Original Article

Electrocardiographic Abnormalities and QTc Prolongation in Lupus Patients on Hydroxychloroquine in Tehran, Iran

Parisa Delkash[1], Soheila Sadeghi[2], Fatemeh Omidi[3]*

[1]Prevention of Cardiovascular Disease Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Department of Internal Medicine, School of Medicine, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Prevention of Cardiovascular Disease Research Center, Shahid BeheshtiUniversity of Medical Sciences, Tehran, Iran

Received: 13 March, 2025; Accepted: 17 May, 2025

DOI: 10.22037/nbm.v13i3.47828

Abstract

Background: Hydroxychloroquine, a commonly prescribed treatment for systemic lupus erythematosus (SLE), has been associated with potential cardiac complications, including QTc prolongation. QTc prolongation increases the risk of arrhythmias and sudden cardiac death. This study aimed to evaluate electrocardiographic (ECG) abnormalities in Iranian SLE patients receiving hydroxychloroquine treatment.

Materials and Methods: A cross-sectional study was conducted at the rheumatology clinic of Imam Hossein Hospital in Tehran, Iran. The study included patients diagnosed with systemic lupus erythematosus (SLE) receiving hydroxychloroquine treatment. Demographic and clinical data were collected through patient interviews and medical records. All participants underwent a 12-lead electrocardiogram (ECG), and the QT interval was corrected using the Bazett formula. QTc prolongation was defined as QTc≥450 ms. Additionally, fragmented QRS complexes, premature ventricular contractions (PVCs), and other ECG abnormalities were recorded.

Results: A total of 81 SLE patients on hydroxychloroquine were analyzed. The mean age was 48.5 years, and the average QTc interval was 426.52 ms (SD: 28.82 ms). QTc prolongation was observed in 16.05% of cases. Fragmented QRS complexes were found in the inferior, and V1-V3 leads in several patients, while no right or left bundle branch blocks (RBBB or LBBB) were detected. Three patients presented with PVCs, and one case showed a Brugada pattern.

Conclusion: QTc prolongation and fragmented QRS complexes were identified in many SLE patients treated with hydroxychloroquine. Regular ECG monitoring may be necessary for early detection of potential cardiac risks in this population.

Keywords: Systemic lupus erythematosus, Hydroxychloroquine, QTc prolongation, Electrocardiographic abnormalities, Fragmented QRS, Premature ventricular contractions, Iran

***Corresponding Author:** Fatemeh Omidi, MD, Prevention of Cardiovascular Disease Research Center, Shahid BeheshtiUniversity of Medical Sciences, Tehran, Iran. Email: Dr.fateme.omidi@gmail.com. ORCID:https://orcid.org/0000-0001-7302-9136

Please cite this article as: Delkash P, Sadeghi S, Omidi F. Electrocardiographic Abnormalities and QTc Prolongation in Lupus Patients on Hydroxychloroquine in Tehran, Iran. Novel Biomed. 2025;13(3):179-83.

Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organ systems and increases the risk of cardiac abnormalities1-4. Hydroxychloroquine (HCQ), a cornerstone in the

management of SLE, is widely prescribed for its immunomodulatory and anti-inflammatory effects5-7. It acts by inhibiting toll-like receptors (TLR) and reducing the production of pro-inflammatory cytokines, helping to control lupus flares and reduce disease activity8-10.

Hydroxychloroquine's relatively favorable safety profile compared to other immunosuppressive agents has made it a first-line therapy for long-term use in SLE5. However, recent studies have raised concerns about the potential cardiotoxicity of hydroxychloroquine (HCQ), linking its prolonged use to QT interval prolongation and various other electrocardiographic (ECG) abnormalities, such as fragmented QRS complexes, premature ventricular contractions (PVCs), and conduction disturbances like right and left bundle branch blocks (RBBB, LBBB)11-15.

These cardiac changes may be more pronounced in patients with major organ involvement and could complicate the management of both the underlying disease and its cardiovascular sequelae. This study aimed to evaluate the prevalence of QTc prolongation and other electrocardiographic abnormalities in a population of Iranian SLE patients receiving hydroxychloroquine treatment.

Methods

Study Population: The study population consisted of systemic lupus erythematosus (SLE) patients under hydroxychloroquine treatment who attended the rheumatology clinic at Imam Hossein Hospital from April 2023 to October 2024. Inclusion criteria were patients diagnosed with SLE and receiving hydroxychloroquine. Exclusion criteria included (1) patients who declined participation and (2) those with known cardiac diseases. Informed consent was obtained from all participants before their inclusion in the study. The study was approved by the Ethics Committee of Imam Hossein Hospital (Ethics code: IR.SBMU.RETECH.REC.1402.701).

Data Collection: Data were collected through patient interviews and the acquisition of a standard 12-lead ECG using an ECG recording device [16]. A researcher-developed checklist was employed to record data under the study objectives. The collected data included demographic information, clinical variables, and electrocardiographic parameters. The ECGs were analyzed for QT intervals and any electrocardiographic abnormalities, such as QTc prolongation, fragmented QRS complexes, and bundle branch blocks.

Study Procedure: After obtaining informed consent, eligible SLE patients receiving hydroxychloroquine were invited to participate during their clinic visits. Disease activity was assessed using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), and patients were categorized into two groups: major and minor organ involvement[17]. Demographic and clinical data, including medication dosage, concomitant treatments, and disease duration, were collected through patient interviews or medical records.

All patients underwent a 12-lead ECG for QT interval assessment and electrocardiographic abnormality screening. QTc intervals were corrected using Bazett's formula, with QTc prolongation defined as ≥450 ms [18]. Additional ECG findings, such as fragmented QRS complexes, PVCs, and BBB, were also recorded and analyzed.

Statistical Analysis: Descriptive statistics were used to summarize the demographic, clinical, and electrocardiographic data. The collected variables' mean, standard deviation, and frequency were calculated. Cases of QTc prolongation, fragmented QRS complexes, PVCs, and other ECG abnormalities were categorized and presented as percentages. All data were processed using SPSS statistical software, version 26.

Results

In this study, 81 cases of SLE patients undergoing treatment with hydroxychloroquine were analyzed for QTc prolongation and electrocardiographic abnormalities. The mean age of the patients was 48.5 years, with an age range spanning from 18 to 74 years. The mean QTc interval across all cases was 426.52 ms, with a standard deviation of 28.82 ms, indicating a relatively homogenous distribution of QTc values within the cohort (Table 1).

QTc prolongation (QTc ≥ 450 ms), a known risk factor for torsades de pointes and other arrhythmias, was observed in 13 cases (16.05%). Among these patients, the QTc intervals ranged from 450 ms to the maximum

Table 1. QTc Interval Analysis.

Parameter	Value
Mean QTc (ms)	426.52
Standard Deviation (ms)	28.82
QTc Prolongation (≥450 ms)	13
Normal QTc (<450 ms)	68
Maximum QTc (ms)	507
Minimum QTc (ms)	367

recorded value of 507 ms. The remaining 68 cases (83.95%) had QTc values within the normal range (<450 ms), with the lowest QTc measured at 367 ms (Table 2).

Table 2. Electrocardiographic Abnormalities.

Abnormality	Frequency	Percentage
QTc Prolongation (≥450 ms)	13	16.05%
Sinus Tachycardia	3	3.70%
PVCs (Premature Ventricular Contractions)	3	3.70%
Fragmented QRS (Inferior/V1-V3)	27	33.33%
Brugada Pattern	1	1.23%
Right Bundle Branch Block (RBBB)	0	0%
Left Bundle Branch Block (LBBB)	0	0%

Fragmented QRS complexes, indicative of myocardial scarring or conduction delays, were identified predominantly in the inferior and V1-V3 leads, affecting 27 cases (33.33%). These findings may suggest underlying myocardial involvement in SLE patients. Importantly, no instances of RBBB or LBBB were reported, except for one case presenting with a Brugada pattern in V1, a marker of increased arrhythmic risk. Additionally, three patients (3.70%) presented with PVCs, which, while often benign, may warrant closer monitoring in this population given their potential to precipitate more serious arrhythmias.

Discussion

The main findings of this study indicate that 16.05% of Iranian SLE patients undergoing hydroxychloroquine treatment exhibited QTc prolongation (QTc ≥ 450 ms). The mean QTc interval was 426.52 ms, with the highest recorded QTc reaching 507 ms. A notable presence of fragmented QRS complexes, particularly in the inferior and precordial leads (V1-V3), was also observed. Other electrocardiographic abnormalities included PVCs in 3 patients (3.7%), while no significant BBB was detected except for one case showing a Brugada pattern in lead V1.

These findings highlight the potential risk of QTc prolongation and other arrhythmogenic abnormalities in SLE patients treated with hydroxychloroquine. QTc prolongation has been associated with an increased risk of ventricular arrhythmias, making monitoring QTc intervals in these patients essential [19, 20]. Although hydroxychloroquine is generally considered safe, particularly at therapeutic doses, its effects on cardiac conduction warrant careful observation in certain patient populations, especially those with additional risk factors like concomitant medications or electrolyte disturbances.

The presence of fragmented QRS complexes is particularly interesting, as it may indicate myocardial scarring and an elevated risk of arrhythmic events. Previous studies have shown a link between fragmented QRS and adverse cardiac outcomes in other diseases. However, its significance in SLE patients remains less clear and should be the focus of future research[21-22].

Although generally benign in isolated cases, PVCs may assume clinical importance when occurring in conjunction with other electrocardiographic abnormalities, such as QTc prolongation or fragmented QRS complexes. In this context, patients with PVCs should be monitored more closely for any progression toward more serious arrhythmias.

The absence of significant BBB in this cohort suggests that these conduction disturbances are not a primary concern in SLE patients treated with hydroxychloroquine. However, the single case of the Brugada pattern noted in lead V1 is clinically relevant, as Brugada syndrome is a known risk factor for sudden cardiac death due to ventricular arrhythmias.

The findings of this study have important clinical implications for the management of SLE patients undergoing hydroxychloroquine treatment. Identifying QTc prolongation in a significant portion of patients suggests that regular ECG monitoring is crucial in preventing potentially life-threatening arrhythmias, particularly in patients with additional risk factors or

concomitant medications that may affect cardiac conduction[19, 20]. Given that hydroxychloroquine is widely prescribed for SLE and other autoimmune diseases, clinicians should consider routine QTc interval assessments, especially in those with prolonged treatment durations or higher drug dosages. The presence of fragmented QRS complexes, which may reflect myocardial scarring or fibrosis, could help identify patients at risk of more serious arrhythmias. This observation raises the need for further investigation into the long-term cardiovascular risks in SLE patients. Clinicians may need to incorporate additional diagnostic tools, such as echocardiography or cardiac MRI, to understand the cardiac involvement in these patients better.

This study contributes valuable data that could inform future guidelines on the cardiac monitoring of SLE patients on hydroxychloroquine therapy. The electrocardiographic abnormalities identified may guide risk stratification and personalized treatment plans, improving patient outcomes. Future research should explore the pathophysiological mechanisms underlying these ECG changes and their long-term impact on cardiovascular morbidity and mortality.

This study was limited by its cross-sectional nature, which restricts the ability to conclude the long-term outcomes of patients with electrocardiographic abnormalities. Additionally, the relatively small sample size and single-center setting may limit the generalizability of the findings. Larger, multicenter studies with longitudinal follow-up are necessary to validate these results and explore the clinical implications of the identified ECG abnormalities.

Conclusion

Our study highlights a significant prevalence of QTc prolongation and fragmented QRS complexes in SLE patients on hydroxychloroquine, underscoring the need for regular electrocardiographic monitoring in this population. Given the potential arrhythmic risks associated with these findings, further studies are needed to investigate their long-term cardiovascular impact and guide appropriate management strategies for SLE patients undergoing hydroxychloroquine treatment.

Acknowledgment

None.

Funding

None.

Conflict of interest

The authors further declare that they have no conflict of interest.

References

1. Siegel, C.H. and L.R. Sammaritano, Systemic lupus erythematosus: a review. Jama, 2024. 331(17): p. 1480-1491.
2. Barber, M.R., et al., Global epidemiology of systemic lupus erythematosus. Nature Reviews Rheumatology, 2021. 17(9): p. 515-532.
3. Yafasova, A., et al., Long-term cardiovascular outcomes in systemic lupus erythematosus. Journal of the American College of Cardiology, 2021. 77(14): p. 1717-1727.
4. Bello, N., et al., Cardiovascular events and risk in patients with systemic lupus erythematosus: Systematic literature review and meta-analysis. Lupus, 2023. 32(3): p. 325-341.
5. Dima, A., et al., Hydroxychloroquine in systemic lupus erythematosus: overview of current knowledge. Therapeutic advances in musculoskeletal disease, 2022. 14: p. 1759720X211073001.
6. Grimaldi, L., et al., Hydroxychloroquine and Cardiovascular Events in Patients With Systemic Lupus Erythematosus. JAMA network open, 2024. 7(8): p. e2432190-e2432190.
7. Petri, M., et al., Association of higher hydroxychloroquine blood levels with reduced thrombosis risk in systemic lupus erythematosus. Arthritis & Rheumatology, 2021. 73(6): p. 997-1004.
8. Han, J., et al., The mechanisms of hydroxychloroquine in rheumatoid arthritis treatment: Inhibition of dendritic cell functions via Toll like receptor 9 signaling. Biomedicine & Pharmacotherapy, 2020. 132: p. 110848.
9. Kyburz, D., F. Brentano, and S. Gay, Mode of action of hydroxychloroquine in RA—evidence of an inhibitory effect on toll-like receptor signaling. Nature clinical practice Rheumatology, 2006. 2(9): p. 458-459.
10. Nirk, E.L., F. Reggiori, and M. Mauthe, Hydroxychloroquine in rheumatic autoimmune disorders and beyond. EMBO molecular medicine, 2020. 12(8): p. e12476.
11. Joyce, E., A. Fabre, and N. Mahon, Hydroxychloroquine cardiotoxicity presenting as a rapidly evolving biventricular cardiomyopathy: key diagnostic features and literature review. European Heart Journal: Acute Cardiovascular Care, 2013. 2(1): p. 77-83.
12. Dey, S., et al., Hydroxychloroquine and cardiotoxicity. Cardiology in Review, 2023: p. 10.1097.

13. Chatre, C., et al., Cardiac complications attributed to chloroquine and hydroxychloroquine: a systematic review of the literature. Drug safety, 2018. 41: p. 919-931.
14. Farhat, H., et al., Hydroxychloroquine and the associated risk of arrhythmias. Global Cardiology Science & Practice, 2024. 2024(2): p. e202417.
15. Nazarenko, N., et al., A series of hydroxychloroquine-associated cardiotoxicity presenting with heart failure. Annals of Medicine and Surgery, 2025: p. 10.1097.
16. Zhang, Y.-H. and S. Babaeizadeh, Synthesis of standard 12-lead electrocardiograms using two-dimensional generative adversarial networks. Journal of Electrocardiology, 2021. 69: p. 6-14.
17. Rovenský, J. and J. Payer, Systemic lupus erythematosus disease activity index (SLEDAI). Dictionary of Rheumatology. Springer Vienna, Vienna, 2009: p. 209-209.
18. Dahlberg, P., et al., QT correction using Bazett's formula remains preferable in long QT syndrome type 1 and 2. Annals of Noninvasive Electrocardiology, 2021. 26(1): p. e12804.
19. O'Laughlin, J.P., P.H. Mehta, and B.C. Wong, Life threatening severe QTc prolongation in patient with systemic lupus erythematosus due to hydroxychloroquine. Case Reports in Cardiology, 2016. 2016(1): p. 4626279.
20. Nishiyama, T., et al., QTc interval prolongation in patients with systemic lupus erythematosus treated with hydroxychloroquine. Modern Rheumatology, 2021. 31(6): p. 1107-1112.
21. Hosonuma, M., et al., Fragmented QRS complex in patients with systemic lupus erythematosus at the time of diagnosis and its relationship with disease activity. PloS one, 2020. 15(1): p. e0227022.
22. Tselios, K. and M.B. Urowitz, Cardiovascular and pulmonary manifestations of systemic lupus erythematosus. Current rheumatology reviews, 2017. 13(3): p. 206-218.