidemiological characteristics(i.e.,exposures,incubation period) ,which might be potential risk factors,were not collected. Secondly, limited samples ,matching scheme and only non-severe patients including in the study might result into bias.

Declarations

We have no conflicts of Interest.

References

- 1.Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Chinese Journal of Epidemiology.2020; 41: 145–151.
2. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med.2020;<https://doi.org/10.1056/NEJMoa2001017>.

3. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. *N Engl J Med*. 2020; <https://doi.org/10.1056/NEJMoa2001191>.
4. Giovanetti M, Benvenuto D, Angeletti S, et al. The first two cases of 2019-nCoV in Italy. where they come from? *J Med Virol*. 2020; <https://doi.org/10.1002/jmv.25699>.
5. Yoon SH, Lee KH, Kim JY, et al. Chest Radiographic and CT Findings of the 2019 Novel Coronavirus Disease (COVID-19): Analysis of Nine Patients Treated in Korea. *Korean J Radiol*. 2020; <https://doi.org/10.3348/kjr.2020.0132>.
6. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020; <https://doi.org/10.1056/NEJMoa2002032>.
7. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA* 2020; <https://doi.org/10.1001/jama.2020.1585>.
8. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*. 2020; [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5)
9. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia: An official clinical practice guideline of the American Thoracic Society and Infectious Disease Society of America. *Am J Respir Crit Care Med*. 2019; 200:e45-e67.
10. Chan JF, Yuan S, Kok K, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *The Lancet*. 2020; 395: 514–23.
11. Fei Zhou, Ting Yu, Ronghui Du, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*. 2020; [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)
12. Hu Z, Song C, Xu C, et al. Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci*. 2020 ; <https://doi.org/10.1007/s11427-020-1661-4>.
13. Lan L, Xu D, Ye G, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. *JAMA*. 2020; <https://doi.org/10.1001/jama.2020.2783>.

Tables

Table 1 Clinical Characteristics and treatment of Patients Infected With COVID-19 virus

characteristics	All patients(n=48)	Group A(n=24)	Group B(n=24)	P value
Age(means±SD)	56.58±11.17	57.83±11.926	55.33±10.466	0.803
Sex(n,%)				
male	35[72.9%]	17[70.8%]	18[75%]	0.745
female	13[27.1%]	7[29.2%]	6[25%]	
Smokers(n,%)	3	1[4.2%]	2[8.3%]	0.051
Signs and symptoms(n,%)				
fever	43[89.6%]	23[95.8%]	20[83.3%]	0.156
cough	40[83.3%]	22[91.7]	18[75%]	0.121
Shortness of breath	16[66.7%]	10[41.7%]	6[25%]	0.221
fatigue	18[37.5%]	13[54.2%]	5[20.8%]	0.017
expectoration	7[14.6%]	4[16.7%]	3[12.5%]	0.683
poor appetite	3[6.25%]	1[4.2%]	2[8.3%]	0.551
Myalgia	2[4.16%]	1[4.2%]	1[4.2%]	1
Headache	2[4.16%]	1[4.2%]	1[4.2%]	1
Diarrhoea	2[4.16%]	1[4.2%]	1[4.2%]	1
Nausea	1[2.08%]	1[4.2%]	0	0.312
Vomiting	1[2.08%]	1[4.2%]	0	0.312
SBP(means±SD)	127.13±14.18	133.38±15.257	120.88±9.79	0.067
DBP(means±SD)	76.77±9.44	79.21±9.673	74.33±8.716	0.851
Respiratory rate(Median ,IQR)	20(20-21)	21(20-21.75)	20(19-20)	0.008
SpO ₂ (means±SD)	97.06±1.84	96.71±1.601	97.42±2.02	0.551
Antiviral treatment(n,%)	35[72.9%]	20[83.3%]	15[62.5%]	0.104
Antibiotics (n,%)	20[41.7%]	11[45.8%]	9[37.5%]	0.558
Intravenous glucocorticoids(n,%)	17[35.4%]	11[45.8%]	6[25%]	0.131
Oxygen therapy (n,%)	28[58.3%]	16[66.7%]	12[50%]	0.242

SD:standard deviations;IQR:interquartile range;SBP:Systolic blood pressure;DBP:Diastolic blood pressure;SpO₂:oxygen saturation by pulse oximetry.

Table 2 Laboratory and Chest CT Findings of Patients Infected With COVID-19 virus

