*Type of the Paper (Research Article)*

# Cardiac Affection in Children with Chronic Renal Failure: Case-Control Study

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**Received:** 15 August, 2024 **Reviewed:** 20 November, 2024
**Accepted:** 25 January, 2025 **Published online:** 20 March, 2025

**Abstract:**

**Introduction:** Chronic renal failure is a devastating disease facing children, with several life-threatening complications, where cardiovascular diseases are on top of them.

**Aim of the study:** To evaluate cardiac affection in children with chronic renal failure through echocardiography, ECG and high sensitivity troponin-I level.

**Subjects and Methods:** This case-control study included 40 children/adolescents aged 2-14 with CRF and 20 healthy subjects from an age-matched population as a control.

**Results:** Regarding echo parameters, LVEDD and LVESD were significantly increased in cases compared to controls ($p < 0.001$) and in hemodialysis cases compared to conservative cases ($p = 0.011$ and 0.03, respectively). EF and FS were significantly decreased in cases compared to controls ($p = 0.029$ and 0.036, respectively), and among hemodialysis cases compared to conservative cases ($p < 0.001$). Impaired diastolic function was found in 20 cases (50%), and impaired systolic function was found in 9 cases (22.5%). Regarding ECG findings, QRS duration, QRS amplitude and QTc values were significantly higher in cases compared to controls ($p = 0.008$, <0.001, and 0.036, respectively), and among hemodialysis cases compared to conservative cases ($p$ <0.001, <0.001, and 0.04, respectively). Regarding hs-cTnI level, 8 cases were positive, no positive subjects were in controls, and there was no significant difference between cases and controls ($p = 0.08$) or between hemodialysis cases and conservative cases ($p = 0.171$).

**Conclusion:** CRF in pediatrics is associated with a highly prevailing LVH, systolic/diastolic dysfunction, and prolonged QTc with no significant elevation of troponin-I level.

**Keywords:** CRF; CVD; LVH; QTc; hs-cTnI.

# 1. Introduction

Cardiovascular disease is considered the major etiology of mortality in pediatrics with chronic renal failure. The rate of death is more occurring by about 30 times in end-stage patients when compared to the general pediatric population [1].

During the early stages of the disease, the development of cardiovascular disease is largely dependent on hypertension, while in later stages, other risk factors are responsible including volume overload mineral bone disease and anemia [2].

The main cardiac affection manifestations noticed in these patients are left-ventricular hypertrophy, diastolic dysfunction and systolic dysfunction [3].

Many ECG changes were frequently demonstrated in pediatric patients with chronic kidney failure, most importantly QT interval prolongation [4].

Troponin-I is a significant cardiac injury marker that may be used as a good indicator of cardiac affection in the mentioned population [5].

Our study aims to evaluate the cardiac affection in pediatric patients with chronic renal failure either on chronic hemodialysis or conservative treatment through echocardiography, ECG and blood troponin-I.

# *2.* Subjects and Methods

## *2.1. Study setting*

The current case-control study was conducted in the period between February 2023 and February 2024 in pediatric cardiology and nephrology units at Fayoum University Pediatric Hospital, Fayoum governorate, Egypt.

## *2.2. Subjects*

The study included 60 children and adolescents of both genders aged 2-14 years. The case group included 40 patients diagnosed with CRF (30 ESRD on regular hemodialysis and 10 on conservative treatment). Patients with known congenital

heart diseases were excluded. The control group included 20 healthy children from the age-matched population who came to the general pediatric clinic for causes other than renal or cardiac diseases or as a part of a general health checkup.

### *2.3. Data collection*

All participants were subjected to full history taking with emphasis on onset, possible cause, symptoms of CRF and cardiovascular symptoms, the main line of treatment and the use of anti-hypertensive and/or anti-failure medications.

A thorough clinical examination was done including anthropometric measurements with plotting on growth charts as well as full general, cardiac, chest and abdominal examination.

Laboratory samples for CBC, urea, creatinine, sodium, potassium, calcium and phosphorus were done.

All studied groups were subjected to a full conventional echocardiography study (on an inter-dialytic day for hemodialysis cases). The study included a complete echocardiographic examination with the exclusion of congenital heart disease and measurement of LA/AO ratio, IVS, LVEDD, LVESD, LVPW, EF and FS as well as tissue Doppler imaging (TDI).

ECG was performed on all studied groups using a 12-lead ECG device while lying down comfortably. the speed of recording was 25 mm/sec and the amplitude were 1 mV/cm. Assessment of the heart rate, rhythm, chamber enlargement, P wave, QRS complex and ST segment was also done. The measurement of the QT interval was performed in all 12 leads starting from the onset of QRS till the end of the T wave and the longest was considered. The corrected QT (QTc) interval was attained by using the Bazett formula ($QTc = QT / \sqrt{RR}$).

A High sensitivity test for cardiac troponin-I (hs-cTnI) level was performed on all participants by a three-site sandwich chemiluminescence immunoassay method. The range of detection is (0.006-50 ng/ml). The cutoff value for cardiac troponin-I was assumed to be (≤ 0.01 ng/ml) and the evaluations were made accordingly.

### *2.4. Statistical methods*

Analyzing collected data was done using SPSS software version 22 [SPSS Inc, USA]. The mean, as well as standard deviation (SD), were calculated for

quantitative data. The independent t-test was used to compare between any two groups. For qualitative data, frequencies and percentages were used for description. Interpreting results of tests of significance; p-value was considered significant at ≤ 0.05.

## 3. Results

In our study, the range of age for cases was 2-14 years with a mean age of 11.3 years. Males represented 65% of cases, and females represented 35%. Congenital renal or urinary tract anomalies were the most common cause of CKD (65%). The duration of CKD ranged from 0.9 years to 13.7 years. 75% of patients were on regular hemodialysis, and 25% were on conservative treatment. 75% of cases were below the 3rd percentile of age for weight, and 70% of cases were below the 3rd percentile of age for height. High systolic BP was found in 40% of cases and high diastolic BP in 45% of cases. 65% of our cases were anemic, 35% had hypocalcemia and 15% had hyperkalemia.

Regarding structural changes in the heart in our study evaluated by conventional Echo, we found that the following parameters AO, LA, IVS, LVPWD, LVEDD and LVESD were significantly increased among cases compared to controls ($p$ <0.001). Regarding left ventricular systolic function, our results showed a significant decrease in EF and FS of cases compared to controls ($p$ =0.029 and 0.036, respectively). 22.5% of cases had systolic dysfunction. TDI results revealed that 50% of cases had diastolic dysfunction (**Table 1**).

Comparing Echo parameters of hemodialysis cases with those on conservative treatment, we found a significant increase in LVEDD and LVESD in hemodialysis cases ($p$ =0.011 and 0.003, respectively). A significant decrease in FS and EF in the hemodialysis group compared to the conservative group was also found ($p$ < 0.001) (**Table 2**).

**Table 1:** Echocardiography characteristics of cases and controls.

| Variables | Cases (n =40) | Controls (n =20) | *P*-value |
|---|---|---|---|
| AO | 2.5 ±05 | 2.2 ±02 | <0.001* |
| LA | 2.7 ±07 | 2.2 ±02 | <0.001* |
| LA/AO | 1 ±02 | 1 ±01 | 0.093 |
| IVS | 1 ±03 | 0.8 ±01 | <0.001* |
| LVPWD | 0.9 ±02 | 0.7 ±01 | <0.001* |
| LVEDD | 4.2 ±08 | 3.4 ±04 | <0.001* |
| LVESD | 2.9 ±08 | 2.2 ±03 | <0.001* |
| EF | 61.5 ±11.4 | 67.7 ±6.8 | 0.029* |
| FS | 33.2 ±7.3 | 37.2 ±5.4 | 0.036* |
| Impaired diastolic function | | 20 (50%) | |
| Impaired systolic function | | 9 (22.5%) | |

**** significant.*** ***AO:*** *Aortic root diameter;* ***LA:*** *Left Atrial Diameter;* ***IVS:*** *Interventricular Septum;* ***LVPWD:*** *Left Ventricular Posterior Wall Diameter;* ***LVEDD:*** *Left Ventricular End Diastolic Diameter;* ***LVESD:*** *Left Ventricular End Systolic Diameter;* ***EF:*** *Ejection fraction;* ***FS:*** *Fractional shortening.*

**Table 2:** Echo characteristics of hemodialysis cases and conservative cases.

| Variables | Cases (n =30) | Controls (n =10) | *P*-value |
|---|---|---|---|
| AO | 2.55 ±0.52 | 2.46 ±0.3 | 0.5 |
| LA | 2.76 ±0.78 | 2.43 ±0.36 | 0.079 |
| LA/AO | 1.07 ±0.24 | 0.98 ±0.09 | 0.093 |
| IVS | 0.98 ±0.24 | 0.92 ±0.28 | 0.554 |
| LVPWD | 0.94 ±0.19 | 0.85 ±0.22 | 0.267 |
| LVEDD | 4.4 ±0.8 | 3.65 ±0.69 | 0.011* |
| LVESD | 3 ±0.79 | 2.3 ±0.48 | 0.003* |
| EF | 59.2 ±12 | 68.4 ±3.1 | <0.001* |
| FS | 31.7 ±7.8 | 37.5 ±2.3 | <0.001* |

**** significant.***

Regarding ECG findings of our cases and controls, the number of cases that had LVH was 23 (57.5%) and those with prolonged QTc were 14 (35%). We found that QRS duration, QRS amplitude and QT corrected values were significantly higher in cases compared to controls ($p$ =0.008, <0.001, and 0.036, respectively) (**Table 3**).

**Table 3:** ECG findings of cases and controls.

| Variables | Cases (n =40) | Controls (n =20) | *P*-value |
|---|---|---|---|
| Heart rate (beat per minute) | 92.6 ±16.3 | 94.1 ±22.1 | 0.771 |
| P wave duration (second) | 0.075 ±0.011 | 0.070 ±0.012 | 0.177 |
| P wave amplitude (millivolt) | 0.16 ±0.05 | 0.14 ±0.04 | 0.072 |
| PR interval (second) | 0.13 ±0.03 | 0.14 ±0.04 | 0.327 |
| QRS duration (second) | 0.085 ±0.03 | 0.068 ±0.02 | 0.008* |
| QRS amplitude (millivolt) | 1.96 ±1.19 | 1.12 ±0.06 | <0.001* |
| QT interval (second) | 0.36 ±0.06 | 0.34 ±0.05 | 0.097 |
| RR interval (second) | 0.73 ±0.33 | 0.69 ±0.027 | 0.644 |
| QT corrected (second) | 0.43 ±0.08 | 0.39 ±0.04 | 0.036* |

**** significant.***

Comparing ECG parameters of hemodialysis cases with conservative cases (table 14), we found that QRS duration and amplitude, as well as QT, corrected values were significantly higher in hemodialysis cases ($p$ <0.001, <0.001, and 0.04, respectively) (**Table 4**).

**Table 4:** ECG characteristics of hemodialysis cases and conservative cases.

| Variables | Cases (n =40) | Controls (n =20) | *P*-value |
|---|---|---|---|
| Heart rate (beat per minute) | 93.4 ±16.1 | 90 ±17.5 | 0.596 |
| P wave duration (second) | 0.076 ±0.01 | 0.07 ±0.01 | 0.121 |
| P wave amplitude (millivolt) | 0.16 ±0.05 | 0.135 ±0.04 | 0.125 |
| PR interval (second) | 0.13 ±0.02 | 0.12 ±0.04 | 0.464 |
| QRS duration (second) | 0.096 ±0.025 | 0.052 ±0.013 | <0.001* |
| QRS amplitude (millivolt) | 2.26 ±1.2 | 1.03 ±0.39 | <0.001* |
| QT interval (second) | 0.36 ±0.06 | 0.35 ±0.046 | 0.589 |
| RR interval (second) | 0.69 ±0.27 | 0.85 ±0.46 | 0.32 |
| QT corrected (second) | 0.44 ±0.08 | 0.39 ±0.06 | 0.04* |

**** significant.***

Regarding high sensitivity troponin-I level in our study, we found eight positive cases (having troponin-I level >0.01 ng/ml), while no positive subjects were found in the control group. There were no statistically significant differences between cases (0.017 ±0.033 ng/ml) and controls (0.0076 ±0.002 ng/ml), or between hemodialysis cases (0.019 ±0.037 ng/ml) and conservative cases (0.0092 ±0.0058 ng/ml) regarding the overall levels of troponin-I ($p$ =0.08 and 0.171, respectively).

There was no significant correlation between systolic function (FS) and QTc value or troponin-I level. There was no significant correlation between QTc value and troponin-I level (**Table 5**).

**Table 5:** Correlation between FS, QTc and Troponin I level.

| Correlations | r | *P*-value |
|---|---|---|
| QT corrected vs FS | -0.04 | 0.804 |
| Troponin-I vs FS | 0.191 | 0.496 |
| QT corrected vs Troponin-I | 0.116 | 0.679 |

## 4. Discussion

Regarding structural changes in the heart, our conventional echo study revealed significant left ventricular chamber enlargement in cases compared to controls. This is consistent with Moustafa et al., (2020) who showed that LVSD and LVPWD were increased in their studied patients [6]. Our Echo measurements are also consistent with Mitsnefes and Mark, (2012) who demonstrated that even in pediatric cases suffering from mild to moderate stages of CKD acquired a high incidence of LVH that increases with progression to ESRD [7]. In contrast, Becker-Cohen et al., (2006) reported a different result with a lower prevalence of LV enlargement that is mostly linked to better control of BP [8].

Regarding the systolic function of the left ventricle, our results showed a significant decrease in EF and FS of patients when compared to controls with highly prevalent systolic dysfunction in the cases group. This coincides with Shahri et al., (2023) who found that a majority of their studied patients had mild to moderate systolic dysfunction based on EF [9], and Hothi et al., (2009) who reported that systolic dysfunction (FS) of the heart is a common finding [10]. Most other studies in pediatrics with pre-dialysis or dialysis-dependent CRF showed a normal ejection fraction at rest as shown in Ramadan et al., (2022) reporting that EF and FS of cases compared to controls had no significant difference [11]. Peter et al., (2019) showed that EF and FS were reduced in the CKD patients compared to controls, but with no statistically significant difference [12].

One of the early manifestations of cardiac affection in CKD pediatric patients is diastolic dysfunction. It's a powerful risk factor for heart failure development in adult life [13]. In this study, half of our cases were suffering diastolic dysfunction as recognized by tissue Doppler imaging.

Comparing Echo parameters of hemodialysis cases with those on conservative treatment, there was a significant left ventricular enlargement in the hemodialysis group. This came in agreement with Scavarda et al., (2014) who demonstrated that the internal diastolic diameter of LV and its posterior wall thickness was increased in dialysis patients compared to conservative ones [14]. Mitsnefes and Mark, (2012) had similar results reporting that pre-dialytic CKD

children presented with a lower incidence of LV hypertrophy compared to dialytic ones [7].

Regarding ECG findings of our cases and controls, a prevalent LVH and prolonged QTc were found. We declared that QRS duration, QRS amplitude and QT corrected values were much higher in cases compared to controls which may reflect the popularity of arrhythmia and chamber enlargement in those cases. Similarly, Leventoğlu et al., (2023) showed a marked prolongation of QTc in their cases compared to controls [15]. Also, Shahri et al., (2023) found an increase in QRS amplitude in most patients and prolonged QTc in about the third [16]. Another comparable result reported by Hafez et al., (2015) said that the prolongation of QTc in CKD cases compared to controls was markedly significant [17]. Mohamed et al., (2016) and Valsangiacomo et al., (2007), on the other hand, showed no significant prolongation of QTc in children with advanced stages of renal impairment on hemodialysis in their studies [18, 19].

Comparing ECG parameters of hemodialysis cases and conservative cases, we found that QRS duration and amplitude as well as QT corrected values were significantly higher in hemodialysis cases. This coincides with Leventoğlu et al., (2023) who concluded that LV hypertrophy found in ECG and higher QTc values in the hemodialysis group were more frequent compared to other CKD subgroups and transplantation cases [15].

Regarding high sensitivity troponin-I level in our study, we found eight positive cases (having troponin-I level > 0.01 ng/ml), that may signify cardiac cell injury in them, while no positive subjects were found in the control group. There were no statistically significant differences between cases and controls, or between hemodialysis cases and conservative cases regarding the overall levels of troponin-I. In the pediatric population with cardiovascular disease risk, data about cardiac biochemical markers are inadequate, especially those using high-sensitivity assays. A study by Kandil et al., (2009) reported a normal level of troponin-I (using regular assay) in their studied CKD patients but concluded that a normal level doesn't exclude cardiac affection in CKD [20]. On the other hand, Mohamed et al., (2021) showed an elevated level of troponin-I in ESRD children before dialysis sessions [21].

In this study, there was no significant correlation between systolic function and QTc value, which came in agreement with Kocak et al., (1999) who reported that their CKD cases have notably longer corrected QT intervals than healthy children and the duration of the QTc positively correlates with the duration of renal failure, but QTc duration is not related to LV mass index or systolic function [22]. Ozdemir et al., (2005) showed a different result, revealing that patients with left ventricular systolic dysfunction had markedly greater QTc value [23].

In our results, there was no significant correlation between FS and cardiac troponin-I or QTc and troponin-I level of cases, which coincides with Kandil et al., (2009) [20]. On the other hand, Artunc et al., (2012) and Buiten et al., (2015) reported a significant correlation between systolic dysfunction and the rise of troponin-I levels in adults on hemodialysis [24, 25]. Contrarily, Mohamed et al., (2021) showed that prolonged QTc is associated with higher levels of troponin-I [21].

## 5. Conclusion

CRF in pediatrics is associated with a highly prevailing LVH, systolic/diastolic dysfunction, and prolonged QTc with no significant elevation of troponin-I level. More studies need to be conducted with the implementation of a larger number of participants and prolonged follow-up courses to help recognize the etiology, implications and long-term prognosis of cardiac abnormalities in CKD children.

**Ethics approval and consent to participate:** The Research Ethical Committee of Fayoum University, Faculty of Medicine reviewed this study. All participants were informed about the objectives, examination and all investigations performed. The confidentiality of all subject's information was strictly respected. They were all informed that they had the right not to participate.

**Availability of data and material:** All data generated or analyzed during this study are included in this published article.

**Competing Interest:** All authors declare no conflict of interest

**Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**AI declaration statement:** Not applicable.

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