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# What Is The Case of More Accessible Treatment Options in COVID 19: Comparison of Hydroxychloroquine and Favipiravir Based on Laboratory Values

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**ABSTRACT**

Two of the drugs are frequently used in COVID-19 treatment algorithm because of their low cost, easy availability and application; Hydroxychloroquine (HCQ) and Favipiravir. Our aim in this study is to compare the laboratory parameters of patients diagnosed with COVID-19 Pneumonia in whom HCQ and Favipiravir treatment was initiated, and to reveal the difference in the effectiveness of the treatments.

64 COVID-19 patients whose diagnoses were confirmed by real-time polymerase chain reaction test (RT-PCR) of nasopharyngeal swab samples and pneumonia image compatible with COVID-19 on Thorax CT were included in the study. Patients were divided into three groups: treated with HCQ, treated with favipiravir, and who were switched to favipiravir treatment when they did not benefit from HCQ. We compared the laboratory values on Day 1, Day 5 and at discharge.

When compared in terms of laboratory values, there was no significant difference between the groups in which HCQ and Favipiravir was initiated. In the patient group who did not improve with HCQ and switched to favipiravir treatment, lymphocyte levels increased and ferritin, CRP and d-dimer values decreased. The decrease in D-dimer and CRP values was statistically significant (p= 0.029, p= 0.048). PLT, Hemoglobin, RDW, MPV, NLR, PLR, INR values did not change significantly in any patient group.

Our study with the most commonly used drugs in our country reveals that HCQ and Favipiravir are not superior to each other. When we changed the treatment with favipiravir in the group of patients receiving HCQ whose clinical and / or laboratory values deteriorated, D-dimer and CRP values decreased during discharge. This finding shows how effective the timely treatment change is in the recovery of the patient by closely following the patient clinically and interpreting the laboratory values correctly. In COVID-19, we should direct the treatment of our patients by following the symptoms, risk factors and especially laboratory values.

**Keywords:** COVID-19, Hydroxychloroquine, Favipiravir, D-dimer, CRP

## Introduction

The world has been battling the COVID-19 disease for over a year. According to the data of the end of January 2021, WHO has reported more than 98.2 million cases and more than 2.1 million deaths globally since the beginning of the pandemic (1).

There is no proven treatment yet. However, many recommendations have been made from the definition of the disease to today. An antimalarial, hydroxychloroquine (HCQ), antiviral drugs such as favipiravir, remdesivir, lopinavir, ritonavir, anti-interleukin-6 receptor tocilizumab and steroids are used for treatment (2,3,4,5).

Two of the drugs have been frequently used in the treatment algorithm since the beginning of the pandemic, due to its low cost and easy availability and application. HCQ, which is the aminoquinolin, used in the treatment of malaria and autoimmune diseases and Favipiravir, an antiviral.

HCQ acts through hem polymerase enzyme inhibition, increases the pH of the endosomes that

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the virus uses for cell entry and also affects the glycosylation of the cellular receptor angiotensin converting enzyme 2 (ACE2) (6). HCQ has been shown to inhibit SARS-CoV-2 replication in vitro (7). It has been suggested that HCQ has the ability to control cytokine storm and shorten the time to clinical recovery in critically ill SARS-CoV-2 infected patients (8). Favipiravir is an antiviral drug that selectively inhibits RNA-dependent RNA polymerase (RdRp) of RNA viruses (9). The genome sequence of 2019-nCoV has been identified as a single-stranded RNA beta-coronavirus with the RdRp gene similar to that of SARS-CoV and MERS-CoV. Therefore, favipiravir has been used for COVID-19 (10, 11).

In the COVID-19 treatment guide of the Ministry of Health of the Republic of Turkey, it is recommended that 200 mg tb 2x 200 mg oral form was started for 5-10 days HCQ for both outpatient and hospitalized patients. Favipiravir is recommended in cases with severe pneumonia. In addition, it has been recommended in cases whose clinical condition is aggravated or whose pneumonia symptoms progressed while receiving HCQ treatment. The recommended dose was 2x1600 mg / day on the first day and 2x 600 mg / day as a 5-10 day treatment (12).

In line with the information accumulated to date, we can say that we can manage the treatments of our patients by following the symptoms, risk factors and laboratory values in COVID-19. Especially laboratory values provide us with more concrete information. Since the beginning of the pandemic, there have been publications examining the correlation between laboratory values and disease severity (13,14). It is evaluate the effectiveness of treatment in COVID-19.

Our aim in our study is to compare the treatments (HCQ, Favipiravir, Favipiravir after HCQ) that we started in the hospitalized patient group with the diagnosis of COVID-19 Pneumonia, in order to measure the efficacy over laboratory parameters (1st day, 5th day and at discharge).

## Materials and Metods

Scientific research approval was obtained from the Ministry of Health, General Directorate of Health Services. Later, ethics committee approval was obtained from the University Clinical Research Ethics Committee (Ethics Committee Approval No: 21.05.2020-04). The study was conducted according to the guidelines of the Declaration of Helsinki and the principles of Good Clinical Practice. All patients were over 18 years old and had been diagnosed with COVID-19 according to the Guidance for Coronavirus disease 2019 criteria that were released by the National Health Commission of Turkey (12)

COVID- 19 patients whose diagnoses were confirmed with RT- PCR real-time polymerase chain reaction-tested nasopharyngeal swabs and patients with pneumonia image compatible with COVID-19 in Thorax CT were included in the study. Patients with pregnancy, hematological diseases, cancer and also using drugs that may affect platelet functions were excluded from the study. Patients were treated according to the set treatment protocols released by the National Health Commission of Turkey.

The patients were divided into three groups: started treatment with HCQ, started treatment with Favipiravir and started Favipiravir when they did not benefit HCQ. We compared the laboratory values on Day 1, Day 5 and at discharge. The discharge period was taken as 15 days. Patients with similar disease severity who were diagnosed with COVID-19 and whose treatment should be done inpatient but not needing intensive care were included in the study. All groups are evenly distributed in terms of age and comorbidities.

Clinical deterioration and monitoring the values defined as poor prognosis criteria in COVID-19 (blood lymphocyte count <800 /µl or CRP> 10 x upper limit of normal value or ferritin> 500ng / ml or D-Dimer> 1000 ng / ml, etc.), we included patients in the group of patients who received favipiravir after HCQ.

Hydroxychloroquine 200 mg tb 2x 200 mg oral form was started for 5 days. Favipiravir 200 mg tb, 2x1600 loading and 2x600 maintenance was started for 5 days (or more if needed). In addition, oxygen therapy, oral or intravenous rehydration, electrolyte correction, antipyretics, analgesics, low molecular weight heparin and antiemetic drugs were added.

**Statistical Analysis:** Descriptive statistics for the continuous variables were presented as Mean and Standard deviation, while count and percentages for categorical variables. Normality test of the variables was performed with Kolmogorov-Smirnov test. After normality test, One-way ANOVA was used to compare group means for normally distributed variables while Kruskal-Wallis test for non-normal variables. Following the analyses, Duncan and Games-Howell multiple comparison tests were used to identify different groups for normally and non-normally distributed variables, respectively. Statistical significance level

was considered as 5% and SPSS (ver: 21) statistical program was used for all statistical computations.

## Results

Demographic characteristic of the COVID-19 patients are summarized in Table 1.

A Total of 64 patients [36 males (56.3%) and 28 females (43.8%), median age 48 years old (range, 18-86)] in Van province, Turkey were enrolled. The majority of these patients (43.5%) had either been exposed to an infected family member(s) (6.3%), out of provincial contact (28.1%) or health employee (9.1%), The admitted patients clinical characteristics were fever (71.3%), cough (65.6%), fatigue (40.6%), shortness of breath (25%), headache (18.8%) nausea and vomiting (9.4%), and pharyngalgia (1.6%).

Hypertension (23.4%) was the most common accompanying comorbidity. Other comorbidities are COPD (18.8%), type II—diabetes (2-DM) (17.2%), Coronary Heart Disease (7.8%), Chronic Kidney Failure (CKD) (7.8%), Cerebrovascular Disease (1.6%) and cancer (1.6%). Pneumonia was limited to two lobes in 36.7% of the patients, and 63.3% had involvement in three or more lobes. Five patients were taken to the intensive care unit and followed up, three of these went to intubation and one patient died.

When compared in terms of laboratory values on Day 1, Day 5 and discharge, it was observed that there was no significant difference between the HCQ initiated group and the Favipiravir initiated group. In the laboratory tests performed at discharge, it was seen that the lymphocyte value increased and the ferritin, CRP and dimer values decreased in the patient group who received favipiravir after HCQ. The decrease in d-dimer and CRP values was statistically significant (p: .029, p: .048). Platelet (PLT), Hemoglobin, Red Cell Distribution Width (RDW), Mean Platelet Volume (MPV), Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR), International Normalized Ratio (INR) values did not change significantly in any group of patients that we grouped according to treatment (Table 2).

## Discussion

In the results of our study, when we compared in terms of laboratory values on Day 1, Day 5 and discharge, it showed that there was no significant difference between the group in which HCQ was initiated and the group in which Favipiravir was initiated. It was seen that the two drugs did not have any superiority.

When we look at the publications on HCQ and favipiravir, it has not been encountered to have any studies comparing the efficacy of the two drugs. In a study conducted to evaluate the efficacy and safety of HCQ in COVID-19 pneumonia, it has been reported that pneumonia improved, imaging findings improved, and the course of the disease shortened compared to the control group (15). In another study, the group that received azithromycin with HCQ was compared with the group that received standard care, and it was reported that the rate of recovery was higher in the group receiving HCQ and azithromycin (16). However, there are also studies showing that HCQ is not effective (17). In a study, patients treated with HCQ 400 mg / day were examined at the end of the 7th day, and it was stated that the drug had no effect on viral load and clinical course. In terms of fever returning to normal, radiological progression and side effects, HCQ superiority was not observed (18). HCQ requires close follow-up of patients because of its ability to prolong QT or cause ventricular tachycardia by blocking the activation of potassium channels. Patients who receive this treatment are recommended to perform a basal ECG and QT measurement, and then follow up daily / every other day ECG (16).

There is limited published data on the use of favipiravir in the treatment of COVID-19 disease. In a study evaluating the data of 240 patients, Favipiravir was compared with arbidol. Fever decreased faster and cough recovered faster in people using favipiravir (19).However, in another study, favipiravir showed no significant antiviral effect against the SARS-CoV-2 virus at concentrations below 100 μML (16).

We must say that there are conflicting results and lack of work regarding the effectiveness of drugs. In our study, we showed that the two drugs did not have any superiority in terms of laboratory parameters we monitored during the course of the disease. However, as suggested in the guideline, we showed that the d-dimer and CRP values decreased during discharge in the group of patients in whom we switched to favorable disease because their clinic got worse and / or laboratory values worsened. This finding, which we put forward in the group that was switched to favipiravir after HCQ, shows how effective the timely treatment change is in the recovery of the patient by closely following the patient clinically and interpreting the laboratory values correctly. At

**Table 1.** Demographic and Clinical Characteristics of the Patients at Baseline

| | |
|---|---|
| Age, year (range) | 48 (18-86) |
| Gender | |
| Male | 36 (56.3) |
| Female | 28 (43.8) |
| Exposure or contact information (%) | |
| Family source | 4 (6.3) |
| Out of provincial contact | 18 (28.1) |
| Health employee | 6 (9.1) |
| Symptoms n (%) | |
| Fever | 46 (71.3) |
| Cough | 42 (65.6) |
| Expectoration | 5 (7.8) |
| Fatigue | 26 (40.6) |
| Shortness of breath | 16 (25) |
| Nausea and vomiting | 6 (9.4) |
| Hemoptysis | 0(0) |
| Pharyngalgia | 1 (1.6) |
| Headache | 12 (18.8) |
| Comorbidity n (%) | |
| Hypertension | 15 (23.4) |
| Coronary Artery Disease | 5 (7.8) |
| Chronic Obstructive Pulmonary Disease | 12 (18.8) |
| Diabetes Mellitus –Type II | 11 (17.2) |
| Chronic Kidney Failure | 5 (7.8) |
| Cerebrovascular Disease | 1 (1.6) |
| Cancer | 1 (1.6) |
| CT findings involving lobes n (%) | |
| 0-2 lobe | 11(36.7) |
| 3 or more lobes | 19 (63.3) |
| Being in intensive care n (%) | |
| Yes | 5 (7.9) |
| No | 58 (92.1) |
| Intubation Status, n (%) | |
| Yes | 3 (4.76) |
| No | 60 (95.23) |
| Mortality Status n (%) | |
| Yes | 1 (1.6) |
| No | 62 (98.4) |

this point, we can say that in line with the information accumulated so far, we can manage the treatments of our patients with those who come to the fore in the follow-up of symptoms, risk factors and especially laboratory values in COVID-19.

Contact history in this infectious disease helps us to evaluate patients within the risk group. 43.5% of our patients exposed to an infected family member (s) (6.3%), out of provincial contact (28.1%) or health employee (9.1%).

Looking at the symptoms of our patients, the most common ones were fever, cough, fatigue, shortness of breath and headache respectively. Similar to our study, a study examining 25849 hospitalized COVID-19 patients reported that the

**Table 2.** Descriptive Statistics and Comparison Results For The Studied Variables

| | Hospitalization days | Hydroxychloroquine | Favipiravir after Hydroxychloroquine | Favipiravir | p value |
|---|---|---|---|---|---|
| Lenfosit, k/mm3 (Mean ± SD) # | Day 1 | 1851.7±778.0 | 1756.7±1085.5 | 1820.0±750. 3 | 0.939 |
| | Day 5 | 2098.5±760.4 | 1531.8±827.0 | 1780.0±529.7 | 0.273 |
| | discharge | 1902.0±627.2 | 2151.2±680.9 | 2104.6±731.0 | 0.505 |
| PLT,μ/mm (Mean ± SD) # | Day 1 | 220.1±82.4 | 250.0±91.9 | 260.1±83.2 | 0.383 |
| | Day 5 | 265.0±109.8 | 239.7±75.6 | 250.8±57.6 | 0.792 |
| | discharge | 299.3±127.7 | 303.6±90.4 | 262.8±73.2 | 0.401 |
| Hb,g/dL (Mean ± SD) | Day 1 | 14.2±3.1 | 14.4±1.7 | 15.0±1.5 | 0.577 |
| | Day 5 | 14.3±2.2 | 14.3±1.7 | 13.7±2.3 | 0.781 |
| | discharge | 13.5±2.7 | 13.9±1.8 | 14.0±2.4 | 0.773 |
| RDW, % (Mean ± SD) | Day 1 | 51.2±6.7 | 50.6±3.7 | 51.3±3.7 | 0.891 |
| | Day 5 | 51.0±5.1 | 49.8±4.3 | 48.2±3.2 | 0.540 |
| | discharge | 51.3±7.7 | 50.1±4.0 | 49.3±4.5 | 0.586 |
| MPV, fL (Mean ± SD) | Day 1 | 9.2±0.8 | 8.9±0.8 | 9.0±0.9 | 0.623 |
| | Day 5 | 9.0±1.0 | 13.2+17.2 | 9.0±0.8 | 0.698 |
| | discharge | 9.2±1.0 | 8.8±0.9 | 14.9±22.9 | 0.210 |
| NLR (Mean ± SD) | Day 1 | 3.2±2.1 | 6.2±8.3 | 6.3±6.5 | 0.288 |
| | Day 5 | 2.0±0.6 | 4.5±6.1 | 3.8±3.4 | 0.529 |
| | discharge | 2.5±1.6 | 11.7±40.0 | 2.6±2.4 | 0.454 |
| PLR (Mean ± SD) | Day 1 | 135.5±68.8 | 200.9±155.9 | 174.4±75.4 | 0.208 |
| | Day 5 | 132.2±55.3 | 223.7±175.4 | 154.2±34.4 | 0.286 |
| | discharge | 155.4±43.1 | 158.3±66.6 | 137.3±45.9 | 0.490 |
| INR (Mean ± SD) | Day 1 | 1.10±0.20 | 1.14±0.21 | 1.11±0.14 | 0.773 |
| | Day 5 | 1.13±0.10 | 1.16±0.13 | 1.03±0.18 | 0.360 |
| | discharge | 1.21±0.38 | 1.01±0.09 | 1.19±0.30 | 0.450 |
| Ferritin,ml/ng (Mean ± SD) # | Day 1 | 457.3±637.0 | 223.3±279.3 | 407.2±691.9 | 0.402 |
| | Day 5 | 168.2±181.5 | 581.1±820.9 | 562.8±707.1 | 0.605 |
| | discharge | 361.0±372.3 | 254.2±277.4 | 541.1±697.8 | 0.243 |
| d-dimer ,μ/L (Mean ± SD) # | Day 1 | 0.76±0.58 | 0.84±1.36 | 0.99±0.77 | 0.828 |
| | Day 5 | 0.67±0.39 | 0.58±0.31 | 1.11±0.92 | 0.093 |
| | discharge | 0.62±0.35 b | 0.55±0.36 b | 1.73±2.90 a | 0.029 |
| CRP,mg/dL (Mean ± SD) # | Day 1 | 30.0±42.0 | 26.5±33.6 | 38.0±56.4 | 0.685 |
| | Day 5 | 22.4±18.2 | 42.5±48.1 | 17.1±21.3 | 0.306 |
| | discharge | 10.0±10.2 b | 7.2±6.1 b | 27.0±49.7 a | 0.048 |

**Abbreviations:** PLT: Platelet, Hb – hemoglobin, RDW: red cell distribution width, MPV – mean platelet volume, NLR neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, INR: international normalized ratio, SD: Standard Deviation; a, b: → Different lower cases in the same row represent statistically significant differences
#: Kruskal -Wallis test

five most common symptoms at presentation were fever, shortness of breath, cough, fatigue / weakness and confusion (20).

Hypertension (16.4%), Cardiovascular Disease (12.1%) and diabetes mellitus (%). 9,8) were found to be the most common comorbidities (19). Hypertension (23.4%) was the most common accompanying comorbidity. Other are COPD, Diabetes mellitus, Coronary Heart Disease,

Chronic Kidney Failure, Cerebrovascular Disease and cancer respectively. Also in another studies, hypertension, cardiovascular disease and diabetes were found to be the most common comorbidities (19).

Monitoring of values defined as poor prognosis criteria in COVID- 19 (blood lymphocyte count <800 / µl or CRP> 10 x upper limit of normal value or ferritin> 500ng / ml or D-Dimer> 1000 ng / ml, etc.) and improvement in these values are the most concrete parameter showing that the disease is getting better. Studies have found that lymphopenia, PT / PTT length and D-Dimer elevation in patients with more severe clinical course (13). It was found that 94 patients infected with SARS CoV-2 had significantly higher coagulation function, D-Dimer and FDP levels compared to 40 normal people (14). In an article in which healthcare workers diagnosed with COVID- 19 pneumonia were examined, leukopenia, lymphopenia and increased D-Dimer were found in all patients (22).

In one of the studies, high plasma CRP level showed severe COVID-19 pneumonia and longer inpatient duration (23). In another, the relationship between the early CRP levels of COVID-19 and the disease severity was determined (24).

These studies revealed the relationship between the values controlled at the time of admission and the severity of the disease. On the other hand, we observed a more significant decrease in d-dimer and CRP values in the group that received Favipiravir after HCQ before discharge compared to the group that received Favipiravir alone or HCQ alone. That is, there was a relationship between CRP and d-dimer reduction and improvement of the disease. As a result of our study, we concluded that especially CRP and d-dimer levels should be followed in COVID-19 disease. In addition, showing this improvement in the group who received favipiravir after HCQ supports that we made the treatment changes on time and the treatment method recommended in the guideline was appropriate.

If we talk about the limitations of our study; A small number of patients were included in the study. Comparing the three groups with more patients could make our study's data stronger. Another limitation is that we did not examine the relationship between the radiological extent of the disease and laboratory parameters. One of the strengths of our study is that there is no other study comparing the efficacy of HCQ and Favipiravir in terms of laboratory parameters. The other is; other studies have revealed the relationship between disease severity and various laboratory parameters, but our study found a relationship between disease recovery and d-dimer and CRP.

The results of this study we conducted with the two most commonly used drugs in our country reveal that HCQ and Favipiravir are not superior to each other. D-dimer and CRP values decreased during discharge in the group of patients in whom we switched to Favipiravir after HCQ, because their clinic and / or laboratory values worsened. This finding shows how effective the timely treatment change is in the recovery of the patient by closely following the patient clinically and interpreting the laboratory values correctly. The observation of this finding in the received Favipiravir group after HCQ emphasizes the importance of changing the treatment regimen when necessary. We think that the follow-up of D-dimer and CRP levels are two important markers showing improvement in COVID-19 patients.

At this point, we can say that, in COVID-19, we should direct the treatment of our patients by following the symptoms, risk factors and especially laboratory values.

## References


1. World Health Organization (2020) Novel coronavirus (2019-nCoV). Situation Report. Weekly epidemiological update -[cited 27Januar2021]. Available from: https://www.who.int/emergencies/diseases/novelcoronavirus-2019
2. Cao B, Wang Y, Wen D, et al. A trial oflopinavir–ritonavir in adults hospitalized with severe Covid-19. N Engl J Med 2020; 382: 1787-1799.
3. Borba MGS, Val FFA, Sampaio VS, et al. Effect of high vs low doses of chloroquine diphosphate as adjunctive therapy for patients hospitalized with severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) infection: a randomized clinical trial. JAMA Netw Open 2020; 3: e208857.
4. The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19-preliminary report. N Engl J Med. DOI: 10.1056/NEJMoa2021436.
5. Sheahan TP, Sims AC, Leist SR, et al. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERSCoV.cNat Commun 2020; 11: 222
6. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020; 395: 565-574.

7. Rodrigo C, Fernando SD, Rajapakse S. Clinical evidence for repurposing chloroquine and hydroxychloroquine as antiviral agents: a systematic review. Clin Microbiol Infect 2020; 26: 979-987.
8. NEJM Journal Watch. COVID-19 update: hydroxychloroquine & recovery time/home face masks at work/reusing respirators. 2020 April 1 [cited 2020 Apr 5]. Available from: https://www.jwatch.org/ fw116513/2020/04/01/covid-19-update hydroxychloroquinerecovery- time-home
9. Furuta, Y., Komeno, T. & Nakamura, T. Favipiravir (T-705), a broad spectrum inhibitör of viral RNA polymerase. Proc. Jpn. Acad. Ser. B Phys. Biol. Sci 2017; 93: 449-463.
10. Vincent MJ, Bergeron E, Benjannet S, et al. Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. Virol J 2005; 2: 69.
11. de Wilde AH, Jochmans D, Posthuma CC, et al. Screening of an FDA-approved compound library identifies four small-molecule inhibitors of Middle East respiratory syndrome coronavirus replication in cell culture. Antimicrob Agents Chemother 2014; 58: 4875-4884.
12. TC Sağlık Bakanlığı, Halk Sağlığı Genel Müdürlüğü " Covid 19 Rehberi" 2020. [cited 27 January 2021]. Available from: www.saglık.gov.tr (in Turkish).
13. Wan S, X_ang Y, Fang W, et al. Clinical Features and Treatment of COVID-19 Patients in Northeast Chongqing. J Med Virol 2020.
14. Han H, Yang L, L_u R, et al. Prominent changes in blood coagulation of patients with SARSCoV- 2 infection. Clin Chem Lab Med 2020.
15. Chen Z, Hu J, Zhang Z, et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial (preprint). MedRxIV; 2020 Mar 31 [cited 2020 Apr 11] Available from: https://www.medrxiv.org/content/10.1101/2020.03.22. 20040758v2.
16. Lu CC, Chen MY, Chang YL. (2020) Potential therapeutic agents against COVID-19: What we know so far. Journal of the Chinese Medical Association. https://doi.org/10.1097/JCMA.0000000000000318.
17. Geleris J, Sun Y, Platt J, et al. Observational study of hydroxychloroquine in hospitalized patients with Covid-N Engl J Med 2020; 382: 2411-2418.
18. Jun C, Danping L, Li L, Ping L, Qingnian X, Lu X, vd. A pilot study of hydroxychloro-quine in treatment of patients with common coronavirus disease-19 (COVID-19). J Zheji-ang Univ(MedicalSci2020;49(1):0-0.Availablefrom: http://www.zjujournals.com/med/EN/10.3785/j.issn.1008-9292.2020.03.03
19. Chen C, Zhang Y, Huang J, Yin P, Cheng Z, Wu J, et al. Favipiravir versus Arbidol for COVID-19: A Randomized Clinical Trial. medRxiv. 2020:2020.03.17.20037432.
20. International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC). COVID-19 Report: 19 May 2020 [Internet]: ISARIC; 2020. Available from: https://media.tghn.org/medialibrary/2020/05/ISARIC_Data_Platform_COVID-19_Report_19MAY20.pdf.
21. Zhang JJY, Lee KS, Ang LW, Leo YS, Young BE. Risk Factors of Severe Disease and Efficacy of Treatment in Patients Infected with COVID-19: A Systematic Review, Meta-Analysis and Meta-Regression Analysis. Clin Infect Dis 2020; 71: 2199-2206.
22. Liu M, He P, Liu HG, et al. Clinical characteristics of 30 medical workers infected with new coronavirus pneumonia. Zhonghua J_e He He Hu XiZa Zhi 2020; 43: 209-214.
23. Chen W, Zheng K, Liu S, et al. Plasma CRP level is positively associated with the severity of COVID-19 Ann Clin Microbiol Antimicrob 2020; 19: 18.doi: 10.1186/s12941-020-00362-2
24. Wang L. C-reactive protein levels in the early stage of COVID-19 Med Mal Infect 2020; 50: 332-334.