Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1625339
J Health Sci Med. 2025;8(2):308-312

Cardiac rhythm disturbances associated with hydroxychloroquine and azithromycin combination in children with COVID-19 pneumonia

Damla Geçkalan[1], Rahmi Özdemir[2], Yasin Yılmaz[3], Cemile Hilal Çelik[3], Batuhan Berk Demir[3], Yeşim Tunç[4]

[1]Department of Pediatrics, Bakırçay University Çiğli Training and Research Hospital, İzmir, Turkiye
[2]Division of Pediatric Cardiology, Department of Pediatrics, Faculty of Medicine, İzmir Katip Çelebi University, İzmir, Turkiye
[3]Department of Pediatrics, Faculty of Medicine, Kütahya Health Sciences University, Kütahya, Turkiye
[4]Department of Biostatistics, Faculty of Medicine, Kütahya Health Sciences University, Kütahya, Turkiye

Cite this article as: Geçkalan D, Özdemir R, Yılmaz Y, Çelik CH, Demir BB, Tunç Y. Cardiac rhythm disturbances associated with hydroxychloroquine and azithromycin combination in children with COVID-19 pneumonia. *J Health Sci Med.* 2025;8(2):308-312.

Received: 22.01.2025 ◆ **Accepted**: 25.02.2025 ◆ **Published**: 21.03.2025

ABSTRACT

Aims: At the beginning of the COVID-19 pandemic; it has been shown that receiving hydroxychloroquine and azithromycin treatment decrease viral carriage of coronavirus in patients. In this study, we aimed to evaluate electrocardiography (ECG) abnormalities in pediatric patients with COVID-19 pneumonia receiving combined therapy with hydroxychloroquine and azithromycin.

Methods: In this study; ECG and laboratory parameters of 24 children with COVID-19 pneumonia who were treated with hydroxychloroquine and azithromycin at Health Sciences University between June 2020 and November 2020 were analyzed retrospectively. P wave dispersion (PWd), QT interval (QT), QT dispersion (QTd), QTc interval (QTc), QTc dispersion (QTcd), Tpeak-Tend interval (Tp-e), Tp-e dispersion (Tp-ed), Tp-e/QT, Tp-Te/QTc ratios were evaluated with 12 lead ECG. ECG parameters and QTc interval were compared before and after (5 days) the treatment.

Results: The mean age was 13±4.5 years and 62.5% were female. Median hospitalization length was 6 days. There was no statistically significant difference between the PWd, QT and QTc interval, QTd, QTcd, Tp-e interval, Tp-e dispersion, Tp-e/QT, Tp-e/QTd measurements and ratios of the before and after treatment. A significant difference was found for the decrease in hearth rate in regard to the measurement before and after the treatment.

Conclusion: In our study, there were no rhythm problems which were observed on ECG in pediatric patients receiving hydroxychloroquine and azithromycin combination therapy for COVID-19 pneumonia. We also found that laboratory parameters were not specific for COVID-19 pneumonia in children.

Keywords: Azithromycin, COVID-19, D-dimer, hydroxychloroquine, side effects, QTc prolongation

INTRODUCTION

COVID-19 (Coronavirus disease 2019) is primarily known as a respiratory infection due to the SARS-CoV-2 virus. But it has been shown to be a multisystemic disease involving the cardiovascular, gastrointestinal, hematopoietic and immune systems.[1] Although data and treatments related to adult patients were mostly published at the beginning of the pandemic, publications began to appear on diagnosis and treatment in children over time.[2] Following the start of the COVID-19 pandemic in Turkiye, a data announced by the Ministry showed that there were 198.284 COVID-19 cases in Turkiye as of June 28, 2020, and 14.388 of them were children aged 15 and under (7.3%).[3] It was observed that clinical and laboratory findings in children were different from those in adults. Laboratory findings regarding COVID-19 in children were found to be similar to findings in other coronavirus infections. In studies; WBC was mostly normal or low and CRP was reported as normal. In severe cases, high D-dimer levels have been reported.[4,5]

However, there were differences in the protocols implemented by countries and recommended by ministries of health during the new COVID-19 epidemic. While hydroxychloroquine was recommended in some countries, it was not recommended in some countries due to its side effects.[6-8] Chloroquine, which was started to be used in the treatment of malaria in the 1950s, also used for anti-inflammatory treatment of lupus erythematosus and rheumatoid arthritis. Studies

Corresponding Author: Damla Geçkalan, drdamlageckalan@gmail.com

have been published showing that it is also effective against viruses in the COVID-19 pandemic.[9,10] After these studies, it was included in the treatment protocol of the COVID-19 treatment in some countries such as Turkiye and China. But later that, hydroxychloroquine and azithromycin combined therapy was published to increased mortality, viral spread, hospitalization and cardiac side effects.[6-8] And later this combination was ceased due to side effects. The most feared side effect in combined therapy is QTc prolongation, which has been reported to occur in 0.67% of adult patients.[11,12] Food and drug administration (FDA) cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems.[13]

In the treatment protocol of the Ministry of Health in Turkiye, hydroxychloroquine and azithromycin treatment was recommended firstly in adult patients. Also, it was added to the pediatric COVID-19 pneumonia treatment protocol in March 2020, in Turkiye.[14] After FDA notification, the Turkish Ministry of Health removed the combined therapy from the pediatric treatment protocol on May 2021.[15,16] But this cases gave the opportunity to evaluate the rhythm disturbances among children who had this combination therapy.

In this study, we aimed to evaluate ECG abnormalities (cardiac repolarization inhomogeneity and QTc prolongation) in pediatric patients with COVID-19 pneumonia receiving combined therapy with hydroxychloroquine and azithromycin.

METHODS

The study was carried out with the permission of the Kütahya Health Sciences University Rectorate Non-interventional Clinical Researches Ethics Committee (Date: 30.06.2021, Decision No: 2021/11-17). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this study, 24 pediatric COVID-19 pneumonia patients treated with hydroxychloroquine and azithromycin combination between June 2020 and November 2020 in the pediatric pandemia service at Kütahya Health Sciences University of Health Sciences were retrospectively analyzed for cardiac dysrhythmia before and after the treatment. Patients with congenital or acquired heart disease, patients diagnosed with myocarditis and patients being treated in intensive care unit were excluded from the study. All patient's echocardiography and 12 lead ECG analysis were evaluated by a pediatric cardiologist. We evaluated ECG and laboratory parameters in patients with COVID-before treatment and on the fifth day of treatment, retrospectively. P wave dispersion (PWd), QT interval (QT), QT dispersion (QTd), QTc interval (QTc), QTc dispersion (QTcd), Tpeak-Tend interval (Tp-e), Tp-e dispersion (Tp-ed), Tp-e/QT, Tp-Te/QTc ratios and also other arrhythmias were evaluated with 12 lead electrocardiography.

Treatment dose of hydroxychloroquine loading dose 10 mg/kg (max: 600 mg/dose), then 3 mg/kg (max: 200 mg/dose) for 4 days period and the total treatment duration was five days) and azithromycin (loading dose 10 mg/ kg and maintenance dose 5 mg/kg daily on the days of 2-5) were given orally for 5 days.[14] All patients were received ceftriaxone to address potential secondary bacterial infections.

Electrocardiographic Analysis

Heart rate (per minute), QRS, corrected QT (cQT), Tpeak-Tend interval (Tpe), corrected Tpe (cTpe), and cTpe/cQT intervals were analyzed from 12-derived ECG by pediatrician and a pediatric cardiologist who were blinded to the patients' data. Examinations were performed on the leads II and V5 at least for measurement. QRS was measured from the beginning of the QRS to the end of the S wave and reflects ventricular depolarization. The QT interval was measured from the beginning of the QRS complex to the end of the tangent of T wave at the point of the isoelectric line. The Tpe interval was measured from the peak point of T wave to the end of the tangent of T wave crossing isoelectric line (the difference between QT interval and QT peak interval).[12] cQT and cTpe were measured by means of Bazett formula: $cQT=QT\sqrt{}$ (R-R interval) and $cTpe=Tpe\sqrt{}$ (R-R interval), respectively.

Laboratory Analysis

Demographic data, blood parameters [white blood cell (WBC) count, lymphocyte count, neutrophil count, hemoglobin, platelet, platecrit, C-reactive protein (CRP), D-dimer, fibrinogen, troponin-I] levels, clinical course, comorbid diseases, medications were evaluated from the medical records.

Statistical Analysis

All statistical analyses were performed using the SPSS software, version 21.0 for Mac (SPSS Inc, Chicago IL, USA). Continuous variables were shown median with interquartile range values. Categorical variables were shown as number and rate. The Kalmogorov-Smirnov test was used to assess the normality of distribution. A paired sample T test or Wilcoxon signed rank test, was employed to calculate the difference between each before-and-after pair of measurements. The categorical values were stated in units of numbers (n) and percentages. The data were analyzed at a 95% confidence level and considered significant at a p-value of less than 0.05.

RESULTS

The mean age was 13±4.5 years (min 1.9 years-max 17 years) and 62.5% were female of patients. Median hospitalization length was 6±1 day (min 5-max 8 day). There was no statistically significant difference between the PWD, QT and QTc interval, QTd, QTcd, Tp-e interval, Tp-e dispersion, Tp-e/QT, Tp-e/QTd measurements and ratios of the before and after treatment. Only a decrease in heart rate was found statistically significant before and after the treatment (**Table 1**). The patients' laboratory parameters were evaluated. Only D-dimer levels were found above the reference range, but no statistically significant difference was found (**Table 2**). No rhythm abnormalities were observed in all COVID-19 pneumonia patients receiving hydroxychloroquine and azithromycin therapy.

Table 1. Comparison of electrocardiographic measurements of the COVID-19 pneumonia patient before and after the treatment

ECG parameters	Before treatment mean (IQR 25%-75%)	After treatment mean (IQR 25%-75%)	p-value*
Heart rate (/min)	93 (79-99)	81 (75-92)	0.008
P wave duration (ms)	80 (80-100)	80 (80-100)	0.202
P dispersion (ms)	20 (20-40)	20 (12-35)	0.275
QT interval (ms)	340 (320-360)	360 (340-377)	0.140
QT dispersion (ms)	20 (20-35)	20 (20-37.5)	0.964
QTc interval (ms)	405 (392-428)	408 (380-430)	0.877
QTc dispersion (ms)	30 (20-58)	30 (21-46)	0.762
Tp-e interval (ms)	70 (60-95)	75 (60-80)	0.369
Tp-e dispersion (ms)	20 (20-40)	20 (20-37.5)	0.418
Tp-e/QT ratio	0.20 (0.17-0.28)	0.20 (0.17-0.25)	0.475
Tp-e/QTc ratio	0.17 (0.15-0.22)	0.16 (0.15-0.20)	0.394

*Wilcoxon signed rank test, p-value <0.05, ECG: Electrocardiography, IQR: Interquartile range, QT: The time from the beginning of the Q wave to the end of the T wave

Table 2. Evaluation of blood parameters of patients with COVID-19 pneumonia

Blood parameters	Median (25-75%)	Reference values
WBC (10^3/ul)	6.635 (4.660-9.402)	4.0-10.0
Lymphocyte (%)	35.75 (22.49-42.35)	19-44
Neutrophil (%)	56.25 (48.50-67.70)	41-73
Hemoglobin (g/dl)	13.75 (12.45-14.85)	11-16
Platelet (10^3/ul)	240 (185.2-296.7)	130-400
Fibrinogen (mg/dl)	366.83 (312.5-360.2)	200-400
D-dimer (ng/ml)	788.9 (338.5-450.0)	170-550
Platecrit (%)	0.20 (0.17-0.26)	0.10-0.28
Troponin-I (ng/ml)	1.6 (0.5-1.5)	0-19.8
CRP (mg/L)	2.5 (1.3-16.8)	<5

WBC: White blood cell, CRP: C-reactive protein

DISCUSSION

Studies have reported that combination therapy of hydroxychloroquine and azithromycin may cause fatal side effects such as arrhythmia, QTc prolongation or ventricular repolarization.[17,18] As a result of these studies, it was predicted that combination treatments should be careful in terms of cardiac side effects and should be excluded from the routine treatment of COVID-19. Here, in this study, no cardiac repolarization inhomogeneity or QTc prolongation was detected in these patients.

In former studies it was thought to be hydroxychloroquine combined with azithromycin is more effective in treating COVID-19 efficiently than hydroxychloroquine alone, and the *in vivo* mechanisms by which this potential synergy occurs is unknown.[19] Azithromycin is a macrolide antibiotic that can inhibit gram-positive and negative bacteria targeting protein synthesis of bacterial ribosomes.[20] Mortality and morbidity caused by bacteria pneumonia with coinfections maybe reduced by using azithromycin in patients infected by Spanish flu and SARS-CoV-2.[21,22] Although hydroxychloroquine and azithromycin are generally well-tolerated medications used in clinical practice, both can cause corrected QT (QTc) prolongation.[17,18]

Since most studies were conducted in adult patients, it was noted that the pharmacokinetics of hydroxychloroquine in children did not differ significantly compared to adults, except for newborns.[23,24] In addition, recent studies report that hydroxychloroquine is used off-label for interstitial lung disease in addition to the routine treatment of malaria and rheumatic diseases in children.[25,26]

In order to determine whether the combined use of these drugs has an additive or synergistic effect on QT prolongation, a study has been conducted on the scanning of the files in the U.S. Food and Drug Administration's adverse event reporting system (FAERS). According to the analysis of these reports, chloroquine/hydroxychloroquine alone was not found to be associated with QT prolongation and safety signal of torsades de pointes. The use of azithromycin alone or in combination with chloroquine/hydroxychloroquine has been associated with a potential risk of adverse effects. According to this analysis, it has been reported that the use of chloroquine/hydroxychloroquine seems to be partially safe in terms of this specific adverse effect, but more studies are needed on its use in COVID-19 disease.[27] Even though we did not find any rhythm abnormalities in our study, the study was performed in pediatric cases which may be important.

According to Tisdale et al.,[28] there are risk factors associated with QTc prolongation in adult patients. They have been developed into a risk score tool that takes age, sex, diuretic use, potassium level, baseline QTc, acute myocardial infarction, use of QTc prolonging drugs, sepsis and heart failure at adult patients. Also, most of pediatric patients don't have these risk factors for QTc prolongation. In a study from Turkiye, compared to adult COVID-19 patients was treated by either hydroxychloroquine (HCQ) + azithromycin or HCQ alone. The results of the study were as follows; off-label drugs (HCQ/azithromycin combination therapy) have an acceptable cardiac adverse effect in short-term hospitalization.[29] In our study, there was no statistical difference in ECG parameters except for heart rate. The observed decrease in heart rate was deemed associated with the clinical progression of pneumonia in pediatric patients rather than being attributed to a side effect. Since the high heart rate at first admission could be caused by factors such as inflammation, fever, and pneumonia, we thought that returning the heart rate to normal after treatment was an expected result.

However, the relationship between laboratory parameters and especially pneumonia and myocarditis in COVID-19 pediatric patients is not clear. White blood cell (WBC), C-reactive protein (CRP), D-dimer, fibrinogen, troponin-I are the most commonly used markers. The most frequently observed laboratory changes in hospitalized adult and pediatric patients with COVID-19 are characterized by elevations in fibrinogen and D-dimer levels.[30-32] In our study, when we evaluated the blood parameters of our patients at the time of admission; the fact that blood parameters other than D-dimer are within normal limits is a result we expected, consistent with most of the literature.[33,35] However, in our study, the detection of WBC

and CRP within the normal range was found to be compatible with viral COVID-19 pneumonia. In our study, the fact that troponin-I values and ECGs of patients were normal showed that pneumonia was not accompanied by myocarditis at the time of admission.

Furthermore, considering the absence of typical risk factors for QTc prolongation seen in adults, such as hypokalemia and heart failure, no cardiac rhythm side effects were observed in pediatric patients in our study. This observation may also be influenced by our patient selection criteria (excluding individuals with pre-existing heart diseases or other comorbid conditions). It is crucial to emphasize the necessity of careful monitoring for patients with heart diseases or illnesses that can lead to electrolyte imbalances. Additionally, a prospective study could shed light on potential rhythm disturbances under combined therapy with hydroxychloroquine and azithromycin in this specific population.

Limitations

Among the limitations of this study, the number of patients was relatively very small. The number of patients is limited because the combined drug is not preferred in pediatric patients due to side effects in adults and the dual combined treatment is used only in adolescent patients diagnosed with COVID-19 pneumonia. In addition, each clinic applied a different treatment protocol and our study is a single centre retrospective study. For these two drugs, which are rarely used in combination in children, a study with a larger patient group is required. In addition, since it was performed in a single centre; multicentre and a larger number of patients should be analysed.

CONCLUSION

In our study, we found that combined treatment with hydroxychloroquine and azithromycin for COVID-19 pneumonia did not statistically prolong QTc in pediatric patients. However, we analyzed that laboratory parameters did not differ significantly for COVID-19 pneumonia in children.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Kütahya Health Sciences University Rectorate Non-interventional Clinical Researches Ethics Committee (Date: 30.06.2021, Decision No: 2021/11-17).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Kannan S, Shaik Syed Ali P, Sheeza A, Hemalatha K. COVID-19 (novel Coronavirus 2019)-recent trends. *Eur Rev Med Pharmacol Sci*. 2020; 24(4):2006-2011. doi:10.26355/eurrev_202002_20378
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel Coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5
3. Üzel VH, Yılmaz K, Şen V, et al. Evaluation of hematological parameters of children diagnosed with COVID-19: single-center experience. *Turk Arch Pediatr*. 2021;56(5):463-468. doi:10.5152/TurkArchPediatr.2021.21076
4. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr*. 2020;109(6): 1088-1095. doi:10.1111/apa.15270
5. Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. *Pediatr Infect Dis J*. 2020;39(5):355-368. doi:10.1097/INF.0000000000002660
6. Okour M, Al-Kofahi M, Austin D. Hydroxychloroquine and azithromycin as potential treatments for COVID-19; clinical status impacts the outcome. *J Pharmacokinet Pharmacodyn*. 2020;47(3):187-188. doi:10.1007/s10928-020-09689-x
7. Gautret P, Honoré S, Lagier JC, Raoult D. Safety profile of hydroxychloroquine and azithromycin combined treatment in COVID-19 patients. *Int J Antimicrob Agents*. 2021;57(1):106236. doi:10.1016/j.ijantimicag.2020.106236
8. Lagier JC, Million M, Gautret P, et al. Outcomes of 3,737 COVID-19 patients treated with hydroxychloroquine/azithromycin and other regimens in Marseille, France: a retrospective analysis. *Travel Med Infect Dis*. 2020;36:101791. doi:10.1016/j.tmaid.2020.101791
9. Terzioğlu Bebitoğlu B, Oğuz E, Hodzic A, Oğuz E, Hodzic A, Hatiboğlu N, Kam Ö. Chloroquine/hydroxychloroquine: pharmacological view of an old drug currently used in COVID-19 treatment. *Anat Clin*. 2020;25(1): 204-215. doi:10.21673/anadoluklin.735826
10. Ben-Zvi I, Kivity S, Langevitz P, Shoenfeld Y. Hydroxychloroquine: from malaria to autoimmunity. *Clin Rev Allergy Immunol*. 2012;42(2):145-153. doi:10.1007/s12016-010-8243-x
11. Gautret P, Hoang VT, Lagier JC, Raoult D. Effect of hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial, an update with an intention-to-treat analysis and clinical outcomes. *Int J Antimicrob Agents*. 2021;57(1): 106239. doi:10.1016/j.ijantimicag.2020.106239
12. Goldman JD, Diaz G, Urba WJ. Use of hydroxychloroquine in combination with azithromycin for patients with COVID-19 is not supported by recent literature. *Int J Antimicrob Agents*. 2021;57(1):106174. doi:10.1016/j.ijantimicag.2020.106174
13. U.S Food&Drug Adminastiration, drugs, drug safety and availability, FDA cautions against use of hydroxychloroquine or chloroquine for COVID-19 outside of the hospital setting or a clinical trial due to risk of heart rhythm problems. Available from: https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-COVID-19-outside-hospital-setting-or
14. Republic of Turkiye Ministry of Health, Department of Public Health, COVID-19 Guideline. 02.02.2020. Available from: https://dosyamerkez.saglik.gov.tr/Eklenti/37044/0/covid-19rehberipdf.pdf
15. Republic of Turkiye Ministry of Health, Department of Public Health Guideline. 06.01.2022. Available from: https://covid19.saglik.gov.tr/Eklenti/42283/0/covid-19rehbericocukhastayonetimivetedavi06012022v1pdf.pdf

16. Aktar F, Sağır H. Pediatric COVID-19 and its approach. *Dicle Med J*. 2021;48(3):166-175. doi:10.5798/dicletip.1005406
17. Asensio E, Acunzo R, Uribe W, et al. Recommendations for the measurement of the QT interval during the use of drugs for COVID-19 infection treatment. Updatable in accordance with the availability of new evidence. *J Interv Card Electrophysiol*. 2020;59(2)315-320. doi:10.1007/s10840-020-00765-3
18. World Health Organization. The cardiotoxicity of antimalarials: Malaria Policy Advisory Committee Meeting. Published March 24, 2017. Available from: https://www.who.int/malaria/mpac/mpac-mar2017-erg-cardiotoxicity-report-session2.pdf
19. Mercuro NJ, Yen CF, Shim DJ, et al. Risk of QT interval prolongation associated with use of hydroxychloroquine with or without concomitant azithromycin among hospitalized patients testing positive for Coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(9):1036-1041. doi:10.1001/jamacardio.2020.1834
20. Li C, Cheng G. Will Hydroxychloroquine still be a game-changer for COVID-19 by combining azithromycin? *Front Immunol*. 2020;11:1969. doi:10.3389/fimmu.2020.01969
21. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054-1062. doi:10.1016/S0140-6736(20)30566-3
22. Retsema J, Girard A, Schelkly W, et al. Spectrum and mode of action of azithromycin (CP-62,993), a new 15-membered-ring macrolide with improved potency against gram-negative organisms. *Antimicrob Agents Chemother*. 1987;31(12):1939-1947. doi:10.1128/AAC.31.12.1939
23. Morens DM, Taubenberger JK, Fauci AS. Predominant role of bacterial pneumonia as a cause of death in pandemic influenza: implications for pandemic influenza preparedness. *J Infect Dis*. 2008;198(7):962-970. doi:10.1086/591708
24. White NJ, Miller KD, Churchill FC, et al. Chloroquine treatment of severe malaria in children. Pharmacokinetics, toxicity, and new dosage recommendations. *N Engl J Med*. 1988;319(23):1493-1500. doi:10.1056/NEJM198812083192301
25. Schrezenmeier E, Dörner T. Mechanisms of action of hydroxychloroquine and chloroquine: implications for rheumatology. *Nat Rev Rheumatol*. 2020;16(3):155-166. doi:10.1038/s41584-020-0372-x
26. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res (Hoboken)*. 2011;63(4):465-482. doi:10.1002/acr.20460
27. Braun S, Ferner M, Kronfeld K, Griese M. Hydroxychloroquine in children with interstitial (diffuse parenchymal) lung diseases. *Pediatr Pulmonol*. 2015;50(4):410-419. doi:10.1002/ppul.23133
28. Sarayani A, Cicali B, Henriksen CH, Brown JD. Safety signals for QT prolongation or torsades de pointes associated with azithromycin with or without chloroquine or hydroxychloroquine. *Res Social Adm Pharm*. 2021;17(2):483-486. doi:10.1016/j.sapharm.2020.04.016
29. Tisdale JE. Drug-induced QT interval prolongation and torsades de pointes: role of the pharmacist in risk assessment, prevention and management. *Can Pharm J (Ott)*. 2016;149(3):139-152. doi:10.1177/1715163516641136
30. Akkuş O, Bal T, Yaqoobi H, Bekler Ö, Akkuş G, Çabalak M. Electrocardiographic findings and cardiac safety of hydroxychloroquine +azithromycin in hospitalized patients with COVID-19. *Cukurova Med J*. 2021;46(2):691-698. doi:10.17826/cumj.856174
31. Imazio M, Klingel K, Kindermann I, et al. COVID-19 pandemic and troponin: indirect myocardial injury, myocardial inflammation or myocarditis? *Heart*. 2020;106(15):1127-1131. doi:10.1136/heartjnl-2020-317186
32. 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;323(11):1061-1069. doi:10.1001/jama.2020.1585
33. Hoang A, Chorath K, Moreira A, et al. COVID-19 in 7780 pediatric patients: a systematic review. *eClinicalMedicine*. 2020;24:100433. doi:10.1016/j.eclinm.2020.100433
34. Hançerli Törün S, Kaba Ö, Sari Yanartas M, et al. Plasma D-dimer: a promising indicator of COVID-19 infection severity or only an acute phase reactant. *Minerva Pediatr (Torino)*. 2021. doi:10.23736/S2724-5276.21.06170-X
35. Lu X, Zhang L, Du H, et al. SARS-CoV-2 infection in children. *N Engl J Med*. 2020;382(17):1663-1665. doi:10.1056/NEJMc2005073