Clinico - Microbiological Profile of Bronchiectasis Patients at Tertiary Care Centre of North India

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Abstract

Context: Bronchiectasis is defined as abnormal and irreversible dilatation of one or more medium sized bronchi mainly from 4th to 9th generation. The most prevalent pathogenic bacteria in Post tuberculosis bronchiectasis are Pseudomonas aeruginosa, Haemophilus influenzae, Streptococcus pneumoniae, and Staphylococcus aureus.

Aim and Objective: To study the clinical and microbiological profile of bronchiectasis in patients attending outpatient department / inpatient department at tertiary care centre of north India.

Methods & Material: This study was a hospital based cross sectional study in which 182 patients were taken over a period of February 2018 to June 2019. Patients above age of 14 years, clinical signs & symptoms suggestive of bronchiectasis and radiological features on Chest X-ray or HRCT thorax suggestive of bronchiectasis were included in the study. Data were collected from patients according to a predesigned proforma gathering clinical history, examination and

microbiological examination of sputum and / or bronchial aspiration liquid.

Result: Out of 182 patients sputum collection was done in 165 (90.65%) patients and in 17 (9.35%) patients where cough was non-productive or sputum was minimal in amount bronchoscopy was done and bronchoalveolar lavage fluid (BAL) was collected. Out of 182 patients pathogenic microorganisms growth were seen in 138 (75.8%) patients.

Conclusion: Gram negative flora were seen predominantly in our study group and most common isolate was Klebsiella followed by Escherichia coli and Citrobacter. Staphylococcus species were predominant among gram positive organisms. Among the gram negative microbial flora maximum antibiotic sensitivity noted was for Fluroquinolones, Carbapenems and Aminoglycosides.

Summary: Gram negative flora was seen predominantly in our study group and most common isolate was Klebsiella followed by Escherichia coli and Citrobacter. Staphylococcus species was predominant among gram positive organisms**.** A statistically significant association (p value=0.013) was seen between severity of bronchiectasis and gram staining profile of microbial flora.

Introduction

Bronchiectasis (broncos, airways; ectasia, dilatation) is a morphologic term used to describe abnormal, irreversibly dilated and thick-walled bronchi. This is an anatomic definition that evolved from Laennec's original description in 1819 of ectatic bronchi in pathologic specimens [1]. Bronchiectasis is defined as abnormal and irreversible dilatation of one or more medium sized bronchi mainly from 4th to 9th generation. It is clinically characterized by persistent cough with the production of sputum which in untreated patients is often copious, purulent and associated with recurrent infective exacerbations [2].

Prevalence figures have varied from 4 to 272 per lakh population, partly dependent upon the age range studied. There are sparse data on the prevalence of bronchiectasis in the Indian subcontinent [3].

The aetiology of bronchiectasis can be congenital or acquired. Congenital causes include genetic diseases, primary ciliary dyskinesia, cystic fibrosis, cartilage abnormalities, asthma, alpha1-antitrypsin deficiency and primary immunodeficiencies. Acquired causes are mainly post infectious, autoimmune diseases, chronic aspirations and allergic bronchopulmonary aspergillosis [4].

The most prevalent pathogenic bacteria in Post TB bronchiectasis are Pseudomonas aeruginosa, Haemophilus influenzae, Streptococcus pneumonia, Staphylococcus aureus, Moraxella catarrhalis, anaerobic organisms like Prevotella and Veillonella and most common fungus is Aspergillus fumigatus. [5] . Though an extensive search of available English literature was done, Indian epidemiological data were lacking on this subject therefore this study was planned.

Aim

To study the clinical and microbiological profile of bronchiectasis in patients attending

Outpatient department / inpatient department at tertiary care centre of north India.

Objectives

1. To assess the clinical profile of bronchiectasis.

2. To detect the prevalence of chronic colonisation in lower respiratory tract in patients with non-cystic fibrosis bronchiectasis in a tertiary care centre.

3. To assess the pathogenic microbial flora present and its antibiotic sensitivity pattern in these patients.

Material & Methods

This study was a hospital based cross sectional study in which 182 patients were taken over a period of February 2018 to June 2019, done at respiratory medicine department of tertiary care centre of north India. Ethical clearance was taken from the institutional ethical committee.

Patients above age of 14 years, clinical signs & symptoms suggestive of bronchiectasis and radiological features on Chest X-ray or HRCT thorax suggestive of bronchiectasis were included in the study . Before enrolment of study, written informed consent from each subject was obtained. Those patients who were clinically suspected of cystic fibrosis and those refused to give consent were excluded from the study.

Data were collected from patients according to a predesigned proforma gathering clinical history and examination, as well as the results of chest X-ray, High Resolution Computerized Tomography scan and microbiological examination of sputum and /or bronchial aspiration liquid. The Computerized Tomography scan diagnostic criteria was bronchus diameter greater than the associated artery diameter, bronchial tubes visualized at the level of external third of the lung parenchyma and the absence of progressive reduction of bronchial tubes, as they gradually than take away of the hilum [6].

Bronchiectasis severity scoring was done using Bronchiectasis Severity Index (BSI). The BSI corresponds to a scale that evaluates the severity and prognosis of Non Cystic Fibrosis Bronchiectasis by analyzing nine parameters/variables: Age, Body Mass Index (BMI), FEV1% predicted, Hospitalization and Exacerbations before study, Degree Of Dyspnea,

Chronic Colonization by Pseudomonas aeruginosa and other microorganisms and Radiological Extension Of The Disease. Mild disease corresponds to score 0-4, Moderate Disease 5-8, 9 and over is Severe Disease [7].

Data Analysis

Standard statistical averages, standard deviation and mean deviation were calculated. Calculation of statistical significance was carried out by the Student's test and Chi-square test for analysis. Key values were expressed with 95% confidence limits. p value < 0.05 was considered to be statistically significant. Data were entered and analysed using SPSS software (SPSS Inc. Statistics for Windows, Version 26.0)

Special Investigations:

- Chest X ray

- High Resolution Computed Tomography (HRCT) – Thorax

- Sputum for AFB, Sputum samples for gram's stain, culture and sensitivity, Sputum for fungal hyphae and culture, Sputum for MGIT and CBNAAT.

- Video-Bronchoscopy: Broncho-alveolar lavage fluid (BAL) for AFB, for gram's stain, culture and

sensitivity, for fungal hyphae and culture, for MGIT and CBNAAT.

Data were entered and analysed using SPSS software (SPSS Inc. Statistics for Windows, Version 26.0)

Results

A total of 182 patients with non-cystic fibrosis bronchiectasis confirmed by high resolution computed tomography (HRCT) of the thorax was evaluated and we found following observation and results –

The mean age of the patients in our study was 48.7 $\pm$ 17.2 years with a range from 15 to 85 years. Maximum 24.2% patients were seen in the 56-65 age group. Out of 182 patients, there were 109 (59.9%) males and 73 (40.1%) females. Socio economic status was evaluated

on the basis of Modified B. G. Prasad scale as per AICP Feb 2018. Maximum patients i.e; 86 (47.2%) belonged to lower class.

Of the 182 patients, 114 patients (62.6%) had no history of smoking at any time in their life as compared to 68 patients (37.4%) who had smoked at some point. Among the smokers, bidi (an indigenous form of tobacco) smoking was most common mode with 64

patients (35.2%) followed by cigarette smoking with 3 patients (1.6%) and ganja or weed smoking the least with 1 patient (0.5%) in both genders. According to the smoking index, majority of the patients were moderate and heavy smokers with 30.2% and 7.1% respectively. A statistically significant association was seen between pattern of smoking and types of bronchiectasis (p=0.024). (Table 1).

Table 1: Characteristics of Bronchiectasis Patients.

S/N	Characteristics	Number Of Patients n=182 (%)
1	Demographic Characteristics Age in years (Mean $\pm$ SD) Sex Male Female	48.7 $\pm$ 17.2 109 (59.90) 73 (40.10)
2.	Clinical Characteristics	
	Smoker	68 (39.90)
	Non Smoker	114(60.10)
	Symptoms	
	Cough	171(91)
	Breathlessness	155(85.20)
	Fever	139(76.40)
	Haemoptysis	99(53.40)
	Etiology of Bronchiectasis	
	Idiopathic	10(5.5)
	Tuberculosis	48(26.4)
	Chronic Obstructive Pulmonary Diseases(COPD)	39(21.4)
	Asthma	
	Post Tuberculosis	27(14.8)
	Allergic Broncho pulmonary Aspergillosis (ABPA)	50(27.8)
	Lung mass	4(2.2)
	Kartagener's syndrome	2(1.1)
	Interistial lung disease (ILD)	1(0.5)
		1(0.5)
	Clubbing	79 (43.4)

Chest X-ray Presentation	
Normal	25 (13.7)
Ring like structures	53 (29.1)
Increased Pulmonary markings	13 (7.1)
Combined Presentation	91 (50)

The most common presenting symptom was Cough with or without expectoration in 171 (94%) patients, followed by breathlessness 155 (85.2%), fever 139 (76.4%) and hemoptysis in 99 (54.3%) patients. A statistically significant association was seen between severity of hemoptysis and etiology of bronchiectasis. (p=0.006)

Out of 182 patients, 25 (13.7%) patients had normal chest radiograph at presentation. On HRCT scan of the thorax, bilateral involvement of the lung was most common finding in 133 (71%) patients. The most common type of bronchiectasis seen as a lone finding (Table 1, Figure 1)

was cylindrical bronchiectasis in 67 (36.8%) patients but in 50% cases all the three types of bronchiectasis was present concomitantly. (Table 1)

In 172 patients (94.5%) cases underlying cause of bronchiectasis was identified. Post tubercular cases accounted for most common cause of bronchiectasis in 50 patients (27.4%) followed by active tuberculous infection as a cause of bronchiectasis was seen in 48 patients (26.4%).

Figure 1 : A Histogram Illustrating The Different Etiologies of Bronchiectasis
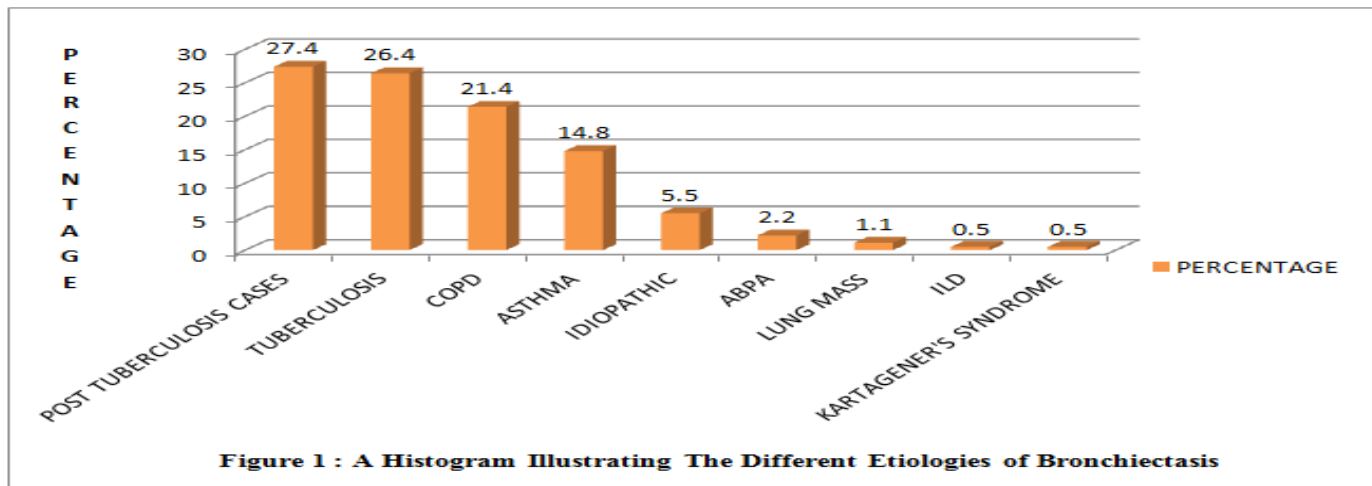
Out of 182 patients sputum collection was done in 165 (90.6%) patients and in 17 patients where cough was non-productive or sputum was minimal in amount bronchoscopy was done and bronchoalveolar lavage fluid (BAL) was collected that accounted for 9.3% patients. Sputum microscopy in those 165 patients yielded pathogenic microorganisms in 126 (69.2%) patients while in BAL fluid microscopy out of 17

patients in a total of 12 patients (6.5%) pathogenic microorganisms growth was seen. Hence in a total of 138 patients (75.8%) pathogenic microorganisms growth were seen. Among the pathogenic organisms isolated cases only gram negative bacterial growth was seen in 121 (66.4%) patients and only gram positive bacteria was seen in 10 (5.4%) patients while both gram

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positive and gram negative bacterial growths were seen
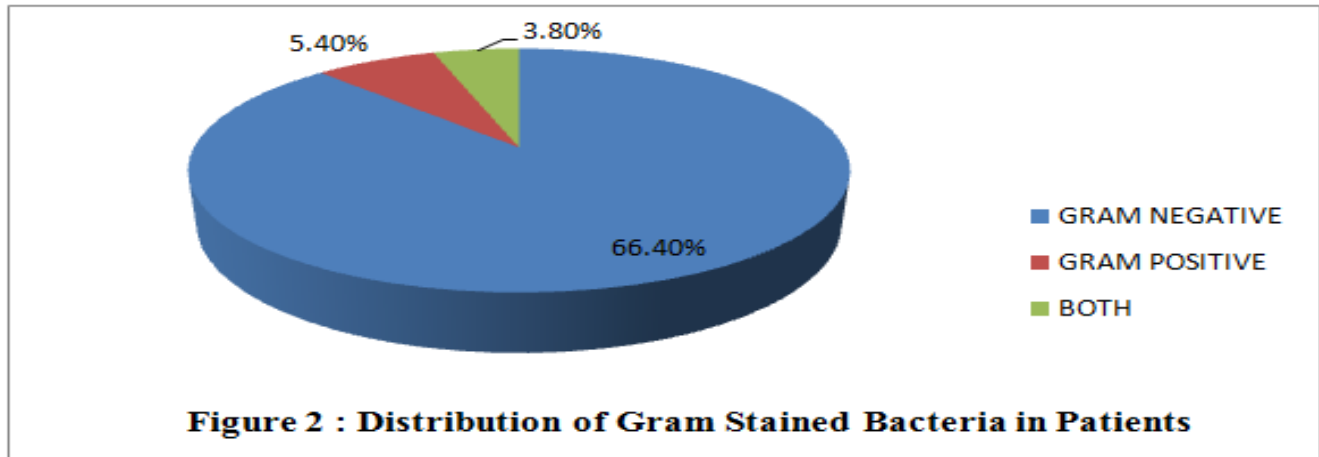
in 7 (3.8%) patients.

(Table 2 , Figure 2)

Figure 2 : Distribution of Gram Stained Bacteria in Patients

Table 2: Distribution   of   Bacterial Flora

S/N	Microrganisms	Frequency n=182* (%)
1	Klebsiella sp.	39(21.4)
2	Escherichia coli	32(17.5)
3	Citrobacter sp.	29(15.9)
4	Pseudomonas aeruginosa	28(15.3)
5	Acinetobacter sp.	9(4.9)
6	Enterococcus sp.	4(2.2)
7	Coagulase negative Staphylococcus (CONS)	4(2.2)
8	Methicillin Resistant Staphylococcus aureus	4(2.2)
9	Staphylococcus aureus	3(1.6)
10	Streptococcus sp.	3(1.6)
11	Proteus mirabilis	2(1.1)
12	Serratia marcescens	1(0.5)
13	Normal flora	44(24.1)
14	Mixed Population	26(14.2)

Of all 182 patients sputum / BAL fluid samples were subjected to mycobacterial growth indicator tube (MGIT) culture which yielded growth of MTB in 43(23.6%) and NTM in 2 (1.1%) patients.

A statistically significant association was seen when severity of bronchiectasis as assessed by

Bronchiectasis Severity Index (BSI) was compared with gram staining profile of microbial flora of patients (p value=0.013). (Table 3)

Table 3: Association of Gram Staining Profile with Severity of Bronchiectasis

S/N	Bronciectasis Severity On The Basis Of *BSI	Gram Stainining Profile				Total	P value at 95%CI
		Normal flora	Gram positive	Gram negative	Mixed infection		
1	Mild	6 (3.3%)	0	16 (8.8%)	4 (2.2%)	26 (14.3%)	x^2 value =16.115[a] d.f.=6 p=0.013
2	Moderate	30(16.5%)	6 (3.3%)	62 (34.1%)	2(1.1%)	100 (54.9%)	
3	Severe	9 (4.9%)	4 (2.2%)	42 (24.1%)	1(0.5%)	56(30.7%)	
	Total	45 (24.7%)	10 (5.49%)	120 (65.9%)	7(3.8%)	182(100%)	

*BSI: Bronchiectasis Severity Index

Among the pathogenic isolates most common organism was Klebsiella in 39 patients (21.4%) followed by Escherichia coli (E.coli) in 32 patients (17.5%) and Citrobacter in 29 patients (15.9%). Pseudomonas aeruginosa were seen in 28 patients (15.3%). Amongst the gram positive bacteria isolated most common were Staphylococcus in 11 patients (6.04%) out of these Coagulase negative Staphylococcus (CONS) and Methicillin resistant Staphylococcus aureus (MRSA) were seen in 4 patients (2.2%) each. (Table 2)

Klebsiella species was most sensitive to tobramycin and colistin (100%) while 100% resistant were seen for

cefoxitin, ofloxacin, gentamicin and teicoplanin. Higher sensitivity was also seen for tigecycline (85%) and amikacin (82.7%) while a higher resistant was also seen for ampicillin (83.3%) and amoxy-clav (76.9%). Sensitivity to piperacillin-tazobactum was 42.80%. Sensitivity pattern of Escherichia coli showed a 100% sensitivity to cefixime and colistin and 100% resistance to ofloxacin, ampicillin, erythromycin and teicoplanin. A higher resistant is also seen towards cefoxitin (85.7%), ceftriaxone (83.3%), doxycycline (71.4%) and amoxy-clav (64.2%). (Table 4)

Staphylococcus species was most sensitive to linezolid (100%) while 100% resistant to cefoxitin. (Table5)

Table 4: Antibiotic Sensitivity Pattern of Gram Negative Organism

Antibiotics	Klebsiella		Pseudomonas		Escherichia coli		Citrobacter		Acinetobacter	
	S	R	S	R	S	R	S	R	S	R
Cefoxitin	0	100%	0	100%	14.2%	85.7%	-	-	0	100%
Ceftriaxone	33.3%	66.6%	66.6%	33.3%	16.6%	83.3%	0	100%	14.2%	85.7%
Cefixime	83.3%	16.6%	100%	0	100%	0	50%	50%	-	-
Ofloxacin	0	100%	-	-	0	100%	40%	60%	-	-
Levofloxacin	66.6%	33.3%	72.7%	27.2%	57.1%	42.8%	90%	10%	100%	0
Ampicillin	16.6%	83.3%	0	100%	0	100%	0	100%	-	-
Meropenem	47.1%	52.9%	77.8%	22.2%	58.8%	41.2%	56.2%	43.7%	62.5%	37.5%
Piperacillin+Tazobactum	42.8%	57.2%	73.1%	26.9%	57.1%	42.8%	40%	60%	0	100%
Cefoperazone+Sulbactum	76.4%	23.5%	82.6%	17.4%	68.4%	31.5%	88.2%	11.7%	87.5%	12.5%
Amoxycillin+clavulanate	23.1%	76.9%	60%	40%	35.7%	64.2%	25%	75%	50%	50%
Tobramycin	100%	0	100%	0	-	-	50%	50%	-	-
Gentamicin	0	100%	-	-	-	-	-	-	-	-
Amikacin	82.7%	17.2%	75%	25%	66.6%	33.3%	68.4%	31.6%	20%	80%
Colistin	100%	0	100%	0	100%	0	93.3%	6.6%	100%	0
Tigecycline	85%	15%	60%	40%	91.6%	8.3%	100%	0	75%	25%
Doxycycline	42.8%	57.1%	66.6%	33.3%	28.5%	71.4%	16.7%	83.3%	0	100%
Teicoplanin	0	100%	-	-	0	100%	0	100%	-	-
Erythromycin	-	-	-	-	0	100%	-	-	-	-
Linezolid	-	-	66.6%	33.3%	-	-	-	-	-	-

Table 5: Antibiotic Sensitivity Pattern of Gram Positive Organism

Antibiotics	Staphylococcus aureus		Methicillin Resistant Staphylococcus		Coagulase Negative Stahylococcus		Streptococcus		Enterococcus	
	S	R	S	R	S	R	S	R	S	R
Cefoxitin	0	100%	0	100%	--	--	-	-	--	--
Ofloxacin	100%	0%	--	--	--	---	--	--	66.6%	33.3%
Ciprofloxacin	---	--	0	100%	0	100%	100%	0	--	--
Azithromycin	--	--	33.3%	66.6%	100%	0	--	--	--	--
Piperacillin+Tazobact										

um	100%	0	66.6%	33.3%	100%	0	--	--	--	--
Amoxycillin+clavulanate	100%	0	0	100%	66.6%	33.3%	0	100%	33.3%	66.6%
Clindamycin	100%	0	66.6%	33.3%	100%	0	100%	0	100%	0
Vancomycin	50%	50%	100%	0	100%	0	100%	0	75%	25%
Meropenem	0	100%	0	100%	100%	0	--	--	--	--
Linezolid	100%	0	100%	0	100%	0	100%	0	--	--

Discussion

The mean age (in years) of the patients in our study was 48.7 years comparable to another study conducted by Bhatta. N et al; 2008 with mean age of 48.3 years. [8] In our study we found male preponderance (59.9%), similar finding also reported by Dhar R et al; 2019, Aslam M et al; 2018 and Utpat K et al; 2017 [9,10,11].

In our study 62.6% patients were non-smokers ,comparable to other studies such as Dimakou K et al; 2016, Amorim A et al; 2015 [12,13].

Cough with or without expectoration was most common symptom followed by breathlessness, similar findings have been reported from various other studies [10,11,12,14]. Digital clubbing was observed in 43.4% patients as seen in other comparative study [15]. On chest examination crepts were heard in 68.4% patients and rhonchi in 54.9% patients similar to other studies [11,14].

HRCT was diagnostic in all our cases (100%) of bronchiectasis. Bilateral abnormalities on HRCT were observed in majority of patients similar finding in other studies [12, 13], and The predominant morphology visualized was cylindrical in our study compared to other studies where cystic type remains the most common [8,11,14].

The etiology of bronchiectasis is heterogeneous but in our study post tuberculosis cases were most commonly seen, as also seen in other studies. Most of the studies have also reported an idiopathic etiology of bronchiectasis predominantly [12,13, 14] .

Gram negative bacteria was the most commonly isolated pathogenic microbial flora similar to other Indian studies [14,16]. In our study among gram negative organisms Klebsiella was most common isolate (21.4%) which showed 100% resistant to cefoxitin and ofloxacin followed by E.coli (17.5%), Citrobacter (15.9%) and Pseudomonas aeruginosa (15.3%) as compared to other studies where Pseudomonas was the most common organism isolated [10,11,12,14].

In gram positive bacteria (5.4% patients) most commonly isolated was staphylococcus species (6.1%) which was 100% resistant to cefoxitin and ciprofloxacin (Table 5). In our study we found fungal growth in 5.5% patients which closely estimates to 4% in study performed by Kumar GS et al [17].

Conclusion

In our study male population was most commonly predisposed to bronchiectasis. We found a statistically significant association between pattern of smoking and types of bronchiectasis and most common etiology was post tuberculosis cases. Cough with or without expectoration remains the most common symptom. In majority of patients we found all the radiological types of bronchiectasis (cylindrical, saccular and varicose) concomitantly.

A statistically significant association (p value=0.013) was seen when severity of bronchiectasis assessed by Bronchiectasis Severity Index (BSI) was compared with gram staining profile of microbial flora.

Gram negative flora were seen predominantly in our study group and most common isolate was Klebsiella followed by Escherichia coli and Citrobacter. Staphylococcus species was predominant among gram positive organisms**.** Among the gram negative microbial flora maximum antibiotic sensitivity was noted for fluro-quinolones, carbapenems and aminoglycosides**.** In gram positive microbial flora maximum antibiotic sensitivity was seen for aminopenicillins, lincosamides and glycopeptides.

Limitations

Our study was based exclusively on patients attending our department, so results are not representative of whole community, thus incidence and prevalence of bronchiectasis could not be evaluated. We could only isolate aerobic bacteria, as anaerobic culture medium was not available at our center which could have given a better bacteriological profile. Other rare causes of bronchiectasis such as immune disorder related, alpha-1 antitrypsin deficiency, cartilage deficiency, connective tissue disorder related cannot be identified due to resources insufficiency.

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