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Original Research Article

Association of serum alpha-1 antitrypsin level with the severity of COPD

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ABSTRACT

Background: Alpha-1 antitrypsin deficiency (AATD) is a hereditary disorder linked to early onset COPD, notably the emphysema variety, but often goes undetected. Low serum AAT levels may impact lung function and correlate with COPD severity. The aim of the study was to detect possible associations of serum AAT level with the severity of COPD patients on the basis of post bronchodilator FEV1 in Bangabandhu Sheikh Mujib Medical University (BSMMU).
Methods: A cross-sectional study was conducted at the Department of Respiratory Medicine, BSMMU, Dhaka, from October 2022 to September 2023. Adult patients (≥18 years) of both genders diagnosed with COPD based on spirometry were included. COPD was defined per GOLD guidelines, with a post-bronchodilator FEV1/FVC ratio <70%. Severity was categorized based on post-bronchodilator FEV1% predicted. Association between serum AAT level and COPD severity was analyzed using SPSS version 26, with significance set at $p < 0.05$.
Results: The study involved 80 COPD patients, with 1.25% showing low serum AAT levels and 98.75% normal. No significant differences in age, sex, or smoking status were observed among severity groups. Mean serum AAT levels varied across severity groups but were not statistically significant (p=0.377). Smoking was prevalent (66.3%), with common comorbidities like hypertension (26.3%), IHD (16.3%), and diabetes mellitus (15.0%). Shortness of breath (95.0%) and cough (92.5%) were common symptoms, with most patients having moderate disease severity (42.5%).
Conclusions: The study indicates a weak association between serum AAT levels and COPD severity, with only 1.25% of 80 patients exhibiting low AAT levels.

Keywords: Antitrypsin level, Serum Alpha-1, Severity of COPD

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an important public health challenge that is both preventable and treatable. Many people suffer from this disease for years and die prematurely from it or its complications (GOLD Report of COPD, 2023).[1] Alpha-1 antitrypsin deficiency (AATD) is an autosomal recessive disorder

characterized by impaired or defective production of Alpha-1 antitrypsin protein in liver which is associated with early onset chronic obstructive pulmonary disease (COPD) particularly emphysema and liver disease.[2] In a study, first described alpha-1 antitrypsin deficiency (AATD) over 50 years ago after observing the absence of the alpha-1 globulin band in the serum protein electrophoresis patterns of a few patients.[3]

It is relatively prevalent but a highly under diagnosed condition especially in Asia. Alpha-1 antitrypsin (AAT) is the most abundant protease inhibitor in human serum with average concentrations in healthy individuals 149 mg/dl (range 100-200 mg/dl). Based on serum AAT level, individual are classified as: no deficiency: AAT >100 mg/dl; intermediate deficiency: AAT between 51-100 mg/dl ; and severe deficiency: AAT <50 mg/dl.[4] The primary function of AAT in the lung is to protect the connective tissue from the enzyme released by the neutrophils. The main evidence for this is the development of emphysema in individuals with a deficiency of the protein. In addition to its anti-protease activity, AAT also has immunomodulatory functions which make it a natural anti-inflammatory molecule.[5]

The impact of systemic inflammation in the pathogenesis of lung function decline in COPD patients has not yet been established Serum levels of AAT can be elevated following acute or chronic inflammation, infections, presence of certain neoplasms, severe burns or during pregnancy and contraceptive use.[6] The amount of circulating protein is thought to be directly related with the patient's genotype. COPD associated with AATD is a potentially fatal disease and a highly under-diagnosed hereditary disorder.[7,8] Yet only 4-5% of those with a deficiency have been identified.[9] The prevalence of AATD in the adult population with COPD in Argentina is estimated to 0.83% but there is no known study in South Asian region regarding the frequency of Alpha-1 antitrypsin deficiency.[10] Various series have found that 2-3% of patients with COPD generally have severe deficiency of the protein. This is reflected in studies that have found long intervals between the first symptom and definitive diagnosis (a period of 6.3-7.2 years) of AATD.[11]

Moreover, the frequency of AATD varies among different racial subgroups and different countries. This has led international guidelines to recommend measuring AAT levels in all symptomatic adults with persistent airflow obstruction on spirometry and in young emphysema patients (aged ≤45 years) or non- smokers[11]. World Health Organization (WHO) recommends all COPD patients should be tested for AAT level at least once during their lifetime.[12] Screening programs have been developed as a strategy to increase detection of AATD in the United States but not routinely used in our country.[13] There is no known study regarding prevalence of AATD among COPD patients and association of serum AAT level with severity of COPD patients in our country. Early diagnosis of AATD will prompt specific interventions; such as smoking cessation, testing of family members, genetic counselling and replacement therapy indicated in patients with severe deficiency. Detection of possible association between serum AAT level with severity of COPD may be helpful in COPD management by AAT augmentation therapy.

This study aimed to determine association of serum AAT level with severity of COPD on basis of postbronchodilator FEV1 (% predicted). Also, to measure serum Alpha-1 antitrypsin level in COPD patients, estimation of frequency of low serum alpha-1 antitrypsin level among COPD patients attending department of respiratory medicine in BSMMU. Additionally, aimed to categorize COPD patients as mild, moderate, severe and very severe group on basis of postbronchodilator FEV1 % predicted. Moreover, to compare serum AAT level with severity of COPD on basis of different levels of severity of airflow obstruction among COPD patients.

METHODS

Study design

This was cross-sectional design and observational study.

Place of study

This study conducted at Department of Respiratory Medicine (Indoor, outdoor, Respiratory Emergency), BSMMU, Shahbag, Dhaka.

Study period

This study conducted for 18 months from April 2022 to September 2023.

Study population

Patients attending in the Department of Respiratory medicine in BSMMU diagnosed as COPD were included.

Sample size determination and sampling technique

Consecutive non probability sampling method was used. Sample size was calculated by using following formula:

$$n= \frac{Z^2(p\times q)}{d^2}$$

Where, n=Sample size, p=10% (prevalence of AATD in COPD patients) = 0.1, q=100-P= 90% = 0.9, z=Usually assumed at 1.96 or 2 which corresponds to 95% confidence limit, d=Degree of precision = 7% = 0.07.

Thus,

$$n= \frac{1.96^2\times(0.1\times0.9)}{0.07^2}$$

$=70.56 \approx 71$

Based on the formula, the targeted sample size was estimated to be 71. However, it was increased to 80 for the final sample.

Inclusion criteria

COPD patients attending department of Respiratory medicine confirmed by spirometry (post bronchodilator FEV1/FVC <0.7 and irreversible postbronchodilator response of FEV1), age≥ 18 years of both sexes, patients who agreed to give informed written consent to participate this study were included.

Exclusion criteria

The study encountered challenges with participant recruitment due to various factors, including patient refusal to participate, unstable health conditions such as heart failure or acute myocardial infarction, and the presence of chronic liver disease among potential candidates. Additionally, serum levels of Alpha-1 antitrypsin (AAT) can be elevated in conditions such as acute or chronic inflammation, infections, neoplasms, severe burns, and during pregnancy were exlcuded.

Procedure

This cross-sectional study was conducted in adult patients diagnosed with COPD. In accordance with GOLD guidelines, COPD may be defined as postbronchodilator FEV1/FVC ratio <70%, based on post-bronchodilator FEV1 lung function tests.[14] They were enrolled upon their voluntary agreement. Participants who fulfill the inclusion criteria was enrolled after having written informed consent. Spirometry was performed according to ATS/ERS 2005 guidelines by Miller et al using NHANES III reference equations to confirmed diagnosis of COPD.[15] Complete blood count, C-reactive protein (CRP) were done to exclude infection as infection process increase AAT level. Liver function test (Serum bilirubin, SGPT, serum albumin, prothrombin time) was also done to exclude chronic liver disease. ECG and troponin-I were done to exclude acute MI. Chest x-ray and CT scan of chest were done to exclude pneumonia, bronchiectasis, bronchial carcinoma and to see evidence of emphysematous change.

Then, serum Alpha-1 antitrypsin level was measured among COPD patients. Blood was collected from participant for determination of plasma AAT concentrations by aseptic measure and sent to biochemistry department. Blood samples were taken in serum tubes, clotted at room temperature for 35-65 minute and centrifuged for 15 min. Then, sample were frozen at -70 degree celsius for further analysis. The serum level of AAT were determined by automated analyzer: Indiko plus, according to instruction of manufacturer using commercial kits. Patients whose spirometry did not meet COPD criteria or was of insufficient quality, patients whose blood sample was insufficient to perform the determination were excluded.

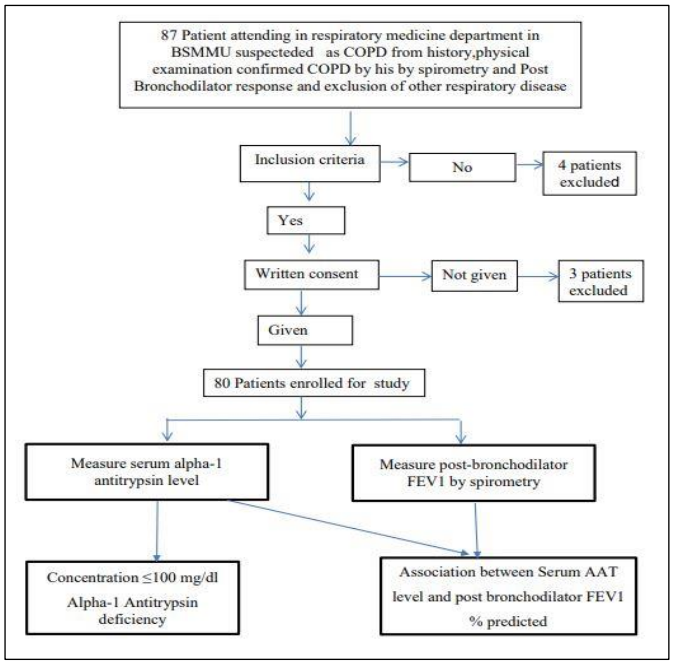

Figure 1: Study flow chart.

Data collection tools

A structured questionnaire containing demographic, clinical and laboratory characteristics of the patients in their own language was used.

Data collection procedure

Data were collected from Respiratory Medicine unit of BSMMU. Non probability sampling technique was applied. On patient group COPD patients confirmed by spirometry fulfilling inclusion and exclusion criteria was enrolled. Data were collected after testing for serum Alpha-1 antitrypsin level of COPD patients. All measures were taken to prevent risk during blood collection method.

Data analysis

Statistical analysis of the data were obtained by using windows based software Statistical Packages for Social Science (SPSS-26), (SPSS Inc. Chicago, IL, USA). The categorical data were analyzed by chi-squared test and continuous data were analyzed by students t test. P values of less than 0.05 were considered statistically significant.

Quality control strategy

This cross-sectional observational study conducted an extensive literature review. Patient evaluation and examinations were supervised by a guide, with secondary

verification if necessary. Prior to enrollment, four subjects underwent piloting, leading to modifications in the data sheet. Analysis of 25% of the patient data ensured study consistency. All collected data were meticulously reviewed to discard inadequate, irrelevant, and inconsistent information.

The study adhered to rigorous ethical standards, including obtaining clearance from the Ethical Review Committee of BSMMU, Dhaka. Participants were thoroughly informed about the study's purpose, their rights, and provided written consent in accordance with the Helsinki Declaration for Medical Research. Confidentiality measures were strictly upheld, and aseptic precautions were followed to ensure participant safety. In the event of any adverse events, immediate steps would be taken by the department to address them. The study was solely conducted for academic research purposes, without any potential conflicts of interest, and participants received no incentives for their involvement.

RESULTS

Table 1 shows the baseline characteristics of COPD patients, including age group and sex distribution. Of the 80 COPD patients included in the study, the majority were in the age group of 51-60 years (35.0%), followed by the age groups of 61-70 years (31.3%) and 41-50 years (17.5%). Only a small proportion of patients were in the age groups of 18-30 years (3.7%) and 31-40 years (3.7%). The mean age of patients was 57.3±11.86 years, with a range of 26-84 years. The majority of patients were male with a male to female ratio of 9:1.

Table 1: Baseline characteristics of the COPD patients (n=80).

Variables	Number of patients	Percentage
Age group (years)		
18-30	3	3.7
31-40	3	3.7
41-50	14	17.5
51-60	28	35.0
61-70	25	31.3
>70	7	8.8
Mean±SD Range (min-max)	57.3±11.86 (26-84) years	
Sex		
Male	72	90.0
Female	8	10.0
Male: female ratio	9:1	

Table 2 shows the distribution of COPD patients by smoking status and the packed year. The majority were smokers accounting for 66.3% of the total population. The remaining 33.7% of patients were non-smokers. The mean packed year among smokers was 26.55±7.62, with a range of 10-40 packed year.

The findings highlight that smoking is a significant risk factor for COPD as the majority of patients were smokers.

Table 3 shows the distribution of COPD patients by comorbidity. The most common comorbidity was hypertension that was 26.3% of patients. The second most common comorbidity was ischemic heart disease (IHD) accounting for 16.3% of patients, both HTN and IHD are also a smoking related diseases, followed by diabetes mellitus (15.0%), chronic kidney disease (CKD) (3.8%), valvular disease (2.5%), and dyslipidemia (1.3%).

Table 2: Distribution of the COPD patients by smoking status (n=80).

Smoking status	Number of patients	Percentage
Smoker	53	66.3
Non-smoker	27	33.7
Passive smoker	0	0
Total	80	0100.0
Packed year		
Mean±SD	26.55±7.62	
Range (min-max)	(10-40)	

Table 3: Distribution of the COPD patients by comorbidity (n=80).

Comorbidity	Number of patients	Percentage
Hypertension	21	26.3
Diabetes mellitus	12	15.0
IHD (acute MI excluded)	13	16.3
Valvular disease	2	2.5
CKD	3	3.8
Dyslipidemia	1	1.3

Table 4: Distribution of the COPD patients by clinical features (n=80).

Clinical features	Number of patients	Percentage
Cough	74	92.5
Shortness of breath	76	95.0
Others (increase sputum production, wheeze etc.)	9	11.3

Table 4 shows the distribution of COPD patients by clinical features. Among the 80 COPD patients, the most common clinical features reported were shortness of breath and cough accounting for 95.0% and 92.5% of patients respectively.

Only a small proportion of patients reported other clinical features including increase sputum production, wheeze, accounting for 11.3% of patients.

Table 5 shows the frequency of alpha-1 antitrypsin deficiency (AATD) among COPD patients included in the study. Of the 80 COPD patients, the majority have normal serum AAT level accounting for 98.75% of patients. Only one patient (1.25%) had AATD with a serum level of less than 100 mg/dl.

Table 5: Frequency of Alpha-1 antitrypsin deficiency (AATD) on basis of low serum AAT level among the COPD patients (n=80).

Alpha-1 antitrypsin deficiency	Number of patients	Percentage
No AATD (>100 mg/dl)	79	98.75
AATD (<100 mg/dl)	1	1.25
Total	80	100.0

Table 6 shows the distribution of COPD patients based on disease severity according to FEV1 % predicted. Out of a total of 80 patients, 3 patients (3.8%) have mild COPD, 34 patients (42.5%) have moderate COPD, 32 patients (40.0%) have severe COPD, and 11 patients (13.8%) have very severe COPD.

Table 7 showed that there was no significant difference in age, sex, or smoking status among the four groups.

The mean serum AAT levels were highest in the moderate group (292.0±231.1 mg/dl) and lowest in the mild group (222.2±106.8 mg/dl.

Table 6: Distribution of the COPD patients by disease severity by postbronchodilator FEV1 % predicted (n=80).

Disease severity	Number of patients	Percentage
Mild (>80%)	3	3.8
Moderate (50%-80%)	34	42.5
Severe (30%-50%)	32	40.0
Very severe (<30%)	11	13.8
Total	80	100.0

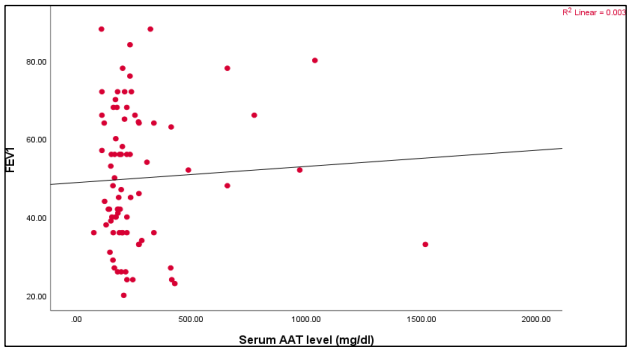

Figure 1: Scatter diagram showing weak positive the correlation of serum AAT level with post bronchodilator FEV1 % predicted.

Note: The correlation coefficient (r)=0.053, indicating a very weak positive correlation. P value is 0.641, which is not statistically significant.

Table 7: Comparison of serum AAT level according to severity of COPD (n=80).

Variables	COPD severity				P value
	Mild (n=3)	Moderate (n=34)	Severe (n=32)	Very severe (n=11)	
Age (years)	64.7±13.6	54.7±14.2	58.3±9.4	60.6±8.7	0.283
Sex (%)					
Male	3 (100.0)	31 (91.2)	28 (87.5)	10 (90.9)	0.892
Female	0 (0.0)	2 (8.8)	4 (12.5)	1 (9.1)	
Smoking	3 (100.0)	24 (70.6)	20 (62.5)	6 (54.5)	0.442
FEV/FVC					
Mean±SD	62.2±11.5	55.5±16.9	55.8±10.9	54.3±13.3	0.503
Median	68.4	62.0	57.8	53.7	
Range (min-max)	49.0-69.3	0.66-69.0	25.6-69.6	31.1-72.6	
FEVI post bronchodialator % predicted (Mean±SD)	86.7±2.31	64.1±8.05	39.9±5.0	25.09±2.43	<0.001
S.AAT level (mg/dl) (Mean±SD)	222.2±106.8	292.0±231.0	246.7±251.7	258.6±105.4	0.377
Median	233.9	210.7	185.5	210.9	
Range (min-max)	110.0-322.6	112.0-1036.9	76.8-1516.6	160.0-428.4	

P value obtained by ANOVA test, Chi-square test and Kruskal Wallis test, p<0.05 considered as a level of significant

DISCUSSION

The aim of study was to detect association of serum AAT level with the severity of COPD patients and to determine the frequency of alpha-1 antitrypsin deficiency (AATD) among COPD in BSMMU. This study included 80 COPD patients with only one patient (1.25%) diagnosed as AAT deficiency on the basis of serum AAT level; while the remaining 98.75% of patients had normal AAT level. We did not separate emphysematous variety of COPD patients. The findings of the study are consistent with previous research which has suggested that AATD is

relatively rare in COPD patients. In a study, conducted a multicenter prospective cross- sectional study to estimate the prevalence of Alpha-1 Antitrypsin Deficiency (AATD) in COPD patients, adjusted based on the population of the COPD prevalence study in Argentina (EPOC.AR).[10] The study included individuals aged ≥30 years diagnosed with COPD and AAT quantification was performed in dry blood spot samples, followed by genotyping in subjects with <1.5 mg/dL AAT in dry blood spot (<80 mg/dL in serum). The prevalence of AATD in adult population with COPD in Argentina is estimated to 0.83%.

AATD was defined as the detection of variants ZZ or SZ on genotyping. The EPOC.AR study population data were utilized to calculate the local adjusted prevalence of AATD in COPD patients in Argentina. Moreover, when adjusting for age, the prevalence of AATD among COPD patients aged 40 years and above was estimated to be 0.83% (95% CI 0.23-2.08). Comparing these findings with our present study, weobserved a prevalence of AATD among COPD patients of 1.25%. The congruence in prevalence rates across studies highlights the consistent presence of AATD among COPD patients emphasizing its relevance within this patient population. Reviewing the epidemiology, the prevalence of AATD in the general population is reported to be from 1 to 2,000 to 1 in 5,000 individuals in some parts of Europe and from 1 to 5,000 to 1 in 10,000 in the United States and Canada while these figures are much lower in Latin American countries.[16,10]

Analyzing patients with COPD only, the prevalence of AATD is 10%, including all mutations. The prevalence of severe AAT deficiency has been estimated at 1-2%.[16,17] Our results closely parallel to the data received from a study carried out in Denmark where the frequency of AAT deficiency among COPD patients was found to be 0.8% for ZZ and 2.4% for MZ genotype.[18] In the United States, the prevalence is similar (0.019-0.030). In Asia, the prevalence is extremely low (0.006).[19] Our study showed that the majority were smokers, accounting for 66.3% of the total population. The mean duration of smoking among smokers was 26.55±7.62 years,with a range of 10-40 years. The findings highlight that smoking is a significant risk factor for COPD as the majority of patients were smokers. The mean duration of smoking among smokers was also relatively long, indicating that prolonged exposure to cigarette smoke increases the risk of developing COPD. In a study, reported among the COPD patients 83.9% were ex-smoker and active smokers comprised 12.2%.[20]

This distribution underscores the significant association between smoking and the development of COPD, as the majority of patients had a history of smoking. The study investigated the distribution of COPD patients by clinical features, family history, and disease severity. The common comorbidities reported were hypertension (26.3%), IHD (16.3%), and diabetes mellitus (15.0%). In a study, reported the general characteristics of a population were investigated.[21] The prevalence of diabetes mellitus in the population was 13.4% in the "No mutation" group and 14.6% in the "Mutation" group. Similarly, the study reported the prevalence of heart failure was 16.9%, tuberculosis was 8.33%. Also another study, reported the most frequent comorbidities in adults were dyslipidemia (27.6%), hypertension (27.4%), diabetes mellitus (11.7%), depression (10.1%), and ischemic heart disease (4%) among COPD patients which was consistent with the present study.[22]

The most common clinical features reported were cough (92.5%) and shortness of breath (95.0%). Only a small proportion of patients reported a family history of COPD (8.8%), while the majority had moderate disease severity (73.8%). A study highlights that the observed circumstances, characterized by overlapping respiratory symptoms resembling those encountered in asthma or COPD, can be attributed to several factors.[23] Our study showed no significant difference in age, sex, or smoking status among the four groups of severity of COPD. There was no significant difference in age, sex, or smoking status among the four groups. The mean serum AAT levels were highest in the moderate group (292.0±231.1 mg/dl) and lowest in the mild group (222.2±106.8mg/dl), but this difference was not statistically significant (p=0.377). This suggests that there may not be a strong association between serum AAT levels and the severity of COPD. In a study shows, on Association of alpha-1 antitrypsin level and lung function in patients with chronic obstructive pulmonary disease showed that circulating AAT inversely correlated with FEV1 in COPD cases without AAT deficiency.[24]

SAPALDIA project investigated associations of circulating AAT level with lung function in general population and detected negative correlation of serum AAT concentration with FEV1. The amount of AAT that passively diffuses from the serum to the lung increases during an inflammation, which may be present in COPD. This may show increased the need of AAT production to meet requirements of overcoming the release of various endogenous enzymes from inflammatory cells in the lungs. Gender distribution did not show a significant difference between stages (p=0.241). In terms of exposure to tobacco, there was no significant difference between the stages (p=0.660). The proportion of patients with exposure to tobacco ranged from 47.4% in stage II to 56.7% in stage IV.

This study has several limitations that should be considered when interpreting the findings. Sample size was relatively small which may limit the outcome of studies to other populations. This study was conducted in a single center which may limit the generalizability of the findings to other healthcare settings. If we separate emphysema variety of COPD, there may be more chance of detection of low serum AAT level. Sample size was not targeted to nonsmoker group and COPD patients aged

less than 40 years. Genetic study for gene mutation was not included in this study which was performed in most of the similar studies in abroad to detect AAT deficiency and its associations. We didn't assess COPD on the basis of mMRC scale, CAT score, history of exacerbation and hospitalization.

CONCLUSION

This study aimed to determine possible association of serum alpha-1 antitrypsin level with the severity of COPD patients in BSMMU. Our study suggests that there is no strong association between serum AAT levels and the severity of COPD. This study also suggest that AATD is relatively rare in COPD patients with only one patient (1.25%) had low serum AAT level. The majority of patients were smokers (66.3%); high lighting the significant role of smoking as a risk factor for COPD. The most common comorbidities reported were hypertension (26.3%), IHD (16.3%), and diabetes mellitus (15.0%) indicating the need for targeted management strategies for co-morbidities to address these conditions in COPD patients.

Recommendations

Based on the study's findings, recommendations include conducting further research on larger populations to validate results. Focus should be on nonsmokers, those with the emphysema variety of COPD, and early-onset cases (<40 years) for improved detection of AATD frequency. Genetic analysis, particularly of SERPINA gene mutations, is advised to understand their impact on COPD development and severity. Multi-center studies for AATD diagnosis and targeted management strategies are crucial for better patient outcomes and reducing COPD burden. Public awareness efforts are needed to promote early detection and management. Future studies should address limitations by employing larger samples, genetic analysis, multi-center studies, family screening, and objective measures analysis.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of BSMMU, Dhaka

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management and Prevention of COPD Executive Summary, 2023. Available at: https://goldcopd.org/2023-gold-report-2/. Accessed 01 March 2023.
2. Carrell RW, Lomas DA, Sidhar S, Foreman R. α1-Antitrypsin deficiency: a conformational disease. Chest. 1996;110(6):243S-7S.
3. Laurell CB, Eriksson S. The electrophoretic α; 1-globulin pattern of serum in α; 1-antitrypsin deficiency. Scand J Cli Labor Investigat. 1963;15(2):132-40.
4. Vidal R, Blanco I, Casas F, Jardí R, Miravitlles M, National Alpha-1 Antitrypsin Registry Committee. Guidelines for the diagnosis and management of α1-antitrypsin deficiency. Archi Bronconeumolo. 2006;42(12):645-59.
5. Brantly M. α 1-Antitrypsin: not just an antiprotease: extending the half-life of a natural anti-inflammatory molecule by conjugation with polyethylene glycol. Am J Respi Cell Mole Biol. 2002;27(6):652-4.
6. Vidal, R., Blanco, I., Casas, F., Jardí, R., Miravitlles, M. and National Alpha-1 Antitrypsin Registry Committee, 2006. Guidelines for the diagnosis and management of α1-antitrypsin deficiency. Archivos de Bronconeumología ((English Edition)), 42(12), pp.645-659.
7. Campos MA, Wanner A, Zhang G, Sandhaus RA. Trends in the diagnosis of symptomatic patients with α1-antitrypsin deficiency between 1968 and 2003. Chest. 2005;128(3):1179-86.
8. Stoller JK, Brantly M. The challenge of detecting alpha-1 antitrypsin deficiency. COPD: J Chr Obstruct Pulm Dis. 2013;10(sup1):26-34.
9. Lieberman J, Winter B, Sastre A. Alpha1-antitrypsin Pi-types in 965 COPD patients. Chest. 1986;89(3):370-3.
10. Menga G, Acquier MF, Echazarreta AL, Sorroche PB, Lorenzon MV, Fernández ME, et al. Prevalence of alpha-1 antitrypsin deficiency in COPD patients in Argentina. The DAAT. AR Study. Arch Bronconeumol. 2020;56(9):571-7.
11. Stoller JK, Aboussouan LS. Alpha1-antitrypsin deficiency. Lancet (London, England). 2005;365(9478):2225-36.
12. Boulyjenkov V. α1-Antitrypsin deficiency: Memorandum from a WHO meeting. Bull. World Health Organ. 1997;75:397-415.
13. Rahaghi F, Ortega I, Rahaghi N, Oliveira E, Ramirez J, Smolley L, et al. Physician alert suggesting alpha-1 antitrypsin deficiency testing in pulmonary function test (PFT) results. COPD: J Chr Obstruct Pulm Dis. 2009;6(1):26-30.
14. Decramer M, Veslbo J, Bourbeau J, Celli B, Lopez Varela MV. Global initiative for chronic obstructive lung disease. Update 2014. Am J Respir Crit Care Med. 2012;186:975-81.
15. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general US population. Am J Respirat Crit Care Medi. 1999;159(1):179-87.
16. Martinez-González C, Blanco I, Diego I, Bueno P, Miravitlles M. Estimated prevalence and number of PiMZ genotypes of Alpha-1 antitrypsin in seventy-four Countries Worldwide. Int J Chr Obstruct Pulm Dis. 2021:2617-30.
17. Strnad P, McElvaney NG, Lomas DA. Alpha1-antitrypsin deficiency. N En J Medi. 2020;382(15):1443-55.

18. Dahl M, Tybjærg-Hansen A, Lange P, Vestbo J, Nordestgaard BG. Change in lung function and morbidity from chronic obstructive pulmonary disease in α1-antitrypsin MZ heterozygotes: a longitudinal study of the general population. Annals Int Medi. 2002;136(4):270-9.
19. Greulich T, Vogelmeier CF. Alpha-1-antitrypsin deficiency: increasing awareness and improving diagnosis. Therap Advan Respirat Dis. 2016;10(1):72-84.
20. Russo R, Zillmer LR, Nascimento OA, Manzano B, Ivanaga IT, Fritscher L, et al. Prevalence of alpha-1 antitrypsin deficiency and allele frequency in patients with COPD in Brazil. J Brasil Pneumol. 2016;42(05):311-6.
21. Alí-Munive A, Leidy P, Proaños NJ, Pedrozo-Pupo J, Giraldo A, Cano D, et al. Prevalence of genetic mutations in alpha-1 antitrypsin deficiency (aatd) in patients with chronic obstructive pulmonary disease in Colombia. BMC Pulm Medi. 2023;23(1):156.
22. Barrecheguren M, Monteagudo M, Simonet P, Llor C, Rodriguez E, Ferrer J, et al. Diagnosis of alpha-1 antitrypsin deficiency: a population-based study. Int J Chr Obstruct Pulmon Dis. 201:999-1004.
23. Topic A, Stankovic M, Divac-Rankov A, Petrovic-Stanojevic N, Mitic-Milikic M, Nagorni-Obradovic L, et al. Alpha-1-antitrypsin deficiency in Serbian adults with lung diseases. Genet Test Mole Biomark. 2012;16(11):1282-6.
24. Serapinus D, Nutautiene R, Pukinskaite R, Bartkeviciene D, Barkauskiene D, Sakalauskas R. Association of alpha-1 antitrypsin level and lung function in patients with chronic obstructive pulmonary disease. Serbi Arch Medi. 2017;145(11-12):580-3.

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