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# Evaluation of QTc Interval Pre- and Post-Albumin Administration in Pediatric Nephrotic Syndrome Patients with Hypocalcemia

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***Abstract***

***Background:*** Nephrotic syndrome (NS) in children is characterized by heavy proteinuria, hypoalbuminemia, and edema. Hypocalcemia, commonly resulting from urinary loss of albumin-bound calcium, can prolong the QT interval, increasing the risk of ventricular arrhythmias. This study aimed to evaluate the effect of albumin administration on the corrected QT (QTc) interval in pediatric NS patients

***Methods:*** A cross-sectional study was conducted on 20 children with NS and hypoalbuminemia who received albumin infusions. Baseline electrocardiograms (ECGs) and serum parameters, including albumin and electrolyte levels, were recorded before and after albumin infusion. QTc intervals were calculated using Bazett's formula. The Wilcoxon signed-rank test was used to assess changes in QTc before and after infusion.

***Results:*** The study included 20 children with NS (15 males, 5 females; mean age $6 \pm 4$ years). The mean serum albumin level was $2 \pm 0$ g/dL, indicating significant hypoalbuminemia. Hypocalcemia was present in 79% of patients and was associated with higher QTc intervals. The mean QTc decreased from $411 \pm 45$ ms pre-infusion to $401 \pm 44$ ms post-infusion, showing a statistically significant reduction ($p < 0.001$), particularly in patients with hypocalcemia.

***Conclusion:*** Albumin administration significantly reduces QTc intervals in children with NS, especially those with hypocalcemia, potentially lowering the risk of arrhythmias. Further research is warranted to evaluate the long-term cardiac effects of albumin therapy in this population.

***Key Words:*** Hypocalcemia, Nephrotic syndrome, Pediatrics, QTc interval.

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## 1- INTRODUCTION

Nephrotic syndrome (NS) is a common kidney disorder in children, characterized by heavy proteinuria, hypoalbuminemia, hyperlipidemia, and edema. Its incidence among children ranges from 1.4 to 6.1 per 100,000 population (1, 2). The substantial loss of proteins in the urine leads to a decline in plasma oncotic pressure and disruption of electrolyte and mineral balance, most notably resulting in hypocalcemia (2-4). Hypocalcemia often arises from the urinary loss of albumin-bound calcium and vitamin D-binding proteins, which reduces total serum calcium levels despite maintaining normal ionized calcium levels (3, 5,6). Such disturbances have significant clinical consequences, affecting the cardiovascular, skeletal, and immune systems (7).

Among the cardiovascular effects, hypocalcemia is known to influence cardiac electrophysiology by prolonging the QT interval on electrocardiograms (ECG) (8, 9). The QT interval represents the duration of ventricular depolarization and repolarization. Its prolongation is associated with an elevated risk of ventricular arrhythmias, such as torsades de pointes (10, 11). The corrected QT interval (QTc) adjusts the QT interval for heart rate and is commonly calculated using Bazett's formula (6). Electrolyte abnormalities, including hypocalcemia, hypokalemia, and hypomagnesemia, are known contributors to QTc prolongation (9, 12).

In clinical practice, albumin infusions are often administered to NS patients to correct hypoalbuminemia and manage severe edema. This intervention helps restore plasma oncotic pressure, thereby reducing fluid retention—one of the hallmark and debilitating symptoms of NS (13, 14). Albumin administration may also increase the bound fraction of serum calcium, potentially restoring total calcium concentrations (15, 16). Thus, correcting hypocalcemia through albumin infusion may influence QTc duration and reduce the risk of arrhythmias. This relationship is particularly relevant in pediatric patients who are more vulnerable to the consequences of electrolyte imbalance and cardiac dysregulation (17).

Despite the theoretical basis and clinical importance of this relationship, limited research has been conducted to investigate the impact of albumin administration on QTc intervals in pediatric NS patients. Gaining insight into this relationship is essential for improving the management of cardiovascular risks in this population. Therefore, the present study aims to evaluate changes in the QTc interval before and after albumin administration in children diagnosed with NS.

## 2- MATERIALS AND METHODS

### 2-1. Study Approach and Participant Selection

This descriptive cross-sectional study was conducted on 20 pediatric patients diagnosed with NS by board-certified pediatric nephrologists. Eligible patients were referred to Akbar and Dr. Sheikh Hospitals in Mashhad during 2018–2019 for albumin administration due to hypoalbuminemia and severe edema.

### 2-2. Inclusion Criteria

Participants were enrolled based on the following criteria:

*1. Age between 1 and 18 years*

*2. Confirmed diagnosis of NS*

*3. Documented hypoalbuminemia*

*4. Informed parental consent for participation*

### 2-3. Exclusion Criteria

Patients were excluded if they had:

*1. Skeletal disorders such as rickets*

*2. Congenital cardiac anomalies or ischemic heart disease*

*3. Hypokalemia*

*4. Diastolic hypertension*

*5. End-stage renal disease requiring dialysis*

*6. Congenital long QT syndrome*

*7. A history of taking medications such as digoxin*

*8. Disagreement to continue the study at any stage*

Informed consent was obtained from the parents or legal guardians of all participants, and all procedures were conducted in accordance with the ethical standards of the institutional research committee. The study protocol was approved by the Ethics Committee of Mashhad University of Medical Sciences (Ethical Code: IR.MUMS.REC.1397.332), in compliance with the Declaration of Helsinki.

**2-4. Data Collection**

Baseline demographic and laboratory data—including age, gender, serum albumin, total protein, electrolytes (calcium, magnesium, potassium, sodium, phosphorus), renal function tests (urea, creatinine), lipid profile (cholesterol, triglycerides), hemoglobin level, and erythrocyte sedimentation rate (ESR)—were collected from medical records before albumin administration.

Standard 12-lead electrocardiograms (ECGs) were performed on all patients before and after albumin infusion using a calibrated ECG machine at a paper speed of 25 mm/sec. The QT interval was manually measured from the onset of the Q wave to the end of the T wave, typically in leads II and V5, and the average of the two was used. The QTc was calculated using Bazett's formula. Patients received a 20% human albumin solution intravenously, with dosing determined by the treating physician based on the clinical condition. The administered dose ranged from 0.5 to 1 g/kg, consistent with standard clinical practice for managing hypoalbuminemia and edema in pediatric NS (18). Post-infusion ECGs were obtained within one hour to evaluate the immediate effect on QTc interval.

**2-5. Statistical Analysis**

Data were analyzed using SPSS version 22. Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables were summarized as frequencies and percentages. Due to the non-parametric distribution of QTc data, the Wilcoxon signed-rank test was used to compare QTc intervals before and after albumin infusion. A p-value of less than 0.05 was considered statistically significant.

**3-RESULTS**

A total of 20 children with NS participated in the study, including 15 males (75%) and 5 females (25%). The participants ranged in age from under 1 year to 15 years, with a mean age of $6 \pm 4$ years.

The mean serum albumin level was $2 \pm 0$ g/dL, confirming significant hypoalbuminemia. Additional baseline laboratory parameters—including total protein, electrolytes, renal function tests, lipid profile, hemoglobin levels, and ESR—are presented in Table 1.

QTc intervals were measured before and after albumin infusion for all patients. The initial QTc (QTc1) ranged from 330 to 520 ms, with a mean of $411 \pm 45$ ms. Following albumin administration, the QTc (QTc2) ranged from 310 to 480 ms, with a mean of $401 \pm 44$ ms (Table 2 and Figure 1).

**Table-1.** Laboratory parameters of the study population.

| Variable | Mean (SD) | Range |
|---|---|---|
| **Total Protein (g/dL)** | 4 (1) | 3-9 |
| **Albumin (g/dL)** | 2 (0) | 1-3 |
| **Total Calcium (mg/dL)** | 7 (1) | 5-11 |
| **Magnesium (mg/dL)** | 2 (0) | 1-2 |
| **Potassium (mEq/L)** | 4 (0) | 3-5 |
| **Sodium (mEq/L)** | 136 (3) | 126-142 |
| **Phosphorus (mg/dL)** | 5 (1) | 4-10 |
| **Urea (mg/dl)** | 49 (27) | 16-121 |
| **Creatinine (mg/dl)** | 0.3 (0) | 0-4 |
| **Hemoglobin (g/dL)** | 13 (2) | 7-19 |
| **ESR (mm/hr)** | 97 (30) | 56-132 |
| **Total Cholesterol (mg/dl)** | 476 (162) | 196-765 |
| **Triglycerides (mg/dl)** | 711 (766) | 140-2672 |

**Table-2.** Mean QTc interval before and after albumin infusion.

| QTc interval (ms) | Mean (SD) | Range |
|---|---|---|
| **QTc1** | 411.00 (45.00) | 330-520 |
| **QTc2** | 401.05 (44.08) | 310-480 |

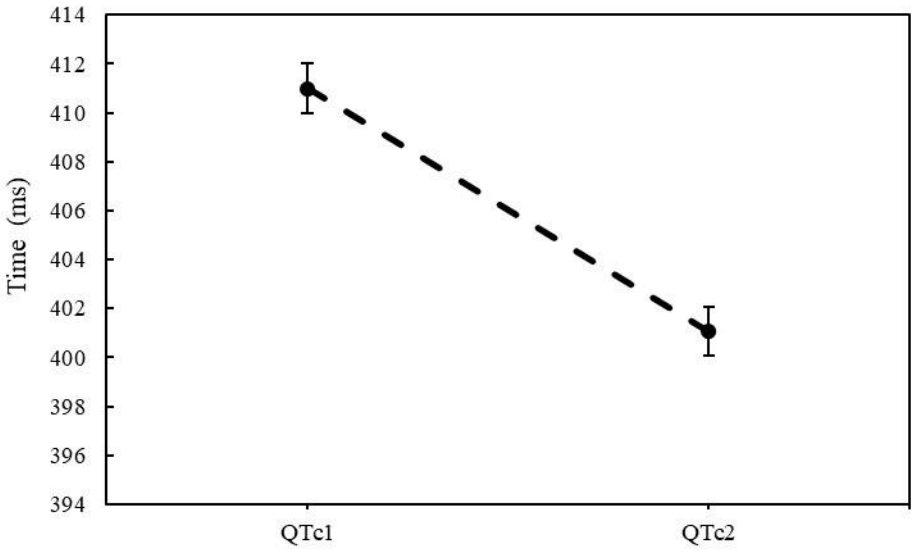


**Figure-1 :** Mean QTc interval before (QTc1) and after (QTc2) albumin infusion.

When comparing individual patient data, QTc decreased in 8 patients, increased in 7 patients, and remained unchanged in 3 patients (Table 3 and Figure 2). Statistical analysis using the Wilcoxon signed-rank test confirmed a significant reduction in QTc intervals following albumin administration ($p < 0.001$).

Additionally, serum calcium levels were analyzed in 19 out of the 20 patients. Of these, 15 (79%) had hypocalcemia, and 4 had normal calcium levels (Figure 3). The mean QTc intervals were consistently higher in the hypocalcemic group both before and after albumin infusion, as shown in Table 4.

**Table-3.** Categorical comparison of QTc interval changes following albumin infusion.

| Category | Number of patients | Mean difference |
|---|---|---|
| **QTc2 < QTc1** | 8 | 7 |
| **QTc1 < QTc2** | 7 | 8 |
| **QTc1 = QTc2** | 3 | 0 |

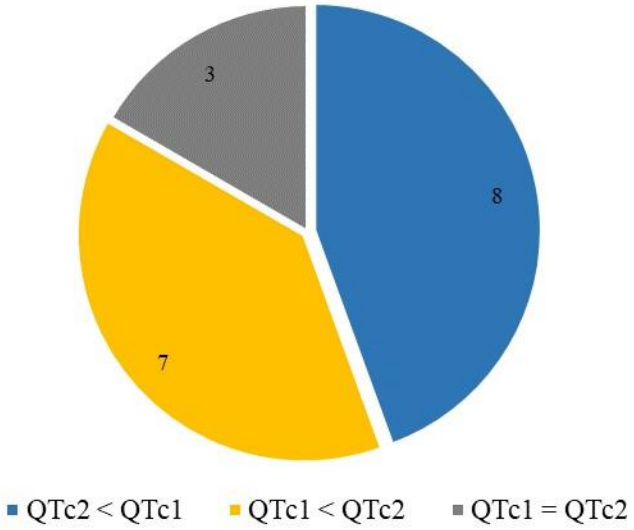


**Figure-2 :** Distribution of patients based on QTc interval change post-infusion.

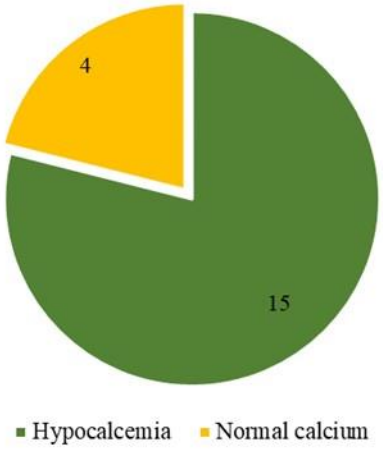


**Figure-3 :** Frequency of hypocalcemia among study participants.

**Table-4:** QTc intervals in relation to serum calcium levels.

| Category | | Mean (SD) | Range |
|---|---|---|---|
| **Hypocalcemia** | **QTc1** | 416 (45) | 330-520 |
| | **QTc2** | 408 (45) | 310-480 |
| **Normal Calcium** | **QTc1** | 395 (47) | 360-460 |
| | **QTc2** | 380 (30) | 350-410 |

## 4- DISCUSSION

This study investigated the impact of albumin administration on QTc intervals in pediatric patients with NS and hypoalbuminemia. Our findings demonstrate that albumin infusion is associated with a statistically and clinically

significant reduction in QTc interval, particularly in patients with coexisting hypocalcemia. This suggests a potential therapeutic role for albumin in reducing cardiac risks associated with prolonged QTc intervals in this population. The mean QTc interval decreased from $411.00 \pm 45.00$ ms before infusion to $401.05 \pm 44.08$ ms after infusion. This reduction was clinically significant, as prolonged QTc intervals are associated with an increased risk of ventricular arrhythmias, such as torsades de pointes and sudden cardiac death. The observed effect may be attributed to correction of hypoalbuminemia and associated hypocalcemia, both of which are common consequences of significant proteinuria in NS patients (19, 20).

Hypocalcemia was observed in over two-thirds of the participants and was associated with higher QTc intervals both before and after albumin administration. This aligns with previous evidence indicating that hypocalcemia prolongs ventricular repolarization and increases QTc duration, thereby elevating the risk of ventricular arrhythmias such as torsades de pointes (8, 21-23). In the setting of NS, hypocalcemia often results from urinary loss of albumin-bound calcium and vitamin D–binding proteins. By restoring serum albumin levels, albumin infusion may increase the bound fraction of serum calcium, thereby normalizing total calcium concentration and mitigating QTc prolongation (24). This mechanism likely explains the statistically significant decrease in QTc seen in our cohort. Through stabilization of myocardial repolarization, albumin administration may reduce the risk of arrhythmias in pediatric NS patients.

Our findings are consistent with those of Avci et al., which showed that both hypoalbuminemia and hypocalcemia were significantly correlated with prolonged QTc intervals, a known marker for arrhythmogenic risk (21). Similarly, Eryol et al. found that calcium replacement therapy reduced QT interval and decreased the frequency of ventricular premature complexes (VPCs) in hypocalcemic patients, supporting the role of electrolyte correction in improving cardiac electrophysiology (17). The mechanism by which albumin affects QTc interval may involve several physiological processes. As a major plasma protein, albumin binds to calcium and magnesium, which are essential for maintaining normal cardiac repolarization (24, 25). While ionized calcium levels may remain normal in hypoalbuminemia, the reduction in total calcium can still impact cardiac function (26). Additionally, albumin administration improves plasma oncotic pressure, reduces edema, and enhances hemodynamic stability, all of which may contribute to better myocardial perfusion and electrophysiologic recovery (27, 28).

From a clinical perspective, our results highlight the importance of routine cardiac monitoring in pediatric NS patients, particularly those with electrolyte imbalances. Albumin infusion may serve not only to alleviate hypoalbuminemia and edema but also to reduce the risk of arrhythmias by improving QTc dynamics. However, several limitations should be acknowledged. The small sample size limits the generalizability of our findings. However, the statistically significant reduction in QTc interval post-albumin infusion suggests a potentially meaningful effect that warrants further investigation. Additionally, we conducted only one post-infusion ECG within one hour of albumin administration, which may not capture delayed or sustained electrophysiologic changes. Serial ECG monitoring over a longer follow-up period would provide more comprehensive insights.

## 5- CONCLUSION

This study demonstrates that albumin administration leads to a

significant reduction in the QTc interval among children with nephrotic syndrome, especially those with hypocalcemia. Given the known association between prolonged QTc and life-threatening ventricular arrhythmias, this finding suggests that albumin infusion may offer a cardioprotective benefit in addition to its established role in managing hypoalbuminemia and edema.

Clinicians should be aware of the potential cardiac implications of electrolyte and protein imbalances in pediatric NS and consider routine monitoring of the QTc interval, especially in patients with hypocalcemia. Correcting hypoalbuminemia through albumin infusion may contribute to improved cardiac electrical stability and reduced arrhythmic risk. However, the study's limited sample size and lack of a control group restrict the generalizability of the findings. Furthermore, the short observation window—limited to a single post-infusion ECG within one hour—does not allow for assessment of long-term effects. Future studies should include larger, powered samples, control groups, and serial ECG monitoring over extended periods to better evaluate both the immediate and sustained cardiac effects of albumin therapy in this vulnerable population.

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