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Changes in Self-Care, Treatment Adherence, and Renal Function in Children with Cystic Fibrosis

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Abstract

Background: Cystic fibrosis (CF) is a chronic and progressive disease that requires continuous care and management. Self-care and treatment adherence play crucial roles in the effective management of these patients, particularly in children. The present study aimed to assess the status of self-care, treatment adherence, and renal function indicators in children with CF, as well as to analyze their changes over a six-month period.

Methods: In this longitudinal study, 30 children with CF were evaluated on an outpatient basis at two time points: baseline and six months later. Data on nutritional self-care and treatment adherence were collected using validated questionnaires. Laboratory indicators including serum creatinine, blood urea nitrogen (BUN), estimated glomerular filtration rate (eGFR), blood glucose, and urinary protein-to-creatinine ratio were measured. Parametric statistical tests and linear mixed-effects regression models were applied for data analysis.

Results: The mean age was 10 years, with a mean body mass index of 15.5 kg/m², and the majority were male. The mean self-care score significantly declined over the six-month period ($p = 0.024$), while treatment adherence showed no significant change ($p = 0.787$). Serum creatinine ($p = 0.019$) and blood glucose ($p = 0.009$) levels increased significantly, whereas eGFR decreased ($p = 0.003$). Time was the only variable that had a significant effect on eGFR and creatinine ($p < 0.05$); self-care and treatment adherence scores had no significant impact. A significant negative correlation was observed between self-care and the urinary protein-to-creatinine ratio ($r = -0.508$, $p < 0.01$).

Conclusion: The observed decline in self-care and renal function among children with CF over time highlights the need for structured, multidimensional, and long-term interventions aimed at improving self-care and treatment adherence. Regular monitoring of renal function is also recommended for these patients.

Key Words: Children; Cystic fibrosis; eGFR; Renal function; Self-care; Treatment adherence.

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1- INTRODUCTION

Cystic fibrosis (CF) is one of the most common life-shortening genetic disorders worldwide (1), caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene (2). These mutations result in severe dysfunction of the respiratory, gastrointestinal, and other organ systems. With advances in treatment—particularly the introduction of CFTR modulators—life expectancy among patients has markedly improved, which has led to greater recognition of several extrapulmonary complications (3).

Historically, CF has been described predominantly in European populations; however, recent evidence indicates that the burden of CF is also substantial in many low- and middle-income countries (2). In China, the prevalence of CF among children is approximately 1 in 128,434—significantly lower than rates reported in Western countries (4). In the Middle East and Arab countries, epidemiological data collected between 2019 and 2023 remain limited, heterogeneous, and insufficiently consolidated, highlighting the need for more systematic investigations (5).

The Cystic Fibrosis Mutation Database has documented more than 2,000 CFTR gene mutations, among which 380 have been confirmed as disease-causing (6). The F508del mutation is the most prevalent variant globally (7). In Iran, a review of 87 affected families demonstrated that F508del, along with several other CFTR variants, is common, with notable regional differences likely influenced by ethnic and geographical diversity (8).

The complications of cystic fibrosis encompass a wide spectrum. In addition to pulmonary, gastrointestinal, and nutritional problems, CFTR-related disorders and long-term drug exposure may contribute to metabolic abnormalities, cystic fibrosis–related diabetes (CFRD), liver disease, and compromised quality of life (3, 9). Among extrapulmonary complications, renal disorders have recently been recognized as an emerging morbidity. A 2025 review reported that drug- or dehydration-induced acute kidney injury (AKI), nephrolithiasis, amyloidosis, IgA nephropathy, and diabetic nephropathy are among the renal manifestations observed in CF patients (3).

Recent studies have shown that novel biomarkers such as cystatin C and urinary neutrophil gelatinase-associated lipocalin (uNGAL) can detect renal function decline in CF patients even when serum creatinine (sCr) levels remain within the normal range (10). Similarly, an Egyptian pediatric study found that over half of the evaluated children had elevated urinary β_2-macroglobulin and kidney injury molecule-1 (KIM-1), despite normal conventional renal tests and ultrasound findings, indicating silent early renal involvement (10). Cystic fibrosis imposes a considerable economic burden in Iran, primarily due to medication expenses and hospitalization costs. Direct non-medical and indirect costs further amplify this burden (11). In chronic conditions with complex, multidimensional management needs—such as CF—treatment adherence and self-care play essential roles. CF therapies, including medications, respiratory physiotherapy, pancreatic enzyme replacement, dietary regulation, and nutritional supplementation, are effective only when accompanied by consistent patient and family engagement. Prior studies have reported that self-reported adherence is influenced by factors such as age, family environment, and parental education, with suboptimal adherence noted in some patients (12).

A recent Iranian study (2025) found that non-adherence to inhaled medications, systemic antibiotics, gastrointestinal drugs, and nutritional supplements is common among children and adolescents with CF. Moreover, adherence to one medication

class does not necessarily predict adherence to others. Barriers such as polypharmacy, low maternal education, and long distance from medical centers were identified as major contributors to incomplete adherence (13). Self-care and treatment adherence are recognized not only as fundamental components of CF management but also as modifiable targets for intervention, as structured educational and behavioral programs have been shown to improve adherence, reduce pulmonary exacerbations, and enhance nutritional outcomes (14).

Evidence also suggests that renal impairment may develop early and asymptomatically (10), particularly in children, underscoring the need for close monitoring and periodic assessment. A 2025 review further emphasized the importance of identifying risk factors, optimizing pharmacotherapy, and ensuring frequent follow-up (3). However, most existing research has focused on adult CF populations. Although a few pediatric studies have been conducted in Egypt and other regional centers, data on renal status in children with CF—particularly in Iran—remain scarce, fragmented, and insufficiently characterized. There is limited understanding of the extent and severity of early renal involvement, its correlations with clinical and laboratory indicators (including biomarkers), and the influence of self-care and treatment adherence on preventing or mitigating renal damage. In the absence of integrated data systems and systematic laboratory surveillance, early stages of renal impairment may remain undetected.

Therefore, conducting a study to evaluate self-care status and both clinical and paraclinical indicators of renal involvement among children under 18 years with CF in Iran or similar settings would address a key knowledge gap. Such evidence could support the development of targeted interventions aimed at improving patient care, preventing renal complications, and ultimately enhancing quality of life in this vulnerable population.

2- MATERIALS AND METHODS

2-1. Study Design

This analytical longitudinal study was conducted between 2023 and 2024 on patients diagnosed with CF in Ardabil Province, located in north-western Iran.

2-2. Study Population and Sampling Method

Given the limited number of CF patients in Ardabil Province, a census sampling method was employed. All patients under 18 years of age with a confirmed diagnosis of CF who attended the Kosar Clinic in Ardabil were included in the study. A total of 30 patients met the inclusion criteria. The diagnosis of CF was confirmed by sweat testing along with clinical and paraclinical evaluations. These patients were under regular follow-up and management by pediatric pulmonologists and gastroenterologists on a monthly basis.

2-3. Inclusion and Exclusion Criteria

Inclusion criteria consisted of children under 18 years with a definitive diagnosis of CF, absence of pre-existing renal or systemic diseases independent of CF-related renal involvement, and parental and child consent to participate in the study.

2-4. Data Collection

Demographic data—including age, sex, and weight—along with age at diagnosis and hospitalization history, were extracted from medical records and, when necessary, supplemented through telephone interviews with families. Paraclinical data, including ultrasound findings and laboratory test results, were recorded throughout the treatment and follow-up period.

To assess renal involvement, renal and urinary tract ultrasonography was performed at the time of enrollment to rule out anatomical abnormalities such as nephrolithiasis, nephrocalcinosis, changes in renal size or echogenicity, medullary thickening, and other associated findings (e.g., inguinal hernia, hydrocele, undescended testes). Renal function biomarkers—including blood urea nitrogen (BUN), serum creatinine, and glomerular filtration rate (GFR, calculated using the modified Schwartz formula)—as well as blood pressure and urinary protein-to-creatinine ratio were measured and recorded at two time points, six months apart. Blood glucose levels and symptoms related to diabetes were also evaluated.

2-5. Measurement Instruments

The study employed two questionnaires. The first was the standard 8-item Morisky Medication Adherence Scale (MMAS-8), comprising 8 questions-7 with yes/no responses and 1 using a Likert scale. Item 5 is reverse-scored. The total score ranges from 0 to 8, with lower scores indicating better medication adherence. Scores of 1-4 indicate high adherence, 4-6 moderate adherence, and 6-8 low adherence. The Persian version of the questionnaire has demonstrated a reliability of 0.94 (15).

The second questionnaire, designed by the researchers, assessed self-care and consisted of 9 items covering daily evaluation of clinical symptoms, sputum culture, physiotherapy, diet, exercise, social support, and interactions with other patients. Scores ranged from 0 to 9, categorized into high self-care (1-3), moderate self-care (4-6), and low self-care (7-9). The content and face validity of this questionnaire were confirmed by a panel of experts. Questionnaires were administered either in person at the clinic, via telephone, or electronically by parents or patients (if capable) at two time points, six months apart.

2-6. Statistical Analysis

Collected data were coded and entered into SPSS version 26 for analysis. Descriptive statistics included mean, standard deviation, minimum, and maximum for quantitative variables, and frequency and percentage for qualitative variables. Normality of data distribution was assessed using the Kolmogorov–Smirnov test. Paired t-tests were used to compare means of quantitative variables across the two time points. Pearson correlation coefficients were calculated to assess relationships between self-care and treatment adherence scores at the first time point, second time point, and the difference between the two, with renal and biochemical laboratory variables.

Additionally, mixed-effects linear regression models were employed to analyze the effects of time, self-care, and treatment adherence on laboratory indices. A significance level of $p<0.05$ was considered for all analyses.

3- RESULTS

3-1. Demographic and Clinical Characteristics

The study included 30 children under 18 years of age with cystic fibrosis, of whom 53.3% were male and 46.7% were female. Renal and urinary tract ultrasonography revealed normal findings in 93.3% of patients, while nephrolithiasis and increased renal echogenicity were each observed in 3.3% of cases.

In terms of body mass index (BMI) percentiles, most patients (50%) fell within the 10th–50th percentile, and all patients (100%) had no evidence of chronic kidney disease (CKD) at the second time point. In the first assessment of AKI, only 3.3% of patients were affected, while 96.7% showed no signs of AKI (Table 1).

Table-1. Demographic and clinical characteristics of the study participants.

Variable	Category	Frequency	Percent (%)	Valid Percent (%)	Cumulative Percent (%)
Sex	Male	16	53.3	53.3	53.3
	Female	14	46.7	46.7	100.0
Renal and urinary tract US	Normal	28	93.3	93.3	93.3
	Stone	1	3.3	3.3	96.7
	Increased echogenicity	1	3.3	3.3	100.0
BMI Percentile	≤10th	9	30.0	30.0	30.0
	10th–50th	15	50.0	50.0	80.0
	>50th	6	20.0	20.0	100.0
CKD (second visit)	No	30	100.0	100.0	100.0
AKI (first visit)	Yes	1	3.3	3.3	3.3
	No	29	96.7	96.7	100.0

Changes in self-care, treatment adherence, and renal laboratory variables between the two time points are presented in Table 2. The mean self-care score decreased significantly over six months (from 5.35 ± 1.25 to 4.88 ± 1.32; mean difference = −0.467, t = 2.379, p = 0.024), indicating a decline in self-care behaviors. There was no significant change in treatment adherence scores (2.84 ± 1.29 vs. 2.81 ± 1.26; mean difference = −0.033, t = 0.273, p = 0.787).

Renal function analysis showed a significant increase in serum creatinine (0.593 ± 0.136 mg/dL to 0.650 ± 0.157 mg/dL; p = 0.019) and blood glucose levels (116.9 ± 75.07 mg/dL to 145.17 ± 97.62 mg/dL; p = 0.009), while estimated glomerular filtration rate (eGFR) significantly decreased (108.04 ± 24.92 to 96.57 ± 12.66 mL/min/1.73 m²; p = 0.003). BUN and urinary protein-to-creatinine ratio did not change significantly over time (p > 0.05) (Table 2).

Table-2. Mean values of self-care, treatment adherence, and laboratory variables at two time points.

Variable	First Visit (Mean ± SD)	Second Visit (Mean ± SD)	Mean Difference	t	p-value
Self-care score	5.35 ± 1.25	4.88 ± 1.32	−0.467	2.379	0.024*
Treatment adherence (MMAS-8)	2.84 ± 1.29	2.81 ± 1.26	−0.033	0.273	0.787
Serum creatinine (mg/dL)	0.593 ± 0.136	0.650 ± 0.157	0.057	−2.482	0.019*
BUN (mg/dL)	24.00 ± 17.22	23.97 ± 11.08	−0.033	0.017	0.986
Blood glucose (mg/dL)	116.90 ± 75.07	145.17 ± 97.62	28.27	−2.797	0.009*
eGFR (mL/min/1.73 m²)	108.04 ± 24.92	96.57 ± 12.66	−11.47	3.228	0.003*
Urinary protein-to-creatinine ratio	0.196 ± 0.057	0.194 ± 0.070	0.002	0.458	0.650

*Significant at p < 0.05

Throughout the six-month follow-up period, the mean self-care score significantly decreased (p=0.024), while treatment adherence did not show a significant change (p=0.787). Serum creatinine and blood glucose levels increased significantly (p=0.019 and p=0.009, respectively), while eGFR decreased significantly (p=0.003). Changes in BUN and urinary protein-to-creatinine ratio were not statistically significant (Table 3).

Table-3. Correlation between changes in self-care and treatment adherence scores and laboratory variables.

Variables	Creatinine	BUN	Blood glucose	eGFR	Protein/Creatinine ratio
Self-care (1st visit)	-0.107	-0.039	-0.044	0.103	-0.101
Treatment adherence (1st visit)	-0.178	-0.176	0.165	-0.015	0.042
Self-care (2nd visit)	0.012	-0.162	-0.082	0.207	-0.508**
Treatment adherence (2nd visit)	-0.089	-0.231	0.023	0.093	-0.164
Δ Self-care (2nd − 1st)	0.255	0.327	-0.084	-0.212	-0.078
Δ Treatment adherence	0.230	0.088	-0.090	-0.165	-0.228

**$p < 0.01$

A significant negative correlation was found between self-care at the second visit and urinary protein-to-creatinine ratio ($r = -0.508$, $p < 0.01$), suggesting a potential protective role of self-care in reducing proteinuria. Other correlations between self-care and treatment adherence scores with creatinine, BUN, blood glucose, and eGFR were weak and non-significant. Similarly, changes in self-care and treatment adherence between the two visits were not significantly correlated with changes in creatinine or BUN ($p > 0.05$). These findings highlight a limited but notable association between self-care and certain renal function indices, underscoring the importance of promoting self-care in patient management.

In the mixed-effects linear regression model with eGFR and creatinine as dependent variables, time was the only significant predictor (eGFR: $p = 0.006$; creatinine: $p = 0.015$), with mean eGFR at baseline significantly higher than six months later. Nutritional self-care and medication adherence scores had no significant effects on eGFR or creatinine ($p > 0.05$) (Table 4).

Table-4. Fixed effects of mixed-effects linear regression model for predicting eGFR and creatinine based on time, nutritional self-care, and medication adherence.

Parameter	eGFR (ml/min/1.73 m²) Estimate	Std. Error	t	P-value	Creatinine (mg/dL) Estimate	Std. Error	t	P-value
Intercept	95.236	11.484	8.293	<0.001	0.616	0.082	7.501	<0.001
Time (0 months)	11.188	3.755	2.980	0.006	-0.062	0.024	-2.576	0.015
Time (6 months, reference)	0	–	–	–	0	–	–	–
Nutritional self-care	0.639	2.345	0.272	0.786	0.012	0.017	0.719	0.475
Medication adherence	-0.636	2.592	-0.245	0.808	-0.009	0.019	-0.460	0.648

4- DISCUSSION

The findings of this study indicate that patients' self-care scores were suboptimal and declined significantly over the six-month follow-up, suggesting that self-care behaviors were not maintained consistently over time. Consistent with prior reports, low adherence to enzyme supplementation and chest physiotherapy has been documented in pediatric CF cohorts (16). Bregnballe et al. also reported that time constraints, forgetfulness, and reluctance to take medication in public were common barriers to adherence (17).

The observed decline in self-care may reflect psychological, social, and family-level determinants (e.g., caregiver burden, disease perceptions), which can erode sustained self-management over time. Rego (2024) highlighted negative disease attitudes among youth with CF that impede independent self-care and may reduce provider–patient self-care support (18). These findings underscore the need for ongoing educational and psychosocial support interventions designed to maintain self-care behaviors longitudinally.

Parental psychosocial and spiritual/religious factors have been described as important determinants of adherence, and targeted caregiver-oriented interventions (including culturally tailored support) may improve regimen uptake (19). Parental beliefs about treatment necessity and child age were independent predictors of adherence to enzymes and physiotherapy in earlier studies (16).

In the present study, medication adherence scores were relatively high and stable at baseline and at six months. This aligns with several reports of acceptable adherence among younger children—often attributed to parental supervision (12, 20). However, a similar study in Iran reported poor adherence to inhaled medications, systemic antibiotics, gastrointestinal drugs, and dietary supplements among children and adolescents with CF (13). Studies by Faint (2017) and Narayanan (21, 22) also documented suboptimal treatment adherence (16, 23).

A key contribution of our work is the longitudinal assessment of self-care, demonstrating that self-care may deteriorate even when medication adherence appears stable over short intervals. Patient knowledge and self-efficacy likely influence adherence trajectories, but their effects may require longer observation to manifest as clinical change.

Our biochemical results showed a statistically significant decrease in eGFR and increases in serum creatinine and blood glucose over six months, whereas BUN and urine protein-to-creatinine ratio were unchanged. These laboratory shifts may signal early renal function decline, but must be interpreted cautiously given the small sample size and short follow-up. Prior pediatric studies report progressive declines in eGFR in susceptible children and variable prevalence of glomerular hyperfiltration in CF cohorts (24, 25). Tubular injury markers (e.g., uNGAL, KIM-1, cystatin C) can detect subclinical renal injury not captured by eGFR alone (26).

In our mixed-effects models, time emerged as the only significant predictor of eGFR and creatinine. Nutritional self-care and medication adherence scores were not significant predictors, and although this pattern may be influenced by sample characteristics, the absence of detected associations should not be interpreted as evidence of no underlying physiological relationship. Although self-care scores decreased in the present study, other CF studies have shown that the effects of self-care behaviors often manifest over longer periods (23). Consistent with our results, Rosner (2025) reported early subclinical tubular and renal injury markers that are not readily detected by eGFR alone. Urinary biomarker analyses in the CF cohort revealed associations with aminoglycoside exposure, lung function, and neutrophil activation (26).

Daily CF care is complex and time-consuming, particularly in adolescence when self-management responsibility shifts from caregivers to patients (23, 27). Our findings therefore support the need for continuous, multidimensional interventions combining education, psychosocial support, and system-level facilitation (e.g., easier access to care, adherence aids) to sustain self-care and

potentially mitigate renal and other extrapulmonary complications.

4-1. Study Limitations

This study has several important limitations. The small sample size (n = 30) and short follow-up period of six months limit statistical power and the ability to detect long-term effects. Self-care and medication adherence were self-reported, introducing recall and social desirability biases. The study also lacked key clinical data including blood pressure, inflammatory markers, and specific tubular injury biomarkers which would have provided a more comprehensive renal assessment. Finally, the analyses focused on linear associations; nonlinear and mediating effects were not explored.

4-2. Recommendations for Future Research

Future studies should employ larger cohorts and longer follow-up periods (≥12 months), integrate objective adherence measures (such as pharmacy refills and electronic monitoring), and include expanded renal biomarker panels and routine blood pressure/inflammatory marker monitoring. Mixed-methods designs incorporating qualitative inquiry can elucidate patient and caregiver barriers and facilitators of self-care. Analytical approaches should examine nonlinear associations and mediation models to clarify pathways linking adherence, systemic inflammation, and renal injury.

5- CONCLUSION

This study demonstrated that among children with cystic fibrosis, self-care scores declined significantly over six months, while medication adherence remained relatively stable. Concurrent increases in serum creatinine and reductions in eGFR suggest early signals of renal vulnerability within this timeframe. Although self-care and medication adherence did not predict renal indices in the mixed-effects models, the temporal changes observed underline the importance of ongoing monitoring and early identification of renal risk. The study highlights the need for structured, sustained self-care support to prevent or delay renal injury in this population.

6- ACKNOWLEDGMENT

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7- CONFLICTS OF INTEREST

The authors have no conflicts of interest.

8- ETHICAL STATEMENT AND CONSENT TO PARTICIPANT

The study was approved by the Ethics Committee No. IR.ARUMS.MEDICINE.REC.1402.136. Informed consent was obtained from the parents of all participants.

9- CONSENT FOR PUBLICATION

All authors consent to the publication of the manuscript and findings.

10- DATA AVAILABILITY STATEMENT

The raw data analyzed during this study are available from the corresponding author upon reasonable request.

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