Changes in Pulmonary Function Tests in Pediatrics with End- Stage Renal Disease in Benha University Hospitals

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ABSTRACT
Background: Patients with end-stage renal disease (ESRD) receiving regular hemodialysis (HD) may experience acute or chronic pulmonary problems, which are one of the leading causes of death in this population. Physical deconditioning, muscular atrophy from lack of usage, weakness, exhaustion, lower-limb edema, and back discomfort can all contribute to a decline in the lung's functional capacity, which makes it difficult for these kids to accomplish everyday tasks.
Objective: The aim of the current work was to examine pulmonary function testing in kids with ESRD receiving routine HD.
Patients and Methods: This comparative cross-sectional study included a total of 26 Children with ESRD on regular HD and equal number of age and gender matched controls, attending at Inpatient Clinic, Pediatric Nephrology Department, Pediatric Hospital, Benha University Hospitals.
Results: The present study showed that, mean values of forced expiratory volume in 1 second (FEV1) (%), forced vital capacity (FVC) (%), Peak expiratory flow (PEF) (%), maximal voluntary ventilation (MVV) (%), forced expiratory flow (FEF) (25-75) were statistically lower among hemodialysis group than Control group. However, there was no statistically significant difference in FEV1/FVC (%) between the hemodialysis group and the Control group. In the current study, 57.7% of the ESRD patients evaluated had restrictive spirometric patterns, 7.7% had mixed obstructive and restrictive patterns, and 7.7% had obstructive patterns.
Conclusion: Our results support the notion that pulmonary function tests considerably decline in ESRD patients receiving HD compared to controls, with a strong negative connection between this and the length of dialysis. The majority of ESRD patients first displayed aberrant pulmonary functions, with a restrictive pattern predominating.
Keywords: Pediatrics, CKD End Stage Renal Disease, Pulmonary Function Tests.

INTRODUCTION
A gradual, irreversible condition known as chronic kidney disease (CKD), ESRD can result from the loss of renal function. It results from several renal abnormalities [(1)]. Reduced glomerular filtration causes a buildup of toxins, fluid, and electrolytes that, if not adequately treated with renal replacement treatments like hemodialysis (HD), peritoneal dialysis, or kidney transplantation, can cause uremic syndrome or patient death [(2)]. Despite the fact that dialysis technology have increased life expectancy, patients' challenges have increased, especially those related to systemic or metabolic problems and HD consequences [(3)].

The mechanical operation and ventilation of the lungs are associated with kidney function in both healthy and pathological situations [(4)]. Pulmonary issues are frequent in chronic renal disease patients. In patients receiving long-term regular HD treatment, several factors, including neutrophil entrapment and bronchial responsiveness, may impair pulmonary function and alter bronchial responsiveness. These individuals may have muscular myopathy, reduced respiratory muscle strength, pulmonary edema, pleural effusion, acute respiratory distress syndrome, increased pulmonary capillary permeability, pulmonary calcification, pulmonary hypertension, hemosiderosis, pleural fibrosis, and hemosiderosis [(5)].

Uremic toxins, anemia, immunosuppression, excessive calcification, malnutrition, electrolyte imbalances, acid-base imbalance, and volume overload may all contribute to their development directly or indirectly [(6)].

The ventilation and function of the lungs may be impacted by ESRD directly or indirectly. Chronic inflammation characterizes ESRD. Hemodialysis decreases fluid retention and enhances pulmonary function, although inflammation can damage the respiratory system and raise mortality rates [(3)].

Lung functional capacity can be impacted by physical deconditioning, muscular atrophy from lack of usage, weakness, lower-limb edema, and back discomfort, making it challenging for these children to carry out everyday tasks [(5)].The study's objective was to examine pulmonary function testing in kids with ESRD receiving routine HD.

PATIENTS AND METHODS
This comparative cross-sectional study included a total of 26 Children with ESRD on regular HD and equal number of age and gender matched controls, attending at Inpatient Clinic, Pediatric Nephrology Department, Pediatric Hospital, Benha University Hospitals.

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The included 52 subjects were classified into two groups: **Group I: the hemodialysis group (HDG)**: included 26 Children with ESRD under regular HD (HDG). **Group II: the control group (CG):** included 26 age and gender matched healthy children who referred for routine checkup as a control group (CG).

The sample size estimate was based on the mean FEV1/FVC among Egyptian children receiving regular hemodialysis for end-stage renal illness.

The total computed sample size was 26 in each group using the G power software version 3.1.9.4 to calculate sample size based to effect size of 0.921 based on the mean of cases and control groups (74.3±21.4 & 89.46±9.1, respectively) using 2-tailed test, error =0.05, and power = 90.0%.

Inclusion criteria:

- Children and adolescents aged between 6 and 16 years.
- Children and teenagers with ESRD who had been receiving regular HD maintenance care for at least six months prior to the trial.
- Both sexes (males and females).

Exclusion criteria:

- Children have general health issues that are getting worse, such as musculoskeletal issues, bronchial asthma history, or other lung conditions.
- Patients with immunological or neoplastic diseases.
- Patients with severe cardiac conditions such as complex congenital heart diseases and cardiac insufficiency.
- Children or their parents who refuse or unable to cooperate.

The following procedures were applied to all patients and controls:

Complete history taking:

General, demographic and disease history

- Age, Sex, Residence.
- History of the ESRD (Age at diagnosis, presenting manifestation, duration of illness, duration of HD and when started).
- Previous medical history, including any current or previous drug use.
- Family background.
- Previous growth and development of the child.

Clinical examination:

Complete general examination:

- Vital signs (temperature, respiratory rate, heart rate).
- A mercury sphygmomanometer was used to gauge arterial blood pressure.

Local examination: (cardiac، chest and abdominal examination) to exclude any other illness.

Lab investigations: CBC, renal function tests (serum creatinine, urea, and BUN), electrolytes (Na, K, Ca), and serum albumin.

Imaging:

Plain chest X-ray (PA view):

- Each time a patient was included, if the result was abnormal, the subject was removed from the research.

Pulmonary function tests:

Pulmonary function test was done one hour after hemodialysis [(3)]**.**

Spirometry was used to measure lung function using a computerized spirometer (Jaeger MS-IOS). Following the standards of the American Thoracic Society and European Respiratory Society (ATS/ERS) [(7)], one flow model and technical processes, acceptance criteria, and repeatability.

Peak expiratory flow (PEF), forced expiratory flow (FEF), forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and FEV1/FVC ratio were all calculated.

The maneuver was carried out three times, with the greatest value being chosen. All data, except for FEV1/FVC%, were calculated as percent of predictions.

Ethical consideration:

This study was ethically approved by Benha University Research Ethics Committee. Verbal and written informed consent of all the participants' parents was obtained. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical analysis

SPSS version 20 was used to tabulate and analyze the data. Numbers and percentages were used to convey categorical data. Quantitative data were evaluated for normality using the Kolmogorov–Smirnov test test, with a P value of 0.05 indicating normality. To analyze quantitative data, the mean±standard deviation, median, and range were used. The student "t" test was used to examine the normally distributed variables in two separate groups. The correlation between non-parametric variables was calculated using the Spearman's correlation coefficient (rho). The Spearman's coefficient of correlation (rho) assesses the linear relationship between two quantitative variables (one is the independent var. X, and the other is the dependent var., Y). P values lower than 0.05 were regarded as significant.

RESULTS

In this study, there were no statistically significant differences between hemodialysis group and control group regarding age (P =0.090) and sex (P = 0.555). Males represented 65.4% in hemodialysis group and 57.7% in control group.

Table 1 shows that the mean of duration of CKD was (5.98± 2.09) **(years)** and the mean of Duration of HD was (4.50± 2.30) **(years)**.

Table (1): Duration of CKD and HD among the studied cases.

	Mean ± SD
Duration of CKD	5.98± 2.09
Range	2-10
Duration of HD	4.50± 2.30
Range	1-9

Mean value of hemoglobin was statistically lower among Hemodialysis group than Control group **Table (2)**.

Table (2): Comparison between Hemodialysis group and Control group regarding complete blood count.

		Hemodialysis group	Control group	t. test	P. value
HB (g /dl)	**Mean ± SD**	9.72± 1.62	11.11± 1.40	-3.314	.002
Platelet ($x10^9$ /l)	**Mean ± SD**	223.1± 53.4	357.9± 49.9	39.7	.001
White blood cells ($x10^9$ /l)	**Mean ± SD**	5.7± 1.3	8.1± 2.0	4.6	.04

Mean values of Urea, BUN and creatinine were statistically higher among Hemodialysis group than Control group **Table (3)**.

Table (3): Comparison between Hemodialysis group and Control group regarding kidney functions.

		Hemodialysis group	Control group	t. test	P. value
Urea (mg/dl)	**Mean ± SD**	50.88± 11.83	25.96± 3.37	8.434	0.000
BUN (mg/dl)	**Mean ± SD**	21.15± 5.13	10.70± 1.44	8.550	0.000
Creatinine (mg/dl)	**Mean ± SD**	3.11± 0.669	0.730 ± 0.134	17.836	0.000

Mean values of FEV1 (%), FVC (%), PEF (%) MVV (%), FEF(25-75) were statistically lower among Hemodialysis group than Control group. While there was no statistically significant difference between Hemodialysis group and Control group regarding FEV1/FVC (%) **Table (4)**.

Table (4): Comparison between Hemodialysis group and Control group regarding Pulmonary function tests.

		Hemodialysis group	Control group	t. test	P. value
FEV1	**Mean ± SD**	1.38± .418	1.91± .499	-4.103-	.000
	Range	0.75-2.1	1.1-2.9		
FEV1 (%)	**Mean ± SD**	77.71± 20.23	97.15± 6.19	-4.684	.000
	Range	48%-95%	88%-105%		
FVC	**Mean ± SD**	1.58± .494	2.09± .543	-3.502-	.001
	Range	0.8-2.4	1.6-3		
FVC (%)	**Mean ± SD**	74.41± 17.05	91.76± 7.44	-4.754	.000
	Range	46-90%	86-100%		
FEV1/FVC (%)	**Mean ± SD**	90.85± 9.58	90.76± 5.65	.041	.968
	Range	66-95%	88-101%		
PEF (%)	**Mean ± SD**	58.26± 15.68	84.46± 6.57	-7.856	.000
	Range	30-80%	79-92%		
MVV (%)	**Mean ± SD**	32.12± 9.15	40.73± 6.07	-3.994-	.000
	Range	13-58	22-54		
FEF(25-75)	**Mean ± SD**	5.45± 1.63	8.51± 1.15	-7.811-	.000
	Range	0.9-2.1	2.8-101%3.6		

Table (5) show there were statistically significant negative correlation between FEV1 (%) and (duration of CKD, duration of HD). while there were no statistically significant correlation between FEV1 (%) and other variables. there were statistically significant negative correlation between FVC (%) and (duration of CKD, duration of HD). while there were no statistically significant correlation between FVC (%) and other variables. There were statistically significant positive correlation between FEF(25-75) and (albumin, ca) and there were statistically significant negative correlation between FEF(25-75) and (urea, BUN, creatinine, Na, k). While, there were no statistically significant correlation between FEF (25-75) and other variables. There were statistically significant positive correlation between MVV (%) and (albumin, ca) and there were statistically significant negative correlation between MVV (%) and (urea, BUN, creatinine, k) while there were no statistically significant correlation between MVV (%) and other variables.

Table (5): Correlations between FEV1 (%), FVC (%), FEF(25-75), MVV (%) and other variable.

Correlation	FEV1 (%)		FVC (%)		FEF(25-75)		MVV (%)	
	r	p	r	p	r	p	r	p
Duration of CKD	-.569-	.002	-.569-	.002	-.151-	.462	-.169-	.410
Duration of HD	-.639-	.000	-.639-	.000	-.170-	.406	-.125-	.542
HB (g/dL)	.153	.455	.174	.394	.266	.057	.111	.435
Urea (mg/dl)	-.241-	.237	-.253-	.212	-.592-	.000	-.334-	.016
BUN (mg/dL)	-.243-	.231	-.256-	.206	-.590-	.000	-.334-	.015
Creatinine (mg/dl)	-.129-	.531	-.103-	.616	-.681-	.000	-.427-	.002
Albumin (g/dL)	-.135-	.510	-.247-	.223	.387	.005	.328	.018
Ca (mg/dL)	.242	.235	.277	.171	.662	.000	.495	.000
Na (mmol/L)	-.028-	.893	-.045-	.826	-.347-	.012	-.018-	.898
K (mEq/L)	.106	.605	-.073-	.722	-.535-	.000	-.298-	.032

Table (6) show there were 7 cases are normal, 2 cases are obstructive, 2 cases are mixed, 15 cases are restrictive pattern and control group are normal.

Table (6): Comparison between Hemodialysis group and Control group regarding spirometry

			Hemodialysis group	Control group	X^2	P. value
	Normal	**No.**	7	26	63.14	.000
		%	26.9%	100.0%		
	Obstructive	**No.**	2	0		
		%	7.7%	.0%		
	Mixed	**No.**	2	0		
		%	7.7%	.0%		
	Restrictive	**No.**	15	0		
		%	57.7%	.0%		

DISCUSSION

This comparative cross-sectional study included a total of 26 Children with ESRD on regular HD (HD group) and equal number of age and gender matched healthy children (control group). In the hemodialysis group, male cases were 65.4%. There was no statistically significant difference between Hemodialysis group and Control group regarding age (years) and sex.

This agreed with **Momeni *et al.*** [(3)] who found a 60% male to female ratio in their study, which may be connected to the higher incidence of CKD in men or the absence of treatment for females due to social, cultural, and economic constraints. Moreover, **Halle *et al.*** [(8)] reported that patients were primarily men. This is consistent with research from poor nations, and it might be explained by boys being at a greater risk of renal illness and perhaps due to some gender discrimination, as has been documented in SSA [(9)].

In the current study, the mean of duration of CKD was (5.98± 2.09) (units) and the mean of duration of HD was (4.50± 2.30) (units).

According to **Mane *et al.*** [(10)] who reported that 91 (44.39%) of the 205 participants had undergone hemodialysis within the preceding 1 to 3 years, followed by 81 (39.51%) of the subjects who had undergone hemodialysis within the previous 6 to 12 months. **Sharma *et al.*** [(4)] reported only 10% of the 45 patients on hemodialysis had had it for less than six months, and that 45 patients (90%) had received it for between six months and three years.

Our study showed that, mean values of urea, BUN and creatinine were statistically higher among hemodialysis group than Control group. This agreed with **Hasan *et al.*** [(11).]

Mane *et al.* [(10)] reported that, mean urea level was 141.65 mg/dl prior to hemodialysis, and it was reduced to 121.78 mg/dl. Before to hemodialysis, the mean creatinine level was 10.0 mg/dl; it was reduced to 7.9 mg/dl. **Steinhorst *et al.*** [(12)] discovered a significant improvement in renal function after 40 hemodialysis sessions. Hemodialysis, according to **Rahgoshai *et al.*** [13] did not significantly enhance urea level.

The current study shown that the hemodialysis group had statistically lower mean values of FEV1 (%), FVC (%), PEF (%), MVV (%), and FEF (25-75) than the Control group. However there was no statistically significant difference in FEV1/FVC (%) between the Hemodialysis group and the Control group.

El-Gamasy [5] showed that CKD significantly lowers lung functional capacity in children and adolescents. In this study, we stated a significant difference in FVC% of predicted value, FEV1% of expected value, FEV1/FVC% of predicted value, and PEFR% of predicted value between HDG and CG. Moreover, we stated that FEF was lower than normal in HDG and within the usual range in CG, indicating that HDG had a little airway blockage.

Our findings were also consistent with those of **Rahgoshai *et al.*** [13]**,** who reported decreased spirometric measures, such as FVC and FEV1, in their 42 studied ESRD patients (32 of whom were on dialysis and 10 of whom underwent kidney transplantation), when compared to their 30 healthy controls (P 0.05), and who also noted that they were not improved after kidney transplantation.

Our findings concur with those of **Karacan *et al.*** [14] who stated that the HD and peritoneal dialysis groups had considerably lower residual volume and total lung capacity than the transplanted group. In the dialysis patients, FEF (25–75%) of vital capacity was somewhat below average.

FEV1 and HD duration had a statistically significant negative connection in our research. The relationship between FVC and HD duration was negatively correlated in a statistically significant way.

Our findings corroborated those of **El-Gamasy** [5]**,** who found that in ESRD patients, there were substantial negative associations between the length of HD and both FVC and FEV1.

CONCLUSION

We may draw the conclusion that pulmonary function tests considerably decline in ESRD patients receiving HD compared to controls of the same age, with a strong negative link to the length of dialysis. The majority of ESRD patients had abnormal pulmonary function tests, with a predominant restrictive pattern.

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REFERENCES

1. **Yilmaz S, Yildirim Y, Yilmaz Z *et al.* (2016):** Pulmonary Function in Patients with End-Stage Renal Disease: Effects of Hemodialysis and Fluid Overload. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research, 22:2779-84.
2. **Zemaitis M, Foris L, Katta S *et al.* (2022):** Uremia. Treasure Island (FL): StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK441859/
3. **Momeni M, Shahraki E, Yarmohammadi F *et al.* (2020):** Early Effects of Hemodialysis on Pulmonary Function in Patients with End-Stage Renal Disease. Zahedan J Res Med Sci., 22(3):e96710. DOI: 10.5812/zjrms.96710
4. **Sharma A, Gahlot S, Prasher P (2017):** A study of pulmonary function in end-stage renal disease patients on hemodialysis: a cross-sectional study. Sao Paulo Med J., 135(6):568-72.
5. **El-Gamasy M (2019):** Study of some pulmonary function tests in Egyptian children with end-stage renal disease under regular hemodialysis in correlation with dialysis duration. Saudi J Kidney Dis Transpl., 30(1):119-128.
6. **Mukai H, Ming P, Lindholm B *et al.* (2018):** Restrictive lung disorder is common in patients with kidney failure and associates with protein-energy wasting, inflammation and cardiovascular disease. PLoS One, 13(4): 29702682. doi: 10.1371/journal.pone.0195585.
7. **Graham B, Steenbruggen I, Miller M *et al.* (2019).** Standardization of spirometry 2019 update. An official American thoracic society and European respiratory society technical statement. American Journal of Respiratory and Critical Care Medicine, 200(8): 70-88.
8. **Halle M, Lapsap C, Barla E *et al.* (2017):** Epidemiology and outcomes of children with renal failure in the pediatric ward of a tertiary hospital in Cameroon. BMC Pediatr., 17: 202. doi: 10.1186/s12887-017-0955-0.
9. **Ladapo T, Esezobor C, Lesi F (2014):** Pediatric kidney diseases in an African country: prevalence, spectrum and outcome. Saudi Journal of Kidney Diseases and Transplantation, 25(5):1110-16.
10. **Mane S, Bhujbal C, Mane R *et al.* (2022):** Effect of Hemodialysis on pulmonary function in patients with End stage renal disease. European Journal of Molecular & Clinical Medicine, 9: 9774-9782.
11. **Hasan A, Alashkar A, Esmael N *et al.* (2019):** Assessment of pulmonary function in end stage renal disease patients on regular hemodialysis. The Egyptian Journal of Hospital Medicine, 76(1):3319-23.
12. **Steinhorst R, Vieira J, Abdulkader R (2007):** Acute effects of intermittent hemodialysis and sustained low-efficiency hemodialysis (SLED) on the pulmonary function of patients under mechanical ventilation. Ren Fail., 29(3):341–5.
13. **Rahgoshai R, Nasiri A, Solouki M *et al.* (2010):** Acute effects of hemodialysis on pulmonary function in patients with end-stage renal disease. Iranian Journal of Kidney Diseases, 4(3):214-17.
14. **Karacan O, Tutal E, Colak T *et al.* (2006):** Pulmonary function in renal transplant recipients and end-stage renal disease patients undergoing maintenance dialysis. Transplant Proc., 38: 396-400.