SCIENTIFIC JOURNAL
CEREM-GO

DOI 10.37951/2675-5009.2025v5i15.162
ISSN 2675-5009
e25162
SCIENTIFIC ARTICLE - CASE REPORT

CONDUCTING GENETIC TESTING FOR ALPHA-1 ANTITRYPSIN DEFICIENCY IN SUS PATIENTS WITH COPD: AN EXPERIENCE REPORT

MARÍLIA GABRIELLA MENDES MARANHÃO[1], ANA PATRÍCIA MIRANDA DE SOUSA[1], ALINE LUIZA RIBEIRO[1], STANLEY JAMES FANSTONE PINA[1]

1. Universidade Evangélica de Goiás-Unievangélica, Anápolis-GO, Brazil.

ABSTRACT

Introduction: Alpha-1 antitrypsin (AAT) is a glycoprotein primarily synthesized by hepatocytes, acting as an inhibitor of neutrophilic elastase and protecting lung tissue from degradation. Alpha-1 antitrypsin deficiency (AATD) is a hereditary disorder transmitted in an autosomal codominant manner and associated with the SERPINA1 gene. This condition is strongly linked to the development and progression of Chronic Obstructive Pulmonary Disease (COPD), leading the WHO to recommend screening for AATD in all diagnosed patients. In Brazil, due to genetic admixture, the prevalence of AATD in COPD patients is similar to that observed in other countries. **Experience Report:** The study was conducted during the event "Saúde na Praça" in Goiânia on November 20, 2024, with genetic testing performed on patients with COPD diagnosed by spirometry. Smokers, former smokers, and non-smokers were included. Sample collection was performed using an oral swab (saliva), and the samples were sent for complete sequencing of the SERPINA1 gene. Patients provided contact information, and the results will be available within 90 days. The initiative also included medical guidance on AATD and its implications, highlighting that 90% of participants were unaware of the condition. **Final Considerations:** The genetic identification of AATD in COPD patients provides a new therapeutic approach, including AAT replacement therapy and preventive counseling for family members. Such initiatives promote education, innovation, and improvements in quality of life, while potentially reducing healthcare costs by preventing COPD complications.

Keywords: Alpha-1-antitrypsin (AAT), Alpha-1-antitrypsin deficiency, Chronic obstructive pulmonary disease (COPD), Genetic test, Genetic testing, COPD.

INTRODUCTION

Placenta Alpha-1-antitrypsin (AAT) is a glycoprotein primarily synthesized by hepatocytes (≥80%) and is also found in other sites such as the lungs, kidneys, and intestines. AAT is encoded by the SERPINA1 gene, located on the long arm of chromosome 14 (14q32.1).[1-4] It is also known as protease inhibitor (Pi), actively inhibiting neutrophil elastase, trypsin, and proteinase-3, thereby protecting

lung tissue from excessive proteolytic degradation of elastin as well as from external injuries, such as exposure to tobacco smoke.

Although AAT deficiency is a rare disorder, it is the most common hereditary disorder in adults, caused by a mutation in the SERPINA1 gene. This condition is inherited in a simple Mendelian manner, following an autosomal codominant pattern, with one allele inherited from each parent[5]. There are approximately 125 known variants of this gene, classified as normal, deficient, null, and dysfunctional.

The normal genotype Pi*MM is present in approximately 80–95% of the population and expresses 100% of serum AAT. The five main deficient genotypes (PiMS, PiSS, PiMZ, PiSZ, and Pi*ZZ) are found in the remaining 5–20% of the population and express 80%, 60%, 55%, 40%, and 15% of serum AAT, respectively.[2,3,5]

The strong relationship between COPD and AAT deficiency led the WHO to issue a 1999 recommendation advising that AATD screening be performed at least once in all patients diagnosed with COPD.[6]

Epidemiologically, AATD has a higher prevalence among Caucasians of European descent.[1,3] However, given the high rate of European immigration to Brazil and the resulting genetic admixture, a cross-sectional study conducted between 2011 and 2012—which gathered data from the five main centers across different regions of Brazil—found that the prevalence of AAT deficiency in COPD patients was similar to that observed in most other countries.[3]

In light of the above, through private initiative, genetic testing kits were donated for the detection of potential COPD patients who may not have received a diagnosis of AAT deficiency. These kits are designed for oral swab (saliva) testing.

Upon identifying patients with deficient genotypes, the possibility of treatment with augmentation therapy is considered, involving intravenous administration of alpha-1 proteinase inhibitor derived from human plasma. This approach also extends to providing genetic counseling for close family members.

The main objective of this report is to highlight the correlation between the development and progression of COPD and AAT deficiency.

The purpose of conducting genetic testing will be to create a database that will allow the identification of patients' genotypes, distinguishing them according to the degrees of AAT deficiency (from moderate to severe) and providing them with appropriate treatment based on their conditions.

In the future, it is anticipated that there will be a reduction in the number of hospitalizations due to exacerbations in this population of patients who have not only COPD but also AATD, leading to reduced healthcare costs and allowing for an improved quality of life.[7]

EXPERIENCE REPORT

The experience report took place at the event titled "Saúde na Praça," which occurred on November 20, 2024, in the city of Goiânia, GO. This event enabled the collection of material for conducting genetic tests to research AATD in COPD patients.

Patients with a documented COPD diagnosis through spirometry were selected. There were no limitations regarding age or diagnosis duration. The group included both current smokers, former smokers, and patients who had never been exposed to tobacco.

Genetic testing was conducted through saliva sample collection (oral swab) using appropriate

kits for storage. The samples were properly allocated and sent to a laboratory center. The complete sequencing of the SERPINA1 gene will be performed, and results are expected to be available within an estimated timeframe of up to 90 days from the date of submission. For the genetic test, patients with a COPD diagnosis based on spirometry were selected, without prior knowledge regarding the coexistence of AAT deficiency.

The patients who underwent the test filled out a form with personal data, including at least two phone numbers, physical address, and email address. The results obtained will later be made available to the medical team through a login and password.

On the same day, outpatient follow-ups were scheduled to allow for the delivery of the results.

The action carried out on the day of the sample collection involved not only the collection of samples by the attending resident doctors, but also provided an opportunity to offer guidance to patients regarding the potential outcomes.

Approximately 90% of the patients present were unaware of AAT deficiency and were able to receive updates during the action.

Future results will expand treatment options for the COPD population, as well as provide opportunities for genetic and behavioral counseling.

DISCUSSION

The initiative to conduct genetic testing for AAT deficiency screening in COPD patients is commendable, especially considering the strong correlation and coexistence of the two conditions. AAT deficiency has a high rate of underdiagnosis, primarily due to the underestimation of the previously known epidemiology. However, when considering Brazil as a country with high genetic admixture, studies have observed epidemiological rates similar to those found in European countries[3].

Knowing patients across a spectrum, in order to map them genetically, allows for the identification of the correct diagnosis. Additionally, it enables the extension of care to family members through genetic counseling and guidance aimed at minimizing exposure.

Treatment with exogenous AAT replacement (via injection) is a viable option for the population with AAT deficiency, as it impacts the progression of the disease[2,4,8].

Access to medication therapy is still limited by high costs. However, we have seen patients who acquired the treatment through legal channels, in collaboration with the Public Prosecutor's Office, with satisfactory results in preventing the progression of COPD.

FINAL CONSIDERATIONS

Placental COPD is a progressive disease, widely known for its complications and impact on the life of the affected patient[7]. With the advent of technological advancements that expanded diagnostic and investigative methods, it was observed that many COPD patients also had AAT deficiency, although this was diagnosed late.

With the detection and genetic mapping of this population, new possibilities in the care pathway can be accessed, thereby implementing injectable replacement therapy to slow the progression of the disease and also provide genetic counseling to family members. This action, in addition to being educational and innovative, represents an important step in combating the progression of COPD.

REFERENCES

1. Vidal R, Blanco I, Casas F, Jardí R, Miravitlles M, Committee on the National Registry of Individuals with Alpha-1 Antitrypsin Deficiency. Guidelines for the diagnosis and management of alpha-1 antitrypsindeficiency. Arch Bronconeumol. 2006 Dec;42(12):645-59.

2. Jardim JR, Casas-Maldonado F, Fernandes FLA, Castellano MVCO, Torres-Durán M, Miravitlles M. Update on and future perspectives for the diagnosis of alpha-1 antitrypsin deficiency in Brazil. J Bras Pneumol. 2021 May 31;47(3):e20200380.

3. Russo R, Zillmer LR, Nascimento OA, Manzano B, Ivanaga IT. Fritscher L, Lundgren F, Miravitlles M, Gondim HD, Santos G Junior, Alves MA, Oliveira MV, Souza AA, Sales MP, Jardim JR. Prevalence of alpha-1 antitrypsin deficiency and allele frequency in patients with COPD in Brazil. J Bras Pneumol. 2016 Sep-Oct;42(5):311-6.

4. Miravitlles M, Dirksen A, Ferrarotti I, Koblizek V, Lange P, Mahadeva R, McElvaney NG, Parr D, Piitulainen E, Roche N, Stolk J, Thabut G, Turner A, Vogelmeier C, Stockley RA. European Respiratory Society statement:diagnosis and treatment of pulmonary disease in α1-antitrypsin deficiency. Eur Respir J 2017 Nov 30;50(5):1700610.

5. Stoller JK, Aboussouan LS. A review of α1-antitrypsin deficiency. Am J Respir Crit Care Med. 2012 Feb 1;185(3):246-59.

6. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, Bourbeau J, Han MK, Martinez FJ, Montes de Oca M, Mortimer K, Papi A, Pavord I, Roche N, Salvi S, Sin DD, Singh D, Stockley R, López Varela MV, Wedzicha JA, Vogelmeier CF. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. Eur Respir J. 2023 Apr 1;61(4):2300239. doi: 10.1183/13993003.00239-2023. PMID: 36858443; PMCID: PMC10066569.

7. Scabello RT, Camelier A, Russo ER, Melo TG. Potencial impacto na redução do número e nos custos de internações hospitalares em pacientes portadores de doença Pulmonar Obstrutiva Crônica (DPOC) por uma empresa privada no Brasil. JAFF. 2023 Feb 1;4(Suppl 1):105.

8. Nascimento LF, Rabahi MF, Souza MV, Kozlowsky I, Farjun B, Fidalgo A. Custos sociais da DPOC: o impacto sobre os anos de vida saudável e a perda de produtividade no Brasil entre os anos de 2017 e 2022. JBES. 2024 Oct 2;16(2):87-9.

MAILING ADDRESS

MARÍLIA GABRIELLA MENDES MARANHÃO
Av. Universitária, s/n - Cidade Universitária, Anápolis - GO - Brasil.
E-mail: mariliagabriellamaranhao@gmail.com

EDITORIAL AND REVIEW

Chief editors:

Waldemar Naves do Amaral - http://lattes.cnpq.br/4092560599116579 - https://orcid.org/0000-0002-0824-1138
Tárik Kassem Saidah - http://lattes.cnpq.br/7930409410650712- https://orcid.org/0000-0003-3267-9866

Authors:

Marília Gabriella Mendes Maranhão - http://lattes.cnpq.br/5077038938163938 - https://orcid.org/0009-0004-5327-4790

Ana Patrícia Miranda de Sousa - http://lattes.cnpq.br/5841207167310018 - https://orcid.org/0009-0002-5602-0572

Aline Luiza Ribeiro - http://lattes.cnpq.br/5042243947788315 - https://orcid.org/0009-0005-1111-4542

Stanley James Fanstone Pina - http://lattes.cnpq.br/2167831340046858 - https://orcid.org/0009.0009.3867.6632

Library Review: Romulo Arantes/ Izabella Goulart
Spell Check: Dario Alvares
Received: 16/12/24. Accepted: 18/02/25. Published in: 28/02/2025.