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EFFECT OF AZITHROMYCIN ON QTC INTERVAL IN CHILDREN: AN OBSERVATIONAL PROSPECTIVE STUDY IN LAHORE, PAKISTAN

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Abstract

Objectives: *To determine the effect of the azithromycin on QTc interval in terms of absence or presence of prolongation in children admitted in Children's Hospital Lahore, Pakistan*

Study Design: *The study utilized observational prospective study to test the effect of Azithromycin on QTc interval in children.*

Place and duration of study: *The study was conducted at the general medical unit 4 of the Children's Hospital Lahore within six months from 1st February 2025 to 1st July 2025 after approval from hospital ethical committee.*

Methodology: *72 patients visiting the Children hospital Lahore, fulfilling the inclusion criteria, were selected using non-probability consecutive sampling technique. A written informed consent was taken from parents (father or mother) followed by child assent. Detailed history was taken including age, gender, weight, diagnosis, and any underlying chronic ailment. A baseline ECG and serum electrolytes were taken before starting azithromycin. Then, a ECG was taken on the fifth day and QTc interval was calculated. All the collected data were entered and analyzed using SPSS (v. 24).*

Results: *In this observational study, the children had an average age of about seven years, with slightly more girls than boys. At baseline, the mean QTc interval was just over 403 ms. When the QTc interval was checked after the first day, it remained almost unchanged, and by the fifth day it was still within a similar range. Most importantly, none of the patients developed QTc prolongation during the observation period. These findings suggest that azithromycin did not adversely affect the heart's electrical activity in the children we studied and appeared safe from a cardiac standpoint.*

Conclusion: *Azithromycin showed no effect on QTc intervals in children, with no cases of QTc prolongation observed. This suggests it is safe for cardiac rhythm in pediatric patients.*

INTRODUCTION

Azithromycin, discovery from class of the macrolides, is one of the most important new drug of the 20th century.[1] It works by inhibiting bacterial protein synthesis, delayed inhibitory effects, immunomodulation, and anti-fibrotic effects.[2, 3] Azithromycin is commonly prescribed in treatment of lower and upper respiratory tract, skin, and soft tissue infections. It is also being used to manage uncomplicated urethritis/cervicitis associated with Neisseria gonorrhea, Chlamydia trachomatis or Ureaplasma urealyticum, Lyme disease, and viral infections as well.[3]

It was widely used during Covid-19 pandemic for SARS-CoV-2 infection, though evidence on its efficacy is still lacking.[3] Azithromycin is administered once a day as it is released slowly in blood[4] It is among the antibiotics most frequently prescribed to children.[4] An analysis in 2020 revealed that roughly 66.8 million antibiotics were given to children aged less than 19 years in the USA. Among them, Amoxicillin and Azithromycin were the most commonly prescribed drugs.[5]

Azithromycin is generally well accepted antibiotic, although many of its typical minor adverse effects include dizziness, headache, vomiting, diarrhea and nausea.[6] Prominent side effects of azithromycin encompass torsades de pointes, hypersensitivity responses, and ototoxicity.[6] Multiple studies in the literature have also documented instances of liver damage caused by azithromycin.[7] Research in the adult population also showed that it has a QTc prolonging effect.[8]

Patients with QTc interval prolongation may experience lightheadedness, dizziness, palpitation, or syncope.[6] In a study conducted by Ramireddy et al., out of 490 adult patients, 12% experienced QTc prolongation of which incidence was increased in patients taking hydroxychloroquine and azithromycin in combination than taking either of the drugs alone.[9]

In another study azithromycin use in adults was seen to cause sudden cardiac death by prolongation of QT interval and triggering ventricular arrhythmias and torsades de pointes. .[10] It can prolong ventricular repolarization by altering the myocyte action potential and predisposing to malignant ventricular arrhythmias.[10] Despite these rare adverse effects, azithromycin remains classified by the World Health Organization (WHO) as one of the most safe and efficacious drugs in the present healthcare system.[9]

To our best knowledge till date, a single study has been done on children that documented azithromycin's effect on QTc interval. The study included 56 pediatric patients, 25 females and 31 males of cystic fibrosis who were taking azithromycin prophylactically. No patient had clinically significant prolonged QTc intervals with azithromycin therapy, but four patients had borderline post-azithromycin elevated intervals (i.e., QTc 441-460 ms).[11]

The present study was strictly limited to the pediatric population to check the effect of azithromycin on QTc interval because of excessive use of azithromycin in children. The study will be beneficial in determining whether azithromycin used under ECG monitoring could avoid adverse outcomes or not. [12]

METHODOLOGY:

After approval from ethical committee of the Hospital, the present observational prospective study was conducted from 1st February 2025 to 1st July 2025. 72 patients visiting the Children Hospital Lahore were selected using non-probability consecutive sampling technique. Only those children were selected who fulfilled the inclusion criteria i.e., children of age between 2-12 years having any gender and diagnosed with upper or lower respiratory tract infections, skin and soft tissue infections, and urinary tract infection.

The study excluded children with known QTc interval prolongation syndrome, diagnosed with enteric fever, taking any other drug known to prolong QTc interval e.g. ciprofloxacin, artemether, fluconazole, ondansetron & sildenafil etc., allergic to azithromycin, critically ill patients i.e. on cardiopulmonary supports and having sepsis.

A written informed consent was taken from parents (father or mother) followed by child assent and detailed history were taken including age, gender, weight, diagnosis, and any underlying chronic ailment. A baseline ECG and serum electrolytes were taken before starting azithromycin. Then, a ECG was taken on fifth day and QTc interval was calculated using the following formula:

$QTc = QT / \sqrt{RR}$

Cardiac monitoring and consultation were taken for these patients, serum electrolyte was obtained, and correction was done if required. All the collected data was entered and analyzed using SPSS (v. 24). Numerical variables i.e., age, weight, and QTc interval were presented as Mean ± SD. Categorical variables i.e., gender and presence of prolongation was presented as frequency and percentages. To check significant differences, t-test and chi-square test were used with a 5% margin of error ($p < .05$).

RESULTS:

The mean age of 72 patients was 6.88 ± 3.44 years and mean weight was 20.65 ± 10.32 kg. Out of 72 patients, 35 (45.1%) were male and 37 (54.9%) were female with male to female ratio as 1:1.22. In current study, most of the patients were from 2-5 years age group i.e. 44.1%.

Table-1: Results of descriptive statistics

Variables		Frequency	Percent
Age Groups	2-5 years	32	44.1
	6-10 years	24	33.3
	11-12 years	16	22.5
Age (years), Mean ± SD		6.88 ± 3.44	
Weight (kg), Mean ± SD		20.65 ± 10.32	
Gender	Male	35	45.1
	Female	37	54.9
	Total	72	100.0

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It was observed that the mean QTc interval at baseline was 403.90 ± 12.18 ms. After the first day of presentation, it remained almost the same at 402.47 ± 11.87 ms, and by the fifth day it measured 405.90 ± 18.77 ms. Throughout the observation period, no child developed QTc prolongation. There was also no meaningful association between age, gender, and QTc changes, indicating that azithromycin was well tolerated from a cardiac perspective in all patients.

Table-2: Results of QTc interval (ms)

Follow-up	QTc Interval (Mean ± SD, ms)	p value
Baseline (Day 1)	403.90 ± 12.18	–
Day 5	405.90 ± 18.77	–

Note: No QTc prolongation was observed in any patient during the study period.

Table-3: Results of QTc Prolongation

QTc Prolongation	Frequency	Percent
Yes	0	0
No	72	100
Total	72	100.0

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Table-4: Stratification results of QTc Prolongation with age and gender

Variables		QTc Prolongation		Total	p value
		Yes	No		
Age Groups	2-5 years	0	32	32	NA
		0	50%	50%	
	6-10 years	0	24	24	
		0	33.3%	33.3%	
	11-12 years	0	16	16	
		0.0%	22.2%	22.2%	
Gender	Male	0	35	35	NA
		0%	46.9%	45.1%	
	Female	0	37	37	
		0%	53.1%	54.9%	

Note: No QTc prolongation was observed in any age group or gender

DISCUSSION:

Azithromycin, similar to other macrolides, obstructs IKr potassium channels in cardiac cells, resulting in a delay in ventricular repolarization. This delay is evident as an elevated QTc interval (the corrected QT interval) on the electrocardiogram (ECG). The QTc interval denotes the duration required for ventricular depolarization and repolarization, with an extended QTc heightening the risk of arrhythmias. Nonetheless, the frequency of such effects in children remains ambiguous due to their physiological differences from adults.

Azithromycin is used for treatment in pediatric patients. It has the ability to extend the QT interval. The present study aimed to evaluate the effect of azithromycin on the process of ventricular repolarization in pediatric patients of lower respiratory tract infections, skin & soft tissue infection, and urinary tract infections.

We found that the mean value of the QTc interval at baseline was 403.90 ± 12.18 ms, and after five days it was 405.90 ± 18.77 ms. No patient developed QTc prolongation during the observation period. Similarly, in a study by Magaret et al. [13], the mean QTc interval at baseline was 416 ± 20 ms and remained stable at 415 ± 21 ms after three weeks of follow-up. They concluded, in line with our findings, that azithromycin use was not associated with an increased risk of QTc prolongation.

In the current study, no cases of QTc prolongation were observed among the pediatric patients receiving azithromycin. Despite the lack of definitive clinical proof, azithromycin has been widely prescribed to patients with confirmed or suspected COVID-19. Concerns have been raised that it may increase the risk of life-threatening arrhythmias related to QT interval prolongation. In contrast, a study by Ramireddy et al. [9] reported QTc prolongation in 12% of patients. Our findings provide reassurance that, in children, azithromycin did not adversely affect ventricular repolarization.We found mean age of patients was 6.88 ± 3.44 years and mean weight was 20.65 ± 10.32 kg with male to female ratio was 1:1.22. The study by Sunkak et al.[14] found mean age of patients as 9.8 ± 5.3 years with male to female ratio was 1:1.14. These results matched with findings of the current study. They also found no impact of azithromycin on the ventricular repolarization parameters on the electrocardiogram (ECG).

Enhos et al.[15] reported azithromycin usage in children due to its anti-inflammatory and immunomodulatory action but its prophylactic use in children resulted in a modest increase in the QTc interval. Nevertheless, all alterations in the QTc interval were within the safe range in their study. Significantly, it is important to conduct a one-month

follow-up treatment to specifically assess for any changes in the QTc interval. Prophylactic administration of azithromycin can be safely initiated if there is no evidence of prolonged QTc interval duration within the first month.

Assessing safety of azithromycin is important as the many studies in pediatric cohort offers crucial assurance against any significant risk of QTc prolongation from long-term azithromycin usage. Early pediatric trial lasting fewer than 6 months provides prior evidence of cardiovascular safety.[16] Contemporary observational studies including children who are on azithromycin also provide evidence for the safety of azithromycin when used for shorter periods of treatment.[17, 18]

Our study has few limitations as the study duration was short with limited sample size. Therefore, we suggest that to confirm and broaden our results, a similar study should be carried out in multicenter environments with a larger sample size to get further understanding of the association between azithromycin and QTc interval is children.

CONCLUSION:

We concluded that there was no statistically significant effect of azithromycin on the ventricular repolarization parameters (QTc) on electrocardiogram (ECG) in pediatric patients of lower respiratory tract infections, skin & soft tissue infection, and urinary tract infections treated with azithromycin. This prospective observational study suggests that azithromycin does not cause prolongation of the QTc interval in children, and the risk of severe arrhythmias remains low. Careful consideration should be given to high-risk pediatric patients, and monitoring may be warranted in certain cases.

REFERENCES:

1. Jelić D, Antolović R. From erythromycin to azithromycin and new potential ribosome-binding antimicrobials. Antibiotics. 2016;5(3):29-33.
2. Heidary M, Ebrahimi Samangani A, Kargari A, Kiani Nejad A, Yashmi I, Motahar M, et al. Mechanism of action, resistance, synergism, and clinical implications of azithromycin. Journal of clinical laboratory analysis. 2022;36(6):e24427.
3. Vitiello A, Ferrara F. A short focus, azithromycin in the treatment of respiratory viral infection COVID-19: efficacy or inefficacy? Immunologic research. 2022;70(1):129-33.
4. Fleming-Dutra KE, Demirjian A, Bartoces M, Roberts RM, Taylor Jr TH, Hicks LA. Variations in antibiotic and azithromycin prescribing for children by geography and specialty—United States, 2013. The Pediatric infectious disease journal. 2018;37(1):52-8.
5. Chan XHS, Win YN, Haeusler IL, Tan JY, Loganathan S, Saralamba S, et al. Factors affecting the electrocardiographic QT interval in malaria: A systematic review and meta-analysis of individual patient data. PLoS medicine. 2020;17(3):e1003040.
6. Ibraimi Q, Ajruli N, Xheladini D. Azithromycin's function among patients. IJMH. 2022;7(1):9-19.
7. Liang R, Ramdass A. Azithromycin-Induced Liver Injury in an Asthma Exacerbation Patient With Autoimmune Features. Cureus. 2022;14(5):1-6.
8. Farzanegan B, Hosseinpoor Z, Baniasadi S, Seyyedi SR, Rajabi M. An observational study of QTc prolongation in critically ill patients: identification of incidence and predictors. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine. 2020;24(4):270-4.
9. Ramireddy A, Chugh H, Reinier K, Ebinger J, Park E, Thompson M, et al. Experience with hydroxychloroquine and azithromycin in the coronavirus disease 2019 pandemic: implications for QT interval monitoring. Journal of the American Heart Association. 2020;9(12):e017144.
10. Lazzerini PE, Boutjdir M, Capecchi PL. COVID-19, arrhythmic risk, and inflammation: mind the gap! Circulation. 2020;142(1):7-9.
11. Lenehan PJ, Schramm CM, Collins MS. An evaluation strategy for potential QTc prolongation with chronic azithromycin therapy in cystic fibrosis. Journal of Cystic Fibrosis. 2016;15(2):192-5.

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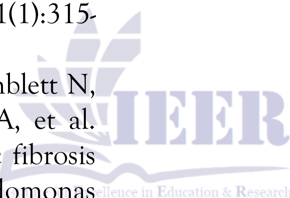
12. Gorelik E, Masarwa R, Perlman A, Rotshild V, Muszkat M, Matok I. Systematic review, meta-analysis, and network meta-analysis of the cardiovascular safety of macrolides. Antimicrobial agents and chemotherapy. 2018;62(6):1-6.
13. Magaret AS, Salerno J, Deen JF, Kloster M, Mayer-Hamblett N, Ramsey BW, et al. Long-term azithromycin use is not associated with QT prolongation in children with cystic fibrosis. Journal of Cystic Fibrosis. 2021;20(2):e16-e8.
14. Sunkak S, Argun M, Celik B, Tasci O, Ozturk AB, Inan DB, et al. Effects of azithromycin on ventricular repolarization in children with COVID-19. Revista Portuguesa de Cardiologia. 2022;41(7):551-6.
15. Enhoş A, Kus HD, Yozgat CY, Cakır E, Yazan H, Erol AB, et al. Short-term azithromycin use is associated with QTc interval prolongation in children with cystic fibrosis. Archives de Pédiatrie. 2024;1(1):315-9.
16. Saiman L, Marshall BC, Mayer-Hamblett N, Burns JL, Quittner AL, Cibene DA, et al. Azithromycin in patients with cystic fibrosis chronically infected with Pseudomonas aeruginosa: a randomized controlled trial. Jama. 2013;290(13):1749-56.



17. Valdés SO, Kim JJ, Niu MC, de la Uz CM, Miyake CY, Moffett BS. Cardiac arrest in pediatric patients receiving azithromycin. The Journal of Pediatrics. 2017;182(1):311-4.
18. Espadas D, Castillo S, Moreno M, Escribano A. Lack of effect of azithromycin on QT interval in children: a cohort study. Archives of Disease in Childhood. 2019;101(11):1079-.