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parameters. The mean FEV1 was marginally lower in NCFB (69.18 vs. 70.76), the mean FVC was lower (66.03 vs. 78.96 in CF), and the mean FEF25- 75 was lower (51.50 in CF group vs. 64.22 in NCFB).

Our study showed strong positive correlation between exhaled breath condensate pH and FEV1 among non- cystic fibrosis group where EBC pH decreases indicating more acidity of the airways and ongoing inflammation, FEV1 decreases indicating more worsening of pulmonary functions and deterioration of the disease. In contrast to our study, there was no correlation between EBC pH and the severity of the disease on lung function, indicating that EBC is not a sensitive indicator of the severity of the disease in bronchiectasis. (Shoemark and Wilson, 2011)

The best cutoff value of EBC pH selected with best sensitivity, specificity and positive predictivity was 7.3, above which the cases were considered healthy and below which the decrease in pH reflected the ongoing airway inflammation in NCFB group. Statistical comparison between the studied groups around cut off value showed a significant decrease in the mean value of EBC pH with the cystic and non- cystic fibrosis bronchiectasis groups when compared to control group. This confirmed the hypothesis that EBC pH is a marker of severity reflecting intensity of airway inflammation. In concordance to our study, (Shoemark and Wilson 2011), revealed that as compared to healthy controls, bronchiectasis patients' EBC pH is more acidic.

The optimal cutoff point was< 6.8 (88.89 sensitivity and 90% specificity). The EBC pH cut off point was selected according to best sensitivity, specificity and positive predictive value cutoff point selected was 6.8. According to (Shoemark and Wilson 2011), compared to healthy controls, the EBC pH in bronchiectasis patients is more acidic. In patients with cystic fibrosis bronchiectasis, EBC pH reflected continuing airway inflammation and inflammatory cell infiltration. In contrast to our study (Antus et.al. 2012), suggested that EBC pH does not distinguish between individuals with CF disease and healthy controls, indicating that the clinical utility of EBC pH measures for measuring airway inflammation in CF is restricted as Mean EBC pH in CF patients and in healthy controls were similar.

Finally, the present study showed significant positive correlation between Exhaled breath condensate pH and FEV1; also it revealed that EBC pH was more acidic among cystic fibrosis and non- cystic fibrosis patients when compared to healthy controls, so EBC pH can be used as a marker of inflammation in patients with bronchiectasis.

Conclusion:

Mean values of FEV1, FEF25- 75%, were significantly lower in the bronchiectasis group when compared to controls, while mean value of FVC was significantly lower in NCFB group, The mean values of EBC pH were significantly lower in bronchiectasis groups when compared to control being lower group (Mean value 6.63) with cut off value= 7.3 in NCFB and 6.8 in CF patients.

Recommendations:

From our study we recommend that:

1. For a better assessment of the EBC pH's usefulness as a non- invasive measure of inflammation in children with bronchiectasis, we recommend that the study to be conducted on a bigger scale.
2. Early diagnosis and course of effective therapy are necessary to improve the prognosis of bronchiectasis.
3. Newborn screening (NBS) for cystic fibrosis (CF) is required and must be included in neonatal screening programs as it aids in early diagnosis, allowing for the setting of dietary and pulmonary interventions aiming at proper management and better outcomes.
4. Proper pulmonary infection management, adherence to the advised immunization schedule, and treatment of acute exacerbations.
5. Raising awareness of clinical history and computed tomography scans characteristics that may suggest bronchiectasis and result in better care.

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		Control Group	NonCystic Fibrosis Bronchiectasis	Cystic Fibrosis Bronchiectasis	Test Value•	P- Value	P1	P2
		No.= 10	No.= 12	No.= 18				
Fev1/Fvc	Mean±SD	92.30±2.75	86.57±20.06	84.46±21.17	0.610	0.549	0.383	0.258
	Range	86- 95	48.8- 102.3	23- 104				
Fef25- 75	Mean±SD	111.50±3.60	64.22±7.81	51.50±24.65	39.581	0.000	0.000	0.000
	Range	105- 115	47- 71.9	11- 86				

P1: Control Vs Non- cystic fibrosis bronchiectasis, P2: Control Vs cystic fibrosis bronchiectasis.

FEV_1: Forced expiratory volume in 1 second; FVC; Forced vital capacity; $FEF_{25-75\%}$: mean expiratory flow between 25% and 75% of FVC.

Our study showed that, There was highly significant decrease in FEV1 Forced Expiratory volume in 1 second and FEF25-& 75 (mean expiratory flow) in both CF and NCFB groups when compared to the control group (p- value=0.000), however there was no significant difference in the mean values of FEV1, FVC, and FEF25- 75% between both CF group and NCFB group. Table (3) shows mean values of different pulmonary function parameters and their statistical value.

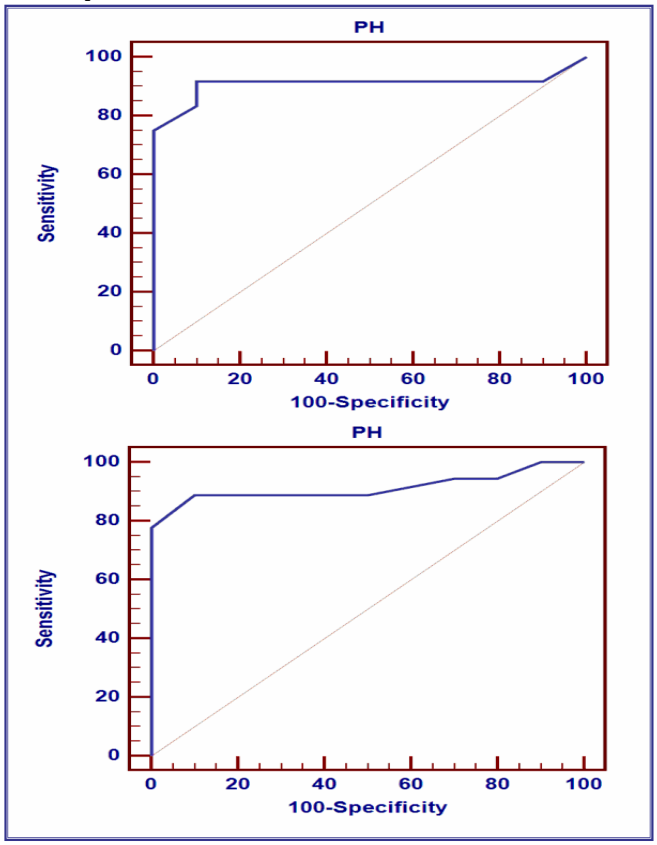

Table (4) ROC curve of EBC (PH) as a predictor of non- cystic fibrosis

Parameter	AUC	Cut Of Point	Sensitivity	Specificity	PPV	NPV
Ph (NCFB)	0.908	≤7.3	91.67	90.0	91.7	90.0
Ph (CF)	0.914	≤6.8	88.89	90.0	94.1	81.8

Table (4) Receiver operating characteristics curve of pH in exhaled breath condensate (EBC) for the diagnostic discrimination of Non cystic fibrosis bronchiectasis and CF bronchiectasis. Area under the curve of the ROC curve of EBC pH in NCFB was 0.908 and 0.914 in CF patients. The optimal cutoff point in NCFB was< 7.3 (91.67% sensitivity and 90% specificity) and was< 6.8 (88.89 sensitivity and 90% specificity). The EBC pH cut off point was selected according to best sensitivity, specificity and positive predictive value, Cutoff point selected was< 7.3 in NCFB< 6.8 in CF and above which the cases were considered healthy and below which the decrease in EBC pH reflected ongoing airway inflammation and inflammatory cell infiltration in non- cystic fibrosis bronchiectasis patients.

Table (5) Correlation between exhaled breath condensate pH and pulmonary function

Variable	Exhaled Breath Condensate pH			
	NCFB		CF	
	R	P- Value	r	P- Value
FEV1	0.679*	0.015	0.356	0.147
FVC	0.394	0.205	0.224	0.372
Fev1/Fvc	0.004	0.991	0.016	0.949
Fef25- 75	-0.300	0.344	-0.067	0.792

Table (5) showed correlation between exhaled breath condensate PH and Forced expiratory volume in first second in NCFB and CF patients, in our study FEV1 was strongly positively correlated with exhaled breath condensate where FEV1 decreases indicating worsening of lung functions and more deterioration, EBC pH decreases indicating more acidity of the airways.

Discussion:

This current case control study aimed to study the value of EBC pH in patients with bronchiectasis and whether it can be used as a noninvasive inflammatory marker to detect inflammation. Our results revealed that the mean values of EBC pH were significantly lower in cystic and non- cystic fibrosis bronchiectasis groups when compared to the control group (p= 0.000), Similar to our study, Exhaled breath condensate pH (EBC) was substantially lower in bronchiectasis patients than in controls, (Liu et.al, 2022). According to (Al- Sadeq., 2019), EBC pH was lower in CF children than in healthy controls suggesting that EBC pH reflects the pH of the fluid lining the airways, and that EBC pH is influenced by the degree of endogenous airway inflammation. In contrast to our study (Antus et.al, 2012), suggested that EBC pH does not distinguish between healthy controls and those with CF, indicating that the clinical utility of EBC pH for measuring airway inflammation in CF is restricted as mean EBC pH in CF patients and healthy controls were comparable.

Spirometry was used to monitor the course of the disease with acute drop in function and worsening of obstructive pattern associated with disease progression, in our study: FEV1, FVC, FEV1 and FEF25- 75 percentage of predicted for age and sex were recorded. FEV1 was highly significantly impaired in NCFB p- value< 0.01 while FEF 25- 75 showed significant affection in CF patients compared to the control group. On the contrary, in a study by (El Basha, 2018), demonstrated a considerable FEV1 impairment in the NCFB group, whereas only extremely severe FEV1 impairment was seen in the CF bronchiectasis group. However, there was no discernible difference between the NCFB and CF bronchiectasis groups in terms of the various pulmonary function testing

Way ANOVA test. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. Receiver operating characteristic curve (ROC) was used in the quantitative form to determine sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and Area under curve (AUC) of EBC (PH) to predict cystic fibrosis and non- cystic fibrosis.

Results:

Our study group comprised 40 children, assigned into 3 groups: First group included 18 patient diagnosed with CF according to CF Foundation guidelines. Their ages ranged from 7 to 15 years old, Second group included 12 patients diagnosed with NCFB according to clinical presentation together with HRCT findings their ages ranged from 7 to15 years old. And the third group included 10 healthy children with matched age and sex, their ages ranged from 5 to 16 years old. The mean age of studied subjects was 10.50± 2.92 in control group, 11.33± 2.64 in NCFB group and 10.89± 2.17 in CF group. 60% the control group were females and 40% were males, In the NCFB group 41.7% were females and 58.3% were males and in the CF group 44.4% were females while males were 55.6%. The Control group, non- cystic fibrosis bronchiectasis and Cystic fibrosis bronchiectasis sociodemographic characteristics are shown in table (1).

Table (1) Showing demographic data of the studied group

		Control Group	Non- Cystic Fibrosis Bronchiectasis	Cystic Fibrosis Bronchiectasis	Test Value	P- Value	P1	P2
		No.= 10	No.= 12	No.= 18				
Sex	Female	6 (60.0%)	5 (41.7%)	8 (44.4%)	0.858*	0.651	0.392	0.430
	Male	4 (40.0%)	7 (58.3%)	10 (55.6%)				
Age (Years)	Mean±SD	10.50±2.92	11.33±2.64	10.89±2.17	0.304•	0.740	0.490	0.691
	Range	7- 15	7- 15	7- 15				
Zscore: Weight In Kg	Median (IQR)	0.63 (-0.02- 2.1)	0.37 (-0.19- 0.82)	-0.8 (-0.91- 0.69)	29.265‡	0.000	0.391	0.000
	Range	-0.37- 3.32	-0.47- 1.09	-0.91- 0.47				
Zscore: Height In Cm	Median (IQR)	0.36 (-0.4- 2.18)	0.08 (-0.16- 0.84)	-0.45 (-0.98- 0.21)	9.556‡	0.008	0.895	0.064
	Range	-1.17- 2.85	-0.98- 1.32	-1.26- 0.08				
Zscore (BMI)	Median (IQR)	0.89 (0.47- 1.49)	0.55 (-0.03- 0.67)	-1.01 (- 1.09- 0.79)	24.778‡	0.000	0.080	0.000
	Range	0.32- 2.69	-0.2- 1.13	-1.38- 1.17				

P1: Control Vs Non- cystic fibrosis bronchiectasis, P2: Control Vs cystic fibrosis bronchiectasis.

Regarding NCFB patients 91.7% showed history of exposure to tobacco smoke, and almost all patients had previous pulmonary infections, while in CF group 61.1% of patients showed positive consanguinity, 50% with history of prematurity and history of sibling death and 66.7% with previous history of NICU admission. Table (2) shows baseline clinical characteristics of the studied group.

Table (2) Baseline clinical charactestrics of the studied group

Variable		NCFB		CF		Test Value	P Value	sig
		N	%	N	%			
Consanguinity	Negative	5	41.7%	7	38.9%	0.023	0.879	NS
	Positive	7	58.3%	11	61.1%			
Tobacco Smoke Exposure	Negative	1	8.3%	10	55.6%	6.914	0.009	HS
	Positive	11	91.7%	8	44.4%			
History Of Pulmonary Infections	Negative	0	0.0%	7	38.9%	6.087	0.014	S
	Positive	12	100.0%	11	61.1%			
History Of Prematurity	Negative	8	66.7%	9	50.0%	0.814	0.367	NS
	Positive	4	33.3%	9	50.0%			
History Of Nicu Admission	Negative	7	58.3%	6	33.3%	11.697	0.003	HS
	Positive	5	41.7%	9	66.7%			
History Of Sibling Death	Negative			9	50.0%			
	Positive			9	50.0%			

Our study showed that, There was highly significant decrease in FEV1 Forced Expiratory volume in 1 second) and FEF25-& 75 (mean expiratory flow) in both CF and NCFB groups when compared to the control group (p- value=0.000), however there was no significant difference in the mean values of FEV1, FVC, and FEF25- 75% between both CF group and NCFB group. Table (3) shows mean values of different pulmonary function parameters and their statistical value.

Table (3) Comparison between studied groups regarding pulmonary function tests.

		Control Group	NonCystic Fibrosis Bronchiectasis	Cystic Fibrosis Bronchiectasis	Test Value•	P- Value	P1	P2
		No.= 10	No.= 12	No.= 18				
FEV1	Mean±SD	105.90±3.11	69.18±7.79	70.76±18.13	28.043	0.000	0.000	0.000
	Range	100- 109	51.6- 74.9	28- 105				
FVC	Mean±SD	89.70±2.91	66.03±12.41	78.96±20.10	6.642	0.003	0.000	0.107
	Range	85- 93	41.2- 78.9	44- 124				

Introduction:

Bronchiectasis in children is defined by the presence of abnormal bronchial dilatation documented by high resolution computed tomography (HRCT) scans which is the gold standard in diagnosis, in addition to airway infection, and/or inflammation together with recurrent or persistent productive cough, (Goyal et.al, 2022). Bronchiectasis results from a number of pathophysiologic processes, including airway obstruction, recurrent or persistent infections, and decreased mucociliary clearance, leading to cumulative, permanent damage to the bronchial walls. (Chang and Redding, 2019), Bronchiectasis can be divided into 2 types according to etiology: noncystic fibrosis bronchiectasis (NCFB) and cystic fibrosis bronchiectasis (CFB), (Goyal et.al, 2020). Although infections, primary ciliary dyskinesia (PCD), immunological deficiencies, and aspirations are potential etiologies for NCFB, the most common cause of bronchiectasis is cystic fibrosis in many patients. (Brower et.al, 2014)

Cystic fibrosis (CF), an autosomal recessive condition characterized by a wide range of clinical symptoms, is brought on by mutations in the CFTR gene on chromosome 7. The male genital system, colon, liver, bone, and kidney are among the affected organs. (Castellani and Assael, 2017)

Children with daily productive or wet cough or occasionally for more than four weeks should be evaluated for bronchiectasis. Hemoptysis, recurrent pneumonia, or recurrent cough with fetid sputum is all crucial indicators of bronchiectasis. (Miller et.al, 2022)

In addition to low and middle income countries and indigenous populations, bronchiectasis is now being recognized as a source of chronic respiratory illness in non- indigenous adult and pediatric populations in affluent countries, (Goyal et.al, 2022). Children's bronchiectasis incidence varies greatly, from 0.2 to 735 per 100000 kids annually. Bronchiectasis has been dubbed the "new global epidemic" because of the rising awareness and diagnosis rates in both children and adults around the world. Pediatric bronchiectasis continues to be disregarded, undertreated, and underserved while being more common than cystic fibrosis. (Goyal et.al, 2022)

Children and their parents experience tremendous anxiety and stress due to bronchiectasis, especially during exacerbations, some of which necessitate hospitalisation and increasing financial burden, (Goyal et.al, 2022). Bronchiectasis related mortality has altered throughout time and depends on the environment; people who receive suboptimal care die earlier. The ideal place for treatment of bronchiectasis is a multidisciplinary clinic. Long- term management focuses on stopping the cycle of infection and inflammation and decreasing exacerbations. (Chalmers et.al, 2022)

Exhaled breath condensate (EBC), a new non- invasive diagnostic method for numerous respiratory disorders, was first introduced more than 20 years ago, (Bannier et.al, 2019). Acidity (pH), hydrogen peroxide (H_2O_2), nitrogen oxides (NO_x), eicosanoids, and cytokines are among the several indicators of airway inflammation included in EBC. In several studies, acidification of EBC has been linked to asthma and chronic obstructive lung disease (COPD). (Lee et.al, 2022)

Our present study aim is to evaluate the pH of exhaled breath condensate (EBC) in children with bronchiectasis either cystic fibrosis or non cystic fibrosis bronchiectasis and determine if it may be utilized as a non- invasive marker of inflammation compared to the pulmonary function tests in these patients.

Materials and Methods:

This cross sectional, case control, 40 children were selected for participation in this study. 18 patients with CF, 12 patients with NCFB and 10 healthy controls participated in the study. Patients who have been clinically and radiologically diagnosed with bronchiectasis. According to CF Foundation recommendations, patients with positive sweat chloride tests (60 mmol/L) are diagnosed with CF in addition to the existence of a homozygous or heterozygous mutation on the gene that codes for the CFTR protein. It was conducted in the pediatric pulmonology unit, Ain Shams University hospitals through the period from 2021 to 2023. A parental signed informed consent was obtained from each participant after each parent or other responsible adult was told of the interventions, goals, advantages, discomforts, and potential hazards of our study.

The Inclusion Criteria were as follows: Children aged from 5 to 18 years old, Patients diagnosed with bronchiectasis clinically and with HRCT chest, Patients diagnosed with CF and Haemodynamically stable children. While critically ill children not suitable for diagnostic modalities, Children with other co- morbid chronic diseases and mentally retarded children who cannot be cooperative like Down syndrome were excluded from our study.

All subjects included in this study were subjected to: Full detailed history, full thorough Examination including general, chest, cardiac and abdominal examinations, Pulmonary function tests to detect the forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), mean expiratory flow between 25% and 75% of FVC (FEF25- 75%), and FVC/ FEV1 ratio using Spirolab III diagnostic colour spirometer. EBC pH (exhaled breath condensate pH): was assessed.

The Collection of EBC was done, using EcoScreen 2 device for exhaled breath condensate (EBC) collection at Pulmonary Adult Unit internal medicine Ain Shams hospitals. EBC pH assessment: was done using the five easy F20 pH meter manufactured by Mettler- Toledo GmbH device at WAKI pharma laboratories.

Statistical Analysis:

The data was collected, revised, coded, and entered into IBM SPSS version 23. Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges. The comparison between groups with qualitative data were done by using Chi- square test. The comparison between more than two groups with quantitative data and parametric distribution were done by using One

Exhaled Breath Condensate PH as a Non- invasive Measure of Inflammation in a sample of Egyptian children with Bronchiectasis

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Summary

Background: Childhood bronchiectasis is defined by the presence of recurrent or persistent episodes of productive cough, together with airway infection, and/or inflammation in addition to abnormal bronchial dilatation on high resolution computed tomography (HRCT) scans.

Aim: To evaluate the pH of exhaled breath condensate (EBC pH) in children with bronchiectasis and determine if it can be utilized as a non-invasive marker of inflammation in Comparison to pulmonary function tests.

Methods: In this cross sectional study EBC was collected using (EcoScreen 2) in 30 stable bronchiectasis patients ,18 patients with Cystic Fibrosis (CF) and 12 with Non cystic fibrosis bronchiectasis (NCFB), during routine clinical visits and in 10 healthy controls with matching sex and pH was measured using five easy F20 pH meter and pulmonary function tests were measured using Spirolab III device.

Results: Mean EBC pH in CF patients vs. controls was 6.63±0.54: 7.76±0.41, p= 0.000 while NON CF patients: 6.68±0.60 versus controls: 7.76±0.41, p= 0.000. EBC pH was more acidic among CF patients than in both Non CF and control groups. (p= 0.000) FEV1 was positively correlated with EBC pH in NCFB, also patients with NCFB showed significantly higher rates of exposure to tobacco smoke P- value< 0.01 and previous history of pulmonary infections P- value< 0.05 while rates of NICU admission were more significant in patients with Cystic fibrosis.

Conclusions: Our data suggest that exhaled breath condensate pH can discriminate between healthy controls and those with bronchiectasis either Cystic fibrosis bronchiectasis or Non cystic fibrosis bronchiectasis indicating that EBC pH measurements can be used to assess degree of inflammation of the airways in bronchiectasis in comparison to pulmonary function tests.

Keywords: Cystic fibrosis, Exhaled breath condensate, Inflammation, pH, bronchiectasis, pulmonary function tests.

قياس الرقم الهيدروجيني للسائل المكثف من الزفير في عينة من الأطفال المصريين المصابين بمرض توسع القصبات الهوائية

الخلفية: يعرف توسع القصبات عند الأطفال على أنه وجود توسع غير طبيعي في القصبات الهوائيه في فحوصات التصوير المقطعي المحوسب عالية الدقة، بالإضافة إلى المتلازمة السريرية للسعال المتكرر أو المستمر، وعدوى أو الالتهاب مجرى الهواء.

الهدف: هو تقييم الرقم الهيدروجيني لتكثيف التنفس المزفور لدى الأطفال المصابين بتوسع القصبات وتحديد ما إذا كان يمكن استخدامه كعلامة غير جراحية للالتهاب مقارنة باختبارات وظائف الرئة.

الطريقة: تم جمع النفس المزفور باستخدام جهاز لجمع مكثفات الزفير في وحدة الرئة للبالغين في مستشفيات كليه الطب جامعه عين شمس. تم إجراء تقييم درجة الحموضة باستخدام أجهزة قياس الأس الهيدروجيني واختبارات وظائف الرئة وتتالف المجموعات البحثية من ١٠ اطفال غير مصابون باي امراض بينما تم تصنيف الأطفال المصابين بتوسع القصبات إلى مجموعتين المجموعة ١: تتألف من ١٢ مريضا يعانون من توسع القصبات غير التليف الكيسي، المجموعة ٢: تتألف من ١٨ مريضا مصابين بالتليف الكيسي.

النتائج: كان متوسط درجة حموضة النفس المكثف في مرضى التليف الكيسي مقابل مجموعة الضوابط ٦,٦٣±٠,٥٤: ٧,٧٦±٠,٤١، p= 0.000 بينما مرضى تمدد القصبات: ٦,٦٨±٠,٦٠ مقابل الضوابط: ٧,٧٦±٠,٤١، p= 0.000. كان الرقم الهيدروجيني لأكثر حمضية بين مرضى التليف الكيسي منه في كل من المجموعات غير التليفزيونية والمجموعة الضابطة. (ع= ٠,٠٠٠) ارتبط FEV1 بشكل إيجابي مع درجة الحموضة. كما أظهر المرضى الذين يعانون من تمدد القصبات الغير ليفي معدلات أعلى بكثير من التعرض لدخان التبغ بقيمة P <0.01 والتاريخ السابق للعدوى الرئوية P- value< 0.05 بينما كانت معدلات الحجز في الحضانات أكثر أهمية في مرضى التليف الكيسي.

الاستنتاجات: تشير بياناتنا إلى أن درجة الحموضة في النفس المكثف يمكن أن تميز بين الضوابط الصحية وأولئك الذين يعانون من توسع القصبات مما يشير إلى أنه يمكن استخدام قياسات درجة الحموضة في النفس المكثف لتقييم درجة التهاب الشعب الهوائية في الاطفال المصابين بمرض توسع القصبات.

الكلمات المفتاحية: التليف الكيسي، الزفير المكثف، الالتهاب، الرقم الهيدروجيني، توسع القصبات، اختبارات وظائف الرئة.

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