ECRONICON OPEN ACCESS

EC PULMONOLOGY AND RESPIRATORY MEDICINE

Research Article

Polycystic Kidney Disease: Is Only the Kidney Impaired?

Ergün Parmaksiz[1]* and Elif Torun Parmaksiz[2]

[1]*Department of Nephrology, Kartal Dr Lutfi Kirdar Kartal Training Hospital, University of Health Sciences, Istanbul, Turkey*

[2]*Department of Chest Diseases, Kartal Dr Lutfi Kirdar Kartal Training Hospital, University of Health Sciences, Istanbul, Turkey*

***Corresponding Author:** Ergün Parmaksiz, Department of Nephrology, Kartal Dr Lutfi Kirdar Kartal Training Hospital, University of Health Sciences, Istanbul, Turkey.

Received: July 10, 2020; **Published:** August 05, 2020

Abstract

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disease presenting with multiple bilateral renal cysts and progressing to end stage renal disease. It has well-documented extra-renal manifestations, however pulmonary manifestations are scarcely documented. Most common pulmonary involvement is bronchiectasis. We aimed to evaluate pulmonary functions in ADPKD patients and their association to renal functions.

Twenty-nine adult ADPKD patients, with no previously diagnosed lung disease or no respiratory signs and symptoms were enrolled in this prospective study. All cases were evaluated with pulmonary function tests (PFT) and chest radiographs. Renal functions (urea, creatinine and glomerular filtration rate-GFR-) were recorded. PFT findings among different severity groups of ADPKB were compared.

PFT results were restrictive in two cases and obstructive in two cases. Correlation analysis revealed a significant relationship between FVC, FEV1 and GFR and. The correlation between GFR and FEV1/FVC ratio was not statistically significant. The mean values for FEV1 and FVC were found to be significantly lower in stage 2-3-4 cases.

The impairment of renal functions in ADPKD can be accompanied by impaired respiratory functions. In this regard, a multisystemic approach should be considered in follow-up.

Keywords: *Polycystic Kidney Disease; Pulmonary Function Test, Renal Function*

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disorder resulting in progressive renal insufficiency. It is associated with defective primary ciliary function in renal epithelial cells [1]. ADPKD is related to defects in genes expressed in the cilia [2]. Two genes, PKD1 and PKD2, which have been implicated in the pathogenesis of ADPKD encode polycystin-1 and polycystin-2, respectively [3]. Genetic defects in polycystin-1 and 2, two transmembrane regulatory proteins responsible for mechanoreception, cell polarization, and orientation lead to cyst formation by effecting the primary cilia [4,5].

The presence of at least three cysts in each kidney in a patient with a family history confirms the diagnosis of ADPKD [6]. In addition to the renal manifestations of the disease, there are several known extrarenal features. Non-cystic manifestations occurring frequently in ADPKD patients include cardiac valve abnormalities, intracranial vascular aneurysms, diverticulosis and abdominal wall hernias [7]. Extra-renal disease burden is often asymptomatic but may result in increased morbidity and mortality. If the disease burden is significant, screening may prove beneficial [8].

The genes implicated in ADPKD are expressed in the primary cilia of both the kidneys and the lungs. Therefore, we hypothesized that disturbed ciliary functions might cause decreased respiratory capacity. We aimed to evaluate pulmonary functions and the relationship between renal and pulmonary functions in ADPKD patients.

Materials and Methods

Twenty-nine consecutive adult ADPKD cases who applied to our outpatient clinic were enrolled in this prospective study. Written consent was taken from patients. Definition of ADPKD required all of the following criteria: Ultrasound findings: (1) the presence of three or more cysts in each kidney (2) cysts involving both the medullary and cortical regions of each kidney and (3) bilateral kidney enlargement [9].

None of the patients had a history of previously diagnosed or current lung disease. The cases with a history of tuberculosis, obstructive or restrictive lung pathology, and dialysis patients were excluded. The patients with symptoms and signs of active respiratory infection were not included. Detailed history was taken, including smoking habits and medications. Physical examinations were done. All cases were evaluated with pulmonary function tests (PFT) and chest radiographs. High resolution computed tomography (HRCT) was performed for those with suspicious findings on chest X-ray. Renal functions (urea, creatinine and glomerular filtration rate-GFR-) of all cases were recorded. The severity of chronic kidney disease was classified as follows: Stage 1 if GFR ≥ 90 ml/min; stage 2 if GFR 60 - 89 ml/min; stage 3 if GFR 30 - 59 ml/min; stage 4 if GFR 15 - 29 ml/min and stage 5 if GFR < 15 ml/min [10].

PFT results were compared between these groups. All cases had PFT performed by the same experienced technician. Each patient received exactly the same instructions. Spirometric tests were applied. The PFT were considered obstructive if forced expiratory volume in 1 second divided by forced vital capacity (FEV1/FVC) was under 70 and restrictive if FVC was under 80%.

Statistical analysis was performed using SPSS package programme. Mann Whitney U test was used for comparing mean spirometric values. Spearman correlation analysis was used to identify association between renal and respiratory functions. P value less than 0.05 was considered to be significant.

Results

The study included a total of 29 cases (19 females and 10 males). The mean age was 45.38 (20 - 76). Smoking history was present in 9 patients, of which 5 were active smokers. Chest radiographs were evaluated as normal in 22 cases. HRCT was performed in 7 cases and bronchiectasis was detected in three of them. Cylindrical bronchiectasis was observed in two cases and cystic bronchiectasis in one case. PFT results were restrictive in two cases and obstructive in two cases.

Correlation analysis revealed a significant relationship between FVC as well as GFR and FEV1 and GFR ($p = 0.009$ and $p = 0.044$, respectively). The correlation between GFR and FEV1/FVC ratio was not statistically significant ($p = 0.06$). Comparative data of PFT in stage 1 CKD cases and stage 2-3-4 cases are shown in table 1. The mean values for FEV1 and FVC were found to be significantly lower in stage 2-3-4 cases. The comparison of pulmonary function test results according to smoking status is demonstrated in table 2.

	Stage 1	Stage 2-3-4	p
FVC (litre)	4.44 ± 1.11	3.38 ± 1.23	0.012
FEV1 (litre)	3.51 ± 0.98	2.77 ± 0.91	0.031
FEV1/FVC	79 ± 5.4	83 ± 8.8	0.15

Table 1: *Comparison of pulmonary function test results according to chronic kidney disease stages.*

	Non-smokers	Smokers and ex-smokers	p
FVC (litre)	4.17 ± 0,96	3,60 ± 1,39	0,13
FVC (%)	109 ± 19	101 ± 11	0,16
FEV1 (litre)	2,88 ± 1,06	3,43 ± 0,74	0,03
FEV1 (%)	99,89 ± 7,32	105,00 ± 19,03	0,47
FEV1/FVC	81 ± 8	82 ± 6	0,94

Table 2: *Comparison of pulmonary function test results according to smoking status.*

Discussion

Our study demonstrated that ADPKD is associated with an decreased lung functions, in accordance with the renal functions. Although co-existence of radiological bronchiectasis in ADPKD has been clearly established, its functional significance is unknown. Predisposition to lung function impairment in ADPKD has not been elucidated. To our knowledge, this is the first study in the literature to demonstrate a correlation between lung and kidney functions in ADPKD.

Apart from renal involvement, ADPKD may effect liver, pancreas, cardiovascular system, central nervous system, gastrointestinal system or genitourinary system.

Pulmonary manifestations of ADPKD are rare [6]. There are few studies on synchronous lung comorbidities and the most common pulmonary manifestation is bronchiectasis. There are even fewer case reports describing associated pulmonary cysts [8,12].

The polycystin proteins are located both in the renal tubules and in epithelial and endothelial surfaces elsewhere in the body, as well. They are associated with both the renal and extra-renal manifestations of this disease [13]. Functional abnormalities in polycystins which are expressed in the cilia of both human airway epithelial and smooth muscle cells may lead to decreased mucociliary clearance and impaired airway injury repair [1]. The most frequently seen synchronous pulmonary pathologies are bronchiectasis and pulmonary cysts [1].

Polycystin-1 known to be expressed in renal primary cilia. Driscoll., *et al*. studied its expression in airway motile cilia. They examined autopsy samples and demonstrated changes consistent with bronchiectasis in one fifth of patients with ADPKD. In retrospective radiographic analysis using chest CT, they found that 37% of ADPKD cases demonstrated bronchiectasis, significantly higher than patients with non-ADPKD kidney disease (13%). Bronchiectasis tended to be mild in patients with a predominance of lower lobe involvement [1].

The prevalence of radiologic bronchiectasis is reported to be higher in ADPKD patients (19%) compared to other patients with chronic kidney disease. Bronchiectasis is generally cylindrical, shows lower lobe predominance and mild; only one third of them are symptomatic. In ADPKD, smoking was found to be associated with an increased risk of radiologic bronchiectasis [1,14].

The incidence of pulmonary cyst formation in ADPKD is much less frequent than bronchiectasis and has been reported in a few case reports [11,12].

There are currently no clear recommendations for routine screening of lung comorbidities for ADPKD patients. Keeping the possibility of coexistence of these lung pathologies may be helpful in systemic evaluation [8].

There are very few studies on lung functions in ADPKD. Teng Moua., *et al*. observed that PFT results (normal, obstructive, restrictive and other) were not statistically different between ADPKD and non-ADPKD patients, or among ADPKD patients with or without radio-

logic or clinical bronchiectasis [14]. FEV1, FVC, and diffusing capacity of the lung for carbon monoxide (DLCO) were statistically lower in patients without ADPKD compared to ADPKD despite comparable smoking status. Smoking status of ADPKD and control subjects were similar, however radiologic bronchiectasis was more frequent in ADPKD smokers than non-smokers [14]. In our study no respiratory functional difference could be observed based on smoking habits.

Our study is prospective and includes a well-selected population with no clinical findings of lung disorder. Still, there are several limitations. First of all, radiologic assessment was done by chest radiographs in majority of the cases. If computed tomography could be performed, more radiologic bronchiectasis could be detected. Even so, asymptomatic radiologic bronchiectasis would have insignificant contribution in clinical evaluation. Another confounder could be lack of data on DLCO. Last, but not the least, the study population includes a small number of cases. Studies on larger groups of ADPKB patients would be enlightening.

Conclusion

As a conclusion, impairment of kidney functions in ADPKD cases can be accompanied by impaired respiratory functions. In this regard, a multisystemic approach is required in follow-up. Claiming that impairment of lung functions as an extra-renal manifestation of ADPKD would be pretentious, however further studies are needed to explore this association.

Funding

No funding was involved in this work.

Bibliography

1. Driscoll JA., *et al.* "Autosomal Dominant Polycystic Kidney Disease Is Associated With an Increased Prevalence of Radiographic Bronchiectasis". *Chest* 133 (2008): 1181-1188.

2. Singla V and Reiter JF. "The primary cilium as the cell's antenna: signaling at a sensory organelle". *Science* 313 (2006): 629-633.

3. Torres VE., *et al.* "Autosomal dominant polycystic kidney disease". *Lancet* 369 (2007): 1287-1301.

4. Hopp K., *et al.* "Functional polycystin-1 dosage governs autosomal dominant polycystic kidney disease severity". *The Journal of Clinical Investigation* 122 (2012): 4257-4273.

5. Gallagher AR., *et al.* "Molecular advances in autosomal dominant polycystic kidney disease". *Advances in Chronic Kidney Disease* 17 (2010): 118-130.

6. Ibrahim WH and Rasoul FA. "Pulmonary Manifestations of Adult Polycystic Kidney Disease: Case Report and Literature Review Ibnosina". *Journal of Medicinal Chemistry* 7.5 (2015): 169-172.

7. Hossack KF., *et al.* "Echocardiographic findings in autosomal dominant polycystic kidney disease". *The New England Journal of Medicine* 319 (1988): 907-912.

8. Randy L Luciano and Neera K Dahl. "Extra-renal manifestations of autosomal dominant polycystic kidney disease (ADPKD): considerations for routine screening and management". *Nephrology Dialysis Transplantation* 29 (2014): 247-254.

9. Pei Y., *et al.* "Imaging-based diagnosis of autosomal dominant polycystic kidney disease". *Journal of the American Society of Nephrology* 26.3 (2015): 746-753.

10. Chapter 1 Definition and classification of CKD". *Kidney International* 3.1 (2013): 19-62.

11. Li HY., *et al.* "Dyspnea in a 43-year-old woman with polycystic kidney disease". *Chest* 135.1 (2009): 238-243.

12. Shanmuganathan A., *et al.* "Recurrent pneumothorax associated with polycystic kidney disease". *Indian Journal of Chest Diseases and Allied Sciences* 50 (2008): 233-235.

13. Torres VE., *et al.* "Autosomal dominant polycystic kidney disease". *Lancet* 369.9569 (2007): 1287-1301.

14. Moua T., *et al.* "Radiologic and clinical bronchiectasis associated with autosomal dominant polycystic kidney disease". *PLoS ONE* 9.4 (2014): e93674.

Volume 9 Issue 9 September 2020