

Chest and Cardiac Findings on High-Resolution Computed Tomography in Children on Regular Hemodialysis with Abnormal Spirometry

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Cite this article as: Sobh E, Hamdy RM, Abdelsalam M, Elsayed FM. Chest and cardiac findings on high-resolution computed tomography in children on regular hemodialysis with abnormal spirometry. *Eurasian J Pulmonol* 2017; 19: X.

Abstract

Objective: To study the high-resolution computed tomography (HRCT) findings of children on hemodialysis with abnormal spirometry.

Methods: This descriptive study included 25 children with chronic kidney disease on regular hemodialysis. They were selected from a pediatric hemodialysis unit during the period from June 2015 to January 2016. Spirometry was done, and those with abnormal values were assessed by HRCT of the chest and echocardiography.

Results: Among 25 children with abnormal spirometry on regular hemodialysis, there was a decrease in spirometric indices in patients on hemodialysis with a tendency to the restrictive pattern (19 patients; 76%). The following HRCT findings were detected: bilateral mild lower-lobe air trapping (centrilobular emphysema) in 14 patients (56%), diffuse bilateral ground-glass appearance in 2 patients (8%), mild hilar and perihilar bronchiectasis in 5 patients (20%), and cardiomegaly in 3 patients (12%).

Conclusion: Our results suggest that HRCT revealed many pathological findings that could not be detected on the chest X-ray, and some of these findings may explain the abnormal indications observed on spirometry.

Keywords: Hemodialysis, HRCT, kidney, pediatric pulmonology, spirometry

INTRODUCTION

Chronic kidney disease (CKD) affects thousands of children all over the world; it affects their health and quality of life, and the number of patients is expected to grow (1). CKD and dialysis may affect different systems of the body and lead to conditions such as cardiovascular, respiratory, and musculoskeletal system dysfunctions (2-5). The diaphragm and intercostal muscles are mainly responsible for ventilatory function, so uremic myopathy may lead to a decrease in the muscle strength and endurance properties (2). Pulmonary complications reported in patients with CKD include pulmonary edema, pleural effusion, pulmonary fibrosis, respiratory infections, pulmonary hypertension, decreased pulmonary capillary blood flow, and hypoxemia (6, 7). Several investigations are required to study the respiratory function in patients on hemodialysis. The pulmonary function tests (PFTs) provide a global overview of both lungs. A significant deterioration of both lungs is usually required for a change in the PFTs parameters (8). Ventilatory deficits occur in CKD due to impairment in respiratory muscles in addition to lung tissue involvement, which contributes to decreased lung capacity and respiratory function impairment (9, 10).

Multiple diagnostic imaging modalities are used to demonstrate clinical anatomical abnormalities within the thorax. A plain chest X-ray is the first-line imaging tool of choice owing to the low radiation burden (11). However, the sensitivity of the chest X-ray is known to be low, making chest high resolution computed tomography (HRCT) the gold standard; the introduction of HRCT has considerably modified the diagnostic approach of pulmonary diseases (12-14). The use of HRCT requiring a low ra-



Received Date: 28.10.2016

Accepted Date: 13.02.2017

DOI: 10.5152/ejp.2017.43434

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• Available online at www.eurasianj pulmonol.com



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diation dose protocol for optimal pediatric chest imaging is currently considered an important diagnostic tool to accurately evaluate the thoracic structures (15-17).

Our aim was to study the main chest and cardiovascular findings using HRCT in children on regular hemodialysis who had abnormal spirometry.

METHODS

A descriptive prospective study conducted during the period from June 2015 to January 2016 involved children with CKD on regular hemodialysis for more than 3 months at the time of the study. They underwent regular hemodialysis 3 times a week and 4 hours/setting using a low-flux polysulphone dialyzer using Fresenius 4008 device (Fresenius Medical Care, Bad Homburg, Germany). They were selected from the hemodialysis unit of Al-Azhar University hospital. Complete medical history was obtained, and all children included in the study were subjected to physical examination by a pediatric nephrologist, pulmonologist, and cardiologist. Investigations were performed after the hemodialysis to avoid bias related to volume overload. Patients with chronic illness other than CKD or severe malnourishment were excluded from the study. Spirometry was done, and only those with abnormal results were included in the study.

- 1. Laboratory investigations:** Complete blood count was performed using Abbott Cell-Dyn 1800 automated hematology analyzer device (Abbott Diagnostics, Abbott Park, IL, USA). Serum biochemical tests were performed using the Roche Cobas C 311 autoanalyzer (Roche Diagnostics GmbH, Mannheim, Germany).
- 2. PFTs:** Spirometry was performed on a pulmonary function testing pediatric-dedicated station using HypAir compact plus flowmeter device (Medisoft, Sorinnes, Belgium). It was performed after hemodialysis and before the HRCT of the chest. The test was performed by an experienced pulmonologist after the demonstration of the technique, all subjects were provided verbal encouragement, and animations were used to encourage children to undergo the test. Spirometric indices were calculated using the best of 3 technically accepted trials (18, 19). Lung volumes [forced expiratory volume in 1st second (FEV₁), vital capacity (VC), forced vital capacity (FVC), Forced expiratory flow at 25-75% (FEF₂₅₋₇₅)] were recorded as absolute values and percentages of predicted values (%) according to age, sex, and ethnicity. Abnormal values were defined as less than 80% of predicted value for FEV₁, VC, FVC and less than 65% of predicted value for FEF₂₅₋₇₅. Obstructive pattern was defined as an FEV₁/FVC ratio of <70% or below lower limits of normal (LLN) (20). Small airway obstruction was also defined as the reduction in FEF₂₅₋₇₅ % below 65% of predicted value or LLN (21), whereas a restrictive pattern was considered when low FVC below 80% or below LLN was observed in the presence of a normal FEV₁/FVC ratio. A mixed ventilatory defect is characterized by the coexistence of obstruction and restriction (22).
- 3. Plain X-ray of the chest:** All patients underwent chest radiography using the Stephanix TPFIS device (Stephanix, La Ricamarie, Franc).
- 4. Echocardiography:** All patients were subjected to transthoracic echocardiography (TTE) using the VIVID S5 cardiovascular ultrasound system (General Electric, Horten, Norway) with 3S-RS phased array sector probe (1.5-3.6 MHz). Simultaneous electrocardiographic recording to allow timing of flow was done using Doppler (continuous wave method, pulse wave method and color flow mapping

method) and tissue Doppler imaging (TDI). The study included measurement of left ventricular (LV) dimensions, ejection fraction (23), and right ventricular (RV) systolic velocity obtained from the lateral tricuspid annular position. We used peak systolic gradient of tricuspid regurgitation and added the value of right atrial pressure to calculate systolic pulmonary artery pressure (sPAP) (24).

- 5. High resolution computed tomography (HRCT) of the chest:** Examinations were performed just after hemodialysis in all patients to prevent volume overload, which may obtain misleading images. The examination was performed using multidetector scanner with 160 detectors (Toshiba, Prime Aquilion Japan). A pediatric protocol without IV contrast was followed. The scans were obtained in the supine position and during full inspiration. Scanning parameters of HRCT examinations were as follows: slice width 5 mm, collimation 2.5 mm, scan time 3.3 seconds, Kv80, feed/rotation 15 mm. A scout was taken at 120 kV and 30 mA and helical scanning in full inspiration in a caudocranial direction to minimize the respiratory artifacts. Lesions were classified according to their presence or absence, anatomical site (parenchymal, pleural, mediastinal, vascular, and thoracic wall), segments, laterality (unilateral or bilateral), and morphology (reticular, ground glass, and nodular). HRCT images were assessed for abnormalities such as reticulation, honeycombing, volume reduction, emphysema, cysts, traction bronchiectases, ground-glass attenuation, nodules, consolidation, and increased main pulmonary artery caliber (25-28).

Informed written consent was obtained from parents of involved children in adherence with the guidelines of the ethical committee of Al-Azhar University and the study protocol had been approved by the ethics committee of Faculty of Medicine for Girls, Al-Azhar University institute.

Statistical Analysis

Data were recorded, fed to the computer as excel sheet. Descriptive analysis was performed using the Statistical Package for the Social Sciences (SPSS) Version 16. (SPSS Inc.; Chicago, IL, USA). Results are presented as mean \pm standard deviation or a percentage.

RESULTS

The study involved 25 children (13 females and 12 males) who had abnormal spirometry and were enrolled in the study; their mean age was 11.4 \pm 3.6 years, weight 26 \pm 10.1 kg, height 1.2 \pm 0.2 m, and body mass index (BMI) 16.6 \pm 3.6 kg/m². Causes of CKD in our study group included unknown (24%), focal segmental glomerulosclerosis (20%), and polycystic kidney (16%). Demographic, clinical, and laboratory data are shown in Table 1.

Patterns of Abnormal PFTs and Echocardiography

Spirometric and echocardiographic data of the study group are shown in Table 2.

Different patterns of abnormal PFTs were found in the study group. Nineteen patients (76%) had restrictive pattern, 4 patients (16%) had obstructive pattern, 2 patients (8%) had mixed pattern, and 20 patients (80%) had small airway affection (Figure 1).

The patients had normal LV internal dimensions and LV ejection fraction. Also, they had a mild elevation of sPAP with preserved RV systolic function on TDI (Table 2).

Table 1. Demographics and clinical / laboratory data

Character	
Age (years)	11.4±3.6
Sex (number):	
• Male	12
• Female	13
Etiology of renal failure (%):	
• Unknown etiology	24
• Focal segmental glomerulosclerosis	20
• Polycystic kidney	16
Duration of dialysis (months)	27.4±9.7
Urea (mg/dL)	143.57±64.5
Creatinine (mg/dL)	6.73±2.62
eGFR (mL/min/1.73 m ²)	9.57±2.57
Sodium (mEq/L)	140.26±3.76
Potassium (mEq/L)	5.07±1.11
eGFR: estimated glomerular filtration rate	

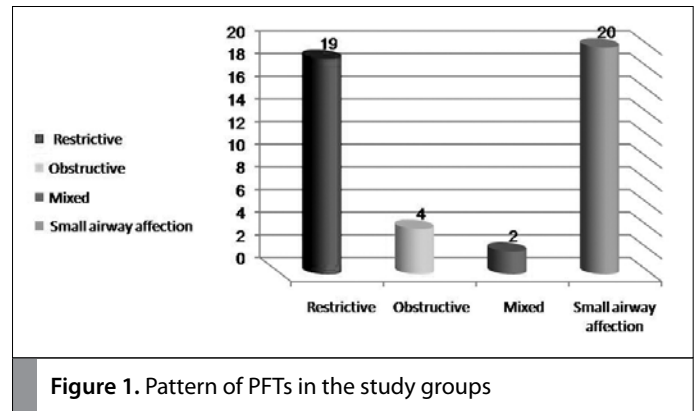
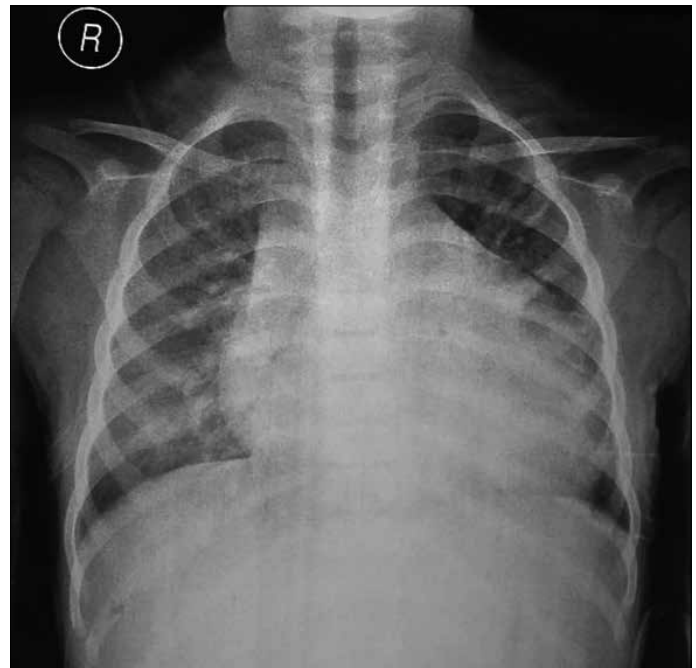
Table 2. Spirometric and echocardiographic parameters of the studied children

Character	
Spirometric indices:	
• FEV ₁ (L)	1.64±0.54
• FEV ₁ %	93.08±5.53
• FVC (L)	1.86±0.59
• FVC%	92.83±6.41
• FEV ₁ /FVC	88.33±4.4
• PEFR (L)	3.42±1.13
Echocardiographic data:	
• LVEDD (mm)	39.5±5.9
• LVESD (mm)	24.6±4.9
• EF (%)	58.2±5.7
• sPAP (mmHg)	40.9±8.8
• RV Sm (cm/seconds)	10.2±1.5
No. of patients with SPAP>35 mmHg (number)	19
EF: Ejection fraction; FEV ₁ : forced expiratory volume in 1 st second; FVC: forced vital capacity; LVEDD: left ventricular end diastolic dimension; LVESD: left ventricular end systolic dimension; PEFR: peak expiratory flow rate; RV Sm: right ventricular systolic myocardial velocity sPAP: systolic pulmonary artery pressure	

Figure 1 demonstrates the patterns of abnormal PFTs in the study group. Restrictive pattern was the most common spirometric abnormality detected (76%). In addition, 80% of cases had small airway affection.

Chest Radiography

Chest X-ray showed cardiomegaly in 2 patients (8%), as shown in Figure 2; besides this, no significant abnormality was detected.

**Figure 1.** Pattern of PFTs in the study groups**Figure 2.** Plain X-ray showing cardiomegaly

Chest and Cardiac Findings Based on HRCT of the Chest

Chest and cardiac findings evaluated by HRCT are presented in Table 3 and Figures 3–5. HRCT findings included air trapping (n=14, 56%), ground-glass opacity (n=2, 8%), bronchiectasis (n=5, 25%), cardiomegaly (n=3, 12%), pericardial effusion (n=1, 4%), and pulmonary artery diameter of >30 mm (n=5, 20%).

DISCUSSION

Respiratory problems are usually underestimated or overlooked in patients with CKD undergoing maintenance hemodialysis. Hemodialysis can severely affect the respiratory system; its effects may be acute or chronic. Acute effects include acute respiratory distress syndrome, recurrent infections, and pleural effusions, whereas chronic effects include respiratory impairment secondary to calcification of the lung parenchyma (29). Therefore, this study was conducted to investigate the negative effects of CKD and hemodialysis on the lung structure and functions in children based on the HRCT findings. This is one of the first studies demonstrating the HRCT findings in uremic children.

In this study, the group of children with CKD had abnormal spirometry with predominant restrictive pattern, and majority of them had

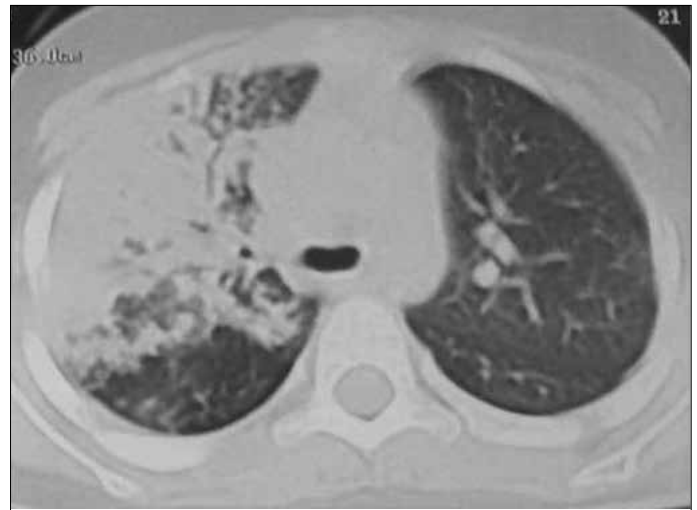
Table 3. High resolution computed tomography (HRCT) findings (chest and cardiac) in the studied group

	No. (%)
Air trapping	14 (56%)
Ground glass opacity	2 (8%)
Bronchiectatic changes	5 (20%)
Cardiomegaly	3 (12%)
Pericardial effusion	1 (4%)
Consolidation	3 (12%)
Pulmonary arterial enlargement (30 mm)	5 (20%)
Pulmonary artery to aortic ratio ≥ 1	5 (20%)

**Figure 3.** HRCT showed bilateral apical centrilobular emphysema

small airway disease. Cury et al. (30) reported impaired functional capacity and lung function in CKD patients undergoing dialysis. Plain X-ray was the first-line imaging tool. Plain chest radiograph revealed air trapping, reticular abnormalities, and hilar enlargement. However, the sensitivity of chest X-ray is known to be low (13). Therefore, CT of the chest was performed, and for this pediatric group, the use of HRCT using a low radiation dose protocol for optimal pediatric chest imaging was considered to accurately evaluate the central airway, cardiovascular and mediastinal abnormalities, and lung parenchyma (16, 17, 31-33).

The most interesting findings of CT chest in the current study are air trapping, bronchiectasis, and ground-glass opacity. Doğan et al. (26) reported similar findings, but their study included only adult patients. Ground-glass opacity can reflect minimal thickening of the alveolar walls or interstitial septa or the presence of cells or fluid filling the alveolar spaces. It can denote active process as pulmonary edema, pneumonia, or diffuse alveolar damage (34, 35). Only a small percentage of the studied group had ground-glass opacity; this may reflect proper fluid balance because we performed CT of the chest

**Figure 4.** Bilateral basal lower segments showing ground-glass opacity**Figure 5.** Right upper lobe consolidation

after hemodialysis to avoid the effect of volume overload and consequently bias in the results.

In the current study, more than half of the cases showed air trapping; we excluded lung regions of air trapping limited to a single secondary pulmonary lobule during analysis. It has been reported (36) that air trapping can be seen in isolated secondary pulmonary lobules in healthy persons (37). Trapped air is an important component of chronic airway diseases. It represents small airways involvement (38, 39). Although the precise cause of air trapping in this patients' group has not been established, it may be due to small airways disease as a result of recurrent infections and chronic inflammation in the small airways due to an impaired coughing mechanism and difficulty pertaining to clearing secretions in children (40). Also, small airway inflammation and airway hyper-reactivity have been reported in uremia (41, 42). The abnormal pattern detected in spirometry of our patients supports this assertion. Air trapping in CT may be a reflection of small airway inflammation (43). Airway mucosal edema can reduce effective airway diameter, predisposing to air trapping and endogenous positive end-expiratory pressure, which can reduce

venous return, further compromising cardiac function and increasing the risk of alveolar rupture (34, 35). Morikawa et al. (44) reported that decreased attenuation of the lung parenchyma on expiratory CT scans is the most important indicator of airflow obstruction. Expiratory HRCT is an established imaging tool for assessment of air trapping (38, 44-46). Although cardiomegaly and pericardial effusion are common in uremic patients (47), we detected cardiomegaly and pericardial effusion in only few patients in this study. The thoracic complications of uremia are mainly related to the poor management of the fluid balance (47).

End stage renal disease patients receiving chronic hemodialysis via an arteriovenous access often develop unexplained pulmonary hypertension (48, 49). In this study, we detected a large number of cases with mild increase in pulmonary artery pressure. Several mechanisms have been proposed for the development of pulmonary hypertension in patients with CKD on regular dialysis. These mechanisms include; increased stiffness of pulmonary vasculature due to vascular calcification or endothelial dysfunction. Also, the inability of the pulmonary circulation to accommodate increased cardiac output (resulting from increased volume, anemia, and arteriovenous shunt) may be another mechanism for the development of pulmonary hypertension in CKD patients (48-52).

In this study; air trapping found in 56% cases by CT imaging reflects small airway disease. These findings supported the involvement of small airways detected by spirometry. Various studies reported similar results (7, 52-54). Small airway disease may be attributed to the following conditions: chronic and often subclinical pulmonary edema, decreased serum albumin with consequent water and protein imbalance in microcirculation, recurrent infections, interstitial fibrosis, and alveolitis (7, 52-54).

Regarding the anthropometric characteristics of the study population, we observed a significant decrease in anthropometric measurements, including weight, height, and BMI, although this study did not include the aim of evaluating nutritional status, but it reflects the prognosis of chronic diseases.

In conclusion, different spirometric abnormalities were detected in children on hemodialysis. HRCT detected a lot of structural abnormalities within the lung and heart of children on regular hemodialysis, including air trapping, ground-glass opacity, bronchiectasis, and cardiomegaly. HRCT seems to be more precise a technique and should be used for this purpose. Spirometry should be included in the assessment and follow-up of children with CKD on hemodialysis. We hope that the ongoing progress in dialysis techniques and renal transplantation will decrease complications in these patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Faculty of Medicine for Girls, Al-Azhar University.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.S., R.M.H., M.A., F.M.E.; Design - E.S., R.M.H., M.A., F.M.E.; Supervision - E.S., R.M.H., M.A., F.M.E.; Resources - E.S., R.M.H., M.A.,

F.M.E.; Materials - E.S., R.M.H., M.A., F.M.E.; Data Collection and/or Processing - E.S., R.M.H., M.A., F.M.E.; Analysis and/or Interpretation – E.S., R.M.H.; Literature Search - E.S., R.M.H., M.A., F.M.E.; Writing Manuscript - E.S., R.M.H., M.A., F.M.E.; Critical Review - E.S., R.M.H., M.A., F.M.E.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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