Primary ciliary dyskinesia: Clinical and tomographic characterization using a combined diagnostic approach

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ABSTRACT

Introduction. Primary ciliary dyskinesia (PCD) is a clinically heterogeneous condition that is difficult to diagnose. This study aimed to describe the clinical and imaging characteristics and the results of diagnostic tests in patients with suspected PCD, by implementing an unvalidated diagnostic strategy that combines screening questionnaires, nasal nitric oxide (nNO), high-speed videomicroscopy (HSVM), and genetic analysis.

Population and methods. A cross-sectional observational study that included all patients referred for clinically suspected PCD between 2022 and 2025. Diagnostic tests: nNOn, HSVM, and genetic testing. Two clinical questionnaires were used to screen for PCD.

Results. A total of 110 patients referred for suspected PCD were evaluated and classified into three groups: highly likely PCD (52 cases), highly unlikely PCD (54 cases), and indeterminate (4 cases). The diagnosis of PCD was made at a median age of 8.8 years. Most patients showed pulmonary involvement on their CT scans. Using the proposed diagnostic algorithm, PCD was highly unlikely in 49% of the referred cases.

Conclusion. The age at diagnosis for patients with a high suspicion of PCD in our country was later than in other countries. At the time of diagnosis, the patients presented with lung damage confirmed by chest CT scans.

Diagnosing PCD is a challenge in resource-limited countries. The initial approach combines screening questionnaires, nNO, and HSVM, and avoids genetic testing when a diagnosis of PCD is highly unlikely.

Keywords: *ciliary motility disorders; Kartagener syndrome.*

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INTRODUCTION

Primary ciliary dyskinesia (PCD) is a clinically heterogeneous disorder with a predominantly autosomal recessive inheritance pattern.[1,2] Its estimated incidence ranges from 1 in 7500 to 1 in 20 000 live births.[3,4] It was initially described as Kartagener syndrome[5] due to its triad of sinusitis, bronchiectasis, and *situs inversus*. Subsequently, it was termed immotile cilia disease[6] and was finally precisely defined as PCD.[7]

It is characterized by an abnormal ciliary movement pattern, which may be immobile or dyskinetic. It affects organs containing cilia; the lungs are responsible for the highest rates of morbidity and mortality. Impaired mucociliary clearance leads to a buildup of secretions, which promotes infections and the development of atelectasis and bronchiectasis. If not treated appropriately, over the years, there is a progressive decline in spirometric values and irreversible lung damage. In turn, the presence of chronic sinusitis, recurrent otitis media, organ lateralization defects, and infertility are common extrapulmonary manifestations.[5]

Currently, the diagnosis of PCD is complex. Diagnostic guidelines[8-11] recommend the use of screening questionnaires and a combination of various tests: nitric oxide nasal (nNO), high-speed videomicroscopy (HSVM), immunofluorescence, electron microscopy (EM), and genetic testing. EM and genetic testing are considered the gold standard tests; however, they can confirm the diagnosis in only 60% to 70% of cases.[12] Approximately 700 proteins are involved in cilia biogenesis and ultrastructure, which are encoded by more than 50 genes.[13] This explains the clinical heterogeneity and the inherent difficulties in diagnosis.[14]

Early diagnosis is essential for delaying lung damage and reducing the risk of a poor quality of life.[15] There are very few centers in Argentina with the infrastructure to evaluate patients with suspected PCD, and access to diagnostic methods is limited. Unfortunately, there are no published data in our country regarding age at diagnosis or clinical characteristics at the time of diagnosis.

The objective of the study was to describe the clinical and imaging characteristics, as well as the results of diagnostic tests, in patients with suspected PCD who underwent an unvalidated diagnostic strategy combining screening questionnaires, nNOn, HSVM, and genetic tests.

POPULATION AND METHODS

Design

Cross-sectional observational study. The study included patients of any age who were referred for suspected PCD and seen between June 2022 and February 2025 at the Ciliary Motility Laboratory of the Hospital de Niños Ricardo Gutiérrez. Subjects with a respiratory infection within 14 days before evaluation were excluded, as this could alter the results of the tests (nNO and HSVM). The project was approved by the Research Ethics Committee at the Hospital de Niños Ricardo Gutiérrez. A structured form was designed on the REDCap platform for data collection. Demographic variables, clinical variables, results of complementary studies, and bacteriological variables were recorded (colonization was defined as the presence of at least two cultures positive for *Pseudomonas aeruginosa* [PAE]).[16] Two screening questionnaires were used: the ATS-CSQ (American Thoracic Society Clinical Screening Questionnaire)[17] and the PICADAR (Primary Ciliary Dyskinesia Rule questionnaire),[18] (*Supplementary Material 1*). The description of the CT findings was performed by the investigators, who were not blinded to the participants' medical history, and was standardized using a specifically designed form, adapted from the work of Dettmer *et al.*[19]

The determination of nNO was performed only in subjects aged over 5 years using an Eco Medics CLD 88 chemiluminescence analyzer in accordance with international standards.[20] An nNO flow rate of less than 77 nl/min was considered pathological.

Using HSVM, the ciliary beating pattern was evaluated in a sample of respiratory epithelial cells from the inferior turbinate region. The evaluation of the ciliary movement pattern was performed by two observers, one of whom was blinded to the questionnaire results and the patient's clinical and tomographic characteristics. Ciliary beating was considered pathological in the presence of a static, rigid, circular, or uncoordinated pattern.[21] Details of the method are provided in *Supplementary Material 1*.

For the sequencing study, DNA was isolated from index cases using 5 mL of peripheral blood anticoagulated with ethylenediaminetetraacetic acid (EDTA). The samples were sent to the University of Münster, Germany, for analysis of a panel of 40 PCD genes (*Supplementary Material 1)* or to the Genomics Laboratory of the Translational Medicine Department at

Hospital de Niños Ricardo Gutiérrez (Exome 2.0 Plus Comprehensive Exome Spike-in Twist, on a NextSeq 500 system, Illumina). Given the difficulties and limitations in accessing genetic testing, priority was given to performing it in undiagnosed cases and in all cases where access to such testing was possible. Confirmed PCD was defined as a genetic study showing two pathogenic variants (PV) or a combination of one PV and one probably pathogenic variant (PPV) or two PPVs in the same gene (in a homozygous or compound heterozygous state).[22]

Patients referred with suspected PCD were classified into 3 groups:

1. ***Highly likely PCD* (PCD+):**
   - Age ≥5 years: pathological nNO and HSVM (both studies confirmed by duplicate testing).
   - Age <5 years: pathological HSVM (confirmed by duplicate testing).
   - Patients with 2 variants of uncertain significance (VUS) or one pathogenic variant *(*PV) or one probably pathogenic variant (PPV) and one VUS, and pathological HSVM.

Since there were few patients with confirmed PCD, they were included in the analysis as part of the highly likely PCD group.

2. ***Highly unlikely PCD* (PCD-)**:
   - Normal nNO and HSVM or only normal HSVM in patients under 5 years of age.
3. ***Undefined PCD***:
   - Normal or decrease nNO, and HSVM with minimal abnormalities or normal findings, along with a clinical questionnaire indicating a high probability of PCD (ATS ≥2 or PICADAR ≥5) and pending genetic test results.

The age at diagnosis was defined as the age at the time of the second pathological test; in cases of uncertainty, it was defined as the age at the time the genetic test results were received.

Statistical analysis

Qualitative variables were reported as absolute numbers and percentages, and quantitative variables were reported as the mean and standard deviation or the median and 25th-75th percentile range (IQR), depending on the variable's distribution. A sample size of at least 50 clinically suspected cases was calculated for an expected confirmation rate of 50%, with a 95% confidence interval and a 10% semi-width of the confidence interval.

To compare categorical variables, the chi-square test or Fisher's exact test was used. To compare numerical variables between two groups, Student's t-test or the Mann-Whitney U test was used; to compare numerical variables between three groups, ANOVA or the Kruskal-Wallis test was used. *P*-values <0.05 were considered statistically significant.

STATA Version 16.1 (Stata Corp, USA*)* was used.

Ethical considerations

This study was approved by the Teaching and Research Committee and the Research Ethics Committee of the Hospital de Niños Ricardo Gutiérrez (registration code 6864). Written informed consent/assent was obtained.

RESULTS

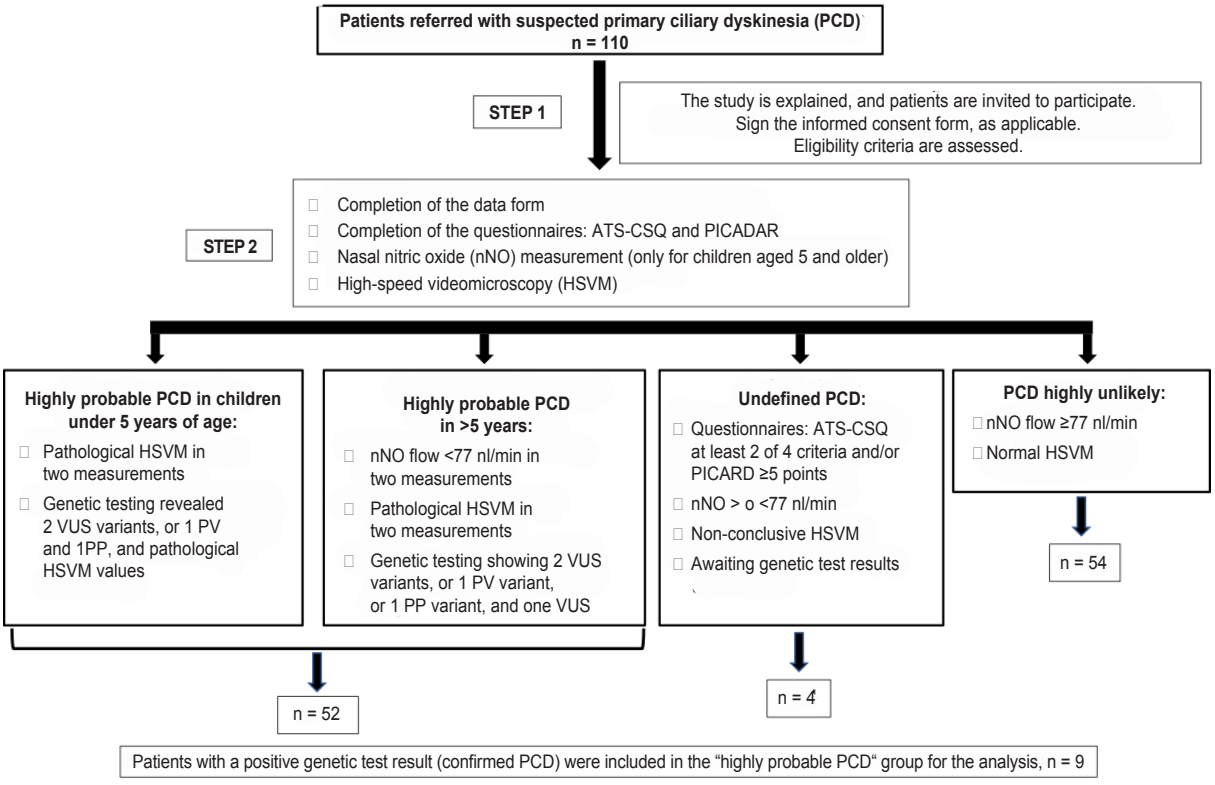
A total of 110 patients referred due to clinical suspicion of PCD were evaluated. Fifty-six percent were from the Buenos Aires Metropolitan Area (AMBA), and 43% were from the rest of the country. The median age at presentation was 9 years (IQR 4.6–14). Of the patients evaluated, 52 cases were highly likely PCD (47%); 54 cases were highly unlikely PCD (49%); and 4 cases (4%) remained undetermined (*Figure 1*). *Table 1* describes the demographic characteristics of the included patients.

The diagnosis of PCD was made at a median age of 8.8 years (IQR 2.8–11.9; range: 3 months to 39 years). When considering only patients with organ lateralization defects, the median age at diagnosis was 4.2 years (IQR 1–11), whereas in those without *situs inversus*, it was 10.5 years (IQR 7.8–16).

In the group over the age of 5, 92% of patients with a high suspicion of PCD had low nNO flow rates, while 9.5% of the PCD (-) group had persistently low flows (*Table 2)*. Regarding the ciliary beating pattern, cases with a high probability of PCD presented the following: 58% had an immotile pattern, 24% had a rigid pattern, 2% had an uncoordinated pattern, and 16% had normal movement. Genetic testing was performed on 23 of 52 patients with a high suspicion of PCD, and the diagnosis was confirmed in 9 cases (39%). The most frequently identified gene was *DNAH5*. *Table 3* details the findings of genetic, HSVM, nNO, and the presence of lateralization.

The clinical characteristics are compared in *Table 2*. Regarding the U.S. screening questionnaire, 94% of subjects with highly likely

Figure 1. Flowchart



PV: pathogenic variant, PP: probably pathogenic, VUS: variant of uncertain significance.

PCD and 22% of the PCD (-) group met two or more criteria. A score of ≥5 on the PICADAR questionnaire was obtained in 90% of PCD (+) cases and 28% of PCD (-) cases.

The most frequently isolated pathogen in sputum cultures from patients with high suspicion of PCD was *Haemophilus influenzae*. *Figure 2* shows the frequency of the isolated pathogens. Thirty-four percent of individuals with PCD (+) had PAE isolated at some point. The median age at the time of the first isolation was 11 years (IQR 3–15 years); six patients were colonized, all of whom were over 13 years of age.

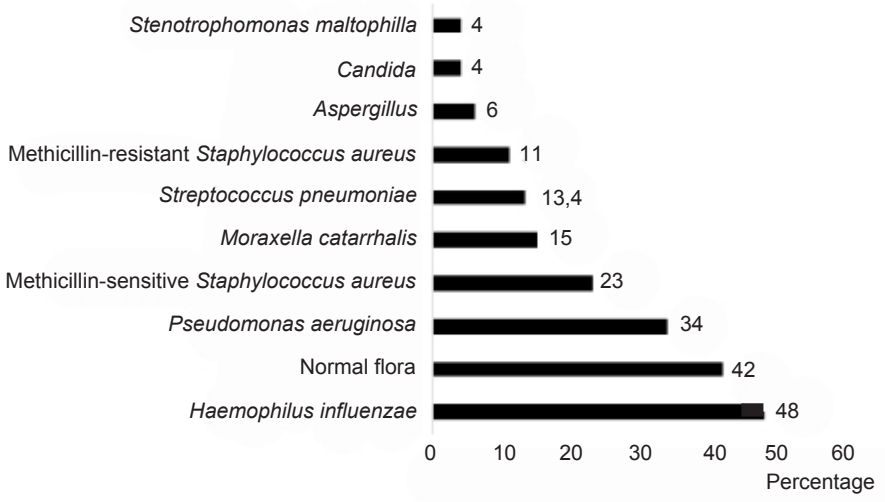
The most common findings on chest CT scans

Table 1. Demographic characteristics of patients

	PCD (+) n = 52	PCD (-) n = 54	Undefined n = 4
Age at presentation, years*	9 (4-17)	9.5 (6.5-12.5)	6.8 (5.5-8)
Female, n (%)	26 (50)	22 (41)	2 (50)
Gestational age, weeks*	39 (38-40)	38 (37-40)	38 (37-40)
Birth weight, grams**	3212 (469)	3200 (640)	3268 (450)
Admission to NICU, n (%)	36 (69)	13 (24)	1 (25)
Need for oxygen, n (%)	33 (63)	13 (24)	1 (25)
Need for MV or CPAP, n (%)	21 (40)	9 (17)	1 (25)
Consanguinity, n (%)	3 (6)	0 (0)	0 (0)
History of infertility, n (%)***	2 (4)	2 (4)	1 (25)

**Median and 25-75% CI.*
***Mean and standard deviation.*
****Personal or family history of infertility, ectopic pregnancies, or miscarriages.*
PCD (+): highly likely primary ciliary dyskinesia; PCD (-): highly unlikely primary ciliary dyskinesia; NICU: neonatal intensive care unit; MV: mechanical ventilation; CPAP: continuous positive airway pressure.

Figure 2. Microorganisms cultured from sputum samples of patients with highly likely primary ciliary dyskinesia



in subjects with a high probability of PCD were mucus plugs, bronchiectasis, and atelectasis, which most commonly affected the lower lobes, lingula, and middle lobes (*Table 4*).

DISCUSSION

This study reports the age at diagnosis and the clinical, imaging, bacteriological, and genetic characteristics of Argentine patients with a high index of suspicion for PCD. Pathogenic and likely pathogenic genetic variants in individuals with PCD were described for the first time in our setting.

In Europe, the average age at diagnosis is 5.3 years, and 5.8 years in individuals without lateralization defects.[15,23] In our study, the age at

Table 2. Clinical characteristics of patients with highly likely PCD (PCD+) and patients with highly unlikely PCD (PCD-)

	PCD (+) N = 52	PCD (-) N = 54	*p*-value
nNO flow, nl/min*	10.5 (4-22)	120 (85-156)	<0.0001
	n (%)	**n (%)**	**n (%)**
Nenonatal respiratory distress	38 (73)	7 (13)	<0.0001
Persistent rhinitis**	40 (81)	16 (30)	<0.0001
Persistent wet cough**	47 (90)	12 (23)	<0.0001
Lateralization defects	30 (57)	6 (11)	<0.0001
Hydrocephalus	1 (3)	0 (0)	NS
Recurrent otitis media	18 (35)	12 (22)	NS
Tympanic tubes	5 (9)	0 (0)	NS
History of recurrent pneumonia	24 (46)	26 (49)	NS
History of recurrent bronchitis	38 (73)	24 (45)	NS
Asthma unresponsive to treatment	27 (52)	8 (15)	<0.0001
Congenital heart disease	6 (11)	7 (13)	NS
ATS-CSQ questionnaire. ≥2 criteria	49 (94)	12 (22)	<0.0001
ATS-CSQ questionnaire. <2 criteria	3 (6)	44 (42)	<0.0001
PICADAR questionnaire ≥5 points	47 (90)	15 (28)	<0.0001
PICADAR questionnaire ≤4 points	5 (10)	39 (72)	<0.0001
ATS ≥2 and PICADAR ≥5 questionnaires	46 (88)	8 (15)	<0.0001

**Median and interquartile range 25–75.*
***Onset before 6 months of age.*
ATS-CSQ: American Thoracic Society Clinical Screening Questionnaire, PICADAR: Primary Ciliary Dyskinesia Rule Questionnaire, NS: not significant, nNO: nasal nitric oxide, PCD (+): highly likely primary ciliary dyskinesia, PCD (-): highly unlikely primary ciliary dyskinesia.

Table 3. Genetic findings, organ laterality defects, nasal nitric oxide levels, and ciliary beating patterns in patients with highly likely primary ciliary dyskinesia and confirmed primary ciliary dyskinesia (shaded in gray)

Subject	Genes	cDNA variant, protein variant	Genotype	ACMG classification	Type of mutation	*SIT*	*nNO* (nl/min)	Ciliary beating pattern
1	*DNAH5*	NM_001369.3:c.8011-2A>G, NP_001360.1:p.(?)	Homocygous	PP (PVS1, PM2_supp)	Splicing	No	<33	Immotile
2	*DNAH5*	NM_001369.3:c.2283_2284del, NP_001360.1:p.(Arg761Serfs*10)	Homocygous	PP (PVS1, PM3, PP2_supp)	Frameshift del.	No		Immotile
3	*DNAH5*	NM_001369.3:c.13060del, NP_001360.1:p.(Ala4354Argfs*23)	Heterocygous	PP (PVS1, PM2_supp)	Frameshift del.	Yes	<33	NA
		NM_001369.3:c.5367del, NP_001360.1:p.(Asn1790Ilefs*14)	Compound	PP (PVS1, PM2_supp)	Frameshift del.			
4	*DNAH5*	NM_001369.3:c.11653C>T, NP_001360.1:p.(Arg3885*)	Heterocygous	P (PVS1, PM3_strong, PM2_supp)	Nonsense	Yes	NA	Immotile
		NM_001369.3:c.8385del, NP_001360.1:p.(Asp2796Ilefs*10)	Heterocygous	PP (PVS1, PM2_supp)	Frameshift del.			
5	*DNAH5*	NM_001369.3:c.13338+5G>A, NP_001360.1:p.(?)	Heterocygous	PP (PM3, PP3_mod, PP4, PM2_supp)	Splicing	No	<33	Immotile
		NM_001369.3:c.8010+3A>G, NP_001360.1:p.(?)	Heterocygous	PP (PM3, PP3_mod, PP4, PM2_supp)	Splicing			
6	*DNAH5*	NM_001369.3:c.8311C>T, NP_001360.1:p.(Arg2771Cys)	Heterocygous	VUS (PM3, PM2_supp)	Missense	No	<77	Normal
		NM_001369.3:c.8497C>T, NP_001360.1:p.(Arg2833Cys)	Heterocygous	PP (PM5, PM3, PP3, PM2_supp)	Missense			
7	*DNAH5*	NM_001369.3:c.12379C>T, NP_001360.1:p.(Arg4127Cys)	Heterocygous	VUS (PM2_supp)	Missense	Yes	<77	Very subtle abnormality
		NM_001369.3:c.13601A>G, NP_001360.1:p.(Tyr4534Cys)	Heterocygous	VUS (PM2_supp)	Missense			
8	*CCDC39*	NM_181426.2:c.594dup, NP_852091.1:p.(Thr199Aspfs*1)	Homocygous	PP (PVS1, PM2_supp)	Framshift dup.	Yes	NA	Immotile
9	*CCDC39*	NM_181426.2:c.1636G>T, NP_852091.1:p.(Gly546*)	Homocygous	PP (PVS1, PM2_supp)	Nonsense	Yes	NA	Rigid
10	*CCDC39*	NM_181426.2:c.357+1G>C, NP_852091.1:p.(?)	Homocygous	P (PVS1_mod, PM3_VS, PM2_supp)	Splicing	Yes	<33	Rigid
11	*CCDC39*	Deleción del exón 9	Homocygous	PP (PVS1, PM2_supp)		No	<33	Rigid
12	*CCDC40*	NM_017950.4:c.2111_2112del, NP_060420.2:p.(Lys704Serfs*51)	Heterocygous compound	PP (PVS1, PM2_supp, PP4)	Frameshift del.	No	<33	Rigid
		NM_017950.4:c.3307C>T, NP_060420.2:p.(Arg1103*)		PP (PVS1_strong, PM3_supp, PM2_supp, PP4)	Nonsense			
13	*CCNO*	NM_021147.5:c.263_267dup, NP_066970.3:p.(Val90Serfs*6)	Homocygous	P (PVS1, PM2_supp, PS4_mod	Missense	Yes	<33	Immotile
14	*DNAAF4*	NM_130810.4:c.229A>G, NP_570722.2:p.(Lys77Glu)	Homocygous	VUS (PP3_mod, PM2_Supp, PP4, PM3, BP1)	Missense	Yes	<33	Immotile
15	*DNAAF4*	NM_130810.4:c.523dup, NP_570722.2:p.(Ile175Asnfs*15)	Heterocygous	PP (PVS1, PM2_supp)	Frameshift dup.	Yes	NA	NA
		NM_130810.4:c.229A>G, NP_570722.2:p.(Lys77Glu)	Heterocygous	VUS (PP3_mod, PM2_Supp, PP4, PM3, BP1)	Missense			
16	*DNAAF1*	NM_178452.6:c.715del, NP_848547.4:p.(Ser239Alafs*12)	Heterocygous	PP (PVS1,PM2_supp)	Frameshift del.	No	<33	Immotile
		NM_178452.6:c.811C>T, NP_848547.4:p.(Arg271*)	Heterocygous	P (PVS1, PM3, PM2_supp)	Nonsense			
17	*DNAH11*	NM_001277115.2:c.11929G>T, NP_001264044.1:p.(Glu3977*)	Heterocygous	P (PVS1, PM3, PM2_supp)	Nonsense	Yes	NA	Immotile
		NM_001277115.2:c.8698C>T, NP_001264044.1:p.(Arg2900*)	Heterocygous	P (PVS1, PM3, PM2_supp)	Nonsense			

18	*DNAH5*	NM_001369.3:c.8311C>T, NP_001360.1:p.(Arg2771Cys)	Homocygous	VUS (PM3_strong, PM2_supp)	Missense	No	ND	Very subtle abnormality
19	*DNAAF4*	NM_130810.4:c.56T>A, NP_570722.2:p.(Leu19Gln)	Heterocygous compound	VUS (PM2_supp, PP4, BP1)	Missense	Yes	< 33	Very subtle abnormality
		NM_130810.4:c.229A>G, NP_570722.2:p.(Lys77Glu)		VUS (PP3_mod, PM2_Supp, PP4, PM3, BP1)	Missense			
20	*HYDYN*	NM_001270974.2:c.10368-2A>G, NP_001257903.1:p.(?)	Heterocygous	PP (PVS1_mod, PM3, PM2_supp, PP4)	Splicing	No	< 33	Normal
		Posible deleción del exón 73 predicha a traves del análisis de los datos de NGS con el algoritmo DECON.	Heterocygous	PP (PVS1, PM2_supp)	CNV?			
21	*DNAH1*	NM_015512.5:c.4739C>G, NP_056327.4:p.(Ala1580Gly)	Heterocygous	VUS (PM2_supp, BP1)	Missense	No	< 77	Rigid
	DNAH9	NM_001372.4:c.7151G>A, NP_001363.2:p.(Gly2384Glu)	Heterocygous	VUS (PM2_supp)	Missense			
22	*DNAAF4*	NM_130810.4:c.229A>G, NP_570722.2:p.(Lys77Glu)	Heterocygous	VUS (PP3_mod, PM2_Supp, PP4, PM3, BP1)	Missense	No	< 33	Immotile
23	*RSPH4A*	NM_001010892.3:c.811C>T, NP_001010892.1:p.(Leu271=)	Heterocygous	VUS(PM2_supp, BP7)	Synonymous splicing?	No	Normal	Very subtle abnormality

The genetic test was considered confirmatory in cases where two PV variants were present, or where there was a combination of one PV and one PPV, or two PPV within the same gene (in a homozygous or compound heterozygous state).
ACMG: American College of Medical Genetics and Genomics; P: pathogenic; PP: probably pathogenic;
VUS: variant of uncertain significance; CNV: copy number variation; NA: not available; NR: not reported in the literature;
SIT: situs inversus totalis; nNO: nasal nitric oxide (normal flow: >77 nl/min; low <77 nl/min; extremely low <33 nl/min);
del.: deletion; dup.: duplication.

diagnosis was later, particularly in patients without *situs inversus,* at 10.5 years.

A later diagnosis has been reported in countries with limited healthcare resources and in individuals without lateralization disorders.[24,25]

Most patients with a high index of suspicion of PCD met two or more criteria on the U.S. questionnaire and scored 5 or more points on the PICADAR questionnaire. The combination of both is extremely useful for clinically identifying individuals suspected of having PCD so that they can be referred early to a referral center for evaluation.

Chest CT scans revealed pulmonary involvement in most patients with a high index of suspicion of PCD. These findings reflect impaired mucociliary clearance. The most affected areas of the lung were the lower and middle lobes

Table 4. Imaging findings in patients with highly likely PCD (PCD+) and highly unlikely PCD (PCD-)

CT findings	**PCD (+) n = 49 Percentage (n)**	**PCD (-) n = 40 Percentage (n)**
Mucous plugs, “tree in bud” pattern	55 (27)	12 (5)
Bronchiectasis	49 (24)	52 (21)
Atelectasis	37 (18)	17 (7)
Ground-glass opacities	12 (6)	7 (3)
Normal	4 (2)	22 (9)
Location of bronchiectasis	**Percentage (n)**	**Percentage (n)**
Right upper lobe	4 (2)	15 (6)
Left upper lobe	2 (1)	12 (5)
Middle lobe	35 (17)	32 (13)
Lingula	20 (10)	25 (10)
Right lower lobe	26 (13)	32 (13)
Left lower lobe	26 (13)	45 (18)

CD: computed tomography.

and the lingula, while the upper lobes remained unaffected. This distribution is characteristic of PCD,[19] with greater accumulation of secretions in the lower areas due to inefficient ciliary beating combined with gravity. Another way to quantify lung involvement is through pulmonary function tests. It was a limitation that we were unable to evaluate this aspect. Furthermore, the study's cross-sectional design did not allow assessment of disease progression or establishment of associations between diagnostic delay and lung damage.

The most frequently isolated pathogens in respiratory secretion cultures from individuals with PCD were *Haemophilus influenzae*, *Streptococcus pneumoniae,* and *Moraxella catarrhalis.* Our findings were similar to those of other cohorts.[26] However, the design of our study may underestimate the actual number of patients colonized with PAE. Chronic PAE infection typically occurs in older patients, and its association with a poorer clinical prognosis and greater decline in lung function is not as evident as in cystic fibrosis.[16,27]

In the complex diagnosis of PCD, there are differences between the U.S. and European algorithms;[11] the main difference is that the former does not use HSVM. The determination of nNO is universally recommended for children aged 5 years and older. Most of our patients with a high index of suspicion of PCD had extremely low values of nNO, which is consistent with other studies.[28] In our study, we implemented an unvalidated diagnostic strategy, adapted to our specific context, based on a combination of both questionnaires search + nNO + HSVM by duplicate. Given the limited resources available, genetic testing was requested when the diagnosis was unclear or when access to such testing was feasible. Using this approach, PCD was deemed highly unlikely in 49% of cases, thereby avoiding the use of a more costly resource that is currently difficult to access in our setting.

Another limitation of the study was the inability to conduct genetic testing systematically. It was performed on only 23 of the 110 patients referred due to suspected PCD. This could result in missed diagnoses in some cases or in the misinterpretation of patients with a high suspicion of PCD due to the strategy used. Patients with cystic fibrosis and immunodeficiencies may also present with low levels of nNO and abnormalities in the ciliary beating. It is therefore essential to rule out these diagnoses. We believe it is important to emphasize that, in cases of high suspicion of PCD, priority should be given to genetic testing to confirm the diagnosis.[10]

The frequencies of the genes identified in our population were similar to those reported in other countries.[29] Currently, according to centers specializing in PCD, genetic testing can confirm the diagnosis in 60% to 70% of cases.[10,30] In our study, the yield of genetic testing was 39%. This may be due to the inability to test parents of cases with two heterozygous variants or patients with variants still classified as of uncertain significance. Another limitation was the inability to evaluate ciliary ultrastructure to complement the diagnosis. EM requires a complex infrastructure and expertise in sample preparation and interpretation; 30% of patients with PCD have a normal ultrastructure.[31] Finally, the use of immunofluorescence in conjunction with other diagnostic tests is recommended.[10] Although this is not a complex study, the cost of the antibodies and the need for trained personnel limited its implementation.

Diagnosing PCD is a challenge in countries with limited resources allocated to rare diseases. The initial approach combines clinical screening questionnaires, nasal nitric oxide measurement, and high-speed videomicroscopy and avoids genetic testing when a diagnosis of PCD is highly unlikely. It is necessary to establish collaborative networks among centers to facilitate access to genetic testing, EM, and immunofluorescence, thereby enabling a more accurate diagnosis.

CONCLUSION

The age at diagnosis for patients with a high index of suspicion of PCD in our country was later compared to that in other countries. At the time of diagnosis, most individuals showed lung damage confirmed by chest CT scans. ■

The supplementary material provided with this article is presented as submitted by the authors. It is available at: https://www.sap.org.ar/docs/publicaciones/archivosarg/2026/10814_AO_Balinotti_Anexo.pdf

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