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EDITORIAL

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Toward Precision Medicine in Asthma: Perspectives From Real-World Clinical Practice in Córdoba

Hacia una medicina de precisión en el asma: Perspectivas desde la práctica clínica real en Córdoba

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Asthma remains a major public health challenge, affecting approximately 300 million people worldwide, and with a prevalence of 8% to 12% in Argentina. However, the management of this disease has undergone a paradigm shift with growing **insight into phenotypes and inflammatory mechanisms**. (1-3) The study by Echegaray and colleagues at Hospital Italiano de Córdoba, a descriptive, cross-sectional observational study, adds an essential piece to the local epidemiologic puzzle by integrating clinical, functional, immunologic, and adherence variables, for the first time in the region.

One of the most notable findings of this research is the **substantial burden of severe asthma (36.4%) and T2 inflammation** in the analyzed cohort. With 34% of patients showing elevated eosinophilia (≥ 300 cells/µL) and 61% having total serum IgE levels ≥ 150 IU/mL, these biomarkers help identify candidates for **targeted biologic therapies**, which only 10% of patients at this center were receiving, mainly mepolizumab and omalizumab.

The 78% prevalence of overweight and obesity is a warning signal, linking asthma to a more complex phenotype and a reduced response to corticosteroids. Likewise, the finding that only 53% of patients achieved optimal clinical control (ACT ≥ 20) and that 57% maintained good adherence (TAI) reminds us that the gap between clinical guidelines and everyday practice remains considerable. (1)

In a disease in which inhaler technique is critical to treatment efficacy, the observation that dry powder inhalers (DPIs) accounted for 57.5% of devices, compared with 38.1% for pressurized metered-dose inhalers (pMDIs) underscores the importance of personalizing treatment in all its dimensions. (2)

In conclusion, the work by Echegaray and colleagues highlights the fact that success in asthma management in tertiary care centers depends on three essential pillars: **biomarker-based stratification, systematic assessment of control and adherence, and education in the use of devices**. It also lays the foundation for future research on the obesity-asthma phenotype and interventions to improve adherence, among others. Finally, the transition to **multicenter studies** will provide a more representative view of asthma epidemiology in Argentina and will allow longitudinal follow-up of the real-world impact of **biologic therapies** in our patients. (1)

Conflict of interest

Author has no conflicts of interest to declare.

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ORIGINAL ARTICLE

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Biomarkers and Asthma Treatment: Experience at the Hospital Italiano de Córdoba

Biomarcadores y tratamiento del asma: Experiencia en el Hospital Italiano de Córdoba

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ABSTRACT

Objective: To describe the clinical, inflammatory, functional, and therapeutic characteristics of asthma patients treated at a tertiary care center in Córdoba, Argentina.

Materials and methods: Observational, descriptive, cross-sectional study including 350 adult patients with a confirmed diagnosis of asthma according to the Spanish Guidelines for Asthma Management (GEMA 5.4) and Global Initiative for Asthma 2025 report (GINA). Sociodemographic variables, body mass index, smoking status, inflammatory biomarkers (peripheral blood eosinophils and total serum immunoglobulin E), clinical control assessed by a validated asthma control test, treatment adherence assessed by a validated inhaler-adherence questionnaire, lung function, and treatment characteristics, including inhaler devices and biologic therapies, were analyzed.

Results: Seventy-six percent of patients were women, with a predominance of individuals older than 60 years. Seventy-eight percent were overweight or obese and 36.4 % were classified as severe asthma. Eosinophil counts were elevated (≥300 cells/µL) in 38.7 % of patients, and total serum immunoglobulin E levels were elevated (≥150 IU/mL) in 39.9 %. Asthma was well controlled in 71.1 % of patients, and treatment adherence was good in 71.2 %. An obstructive pattern was observed in 29.1 % of patients. Ten percent were receiving biologic therapies, mainly omalizumab and mepolizumab.

Conclusions: This population shows a high burden of type 2 inflammation, a significant prevalence of severe asthma, and suboptimal disease control. The integration of inflammatory biomarkers, structured clinical assessment, and appropriate inhaler device selection is essential to optimize therapeutic strategies, particularly in candidates for targeted biologic therapies.

Key words: asthma | biomarkers | biologic therapy | asthma control | inhalation devices

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RESUMEN

Objetivo: Describir las características clínicas, inflamatorias, funcionales y terapéuticas de pacientes con asma atendidos en un centro de alta complejidad de la ciudad de Córdoba, Argentina.

Materiales y métodos: Estudio observacional, descriptivo y transversal que incluyó 350 pacientes adultos con diagnóstico de asma según guías GEMA 5.4 y GINA 2025. Se analizaron variables sociodemográficas, índice de masa corporal, tabaquismo, biomarcadores inflamatorios (eosinófilos en sangre periférica e inmunoglobulina E sérica total), control clínico mediante una prueba validada de control del asma, adherencia al tratamiento mediante un cuestionario validado de adherencia al tratamiento inhalatorio, función pulmonar y tipo de tratamiento recibido, incluidos los dispositivos inhalatorios y terapias biológicas.

Resultados: El 76 % de los pacientes fueron mujeres, con predominio del grupo mayor de 60 años. El 78 % presentó sobrepeso u obesidad y el 36,4 % fue clasificado como asma severa. El 38,7 % presentó eosinofilia elevada (≥300 células/µL) y el 39,9 % inmunoglobulina E sérica total elevada (≥150 UI/mL). El 71,1 % mostró buen control clínico y el 71,2 % buena adherencia al tratamiento. El 29,1 % presentó patrón obstructivo en la espirometría. El 10 % recibía terapias biológicas, principalmente mepolizumab y omalizumab.

Conclusiones: La población asmática evaluada presenta alta carga de inflamación tipo 2, elevada prevalencia de asma severa y control subóptimo. La integración de biomarcadores inflamatorios, evaluación clínica sistematizada y selección adecuada de dispositivos inhalatorios resulta clave para optimizar el abordaje terapéutico, especialmente en candidatos a terapias biológicas dirigidas.

Palabras clave: asma · biomarcadores · terapia biológica · control del asma · dispositivos de inhalación

INTRODUCTION

Asthma is a heterogeneous, chronic respiratory disease affecting approximately 300 million individuals worldwide. It remains a major public health challenge due to its substantial morbidity, detrimental impact on quality of life, and associated healthcare costs.[1,5] In Argentina, the estimated prevalence ranges from 8% to 12%, with regional, age-related, and environmental variations.[2,3]

Over the past few decades, our understanding of asthma has evolved from a broad clinical construct toward a more refined characterization of its endotypes and underlying pathophysiological mechanisms, particularly those linked to type 2 inflammation. In this context, biomarkers such as peripheral blood eosinophil counts and total serum immunoglobulin E levels have assumed a central role in patient phenotyping and therapeutic decision-making, especially regarding the selection of targeted biologic therapies.[5,6]

Current asthma management also requires the integration of objective tools to assess disease control and treatment adherence. Validated instruments, including the Asthma Control Test and the Test of Adherence to Inhalers, facilitate systematic evaluation in clinical practice and may contribute to improved risk stratification and treatment optimization.[7,8]

Despite advances in the understanding and treatment of asthma, a gap remains between evidence derived from population-based studies and clinical trials and the reality of routine clinical practice. In particular, integrated local data encompassing clinical characteristics, inflammatory biomarkers, disease control, treatment adherence, type of treatment, and inhaler device use remain limited in our setting. This lack of information hinders the adaptation of therapeutic strategies to the specific characteristics of patients managed at tertiary care centers.

Hospital Italiano de Córdoba is a referral center for respiratory diseases in central Argentina, managing a significant number of patients with asthma. However, no systematic data are available to comprehensively characterize this population from clinical, functional, and immunologic perspectives.

Therefore, the objective of this study was to describe the clinical, inflammatory, functional, and therapeutic characteristics of patients with asthma treated at the Hospital Italiano de Córdoba. Secondary objectives included characterization of sociodemographic and anthropometric profiles, assessment of inflammatory biomarkers, evaluation of asthma control and treatment adherence, and description of therapeutic strategies, including inhaler devices and biologic therapies. To provide local evidence that optimizes diagnostic and therapeutic approaches in real-world clinical practice.

MATERIALS AND METHODS

Study design

Retrospective, cross-sectional, observational study based on the review of electronic medical records of patients with a diagnosis of asthma treated at the Hospital Italiano de Córdoba.

Study population

The study included 350 adults (aged ≥ 18 years) with asthma diagnosed according to the GEMA 5.4 and GINA 2025 criteria.1,2 Patients were evaluated in the outpatient setting or during hospitalization between July 1, 2024, and July 1, 2025. The Hospital Italiano de Córdoba records approximately 12,000 respiratory consultations annually, of which 40% correspond to patients with asthma (approximately 4,800 patients/year). The 350 included patients met the criteria for a confirmed diagnosis of asthma and had complete data for the primary study variables at the time of review, representing 7.3% of the total population of patients with asthma treated during that period. Data were obtained retrospectively from the institutional electronic medical record using a standardized data extraction form. No additional exclusion criteria were applied. All patients meeting diagnostic criteria and with complete documentation of the variables of interest were included in the analysis.

Variables and definitions

The following variables were analyzed: sociodemographic characteristics (age and sex), anthropometric measures (body mass index [BMI], with obesity defined as BMI ≥ 30 kg/m^2), smoking status, and age at asthma diagnosis (childhood, < 18 years; adulthood, ≥ 18 years). Asthma control was assessed using the Asthma Control Test (ACT), a validated instrument with the following cut-off points: well-controlled asthma (score ≥ 20), partially controlled asthma (score 16-19), and poorly controlled asthma (score ≤ 15). Adherence to inhaled therapy was evaluated using the Test of Adherence to Inhalers (TAI). The TAI identifies patients with poor adherence, classifies adherence as good, intermediate, or poor, and characterizes patterns of non-adherence as erratic (items 1-5), deliberate (items 6-10), or unwitting (items 11-12). The instrument comprises a 10-item patient-completed questionnaire and a complementary 12-item version completed by both the patient and the healthcare professional. Asthma severity was classified based on the intensity of the required treatment following the GINA 2025 and GEMA 5.4 treatment steps. Mild asthma was defined as control achieved at steps 1 to 2 (low-dose inhaled corticosteroid [ICS], with or without as-needed formoterol, equivalent to budesonide 200–400 µg/day); moderate asthma corresponded to step 3 requirements (medium-dose ICS-LABA [long-acting beta-2 adrenergic bronchodilators], equivalent to budesonide 400–800 µg/day, or low-dose ICS combined with an LTRA [leukotriene receptor antagonists] or occasional LAMA [long-acting muscarinic antagonists]); and severe asthma was defined requiring steps 4 to 5 (high-dose ICS-LABA, equivalent to budesonide > 800 µg/day, with the addition of tiotropium or prescription biologics, including omalizumab, mepolizumab, or dupilumab). Inflammatory biomarkers included peripheral blood eosinophil counts (percentage and cells/mm^3) and total serum immunoglobulin E (IgE) levels (IU/mL). Pulmonary function was assessed by spirometry and categorized as normal, obstructive, or suggestive of a restrictive pattern according to the 2019 standards of the American Thoracic Society/European Respiratory Society (ATS/ERS). Treatment-related variables included type of drug, daily inhaled corticosteroid dose (µg/day), inhaler device type, and use of biologic therapies.

Statistical analysis

A descriptive and statistical analysis was performed. Quantitative variables were presented as mean and standard deviation or median and interquartile range as appropriate according to data distribution. Categorical variables were expressed as absolute and percentage frequencies.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki (2024 review), Good Clinical Practice guidelines of the National Administration of Drugs, Food, and Medical Devices (ANMAT), Provincial Law No. 9694, and National Law No. 25.326 on personal data protection. Given its retrospective observational design, the study was considered to involve minimal risk, according to the World Health Organization (WHO) classification. Investigators have no conflicts of interest to declare.

RESULTS

Sociodemographic characteristics

A total of 350 adult patients with a confirmed diagnosis of asthma according to GEMA 5.4 and GINA 2025 criteria were included in the analysis.[1,2] Women accounted for 76% of the cohort, whereas men represented 24% (Figure 1). Regarding age distribution, the predominant group was patients older than 60 years, followed by those aged 40 to 59 years (Figure 2). A total of 32.7% of participants reported a childhood diagnosis of asthma (< 18 years of age), whereas 67.3% were diagnosed during adulthood (Figure 3).

Body composition and smoking status

Based on body mass index (BMI), 47% of patients had normal weight (BMI, 18.5-24.9), 47% were overweight (BMI, 25.0-29.9), and 31% had obesity (BMI ≥ 30.0), resulting in a combined prevalence of excess weight of 78% (Figure 4). Regarding smoking status, 70.9% of the cohort had never smoked, 23.6% were former smokers, and 5.4% were current smokers (Figure 5).

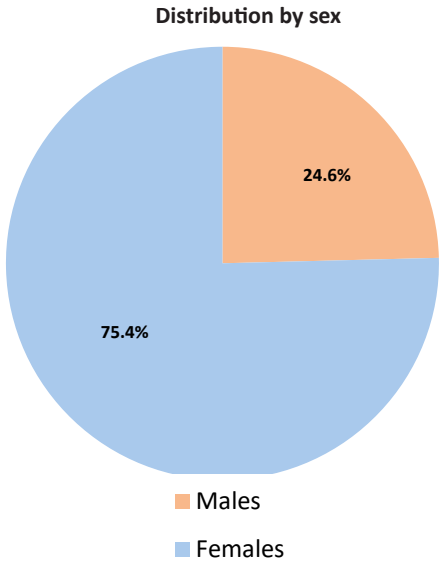
Asthma control and treatment adherence

Asthma control, assessed using the ACT, was classified as well controlled (ACT score ≥ 20) in 71.1% of patients, partially controlled (ACT score 16 -19) in 22,3%, and poorly controlled (ACT score ≤ 15) in 6,6% (Figure 6). Adherence to inhaled therapy, evaluated using the TAI, was classified as good in 71.2% of patients, intermediate in 28.8%, and poor in 0.6% (Figure 7).

Asthma severity classification

Asthma severity was classified according to treatment intensity, following the therapeutic steps outlined in GINA 2025 and GEMA 5.4, and taking into account ICS dose, use of LAMAs, and prescription of biologic therapies. 27.3% of patients were classified as having mild asthma, 36.4% as moderate asthma, and 36.4% as severe asthma (Figure 8).

Figure 1. Distribution by sex in the studied population.



Inflammatory biomarkers

Peripheral blood eosinophil counts were elevated (≥ 300 cells/µL) in 38,7% of patients, intermediate (150–299 cells/µL) in 32.2%, and low (< 150 cells/µL) in 29.1% (Figure 9). Total serum IgE levels were elevated (≥ 150 IU/mL) in 39.9% of patients (Figure 10). When analyzing the relationship between disease severity and biomarkers, an increasing trend was observed in mean eosinophil and IgE levels as severity categories advanced; with the highest values for both variables observed in patients with severe asthma (Figure 16).

Pulmonary function

Spirometric analysis demonstrated an obstructive pattern in 54% of patients, normal spirometry in 29.1%, and a pattern suggestive of restriction in 16.9% (Figure 11). Spirometric patterns were classified according to the 2019 guidelines of the ATS/ERS.

Pharmacologic treatment and inhaler devices

The most frequently used combinations were fluticasone/salmeterol (36.2%) and budesonide/

Figura 2. Distribution by age group.

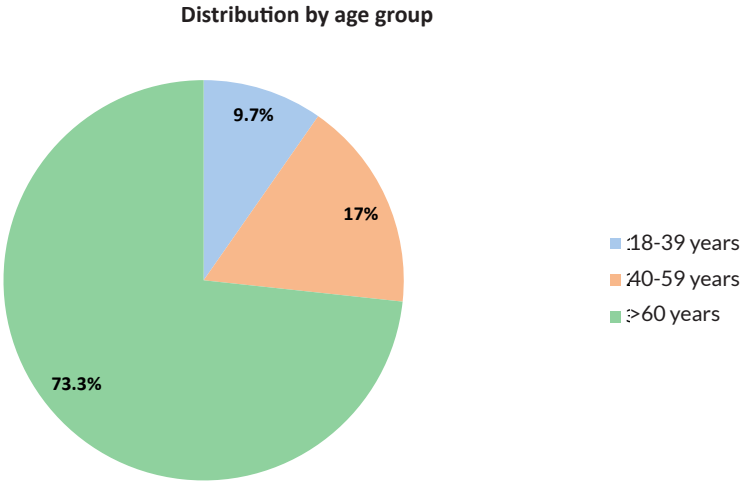
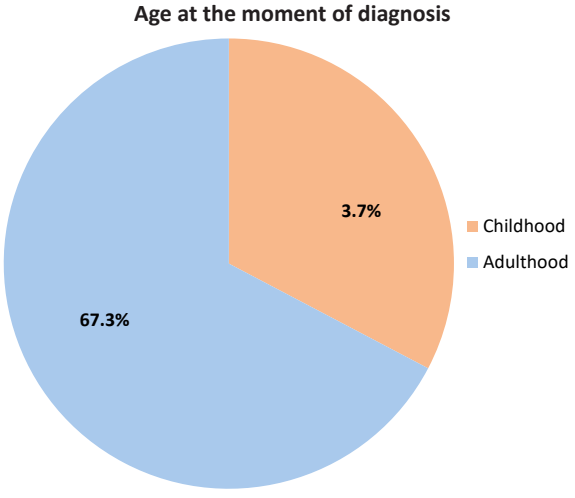


Figure 3. Age at the moment of diagnosis



formoterol (41.6%), followed by fluticasone furoate/vilanterol, fluticasone furoate/vilanterol/umeclidinium, and tiotropium bromide combinations (Figure 12). Regarding the type of inhaler device, pressurized metered-dose inhalers (pMDIs) were the most commonly used (38.1%). Dry powder inhalers (DPIs) accounted for 57.5% of all devices and included capsule-based devices (26.2%), Diskus (17.6%), Ellipta (8.8%), and Turbuhaler (4.9%) (Figure 13).

With respect to daily ICS dosing, 29.2% of patients received low-dose therapy, 40.4% medium-dose therapy, and 30.4% high-dose therapy, according to GEMA-defined dose ranges for budesonide, fluticasone propionate, and fluticasone furoate (Figure 14).

Biologic therapies

At the time of evaluation, 10% of patients were receiving biologic therapy. The most frequently prescribed biologics were mepolizumab and omalizumab, followed by dupilumab at a lower frequency. The remaining 90% were not receiving biologic therapy (Figure 15).

Asthma severity according to BMI category

When asthma severity was analyzed according to BMI category, it was observed that 40.3% of patients with normal weight had mild asthma, 37.7% had moderate asthma, and 19.5% had severe asthma. Among patients with overweight, the proportion of severe asthma increased to 40.6%, whereas the cases of mild asthma decreased to 23.6%. In patients with obesity, moderate (41.3%) and severe asthma (34.9%) predominated, while only 18.3% had mild disease (Figure 17).

DISCUSSION

To our knowledge, this is the first study conducted in Córdoba to comprehensively evaluate asthma prevalence, inflammatory biomarkers, asthma control (ACT), treatment adherence (TAI), inhaler device use, and biologic therapy according to the GINA 2025 and GEMA 5.4 guidelines.[1,2] This multidimensional approach, based on real-world clinical data, not only expands local knowledge but

Figure 4. Classification of the Body Mass Index (BMI).

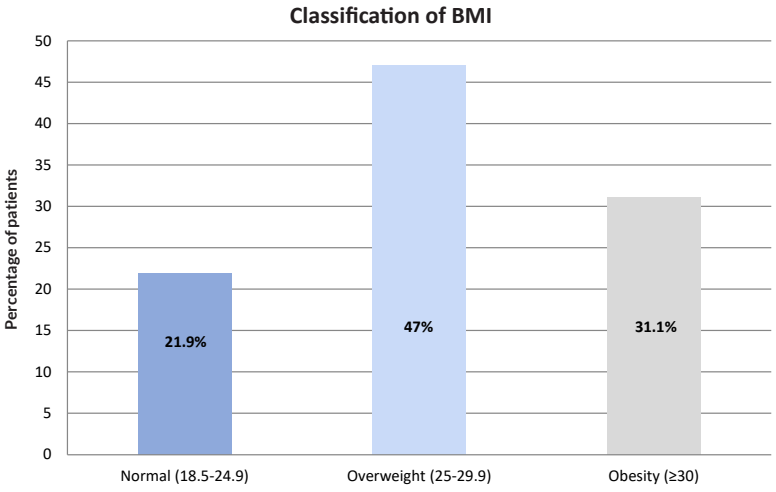


Figure 5. Classification by smoking status

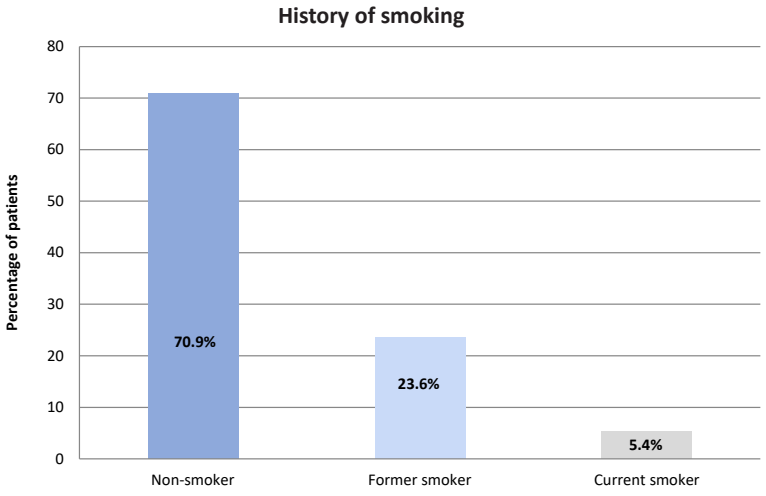


Figure 6. Asthma control level according to the ACT.

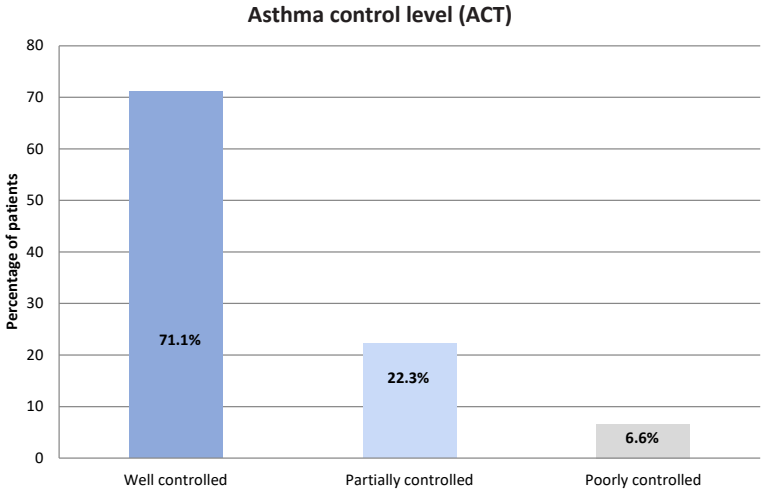


Figure 7. Level of adherence to inhalatory treatment (TAI).

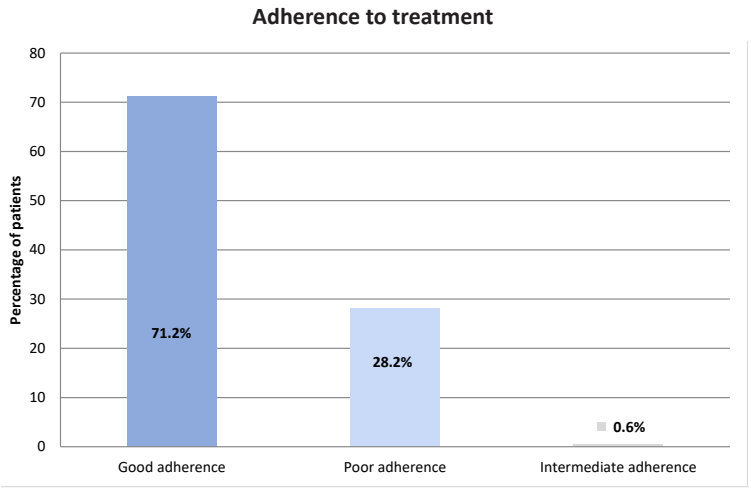


Figure 8. Classification of Asthma according to the therapeutic regimen (GINA/GEMA).

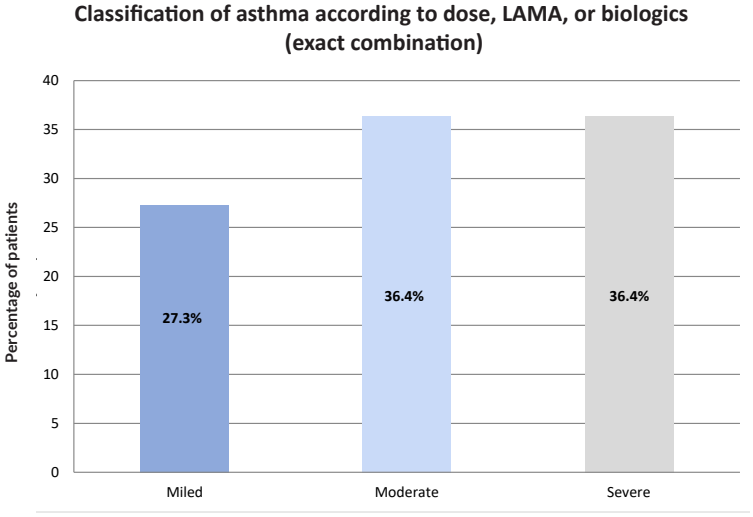


Figure 9. Eosinophil counts in peripheral blood.

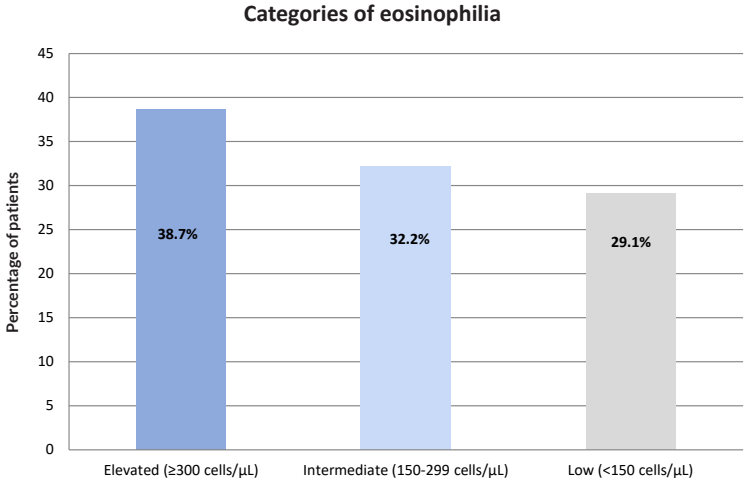


Figure 10. Distribution of total serum IgE levels.

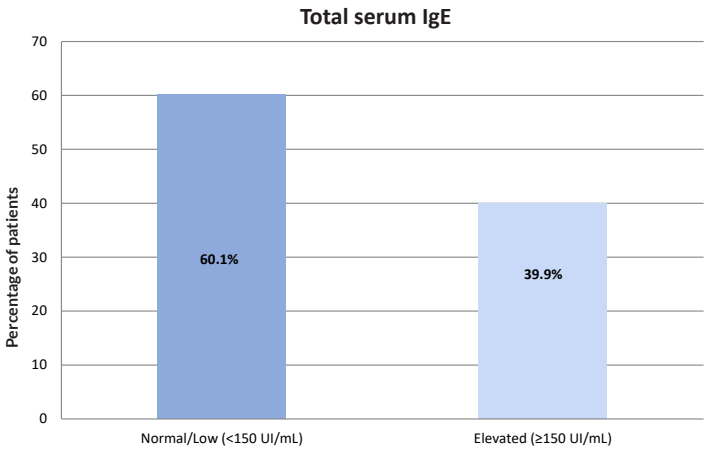


Figure 11. Spirometric pattern..

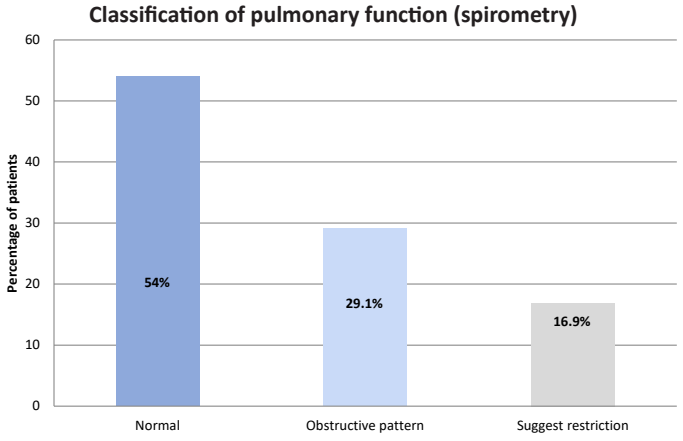


Figure 12. Treatment distribution according to pharmacologic combination.

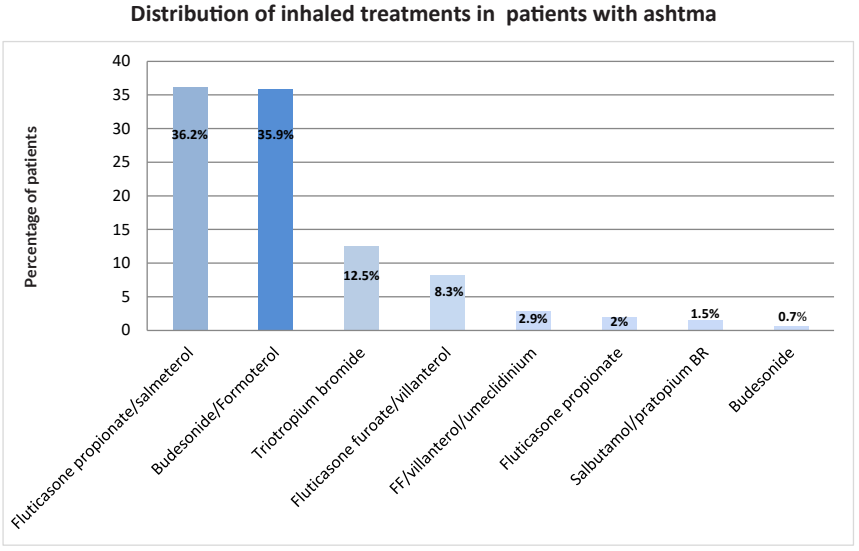


Figure 13. Type of inhaler used.

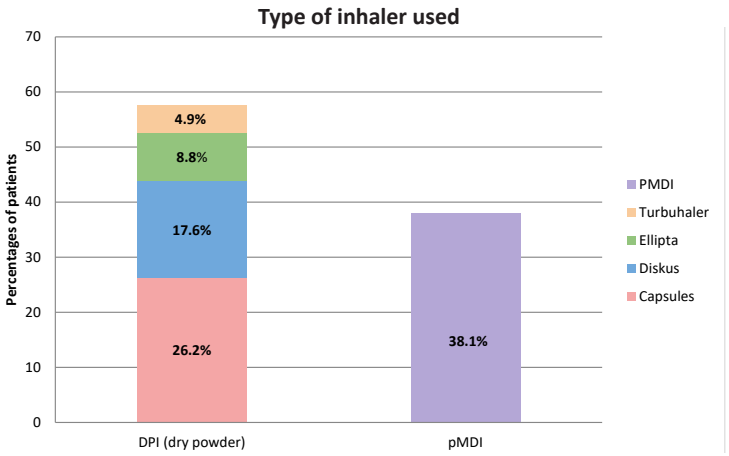


Figure 14. Classification of patients according to daily dose of inhaled corticosteroids.

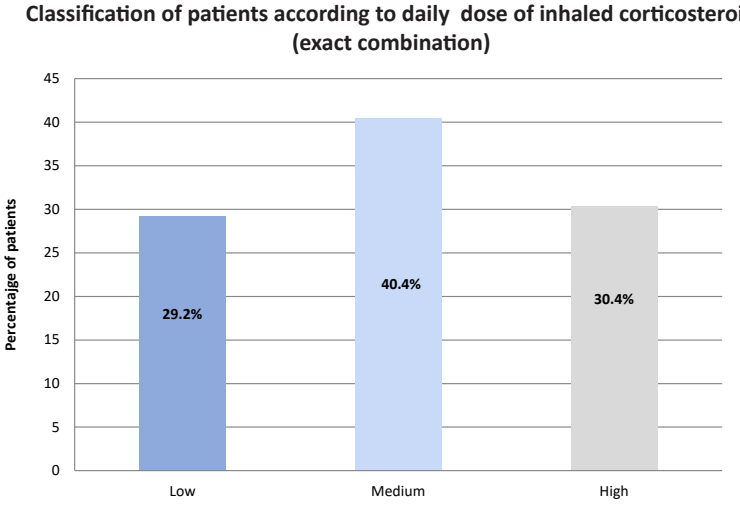


Figure 15. Use of biologic therapies.

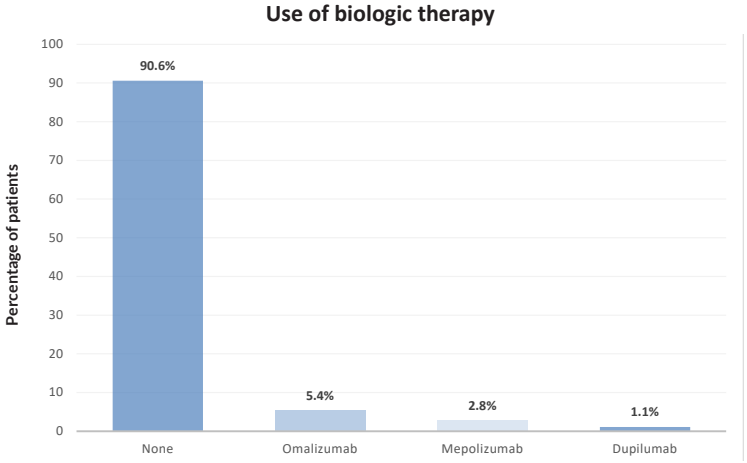


Figure 16. Relationship between asthma severity and inflammatory biomarkers.

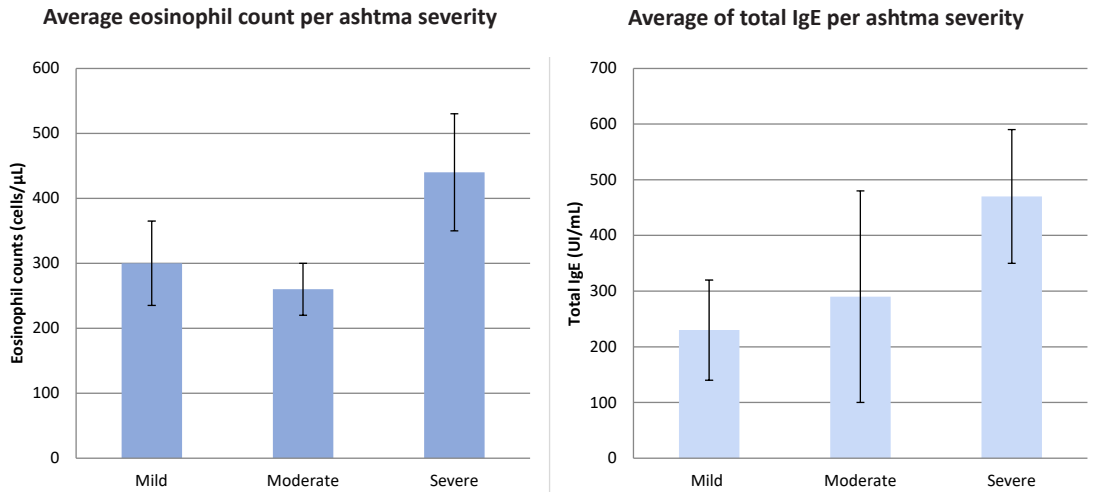
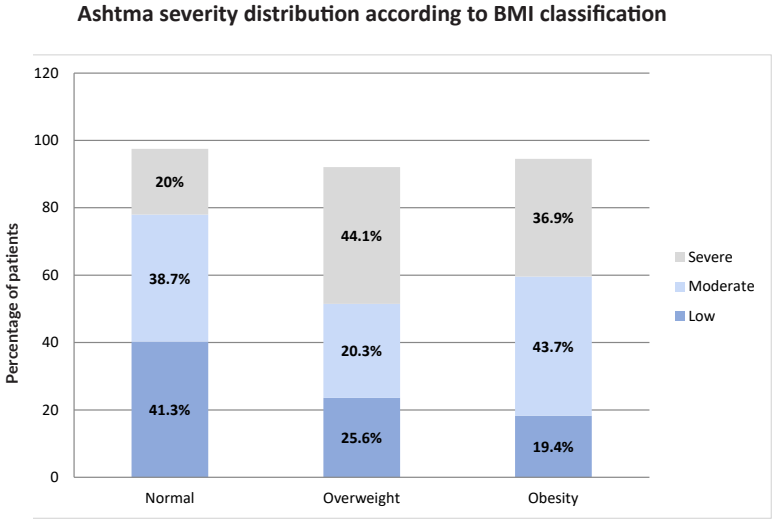


Figure 17. Asthma severity according to BMI classification.



also provides evidence that is comparable with international studies.

At the national level, the only comparable study is that conducted by Parisi et al at Hospital Italiano de Buenos Aires, 3 which reported a 6% prevalence (n = 66) in an adult population and focused primarily on general clinical variables. Although both studies share a cross-sectional design conducted in private healthcare institutions, our study differs in several important respects, including a larger sample size (n = 350), the incorporation of immunologic data (blood eosinophil count and total IgE levels), therapeutic severity classification, and the assessment of treatment adherence, asthma control, and biologic therapy use. In our cohort, 36.4% of patients were classified as having severe asthma, 34% had blood eosinophil counts > 300 cells/µL, and 61% had elevated total IgE levels, indicating a substantial burden of type 2 inflammation.[14]

These findings are consistent with international reports from Hong Kong and Lebanon,[6,7] which described a high prevalence of eosinophilic phenotypes and elevated IgE levels. The coexistence of these biomarkers has been recognized as a key determinant for selecting targeted biologic therapies. The similarity in

these patterns reinforces the concept of a shared global pathophysiology.

The comparison with the PREPARE study[4] conducted in Brazil, Peru, and Colombia also revealed similarities regarding the use of inhaled corticosteroids and the characterization of severe asthma. However, the prevalence of eosinophilia (≥ 300 cells/µL) in our cohort (38.7%) was slightly lower than previously reported, potentially reflecting regional differences in inflammatory profiles or prior exposure to systemic corticosteroids.

From a clinical point of view, the predominance of female patients (76%) is consistent with previous reports and may be related to hormonal and environmental factors. The high rate of overweight and obesity (78% with BMI ≥ 25) underscores the relevance of the asthma-obesity phenotype, which has been associated with poor asthma control and reduced responsiveness to inhaled steroids.[9] Only 53% of patients achieved well-controlled asthma (ACT score ≥ 20), a concerning finding that nevertheless agrees with international studies reporting optimal control rates ranging from 40% to 60%.[10] Intermediate or poor adherence (28.8%) was clearly associated with poorer asthma control, suggesting that educational and follow-up interventions could improve prognosis.

An additional strength of the present study is the inclusion of the specific inhaler device type used; an aspect that remains poorly explored in the domestic literature. Device selection –pMDI, DPI, Diskus, Ellipta, and Turbuhaler– is relevant because it directly influences inhaler technique, treatment adherence, and therapeutic efficacy. In this study, the pressurized metered-dose inhaler (pMDI) was the most commonly used (38.1%). Appropriate device selection tailored to patient characteristics, together with adequate inhaler education, remains essential for optimizing treatment outcomes.11

Overall, our findings support the integration of standardized tools such as the ACT and TAI, enabling systematic, reproducible, and internationally comparable assessment of asthma. The use of biomarkers and precise therapeutic criteria helps rationalize resource allocation, particularly for biologic therapies, thereby optimizing asthma management within demanding clinical settings.[12,13]

Study limitations

This study has several limitations. First, its retrospective, single-center design may limit the generalizability of the findings. Also, the absence of inferential analysis precludes the establishment of statistical associations among the evaluated variables. Nonetheless, our findings provide relevant insights into real-world clinical practice and establish a foundation for future analytical studies.

CONCLUSION

This study provides a comprehensive characterization of adults with asthma treated at a tertiary care center in Córdoba by integrating clinical, functional, and immunologic variables according to current international standards. The high prevalence of severe asthma, the frequent presence of type 2 inflammation, low control rates, and suboptimal adherence reinforce the need for a personalized, long-term management approach. In addition, including the type of inhaler device used and the use of biologic therapies provide information that has been underreported in the domestic literature. The data obtained are clinically useful and also help as a foundation to improve decision-making, optimize resources, and guide future research and healthcare planning at the regional level.

Conflict of interest

Authors have no conflict of interest to declare that are relevant to the content of this article.

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Author contributions

All authors reviewed and approved the final manuscript and made substantial contributions to the study.

Ethics approval, informed consent, and confidentiality

All procedures involving human participants conformed to the ethical standards of the institutional research committee, the World Medical Association Declaration of Helsinki (2024 revision) and its subsequent amendments, or comparable ethical standards.

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Alpha-1 Antitrypsin Deficiency: the Challenge of Reducing the Underdiagnosis

Déficit de alfa-1 antitripsina: El desafío de reducir el subdiagnóstico

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ABSTRACT

Introduction: Alpha-1 antitrypsin deficiency (AATD) is a hereditary genetic disorder characterized by a reduction in serum concentrations of this protein, predisposing affected individuals to a significantly increased risk of pulmonary and hepatic diseases. Despite being a well-recognized condition, AATD remains substantially underdiagnosed globally and regionally, largely because of low clinical suspicion.

Objective: This cross-sectional, retrospective study aimed to determine the prevalence and clinical characteristics of AATD in patients evaluated at a university hospital in Córdoba, Argentina, between June 2023 and June 2025.

Materials and methods: The study included 339 patients, of whom 18 had serum alpha-1 antitrypsin levels < 120 mg/dL.

Results: A 0.88% prevalence of severe AATD was confirmed. Low alpha-1 antitrypsin levels were significantly associated with pulmonary emphysema, independent of smoking history, age, and sex. In addition, serum alpha-1 antitrypsin levels were positively correlated with forced expiratory volume in 1 second (FEV_1). Among patients with concentrations in the lower reference range, liver disease and eosinophilia were the most frequent associated findings.

Conclusions: Systematic screening for AATD in patients with chronic obstructive pulmonary disease (COPD) or liver disease is crucial for ensuring timely diagnosis.

Key words: alpha-1 antitrypsin deficiency | pulmonary Emphysema | chronic obstructive pulmonary disease | phenotype | Argentina

RESUMEN

Introducción: El déficit de alfa-1 antitripsina es un trastorno genético hereditario caracterizado por una reducción en las concentraciones séricas de esta proteína, lo que genera una predisposición significativa a enfermedades pulmonares y hepáticas. A pesar de ser una condición reconocida, el subdiagnóstico persiste a nivel global y regional debido a la falta de sospecha clínica.

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Objetivo: Este estudio transversal y retrospectivo se realizó con el objetivo de describir la prevalencia y las características clínicas de esta deficiencia en pacientes de un hospital universitario de Córdoba, Argentina, entre junio de dos mil veintitrés y junio de dos mil veinticinco.
Materiales y métodos: Se analizaron los registros de 339 pacientes, de los cuales dieciocho presentaron niveles de alfa-1 antitripsina inferiores a 120 mg/dL.
Resultados: Se confirmó una prevalencia de deficiencia grave del 0,88 %. Se identificó una asociación estadísticamente significativa entre los niveles bajos de la proteína y la presencia de enfisema pulmonar, independientemente del historial de tabaquismo, la edad o el sexo. Asimismo, se observó una correlación positiva entre los niveles de alfa-1 antitripsina y el volumen espiratorio forzado en el primer segundo. En los casos con valores en el límite inferior, predominó la asociación con enfermedades hepáticas y eosinofilia.
Conclusiones: El estudio concluye que es fundamental implementar un cribado sistemático en pacientes con enfermedad pulmonar obstructiva crónica y hepatopatías para mejorar la detección temprana de esta patología.

Palabras clave: Déficit de alfa 1-antitripsina | enfisema pulmonar | enfermedad pulmonar obstructiva crónica | fenotipo | Argentina

INTRODUCTION

Alpha-1 antitrypsin deficiency is a complex hereditary genetic disorder and a potentially life-threatening congenital condition that typically manifests during adulthood.[1,2] It is characterized by reduced serum concentrations of alpha-1 antitrypsin, a glycoprotein synthesized primarily by hepatocytes.[1,3] The main biologic function of this glycoprotein is to protect the pulmonary extracellular matrix from proteolytic degradation by neutrophil elastase.[1,2] AATD is caused by mutations in the SERPINA1 gene, located on chromosome 14, and is transmitted via an autosomal codominant inheritance pattern.[1,3,4]

From a genetic perspective, approximately 125 SERPINA1 variants have been identified.[4] The normal allele, PiM, is present in 80% to 95% of the population.[4] The most common deficient variants are PiS and PiZ. Most cases of severe clinical disease are associated with the homozygous PiZZ genotype, which results in plasma AAT levels of approximately 10% to 15% of normal values.[1] The pathophysiology involves a dual mechanism: a "loss of function" in the lungs that predisposes to premature panacinar emphysema, and a "toxic gain of function" in the liver, where the polymerization of the abnormal protein within the endoplasmic reticulum of hepatocytes can lead to cirrhosis and hepatocellular carcinoma.[1,4,5]

The epidemiology of AATD is characterized by marked geographic and ethnic variation. Recent estimates indicate that approximately 235,000 individuals worldwide have the Pi*ZZ genotype, with 50% residing in Europe and 37% in the Americas.[6] Within Europe, the highest prevalence of the PiZZ genotype is reported in Northern and Western European countries, including Italy, Spain, France, and the United Kingdom.[7,8] In these countries, there is a strong association between the PiZZ genotype and chronic obstructive pulmonary disease, with a mean prevalence of one Pi*ZZ patient for every 850 individuals with COPD.[9]

In Latin America, the prevalence of AATD is estimated to be up to fivefold lower than that reported in Europe.[4] However, the DAAT.AR study conducted in Argentina reported an adjusted prevalence of severe AATD (SZ and ZZ genotypes) of 0.83% among patients with COPD aged ≥ 40 years.[7] This represents around 17,000 to 18,000 affected individuals in Argentina, the vast majority of whom remain undiagnosed.[7] In Brazil, approximately 6,000 individuals are estimated to have the Pi*ZZ genotype, highlighting that AATD is not confined to white populations in the Northern Hemisphere but affects diverse racial and ethnic groups worldwide.[1,3,4]

Despite its clinical relevance, AATD remains markedly underdiagnosed, with more than 85% of affected individuals estimated to remain un-

detected.[4,6] Diagnostic delays of 5 to 8 years from the onset of respiratory symptoms have been consistently reported.[6,9,10] Patients often consult multiple physicians before receiving a precise diagnosis, frequently after unsuccessful treatment for asthma or COPD.[6,10]

Accordingly, the World Health Organization (WHO) and the American Thoracic Society/European Respiratory Society (ATS/ERS) and Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) guidelines recommend measuring serum AAT levels at least once in a lifetime in all patients with COPD, regardless of age or smoking history.[1,2] Early screening is essential to facilitate the integration of preventive measures, enable family screening, and identify candidates for purified AAT augmentation therapy, the only disease-specific treatment shown to slow the decline in lung density in appropriately selected patients.[1,2,4]

Hypothesis

We hypothesized that AATD is underdiagnosed at our institution because of the lack of systematic screening among patients with emphysema, uncontrolled asthma, persistent eosinophilia, or liver disease, resulting in reduced detection of clinically relevant cases.

OBJECTIVES

Overall objective

To determine the prevalence and describe clinical characteristics of alpha-1 antitrypsin deficiency among patients evaluated at Hospital Privado Universitario de Córdoba, Argentina, during the study period.

To characterize the epidemiologic and clinical profile of patients with low or borderline serum A1AT levels and evaluate their association with respiratory manifestations and ancillary clinical findings.

Secondary objectives

To evaluate the demographic distribution and clinical association of alpha-1 antitrypsin deficiency in patients from a private healthcare facility in Córdoba, with particular emphasis on its relationship with pulmonary imaging and lung function findings.

To evaluate the prevalence of the association between peripheral eosinophilia and low A1AT levels.

To investigate the coexistence of a history of liver disease and its association with alpha-1 antitrypsin deficiency.

MATERIALS AND METHODS

We conducted a retrospective, observational, analytical, cross-sectional study.

Study design and setting

This retrospective and descriptive study was conducted by the Department of Pulmonology at Hospital Privado Universitario de Córdoba.

Study population

Consecutive adults (aged ≥ 18 years) who received care at this institution between June 2023 and June 2025 were included.

Data collection

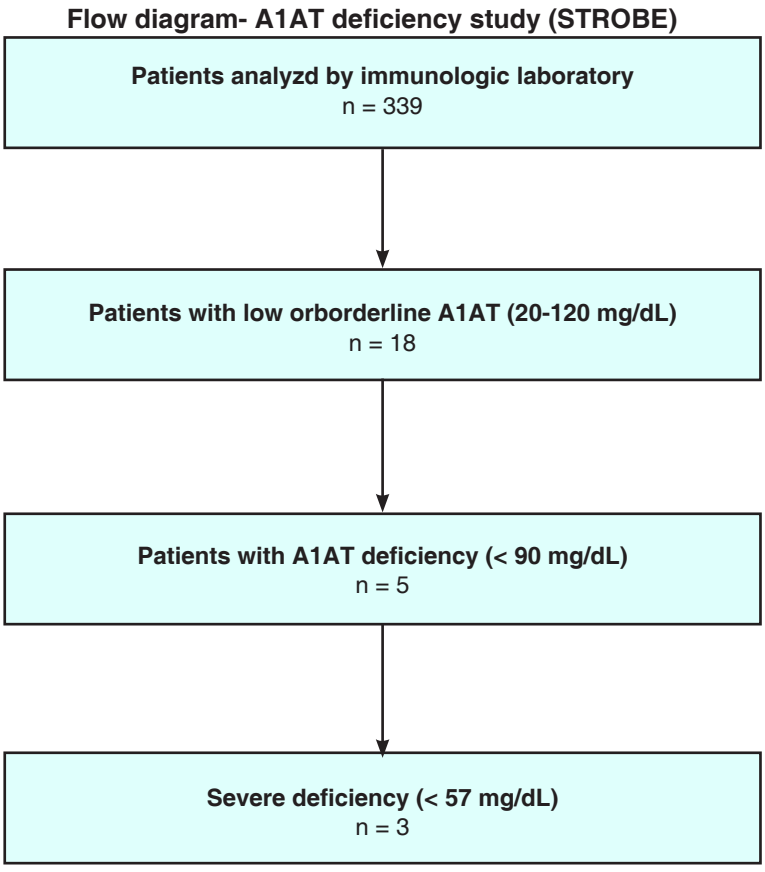
Data were obtained from the hospital's electronic health record system. Medical records were extracted. Then, medical records were reviewed, and eligible patients were identified after application of the predefined inclusion and exclusion criteria. The following variables were collected: epidemiologic data, smoking history, clinical symptoms, spirometry results, immunologic test results, and high-resolution CT (HRCT) findings.

Statistical analysis

Data from the electronic medical records were entered into an Excel-like database, which was later used for statistical analysis. Absolute and percentage distributions were calculated for categorical variables. To evaluate the association between clinical symptoms and immunological, spirometric, and tomographic findings, the chi-square test was applied. The same approach was applied to all other analyses involving categorical variables of interest. A significance level of 0.05 was used in all cases. Statistical analyses were performed using InfoStat software (version 2020). Results are presented as tables or figures, as appropriate.

RESULTS

A total of 339 laboratory results from the Immunology Department were analyzed to evaluate



serum alpha-1 antitrypsin levels (measured in mg/dL).

Serum levels greater than 120 mg/dL were considered normal, borderline values were defined as 91 to 119 mg/dL, decreased values as less than 90 mg/dL, and severely decreased values as less than 57 mg/dL.

From the initial cohort (n = 339), 18 patients (5.3%) exhibited values less than 120 mg/dL and were classified as suspected cases.

Within this group, 5 patients (1.47% of the total cohort) had levels less than 90 mg/dL, and 3 patients (0.88% of the total cohort) had levels less than 57 mg/dL. At the time of data collection, only the latter three patients had undergone genetic testing.

The genomic variants identified were: homozygous Z, homozygous S, and heterozygous ZS.

Consequently, the confirmed true prevalence was 0.88% based on immunological A1AT serum testing. The prevalence of suspected cases based on borderline values was 5.3%; however, neither genetic testing, buccal swab, nor dried blood spot testing was performed in these remaining patients.

Regarding age distribution, 14 men and 4 women were identified, with a mean age of 53 +/- 1 years.

To facilitate the analysis of associations, patients were divided into two groups based on a cutoff value of ≥ 90 mg/dL.

A male predominance was observed in the overall cohort (77.8%).

In the subgroup with A1AT levels < 90 mg/dL, 3 patients were men and 2 were women, whereas the subgroup with levels ≥ 90 mg/dL was also predominantly male (11 men vs. 2 women).

Proportionally, 50.0% of the women had A1AT levels < 90 mg/dL compared with 21.4% of the men. However, due to the small sample size –particularly within the female subgroup– it was not possible to demonstrate a statistically significant association between sex and serum A1AT levels.

Regarding smoking history, 8 patients were smokers with a smoking load of more than 15 pack-years.

In terms of underlying conditions, 9 patients had liver disease (autoimmune hepatitis, n = 3; HCV-related cirrhosis, n = 2; NASH cirrhosis, n = 2; alcoholic cirrhosis, n = 1; and hemochromatosis, n = 1).

To simplify the statistical analysis, the 18 patients were stratified into 2 groups according to their serum A1AT concentration: > 90 mg/dL and < 90 mg/dL.

Only 1 of the 5 patients (20.0%) with A1AT less than 90 mg/dL had an underlying liver disease. This difference in liver disease distribution between the two A1AT cohorts did not reach statistical significance (p = .35, Fisher exact test).

4 of these 5 patients (80.0%) with A1AT < 90 mg/dL did not show liver disease.

The remaining 8 patients showed values > 90 mg/dL.

Regarding the analysis of patient phenotypes, a total of 17 patients had peripheral blood eosinophil counts available for evaluation.

A trend toward higher eosinophil counts (> 300 cells/µL) was observed in patients with A1AT levels ≥ 90 mg/dL (7 cases) compared with those with levels < 90 mg/dL (0/4 cases). However, no statistically significant association was identified. The proportions of eosinophilia were comparable between both A1AT groups (p > 0.05).

Patients with < 90 mg/dL had eosinophilia (> 150); nonetheless, this did not reach statistical significance due to the high prevalence of

Table 1. Association between A1AT levels and sex

Sexo	G1 (<90 mg/dL)	G2 (≥90 mg/dL)	% of deficiency
Male (14)	3	11	21.40%
Female(4)	2	2	50%

Table 2. Association between A1AT levels and sex

		A1AT category	
Patient	SEX	G2 (≥90 mg/dL)	G1 (<90 mg/dL)
1	female	1	0
2	male	1	0
3	male	1	0
4	female	0	1
5	male	1	0
6	male	1	0
7	female	1	0
8	female	0	1
9	male	1	0
10	male	1	0
11	male	1	0
12	male	1	0
13	male	1	0
14	male	1	0
15	male	1	0
16	male	0	1
17	male	0	1
18	male	0	1

Figure 1. Association between A1AT levels and sex

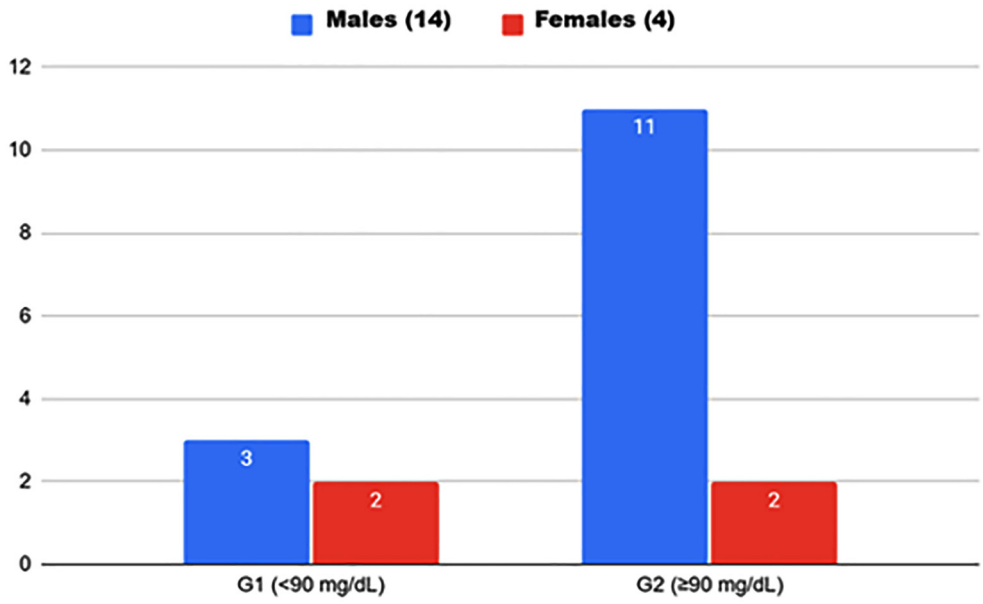


Table 3. Distribution of liver disease by A1AT level

A1AT category	Wit hliver disease	Without liver disease	Total
< 90 mg/dL	1	4	5
≥ 90 mg/dL	8	5	13
Total	9	9	18

Table 4. Distribution of eosinophilia by A1AT levels

Distribution of eosinophilia by A1AT levels			
A1AT category	≤150 cells/µL	>150 cells/µL	>300 cells/µL
<90 mg/dL	0	4	0
≥90 mg/dL	3	3	7
Total	3	7	7

eosinophilia within the cohort with values ≥ 90 mg/dL.

Regarding chest imaging patterns, high-resolution chest CT scans were available for all patients (n = 18).

Emphysema was identified in 6 patients, of whom 3 had A1AT levels < 90 mg/dL.

Only 2 of the 12 patients without emphysema had A1AT levels < 90 mg/dL.

A statistically significant association was identified between low A1AT levels (< 90 mg/dL) and the presence of emphysema (p = .049, Fisher exact test), demonstrating a significantly higher prevalence of emphysema among patients with A1AT deficiency.

Emphysema was present in 3/5 of patients with A1AT levels < 90 mg/dL compared with 3/13 of patients in the cohort with A1AT levels ≥ 90 mg/dL.

Figure 2. Association between A1AT levels and eosinophil counts.

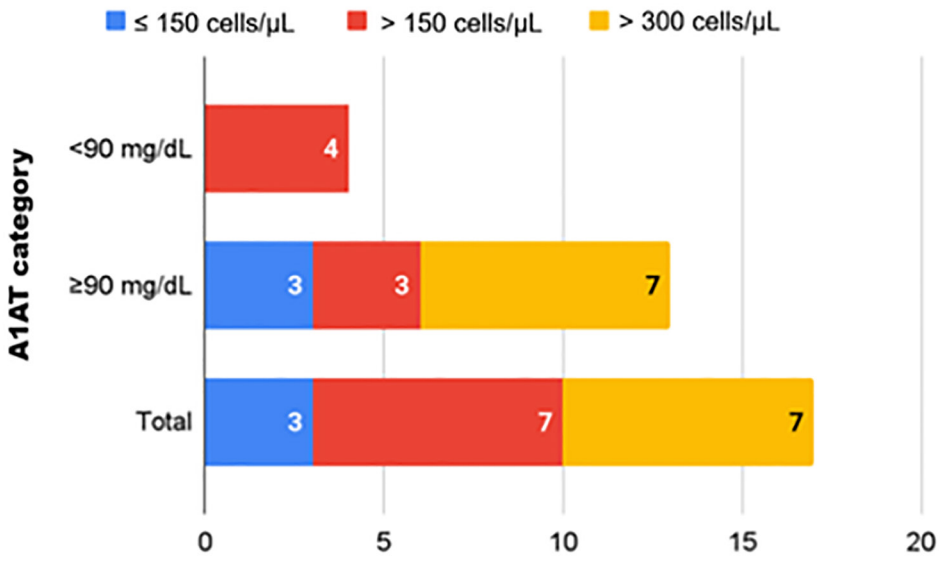
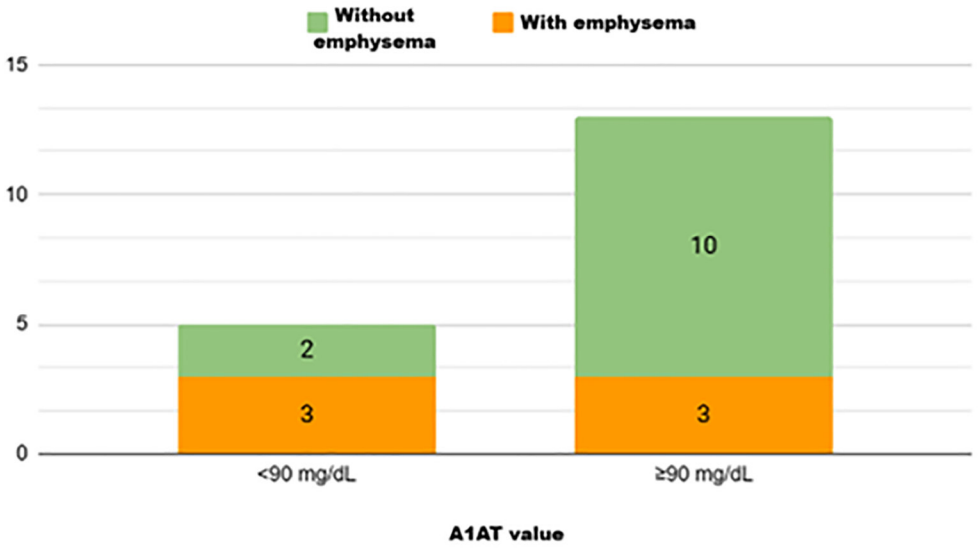


Figure 3. Distribution of emphysema by A1AT level



The three patients with emphysema exhibited individual serum values of 90 mg/dL, 114 mg/dL, and 120 mg/dL, respectively.

Regarding functional assessment, spirometry data were available for 15 patients. The distribution of spirometric patterns was as follows: 8 normal, 3 obstructive, and 4 restrictive.

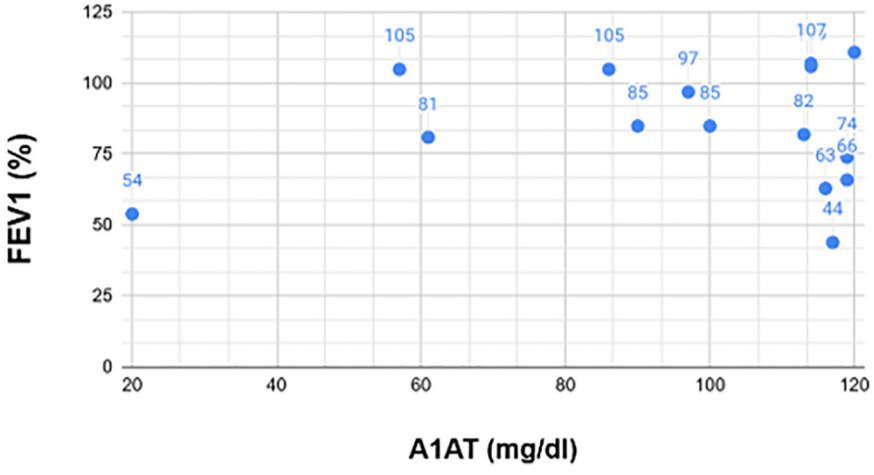
A moderate positive correlation was identified between serum A1AT levels and FEV1% ($p = .42$; $p = .061$).

Notably, after excluding a single case with severe A1AT deficiency (20 mg/dL), this correlation reached statistical significance ($p = .48$; $p = .037$).

Table 5. Association between A1AT levels and the presence of emphysema

A1AT (mg/dL)	A1AT (mg/dL)
100	0
114	1
120	0
61	0
119	0
119	0
117	0
20	1
97	0
116	0
113	0
93	0
114	0
20	1
90	1
86	1
20	1
57	0

Figure 4. Correlation between FEV1 (%) and A1AT (mg/dL)



The distribution of FEV1 percentages plotted against A1AT levels demonstrates a reciprocal relationship between normal values, respectively.

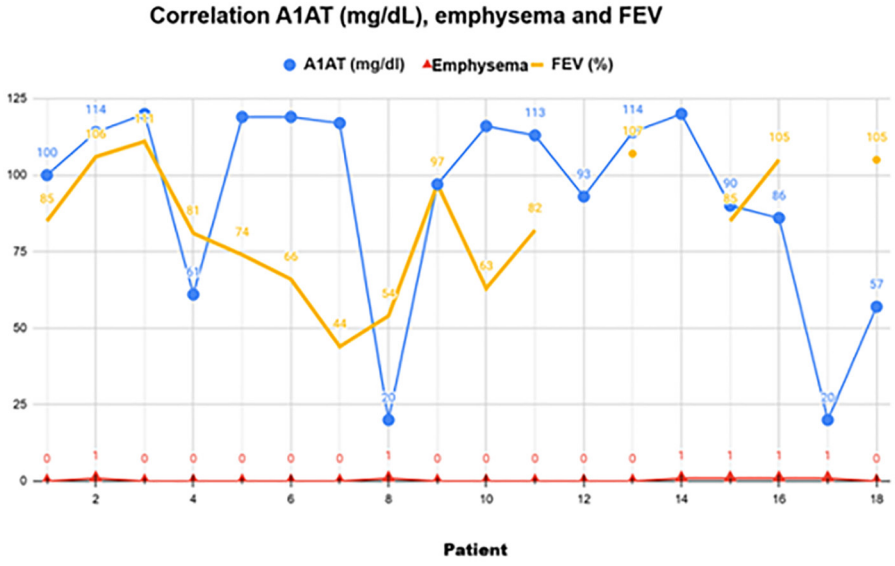
The exploratory analysis demonstrated a trend toward greater respiratory functional impairment in patients with reduced serum alpha-1 antitrypsin levels, particularly in those with concomitant emphysema.

Cases with severe deficiency consistently exhibited coexistence of emphysema and functional decline. However, notable clinical heterogeneity was observed across the cohort, which was likely

Table 6. Correlation among spirometric findings, chest CT patterns, and serum A1AT levels

Patient	A1AT (mg/dL)	Emphysema	FEV
1	100	0	85
2	114	1	106
3	120	0	111
4	61	0	81
5	119	0	74
6	119	0	66
7	117	0	44
8	20	1	54
9	97	0	97
10	116	0	63
11	113	0	82
12	93	0	NR
13	114	0	107
14	120	1	NR
15	90	1	85
16	86	1	105
17	20	1	NR
18	57	0	105

Figure 5. Correlation among spirometric findings, chest CT patterns, and serum A1AT levels



influenced by concomitant factors such as smoking history and phenotypic variability.

Among all of the patients who were analyzed (n = 18), 8 were smokers and 6 had emphysema.

Smokers with emphysema: 3/8

Smokers without emphysema: 5/8

Non-smokers (n= 10) with emphysema: 3. (These 3 patients had A1AT levels < 90)

1 every 5 patients with A1AT levels < 90 was a smoker without emphysema

1 every 5 patients with A1AT levels < 90 was non- smoker without emphysema

These findings suggest an association between low A1AT levels and emphysema that may be stronger than the association observed with smoking history.

Smoking was associated with emphysema in only 37.5% of cases.

No statistical significance can be established with this small sample size (n = 18), but there is a clinically relevant trend.

DISCUSSION

The findings of this study support that alpha-1 antitrypsin deficiency (AATD) remains underdiagnosed in our setting. The prevalence of severe deficiency observed in our cohort (0.88% for serum A1AT concentrations < 57 mg/dL) is highly consistent with the findings of the DAAT.AR study, which reported an adjusted prevalence of 0.83% among Argentine patients with COPD aged ≥ 40 years. In contrast, higher prevalences have been reported in European populations, where the PI*ZZ genotype is more common because of ethnic and geographic factors.(2,3)

Our findings may underestimate the local epidemiologic reality because systematic genotyping was not routinely available. Only 3 patients from the sample underwent confirmatory genetic testing.(2,4) The statistically significant association between low serum A1AT concentrations and the presence of emphysema (p = .049) is consistent with the established pathophysiology of AATD, in which an imbalance between proteases and antiproteases promotes neutrophil elastase-mediated degradation of the pulmonary extracellular matrix. Consistent with previous studies, higher serum A1AT concentrations were associated with higher FEV1%, suggesting that more severe obstruction is associated with greater degrees of AAT deficiency. Furthermore, the data suggest that the relationship between AATD and emphysema may be more determinant than smoking history, as non-smoking patients with emphysema were found to have deficient serum AAT levels.

A point of particular interest in this discussion is the behavior of patients with "borderline" serum levels (90-120 mg/dL). Within this subgroup, a predominant association with hepatic diseases and peripheral blood eosinophilia was observed, raising critical questions regarding the role of heterozygous variants (such as PiMZ or PiSZ) in extrapulmonary manifestations and systemic inflammatory processes. It is well established that hepatic pathology in AATD does not stem from a loss of protein function; rather, it is driven by a toxic gain of function resulting from polymer accumulation within hepatocytes –a mechanism that can be active even in individuals with moderately reduced serum levels.

Despite the relevance of these findings, this study has several limitations, including a small sample size (n = 18) and potential selection bias inherent to data from a single private center, which limits the generalizability of the results to the broader population. Nevertheless, the diagnostic delay and lack of clinical suspicion identified herein remain persistent global challenges. International studies document diagnostic delays ranging from 5 to 8 years –and up to 10 years in certain regions– demonstrating that early detection rates have not significantly improved over recent decades.[8,9]

Finally, these results underscore the imperative need to implement systematic screening protocols. In alignment with guidelines from the WHO and international scientific societies, serum AAT quantification should be performed at least once in a lifetime in all patients with COPD or difficult-to-control asthma, regardless of their smoking history.

Early identification not only optimizes clinical management and allows for the timely consideration of augmentation therapy, but it also facilitates the screening of consanguineous relatives to detect other individuals at risk before irreversible organic damage develops.

CONCLUSIONS

This study suggests that AATD remains an underdiagnosed condition within our population. Low A1AT levels were significantly associated with pulmonary emphysema, independent of smoking history, age, and sex. In patients with "borderline" serum values, liver disease predominated over pulmonary involvement, and peripheral blood eosinophilia was detected within this subgroup.

These findings reinforce the need to use systematic screening protocols in patients with diagnosed COPD, early-onset emphysema (with and

without significant tobacco exposure), and chronic liver disease, in strict alignment with international guidelines.

Future recommendations

Universal screening in COPD/severe asthma patients, even in the absence of emphysema.

Multicenter studies to estimate the true prevalence of AATD in Argentina, incorporating systematic genotypic analysis.

Finally, it is crucial to underscore that within this Argentine cohort, a negative correlation was observed between AAT levels and age, tobacco consumption (pack-years), and FEV1%. This evidence strongly reinforces the importance of maintaining a high index of suspicion for AATD in patients with early-onset COPD, non-smokers or individuals with minimal tobacco exposure, and those exhibiting more severe functional impairment and lower FEV1 values.

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CASE REPORT

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Empyema due to *Rhodococcus hoagii*, an unusual presentation

Empiema por Rhodococcus hoagii, una presentación poco habitual

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ABSTRACT

Rhodococcus hoagii is an unusual infectious agent in humans. It typically presents as an opportunistic infection in immunosuppressed patients, although it has also been reported as an occupational disease following exposure to farm animals (such as horses, goats, sheep and cattle). The most common clinical presentation is slowly resolving cavitary pneumonia, so it should be included in the differential diagnosis of tuberculosis. Less common manifestations include pleural effusion, empyema, and lung abscess. We report the case of a 57-year-old man, HIV-positive, who was employed as a racetrack stable worker, diagnosed with empyema caused by *Rhodococcus hoagii* (presently *R. equi*).

Key words: empyema | infection | *Rhodococcus hoagii* | HIV | occupational exposure

RESUMEN

En humanos, *Rhodococcus hoagii* es un agente infeccioso inusual. Suele producir infecciones oportunistas en pacientes inmunosuprimidos aunque también está descrita como una enfermedad relacionada con la exposición ocupacional (contacto con animales de granja como caballos, cabras, ovejas, vacas en ámbito laboral). La forma de presentación más común es como neumonía cavitada de lenta resolución, por lo que debe considerarse como diagnóstico diferencial de la tuberculosis; y con menor frecuencia como derrame pleural, empiema o absceso pulmonar. Se presenta el caso de un paciente masculino de 57 años, retrovirus positivo, trabajador en establos del hipódromo, con diagnóstico de empiema por *Rhodococcus hoagii* (actualmente *R. equi*).

Palabras clave: empiema | infeccion | *Rhodococcus hoagii* | HIV | exposición ocupacional

INTRODUCTION

Rhodococcus hoagii (formerly *Rhodococcus equi*) is a Gram-positive intracellular coccobacillus commonly found in the soil and is best known in veterinary medicine as a pathogen causing infection in horses. In humans, it is an opportunistic pathogen that primarily causes pulmonary infection, typically presenting as chronic cavitary or necrotizing pneumonia in immunocompro-

mised hosts, particularly individuals with AIDS or solid organ transplantation. Less commonly, pulmonary abscess and empyema have also been reported as clinical manifestations.

CASE REPORT

A 57-year-old man, former smoker (40 pack-years), with HIV (undetectable viral load, CD4 count 142 cells/mm^3; excellent antiretroviral therapy adherence) was recently diagnosed with chronic obstructive pulmonary disease (COPD), Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) group B, stage 2. His COPD is well controlled with salmeterol/fluticasone and has no recent exacerbations. His occupational history included maintenance work in horse stables at a racetrack for 3 years, with regular exposure to horses. He presented with a 45-day history of dyspnea, New York Heart Association (NYHA) class II, left-sided chest pain, productive cough with hemoptoic sputum, and febrile episodes. During this period, he sought care at multiple emergency departments and received several antibiotic regimens without clinical improvement. Physical examination: oxygen saturation 96% on room air, afebrile, abolition of vesicular breath sounds in the left lower-middle lung field with local dullness to percussion and dullness over the spine. Laboratory testing revealed leukocytosis of 25,100 µL with neutrophilia; hematocrit 33%, hemoglobin 11 g/dL, urea 9.3 mmol/L; the remainder was unremarkable. Sputum acid-fast bacilli smear repeated twice was negative. Contrast-enhanced CT of the chest demonstrates centrilobular emphysema and a tree-in-bud pattern in the left upper lobe. There is left pleural thickening and a loculated pleural effusion, associated with an area of increased attenuation within the lingula, described as a mass with spiculated margins that exhibits enhancement following intravenous contrast administration. Fiberoptic bronchoscopy revealed abundant mucopurulent secretions but no evidence of endoluminal lesions. Bronchoalveolar lavage (BAL) and bronchoscopic transbronchial biopsy (BTB) samples were submitted for microbiological analysis, which yielded negative results. Following evaluation by thoracic surgery, the patient underwent left video-assisted thoracoscopic surgery (VATS) for pulmonary decortication and pleural biopsy. Pathological anatomy of the pleural biopsy revealed an acute-on-chronic, nonspecific, abscessed inflammatory process. Pleural fluid samples were also collected for microbiological culture; both the tissue and fluid samples were positive for *Rhodococcus hoagii* (sensitive to vancomycin, erythromycin, and levofloxacin). Consequently, a 28-day course of dual intravenous antibiotic therapy with vancomycin and levofloxacin was initiated, resulting in a favorable clinical response. A follow-up chest CT was performed (Figure 1). The patient was subsequently transitioned to oral antibiotic therapy. To date, the patient has completed a 6-month course of antibiotic therapy and is scheduled for follow-up radiological and pulmonary function testing.

Ethical considerations

Patient permission was obtained for the publication of this case, supported by a signed informed consent.

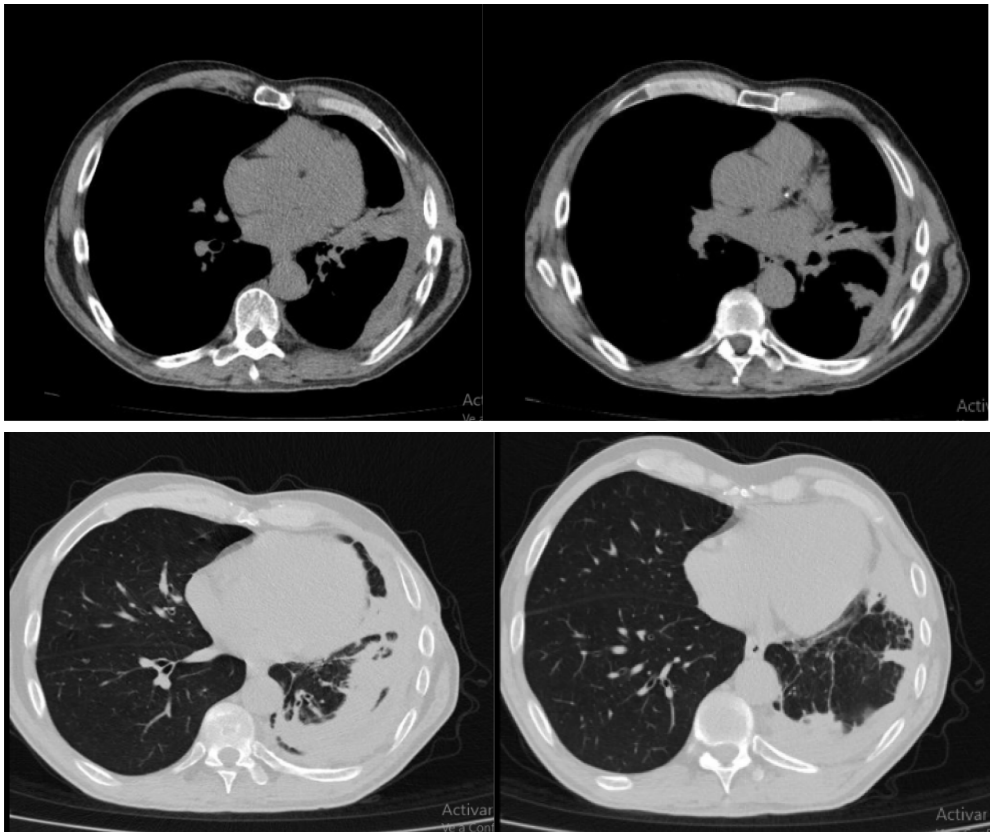
DISCUSSION

Rhodococcus hoagii is a soil-dwelling organism that colonizes the gastrointestinal tract of numerous herbivores and is commonly found in their feces, pasture soils, and other agricultural environments. Not only horses but also pigs, goats, and cattle should be considered potential sources of *R. hoagii* infection in humans.[1] More than 300 cases of R. hoagii infection have been reported since the first description of this disease in humans, in 1967.1 In that initial report, Golub et al identified the organism as the causative agent of a cavitary right upper lobe pneumonia, isolated from bronchoalveolar lavage fluid in a 29-year-old man with autoimmune hepatitis who had been receiving long-term corticosteroid therapy.[2]

Most reported cases occur in immunocompromised individuals, including patients with human immunodeficiency virus (HIV) infection, solid organ transplant recipients, and those undergoing cancer treatment.[1]

The primary route of infection acquisition is believed to be inhalation of the microorganism from contaminated soil. However, alternative routes have been described, including direct inoculation through skin or mucosal injuries and ingestion of contaminated food.[4] In several cases, exposure to farm and domestic animals, particularly dogs, has been considered a potential source of infection

Figure 1. Chest CT with mediastinal (1A) and lung parenchyma (1B) windows showing left lung volume loss associated with fibrotic bands extending from the pulmonary hilum to the periphery. A small left pleural effusion with underlying pleural thickening is also visualized.



through inhalation of contaminated fecal material or direct contact with infected skin lesions in these animals.[4] Nosocomial acquisition has been reported rarely, and only one case of occupationally acquired infection has been described in a laboratory worker.[5]

The most common clinical manifestation of *R. hoagii* infection in humans is focal nodular or cavitary pneumonia, which may be complicated by empyema, pleural effusion, pneumothorax, or endobronchial granuloma formation.[4] Extrapulmonary manifestations have also been reported and include subcutaneous abscesses, lymphangitis, endophthalmitis, septic arthritis, osteitis, pericarditis, renal abscesses, sepsis, and central nervous system infections, including meningitis and brain abscesses (Table 1).

The most common radiographic findings are poorly defined areas of consolidation and irregular cavitary lesions in the lungs, which may be unilateral or bilateral and typically involve the upper lobes. Approximately 70% to 75% of *R. hoagii* infections present as slowly resolving cavitary pulmonary disease, with radiographic features resembling those of *Mycobacterium tuberculosis* infection. In patients with cavitary lung lesions, the microorganism may be readily identified in sputum specimens. However, when isolated from the sputum of patients with pneumonia, *R. hoagii* may be dismissed as normal respiratory flora because of its morphologic resemblance to oropharyngeal commensal diphtheroids.[3]

Management is often challenging because of the organism's intrinsic resistance to multiple antimicrobial classes.[6] Antimicrobial susceptibility testing should be performed for all *R. hoagii* isolates to guide therapy and avoid the use of agents to which the organism demonstrates *in vitro* resistance. *R. hoagii* is generally susceptible to erythromycin, rifampin, fluoroquinolones, aminoglycosides, glycopeptides, and imipenem.5 Combination antimicrobial therapy should be considered to minimize the risk of emerging resistance.[6]

Most patients require initial intravenous treatment with bactericidal agents, such as imipenem and vancomycin, for at least 2 weeks, with the duration guided by clinical response, followed

Table 1. Previously Reported Clinical Manifestations of Rhodococcus equi Infection. Extracted from Weinstock DM, et al[8]

Pulmonary nodules
Lung abscess
Pneumonia, with or without cavitation
Spontaneous pneumothorax
Wound infection
Traumatic keratitis and endophtalmitis
Bacteremia, isolated and catheter related
Fever of unknouwn origin and infected bone marrow
Peritonitis, spontaneous and peritoneal dialysis associated
Mesenteric adenitis, isolated or with peritonitis
Cervical adenitis
Osteomyelitis, by direct extension from pneumonia or due to disseminated infection
Septic arthritis
Brain abscess, spontaneous or postneurosurgical
Hepatyc abscess, by direct extension from pneumonia or due to disseminated infection
Renal abscess
Urinary tract infection
Subcutaneous or deep-tissue abscess
Sternal-bound infection following coronary bypass grafting
Ventricular shunt infection
Bronchobiliary fistula by direct extension from pneumonia
Pedunculated and sessile colonic polyps
Otomastoiditis
Thyroid abscess
Colitis mimicking Whippie´s disease
Spleen abscece
Prostate abscece

by oral combination therapy (eg, a macrolide plus a quinolone).[5] The duration of treatment should be individualized according to the extent of infection, the patient's immune status, *in vitro* susceptibility profile, and clinical response to therapy.[6] Some authors recommend prolonged treatment for at least 6 months to reduce the risk of relapse.[5,6] In patients with HIV infection, initiation or continuation of antiretroviral therapy is also recommended to improve prognosis and reduce mortality.[7] Finally, surgical intervention should be considered when medical therapy fails, particularly in patients with pulmonary abscesses or empyema, as occurred in the present case.

CONCLUSION

Increasing recognition of *Rhodococcus hoagii* as a human pathogen has improved laboratory identification of infection in both immunocompromised and immunocompetent individuals. Close communication with the microbiology laboratory is essential in order to reach a precise diagnosis when clinical specimens are submitted, because the organism may be overlooked or misclassified as a contaminant agent. *Rhodococcus* infections remain challenging to treat and often require prolonged dual antibiotic therapy and surgical drainage, as in the case we present. In patients with HIV infection, concomitant antiretroviral therapy has been associated with improved survival outcomes. Finally, this entity should be considered in the differential diagnosis of tuberculosis, which represents a significant challenge.

Conflict of interest

Authors have no conflicts of interest to declare.

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CASE REPORT

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Alpha-1 Antitrypsin Deficiency with Pulmonary Nodules and Cirrhosis: a Case Report

Déficit de alfa-1 antitripsina con enfermedad nodular pulmonar y cirrosis: reporte de caso

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ABSTRACT

Alpha-1 antitrypsin deficiency (AATD) is an underdiagnosed codominant genetic disorder. The PiZZ phenotype represents the most common form of severe deficiency and is associated with pulmonary and hepatic involvement. In addition to the classic emphysematous phenotype, nodular findings have been described on high-resolution computed tomography (HRCT). We present the case of a 62-year-old nonsmoking man with persistent dry cough and mild dyspnea, in whom the HRCT revealed a dominant solid nodular lesion measuring 24 × 17 mm in the right upper lobe, accompanied by multiple irregular solid nodular opacities of chronic evolution. Abdominal imaging suggested chronic liver disease with normal liver panel and platelet count. Serum alpha-1 antitrypsin level was 69 mg/dL, and the PiZZ phenotype was confirmed. Liver biopsy showed PAS-positive and PAS-D-positive intracytoplasmic inclusions, consistent with alpha-1 antitrypsin polymer accumulation and cirrhosis in the setting of AATD. Granulomatous, infectious, and neoplastic differential diagnoses were considered; available bronchoscopic, cytological and microbiological studies did not show active infection or malignancy, and radiological surveillance was adopted due to lesion stability. Phenotypic confirmation enabled a definitive syndromic diagnosis, identified pulmonary and hepatic involvement, and guided targeted management according to international recommendations.

Key words: alpha-1 antitrypsin deficiency | Pi*ZZ | pulmonary nodules | high-resolution computed tomography | cirrhosis

RESUMEN

El déficit de alfa-1 antitripsina (DAAT) es una enfermedad genética codominante e infradiagnosticada; el fenotipo PiZZ representa la forma más frecuente de déficit grave y se asocia a compromiso pulmonar y hepático. Además del fenotipo enfisematoso clásico, se han descrito imágenes nodulares

en tomografía computarizada de alta resolución (TCAR) de tórax. Presentamos el caso de un varón de 62 años, no fumador, con tos seca persistente y disnea leve, en quien la TCAR mostró una lesión nodular sólida dominante de 24 × 17 mm en lóbulo superior derecho, asociada a múltiples imágenes nodulares sólidas irregulares de evolución crónica. En estudios abdominales se evidenció hepatopatía crónica con hepatograma y plaquetas normales. La alfa-1 antitripsina sérica fue de 69 mg/dL y se confirmó fenotipo PiZZ. La biopsia hepática mostró inclusiones intracitoplasmáticas PAS positivas y PAS-D positivas, hallazgos compatibles con acumulación de polímeros de alfa-1 antitripsina y cirrosis, en el contexto de DAAT. Se consideraron diagnósticos diferenciales granulomatosos, infecciosos y neoplásicos; los estudios broncoscópicos, citológicos y microbiológicos disponibles no evidenciaron infección activa ni malignidad, por lo que, ante la estabilidad de las lesiones, se adoptó vigilancia tomográfica. La confirmación fenotípica permitió un diagnóstico sindrómico definitivo, identificar el compromiso pulmonar y hepático y orientar medidas específicas según recomendaciones internacionales.

Palabras clave: déficit de alfa-1 antitripsina | Pi*ZZ | nódulos pulmonares | tomografía de alta resolución | cirrosis

INTRODUCTION

AATD is an underdiagnosed codominantly inherited genetic disorder.[1,2] The Pi*ZZ phenotype is the most common form of severe deficiency and is associated with both pulmonary manifestations (emphysema, bronchiectasis) and liver disease resulting from the accumulation of alpha-1 antitrypsin polymers within hepatocytes.[1-3] Although emphysema represents the most widely recognized pulmonary phenotype, nodular patterns on HRCT have also been described, potentially posing diagnostic challenges.[4]

CASE REPORT

A 62-year-old man, never-smoker, employed as a baker, with a history of presumed ocular sarcoidosis treated with prolonged corticosteroid therapy, insulin-dependent type 2 diabetes mellitus, and liver cirrhosis secondary to alpha-1 antitrypsin deficiency presented with persistent dry cough and dyspnea classified as grade 1 on the mMRC scale (modified Medical Research Council dyspnea scale). The patient was being followed by the Pulmonology Service for long-standing pulmonary nodular lesions. HRCT showed multiple solid pulmonary nodules, predominantly involving the right lung, some with irregular margins and diffuse distribution. Several lesions were associated with pleuropulmonary fibrotic sequelae. A dominant lesion measuring 24 × 17 mm was identified in the posterior segment of the right upper lobe. Subsequent follow-up evaluations over 2 years demonstrated no significant evidence of disease progression.

Flexible bronchoscopy with bronchoalveolar lavage (BAL) was performed and revealed no endobronchial abnormalities. The CD4/CD8 ratio was within normal limits, without lymphocytosis. Cytologic analysis was negative, and cultures for common bacterial pathogens, mycobacteria, and fungi yielded negative results. Serial chest CT examinations demonstrated no significant changes in the size or morphology of the pulmonary lesions.

Available lung function testing was limited to spirometry, which showed an FVC (forced vital capacity) of 3.33 L (77%), FEV_1 (forced expiratory volume in the first second) of 2.29 L (74%), and a FEV_1/FVC ratio of 73%. Measurements of lung volumes and diffusing capacity of the lung for carbon monoxide (DLCO) were not available, limiting the comprehensive assessment of pulmonary impairment related to AATD. Abdominal MRI demonstrated a heterogeneous liver with lobulated margins, a hepatic nodular lesion measuring approximately 35 mm, splenomegaly, and collateral venous circulation. Liver biochemical tests and platelet count were within normal limits. In the absence of hepatotropic virus infection or alcohol-related liver disease, the alpha-1 antitrypsin level was measured at 69 mg/dL, and the Pi*ZZ phenotype was confirmed.

Liver biopsy revealed hepatocytes containing PAS-positive and PAS-D positive intracytoplasmic inclusions, findings consistent with alpha-1 antitrypsin deficiency. In addition, chronic steatohepatitis with moderate inflammatory activity (Ishak score, 6/18; portal inflammation, grade 2) and advanced fibrosis/cirrhosis characterized by portoportal bridging and nodular regeneration were identified. No documentation of family screening for AATD was available in the medical record. Given the hereditary nature of the disease, genetic counseling was provided, and screening of first-degree relatives was recommended via serum alpha-1 antitrypsin quantification and potential phenotypic and/or genotypic confirmation. Further pulmonary evaluation with measurement of lung volumes, DLCO, and longitudinal assessment of FEV_1 was proposed to better define the extent of pulmonary involvement and determine potential eligibility for alpha-1 antitrypsin augmentation therapy.[1-3] The clinical course was complicated by multiple liver disease-related events, and the patient ultimately died.

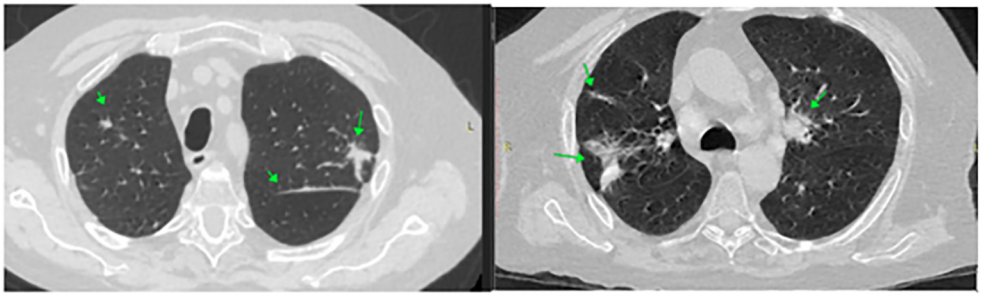
DISCUSSION

AATD is an underdiagnosed genetic disorder whose pulmonary manifestations are classically associated with emphysema (frequently panacinar) and, to a lesser extent, bronchiectasis.[1-3] Current clinical guidelines and consensus statements recommend maintaining suspicion of AATD in adults presenting with compatible lung disease or otherwise unexplained liver disease, quantifying serum alpha-1 antitrypsin levels and confirming the diagnosis via phenotype or genotype to guide targeted management strategies.[1-3]

Although emphysema remains the most widely recognized pulmonary phenotype, the radiologic spectrum of AATD may include nonclassical findings. Specifically, the prevalence and radiological evolution of pulmonary nodules have been evaluated in AATD cohorts, highlighting the importance of integrating clinical context, lesion morphology, and temporal changes before indicating routine invasive procedures.[4] Furthermore, atypical presentations of AATD with findings that mimic infection or malignancy have been reported, reinforcing the need for a stepwise diagnostic approach.[5]

In our patient, the pulmonary nodular pattern prompted the consideration of granulomatous, infectious, and neoplastic differential diagnoses. Sarcoidosis was considered because of the patient's ophthalmologic history and chronic radiologic pattern. However, bronchoscopic evaluation did not demonstrate lymphocytosis or a significant alteration in the CD4/CD8 ratio. Given the history of chronic immunosuppression, diabetes mellitus, and prior infectious complications, infectious etiologies, including mycobacterial and fungal disease, were also investigated. No microbiologic evidence of active infection was identified in the available studies. Malignancy was likewise considered because of the presence of a dominant irregular solid pulmonary nodule. Nevertheless, negative cytology, absence of significant radiologic progression, and overall clinical context favored a conservative approach with serial imaging surveillance. Although flexible bronchoscopy with BAL do not definitively exclude a malignancy in peripheral pulmonary lesions, the risk-benefit assessment supported initial observation, consistent with international recommendations for the

Image 1. High-resolution computed tomography (HRCT) of the chest: dominant solid nodular lesion associated with multiple irregular, solid nodular and pseudonodular opacities.



management of selected (non-smoker) incidental pulmonary nodules based on clinical risk and radiologic characteristics.[6]

Concomitantly, liver involvement associated with the PiZZ phenotype may be present despite normal liver biochemical tests and platelet counts. Therefore, phenotypic confirmation and histopathologic correlation remain essential when imaging findings suggest advanced fibrosis or portal hypertension.[1-3] In this patient, reduced serum alpha-1 antitrypsin levels, confirmation of the PiZZ phenotype, and liver biopsy findings demonstrating PAS/PAS-D positive inclusions and cirrhosis facilitated a definitive syndromic diagnosis and guided subsequent hepatologic management. The decision to initiate augmentation therapy requires adequate characterization of pulmonary involvement, ideally including serial spirometry, DLCO measurement, and assessment of lung volumes. The absence of comprehensive physiologic testing at initial evaluation, together with incomplete data regarding family screening, represents a limitation of the present report.[1-3]

CONCLUSION

Alpha-1 antitrypsin deficiency due to the Pi*ZZ phenotype must be considered in the presence of atypical pulmonary findings, including nodular patterns, particularly when concurrent imaging suggests liver disease despite normal liver function tests and platelet counts.[1-4] In clinically stable patients, the absence of tomographic progression on serial monitoring warrants the consideration of a conservative, surveillance-based approach. This strategy requires integrating the patient's risk profile, differential diagnoses, and available microbiologic and cytologic studies, in accordance with international recommendations for incidental nodules.[6] Phenotypic confirmation, histopathologic correlation when indicated, complete pulmonary function testing, and genetic counseling are fundamental to establishing a definitive syndromic diagnosis, guiding subsequent follow-up and targeted clinical interventions.[1-3]

Conflict of interest

Authors have no conflicts of interest to declare.

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High-resolution computed tomography (HRCT) of the chest: dominant solid nodular lesion associated with multiple irregular, solid nodular and pseudonodular opacities.

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CASE REPORT

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Pulmonary Tuberculosis with Genitourinary Involvement Presented as a "Putty Kidney"

Tuberculosis pulmonar con compromiso genitourinario: presentación como "riñón en masilla"

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ABSTRACT

Genitourinary tuberculosis is an extrapulmonary manifestation that is often underdiagnosed due to nonspecific urinary symptoms. Renal involvement may progress to advanced destructive disease with diffuse calcification ("putty kidney"), leading to severe urologic sequelae, chronic kidney disease, and even nephrectomy. We report a 28-year-old man with microbiologically confirmed pulmonary tuberculosis (positive smear microscopy, molecular testing, and respiratory culture) who developed worsening urinary symptoms (dysuria, hematuria, urinary frequency, and flank pain) and fever during hospitalization. Urinalysis revealed sterile pyuria, proteinuria, and acidic urine; urine mycobacterial smear and culture were positive. Ultrasound and non-contrast abdominal CT demonstrated advanced right renal involvement with calcifications and urinary tract stenosis, consistent with advanced genitourinary tuberculosis. A multidisciplinary approach was implemented, including double-J ureteral stent placement and continuation of standard anti-tuberculosis therapy. Renal function remained stable throughout hospitalization and follow-up. This case highlights the need to consider genitourinary tuberculosis in patients with persistent urinary symptoms and sterile pyuria, particularly in the setting of active tuberculosis, to prevent irreversible renal damage.

Key words: extrapulmonary tuberculosis | genitourinary tuberculosis | sterile pyuria | putty kidney | renal tuberculosis

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RESUMEN

La tuberculosis genitourinaria es una forma extrapulmonar frecuentemente subdiagnosticada debido a su presentación inespecífica. El compromiso renal puede progresar a estadios avanzados con destrucción parenquimatosa y calcificación difusa («riñón en masilla» o putty kidney), asociadas a secuelas urológicas graves, insuficiencia renal crónica e incluso nefrectomía. Presentamos el caso de un varón de 28 años con tuberculosis pulmonar confirmada mediante baciloscopia, prueba molecular y cultivo respiratorio positivos, que durante su internación presentó reagudización de síntomas urinarios (disuria, hematuria, polaquiuria y dolor lumbar) y fiebre. El examen de orina evidenció piuria estéril, proteinuria y pH ácido; la baciloscopia y el cultivo para micobacterias en orina fueron positivos. La ecografía y la tomografía computarizada abdominopélvica sin contraste evidenciaron compromiso renal derecho con calcificaciones y estenosis de la vía urinaria, compatibles con tuberculosis genitourinaria avanzada. (Figura 1) Se realizó un abordaje interdisciplinario con colocación de catéter doble J y continuidad del esquema antifímico. La función renal se mantuvo estable durante la internación y el seguimiento. Este caso resalta la importancia de sospechar tuberculosis genitourinaria ante piuria estéril y síntomas urinarios persistentes, especialmente en pacientes con tuberculosis activa, para evitar daño renal irreversible.

Palabras clave: tuberculosis extrapulmonar | tuberculosis genitourinaria | piuria estéril | riñón en masilla | putty kidney

INTRODUCTION

Tuberculosis (TB) remains a major public health concern in Argentina.[1] In recent years, a steady increase in the number of reported cases has been observed, underscoring its persistence as a significant public health challenge. Although pulmonary TB accounts for most cases, extrapulmonary manifestations continue to represent a substantial proportion of the disease burden and are often associated with greater diagnostic challenges. Genitourinary tuberculosis (GUTB) is frequently underdiagnosed due to its insidious course and nonspecific presentation, both of which can delay diagnosis and lead to irreversible sequelae.[2-4]

Hematogenous dissemination can involve the genitourinary tract, resulting in GUTB.2,3 Renal involvement can progress to ureteral strictures, obstruction, functional sequelae, and renal impairment.4,5 In advanced stages, diffuse calcification with parenchymal destruction and loss of function may be observed, a condition known as “putty kidney”. Although less common today due to early diagnosis and treatment, it remains a possible manifestation in patients with delayed diagnosis.[2,5]

CASE REPORT

A 28-year-old man with no known comorbidities presented with chronic cough and weight loss. He also reported intermittent urinary symptoms and prolonged fever.

Chest computed tomography (CT) revealed predominantly apical cavitation alongside alveolar infiltrates displaying a ‘tree-in-bud’ pattern. Sputum acid-fast bacilli smear microscopy and molecular testing (GeneXpert) were positive, showing no rifampicin resistance; cultures of respiratory specimens were also positive. First-line anti-tuberculosis therapy was initiated. Serologic testing for HIV, hepatitis B virus, and hepatitis C virus was negative.

During hospitalization, the patient’s urinary symptoms worsened, with dysuria, hematuria, urinary frequency, and flank pain, although no recurrent fever was documented. Urine sediment examination showed pyuria with negative routine bacterial cultures (compatible with sterile pyuria), proteinuria (+++), and acidic urine (pH, 6.0). Further evaluation revealed positive urine acid-fast bacilli smear microscopy and mycobacterial culture.

Figure 1. TChest CT (coronal reconstruction, lung window). Predominantly apical cavitation and nodular/branching opacities compatible with endobronchial dissemination (a 'tree-in-bud' pattern), in the context of active pulmonary tuberculosis.

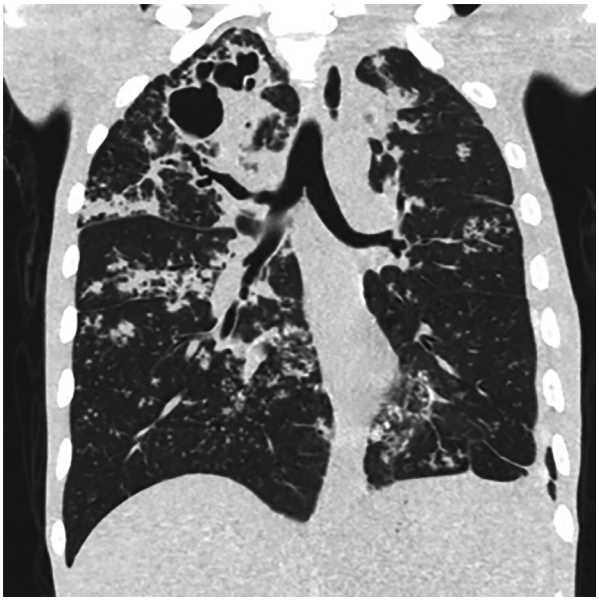
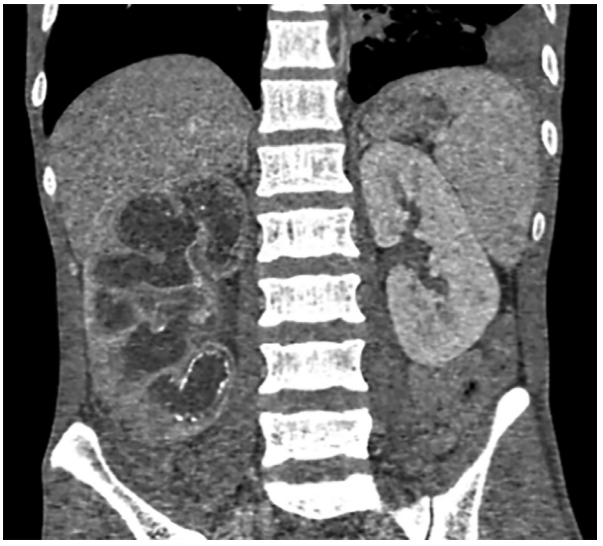


Figure 2. Contrast-enhanced abdominopelvic CT (coronal reconstruction). Right kidney showing advanced structural involvement of the pyelocaliceal system and calcifications, with findings compatible with advanced genitourinary tuberculosis associated with urinary tract strictures.



Renal ultrasound demonstrated an enlarged right kidney with echogenic material within the collecting system and renal calcifications. Non-contrast abdominopelvic CT demonstrated right renal involvement with calcifications and urinary tract stricture (Figure 2), consistent with advanced genitourinary tuberculosis. No evidence of urinary tract obstruction was identified. Renal function was preserved at the time of diagnosis and remained stable throughout hospitalization.

The patient underwent multidisciplinary management involving the Urology Service, and a double-J ureteral stent was placed for urinary drainage. The patient's clinical status improved, allowing for hospital discharge and transition to outpatient surveillance for monitoring and treatment follow-up.

DISCUSSION

Genitourinary tuberculosis (GUTB) is an extrapulmonary manifestation of tuberculosis that remains underdiagnosed because of its nonspecific presentation and typically insidious course. In Argentina, 14,914 cases of tuberculosis were reported in 2023, representing a rate of 32 cases per 100,000 inhabitants).[1] Globally, the World Health Organization estimates that approximately 84% of notified cases correspond to pulmonary tuberculosis, and 16% to extrapulmonary forms.[2] In this context, the coexistence of laboratory-confirmed pulmonary tuberculosis and persistent or worsening urinary symptoms should raise suspicion for genitourinary involvement, particularly when associated with sterile pyuria.[3,4]

Clinically, GUTB typically presents with dysuria, increased urinary frequency, urinary urgency, and hematuria, alongside flank or suprapubic pain.[3,4] A classic laboratory finding is sterile pyuria, occasionally accompanied by microscopic hematuria, proteinuria, and acidic urine; in compatible clinical scenarios, this profile necessitates targeted mycobacterial testing, including urine acid-fast bacilli (AFB) smears, cultures, and/or molecular assays.[3,4] In the present case, positive urine AFB smear and mycobacterial culture confirmed the diagnosis, explaining the discrepancy with the routine negative bacterial culture.

Diagnosis and assessment of disease severity generally require integration of microbiologic and imaging findings. The ultrasound may demonstrate renal enlargement, echogenic material within the collecting system, and calcifications, whereas CT more accurately characterizes the

extent of the disease (parenchymal involvement, calcifications, ureteral or urinary tract strictures) and guides urologic management.[5-7]

Among the advanced sequelae, the putty kidney represents late-stage disease characterized by diffuse calcification and parenchymal destruction, potentially associated with functional impairment, and urologic complications.[6,8] However, renal function may remain preserved in early-stage disease or in patients with unilateral involvement, as observed in this case. Preservation of renal function should not delay diagnosis or treatment, given the risk of progression to ureteral strictures, obstruction, and functional loss.[3,4]

Treatment consists of standard anti-tuberculosis regimen, whereas urologic intervention depends on the extent of anatomic and functional involvement. In selected patients, placement of a double-J ureteral stent or percutaneous nephrostomy may be required to relieve urinary obstruction, ensure adequate drainage, alleviate symptoms, and preserve renal function.[3,4] In the present case, multidisciplinary management, including placement of a double-J ureteral stent and continuation of anti-tuberculosis therapy, was associated with clinical improvement and stable renal function throughout hospitalization and follow-up.

To conclude, in the presence of sterile pyuria and persistent or worsening urinary symptoms –particularly in patients with active tuberculosis–genitourinary tuberculosis (GUTB) must be considered, warranting targeted urine mycobacterial testing and urinary tract imaging to prevent irreversible sequelae.[3-6]

Conflict of interest

Authors have no conflicts of interest to declare.

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CASE REPORT

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Non-Invasive Ventilatory Support in a Pediatric Patient with Guillain-Barré Syndrome in a Public Hospital in the Province of Córdoba. Case Report

Soporte ventilatorio no invasivo en un paciente pediátrico con síndrome de Guillain-Barré en un hospital público de la provincia de Córdoba. Reporte de caso

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ABSTRACT

Introduction: Patients with Guillain–Barré Syndrome (GBS) may develop acute respiratory failure as a result of muscular weakness. The optimal timing for initiating mechanical ventilation (MV) in these cases remains controversial.

Objective: To report a case of successful management using non-invasive mechanical ventilation (NIMV) in a pediatric patient with GBS treated at Hospital de Niños de la Santísima Trinidad of the Province of Córdoba.

Case description: A 6-year-old male patient presented with ocular pain, diplopia, ataxia and progressive muscle weakness, initially affecting the lower limbs and subsequently involving the upper limbs. He had a prior episode of gastroenteritis one week before symptom onset, along with specific anti-ganglioside antibodies. The medical team diagnosed an atypical presentation of GBS, characterized by rapid progression of clinical symptoms and an unusual pattern of neurological involvement. Given bibasal hypoventilation on auscultation despite preserved lung volumes on chest radiography, together with hypophonia and an ineffective cough (cough peak flow, 60 L/min), but with adequate airway protection as evidenced by effective swallowing of saliva and respiratory secretions, NIMV was initiated via an oronasal interface without supplemental oxygen. Additionally, lung volume recruitment (LVR) and mechanical insufflation-exsufflation (MIE) were performed. On day 32, the patient was discharged from the hospital, breathing spontaneously on room air.

Conclusion: This case report describes a patient with GBS who received early NIMV while maintaining adequate functional airway protection. This intervention, combined with LVR and MIE strategies, helped manage ventilatory failure and prevent the need for invasive mechanical ventilation (IMV) and contributed to a favorable clinical outcome.

Key words: Neuromuscular diseases; Guillain-Barre syndrome; noninvasive ventilation; respiratory therapy

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RESUMEN

Introducción: Los pacientes con Síndrome de Guillain-Barré (SGB) pueden desarrollar insuficiencia respiratoria aguda como consecuencia de la debilidad muscular. El momento óptimo para iniciar la ventilación mecánica (VM) en estos casos sigue siendo un tema controvertido.

Objetivo: Reportar un caso de manejo exitoso con Ventilación Mecánica No Invasiva (VMNI) en un paciente pediátrico con SGB atendido en el Hospital de Niños de la Santísima Trinidad de la Provincia de Córdoba

Presentación del caso: Paciente masculino de 6 años de edad que consultó por dolor ocular, diplopía, ataxia y debilidad muscular progresiva, que inició en los miembros inferiores y posteriormente comprometió los miembros superiores. Con un episodio de gastroenteritis una semana previa a los síntomas y resultados anticuerpos antigangliósidos específicos. El equipo médico diagnostica SGB de presentación atipica caracterizado por la rápida progresión del cuadro clínico y el patrón inusual de afectación neurológica. Ante hipoventilación bibasal auscultatoria con volumen radiográfico conservado, sumada a hipofonía y tos débil (pico de flujo tosido 60 L/min), aunque con una correcta protección de la vía aérea -evidenciada en una deglución eficaz de la saliva y las secreciones, se inició VMNI por interfase buconasal sin oxígeno suplementario. Además, se realizó reclutamiento de volumen pulmonar (RVP) y Asistencia Mecánica de la Tos (AMT). El día 32 fue dado de alta hospitalaria, respirando espontáneamente en aire ambiente.

Conclusión: Se reportó el caso de un paciente con SGB que, al conservar una adecuada protección funcional de la vía aérea, recibió de forma temprana VMNI. Esta intervención, combinada con estrategias de RVP y AMT, permitieron tratar la insuficiencia ventilatoria, evitar la VMI y facilitar una evolución clínica favorable.

Palabras clave: Enfermedades neuromusculares · síndrome de Guillain-Barré · ventilación no invasiva · terapia respiratoria

INTRODUCTION

Guillain-Barré syndrome (GBS) is an inflammatory disorder of the peripheral nervous system that, in its classic forms, is characterized by symmetric, rapidly progressive, and typically ascending muscle weakness accompanied by diminished or absent deep tendon reflexes.[1]

Several GBS subtypes have been recognized, including acute inflammatory demyelinating polyradiculoneuropathy, acute motor axonal neuropathy, and acute sensorimotor axonal neuropathy. Disease progression may be rapid, with most patients reaching peak disability within 2 weeks of symptom onset.[2,3]

Atypical GBS, in contrast, is characterized by less common manifestations, including upper extremity weakness, ptosis, neck stiffness, inability to stand because of proximal muscle weakness, headache, and dysphagia.[4]

GBS is believed to result from an abnormal immune response triggered by infection, leading to peripheral nerve injury. However, its pathogenesis is not yet fully understood. Approximately two-thirds of patients report a respiratory or gastrointestinal infection within the preceding 2 to 3 weeks. *Campylobacter jejuni* is the most frequently identified pathogen (30%).[5]

Neuromuscular disorders in children and adolescents may affect, to varying degrees, the 3 muscle groups involved in ventilation and airway protection: inspiratory muscles, expiratory muscles, and innervated bulbar muscles. Patients with GBS may develop acute respiratory failure (ARF) as a consequence of progressive weakness of the inspiratory and expiratory muscles, as well as bulbar dysfunction. The optimal timing for initiating mechanical ventilation in these cases remains controversial.[6]

To date, evidence regarding the use of NIMV for the management of respiratory failure in patients with GBS is limited, and available studies have been conducted exclusively in adult populations.[7,8] In this context, we report the successful use of NIMV in a pediatric patient with GBS treated at our institution.

This study was conducted in accordance with the Guidelines of the Declaration of Helsinki and Good Clinical Practice, with strict protection of patient confidentiality. Written informed consent for publication was obtained from the patient's parents.

CASE DESCRIPTION

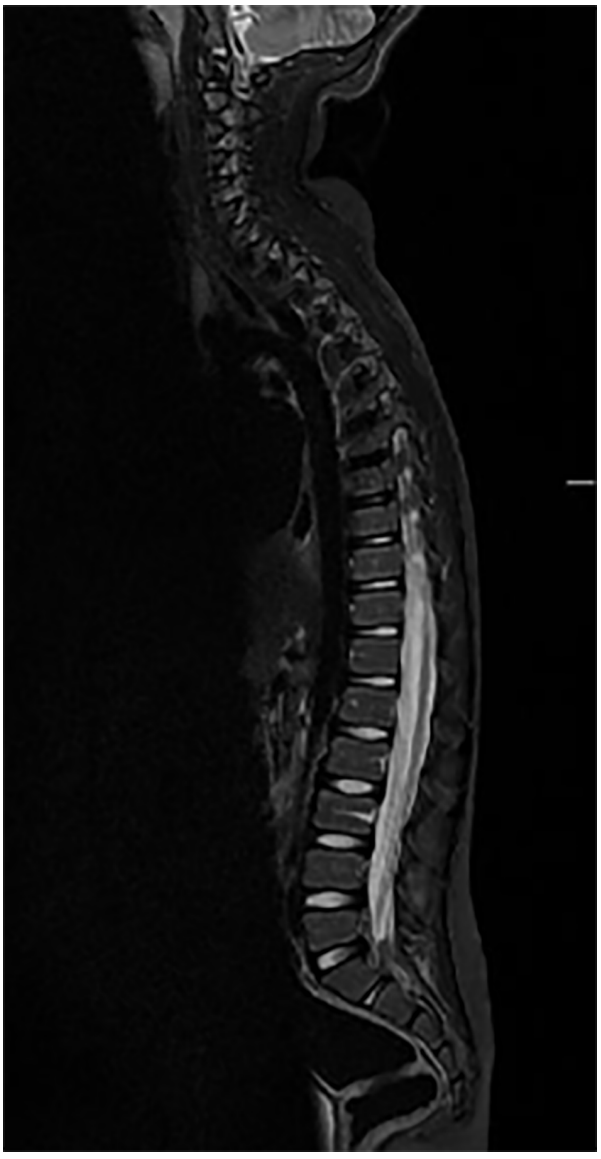
A 6-year-old boy presented to the Emergency Department of Hospital de Niños de la Santísima Trinidad, Córdoba, Argentina, on April 10, 2025. He reported ocular pain, diplopia, gait impairment, and progressive muscle weakness that initially involved the lower extremities and subsequently progressed to the upper extremities.

Upon admission to the Pediatric Intensive Care Unit (PICU), the patient was breathing spontaneously on room air and had a Glasgow Coma Scale score of 15/15. He was awake, alert, and responsive to stimuli. Deep tendon reflexes (DTR) were diminished, with apparent hyporeflexia affecting the left side of the body and flattening of the nasolabial fold. No Clonus or Babinski sign. Sensation was preserved in all four extremities. Pupils were equal, round, and reactive to light. The patient reported diplopia and exhibited marked proximal muscle weakness involving the shoulder and pelvic girdles, with inability to maintain head control. His mother reported an episode of gastroenteritis one week before symptom onset.

Lumbar puncture was performed. Serologic testing was positive for cytomegalovirus (CMV) IgM. Serum antiganglioside antibody testing yielded positive results as follows: GT1a IgG and IgM, GQ1b IgM, and in CSF: GT1a IgG and sulfatide IgG. Magnetic resonance imaging demonstrated enhancement of the cauda equina and both the anterior and posterior nerve roots (Image 1). Based on clinical findings, the medical team diagnosed an atypical presentation of GBS, characterized by rapid progression of clinical symptoms and an unusual pattern of neurological involvement.[4]

Treatment consisted of intravenous immunoglobulin (2 g/kg administered over 5 days) and analgesia. As a supportive measure, a nasogastric tube was placed, and proper positioning was ensured.

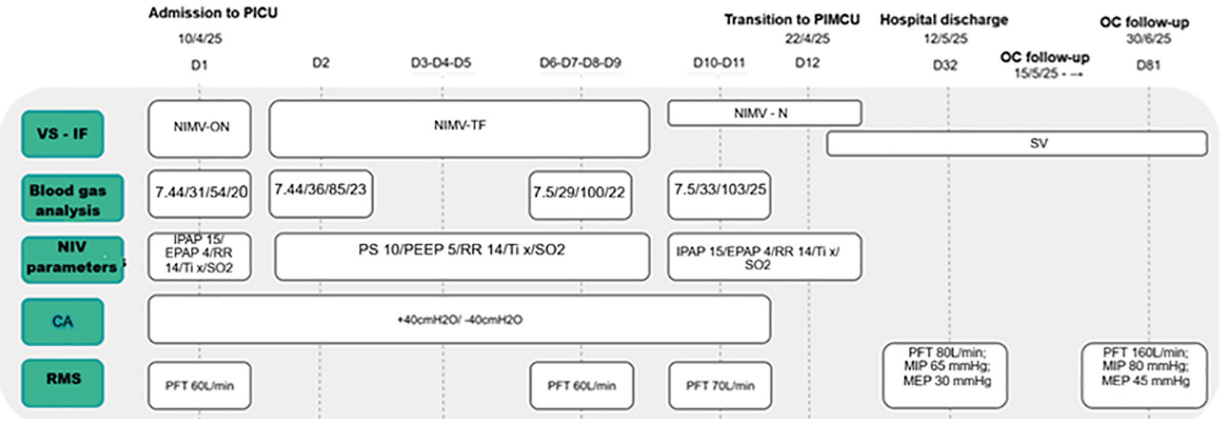
Image 1. Sagittal spine MRI (STIR sequence) showing hyperintense nerve roots



Given bibasal hypoventilation on auscultation despite preserved lung volumes on chest radiography, together with hypophonia and an ineffective cough (cough peak flow, 60 L/min), but with adequate airway protection as evidenced by effective swallowing of saliva and respiratory secretions, NIMV was initiated via an oronasal interface without supplemental oxygen. (Figure 1)

On hospital day 2, NIMV support was transitioned to a microprocessor-controlled ventilator operating in noninvasive mode with a total face

Figure 1. Timeline. Diagram illustrating the principal interventions and outcomes from hospital admission through discharge from the institution.



CA: cough assist; D: day; EPAP: expiratory positive airway pressure; IF: interface; IPAP: inspiratory positive airway pressure; N: nasal; NIMV: non-invasive mechanical ventilation; OC: outpatient clinic; ON: oronasal; PEEP: positive-end expiratory pressure; PICU: Pediatric Intensive Care Unit; PIMCU: Pediatric Intermediate Care Unit; PS: pressure support; RMS: respiratory muscle strength; *values from the latest outpatient clinic follow-up; RR: respiratory rate; SpO_2: no supplemental oxygen; SV: spontaneous ventilation; TF: total-face; Ti: inspiratory time; VS: ventilatory support

mask interface to optimize ventilatory support in response to the patient's clinical course. In addition, lung volume recruitment (LVR) was performed using a manual resuscitation bag and an inflatable mask to prevent atelectasis, facilitate secretion clearance, and improve thoracopulmonary compliance. Mechanical insufflation-exsufflation (MI-E) was also administered with pressures up to +50/−50 cm H_2O to optimize airway secretion clearance and prevent respiratory complications.[9]

On days 3, 4, and 5, functional assessments, MI-E sessions, and LVR maneuvers could not be performed because of severe radicular pain reported by the patient. Under these circumstances, any intervention that could exacerbate pain was avoided. The patient remained on NIMV with the previously established settings.

Adequate pain control was achieved on days 6 through 9. The patient continued with NIMV using a total-face interface and resumed respiratory therapy with MI-E and LVR.

On day 10, given the favorable clinical course, a well-expanded chest radiograph, and arterial blood gas values within normal limits, ventilatory support was transitioned to a continuous-flow device with a nasal interface operating in spontaneous/timed (S/T) mode.

On day 12 of PICU admission, the patient was transferred to the Pediatric Intermediate Care Unit, where progressive weaning from positive-pressure ventilatory support was continued and oral feeding was initiated. On day 32, the patient was discharged from the hospital, breathing spontaneously on room air. At the time of this report, the child remains under outpatient follow-up with neurorehabilitation, speech therapy, and respiratory therapy services.

DISCUSSION

A common clinical error is to confuse respiratory failure, typically related to abnormalities of the pulmonary parenchyma and often managed with supplemental oxygen, with ventilatory failure, which results from respiratory muscle weakness. In the latter setting, administration of supplemental oxygen without ventilatory support may mask alveolar hypoventilation and further worsen ventilatory pump failure.[9]

Respiratory impairment in NMDs is characterized by alveolar hypoventilation (resulting in hypoxemia) due to reduced ventilatory muscle pump activity despite structurally normal lungs. Supplemental oxygen does not correct alveolar hypoventilation; instead, it increases arterial oxygen tension without addressing the underlying respiratory muscle pump dysfunction. Moreover, oxygen therapy may worsen hypercapnia by blunting ventilatory drive and can mask clinical deterioration, including the presence of retained airway secretions. These patients are frequently misclassified and managed as having impaired

oxygenation due to acute respiratory failure rather than ventilatory insufficiency resulting from respiratory pump failure.[10] In our patient, early initiation of NIMV was pivotal to the favorable clinical course, providing ventilatory support that was sufficient to reduce respiratory muscle workload, optimize minute ventilation, and reverse respiratory muscle fatigue without suppressing central respiratory drive.

Acute respiratory failure develops in approximately 30% of patients with GBS, and nearly 20% require IMV.[11] In pediatric patients with GBS, IMV should be initiated at the earliest signs of respiratory muscle fatigue, before clinical decompensation occurs. Endotracheal intubation is indicated in the presence of dysphagia with salivary aspiration or ineffective airway clearance resulting from an absent or severely impaired cough.[6]

IMV is often required in GBS because recovery of respiratory muscle function is typically not expected within hours.[11] In our patient, the decision to initiate NIMV was based on the absence of impaired consciousness and bilateral facial paralysis. Although cough effectiveness was reduced, glottic closure and gag reflexes remained intact, and the patient demonstrated adequate secretion and saliva management, indicating preserved airway protection.

Consistent with our experience, a previously reported case in an adult with GBS demonstrated that NIMV could be safely used for 2 weeks in a patient who remained alert, cooperative, and capable of protecting the airway, with no evidence of dysphagia or bulbar dysfunction. This approach avoided the need for IMV and tracheostomy, and was associated with a favorable clinical outcome.7 Another study reported the use of NIMV in patients with GBS who had neither acute respiratory failure nor swallowing dysfunction and therefore maintained adequate airway protection against aspiration. In these patients, NIV avoided exposure to complications associated with endotracheal intubation, including hypoxemia, hypotension, sedation, and worsening muscle weakness.[8] In a pediatric cohort of patients with GBS, 41% required IMV, with a median duration of ventilatory support of 25 days. Among ventilated patients, 87.5% subsequently underwent tracheostomy.[12] In this context, it is noteworthy that early implementation of NIMV in our patient not only prevented progression to ventilatory failure but also avoided the need for IMV and its associated risk of tracheostomy, contributing to a favorable clinical course.

One of the key strategies in our patient was mechanical insufflation-exsufflation (MI-E). As noted by several authors, ventilatory support is often prioritized over cough-assistance techniques, despite the fact that airway clearance may be equally or even more important, particularly during the early stages of disease before ventilatory failure develops. A patient with a vital capacity of only 500 mL cannot be expected to generate an effective cough, not even with manually assisted coughing. Under normal conditions, cough produces an expiratory volume of approximately 2.3 L and peak flows ranging from 6 to 20 L/s. MI-E reproduces this physiologic mechanism by delivering a deep insufflation, typically using positive pressures of +40 to +50 cm H_2O, followed by rapid exsufflation at −40 to −50 cm H_2O.10

With respect to respiratory muscle strength assessment, a mean peak cough flow (PCF) of 179.5 ± 52.3 L/min has been reported in children younger than 10 years with neuromuscular disease (NMD).[13] These values should be interpreted cautiously, however, because normative PCF values have not yet been standardized for healthy children, adolescents, or patients with NMD in our setting.

In addition, maximal inspiratory pressure (MIP) values below 25 cm H_2O have been associated with nocturnal hypoventilation in patients with NMD. Maximal expiratory pressure (MEP) values <60 cm H_2O in individuals older than 12 years have been associated with impaired airway secretion clearance.[14]

CONCLUSIONS

This case report describes a patient with GBS who received early NIMV while maintaining adequate functional airway protection. This intervention, combined with LVR and MIE strategies, helped manage ventilatory failure, and prevent the need for IMV, and contributed to a favorable clinical outcome.

Conflict of interest

Authors have no conflicts of interest to declare.

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HIGHLIGHTS

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AAMR Obstructive Airway Disease Symposium

Jornada de enfermedades obstructivas de la vía aérea de AAMR

Manuel Ibarrola

On April 9 and 10, 2026, the Argentine Association of Respiratory Medicine (AAMR) held the "Dr. Juan Carlos Figueroa Casas" Meeting on Airway Obstructive Diseases. The meeting addressed the most relevant topics in asthma, chronic obstructive pulmonary disease (COPD), and bronchiectasis through presentations delivered by nearly 30 national respiratory health professionals and five Spanish-speaking international experts who are recognized leaders in the field.

The first day was organized in four scientific sessions and two industry-sponsored symposia, covering the following topics:

NAVIGATING UNRESOLVED ISSUES IN CURRENT GUIDELINES

There were three concise presentations focused on ongoing controversies in major guidelines for asthma and COPD management. Dr Martín Sívori, who has an extensive career in COPD research and clinical management, examined the role of spirometrically measured airflow obstruction in disease management. International guidelines have overlooked this point in recent years. Therefore, it was crucial to emphasize its key role in specific patient subgroups –supported by an appropriate literature review– and to clarify that the degree of spirometric obstruction remains a critical factor in therapeutic management

Dr. Luis Nannini reviewed the evidence supporting the use of different symptom-reliever medications in asthma. He emphasized that newer combinations of rapidly acting bronchodilators with inhaled corticosteroids offer advantages over the traditional use of short-acting bronchodilators as rescue therapy. This aligns with the latest 2026 Global Initiative for Asthma (GINA) recommendations, which increasingly de-emphasize the role of salbutamol monotherapy.

The session concluded with an evaluation, defense, and critique of various strategies used to define spirometric obstruction. Drs. Malet, Salvado, and Arce presented evidence-based perspectives, informed by both research and clinical experience, regarding the use of fixed thresholds, the lower limit of normal, and z scores in the interpretation and reporting of lung function tests. ¿Conclusion? The conclusion was left to the audience. The discussion demonstrated that every method presents unique advantages and limitations depending on its clinical application.

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ASTHMA MODULE 1

Following the formal opening of the event, and with the auditorium already filled to capacity early in the morning, the first asthma session began with a presentation by Dr. María Eugenia Franchi on the concepts of asthma control, clinical remission, and complete remission. This concise review detailed diverse clinical scenarios to evaluate potential management targets for patients. Broadly speaking, it is critical to differentiate clinical remission—defined as sustained disease control over time—from complete remission, which requires the absence of all evidence of disease activity, including biomarkers. This remains an area of active research and ongoing evolution.

In a novel addition to the scientific program, Dr. Joaquina López Moras, a specialist in thoracic imaging, discussed the role of imaging studies in asthma management. Her presentation reviewed characteristic CT findings, including mosaic attenuation, bronchial wall thickening, and mucus plugging, as well as emerging imaging modalities. Particular attention was given to functional magnetic resonance imaging (MRI) techniques using inhaled tracers capable of identifying regions of hypoventilation, along with other imaging approaches that may support diagnosis and disease assessment.

The third lecture featured the first international guest speaker from Spain, Dr. Francisco Casas, who addressed the relationship between asthma and exercise. Key topics included the distinction between exercise and physical activity, the diagnosis of exercise-induced bronchoconstriction, therapeutic approaches, and the clinical relevance of these conditions. Concluding remarks Exercise-induced bronchoconstriction and asthma associated with exercise represent physiopathologically distinct entities. Unlike asthma, exercise-induced bronchoconstriction may occur in the absence of chronic airway inflammation and therefore may require a different management approach. However, diagnostic challenges warrant caution when applying this conceptual distinction, as differentiating between these conditions in clinical practice can be difficult.

COPD MODULE 1

To foster collaboration among respiratory healthcare stakeholders, Mr. Ignacio Capparelli discussed pulmonary rehabilitation beyond traditional center-based settings. He emphasized that limited access to these programs should not prevent implementation, as remote delivery via telerehabilitation has yielded excellent outcomes in patients with COPD.

Dr. Pedro Grynblat, a pulmonologist and interventional bronchoscopist with extensive experience in the field presented and analyzed bronchoscopic lung volume reduction, an intervention infrequently used in routine clinical practice. Although not widely used in routine clinical practice, bronchoscopic lung volume reduction remains a viable therapeutic option for carefully selected patients and can be performed using various techniques.

The session concluded with a presentation by the next international guest speaker, Dr. Juan José Soler Cataluña, internationally recognized for his extensive contributions to the study and management of COPD exacerbations and, more recently, for his leading role in generating evidence on cardiovascular risk in COPD. The discussion focused on this topic under the session title, “Bidirectionality and Therapeutic Impact.” COPD and cardiovascular disease share common risk factors, epidemiologic characteristics, and systemic consequences. Their coexistence results in a detrimental bidirectional interaction that is associated with increased mortality, underscoring the need for coordinated management by pulmonologists and cardiologists.

CASE REPORT MODULE

The first day of the meeting concluded with a session led by Dr. Ana López and Dr. Fernando Saldarini, featuring a segment that has become a hallmark of the event: the Case Report Competition. In the weeks preceding the meeting, case report presentations related to the conference theme were submitted by residents from across the country. The cases were reviewed and scored, and the five highest-rated cases were selected for live presentation during the event. At the conclusion of the presentations, a winning case was chosen and awarded a prize by the AAMR. This year’s winner was a colleague from the province of Córdoba, who delivered an outstanding presentation of a highly uncommon case: Diffuse Idiopathic Pulmonary Neuroendocrine Cell Hyperplasia

(DIPNECH) in a patient initially diagnosed with asthma.

The second day of the meeting opened with a general session covering a range of topics related to airway disease.

A central aspect of disease management served as the starting point for discussion: "Inhaler Devices: A Tailored Approach for Each Patient," presented by Dr. Juan Pablo Casas. The lecture provided a comprehensive review of available inhaler therapies and the criteria that should guide device selection for individual patients.

Subsequently, Dr. Daniel Schonfeld presented highly relevant data regarding the management of patients with airway obstruction and bronchiectasis, a clinical scenario increasingly encountered during patient evaluations. Whether considered a comorbidity or a treatable trait, the presence of bronchiectasis in these patients has important implications for quality of life, survival, and clinical management.

The general session concluded with an opportunity to analyze and reflect on a highly relevant topic in contemporary respiratory health: vaping. Dr. Cristina Borrajo, former coordinator of the Smoking Cessation Section of our Association and a recognized expert in the field, delivered several clear messages: vaping causes airway injury and has no established role as a smoking-cessation intervention.

COPD MODULE 2

Continuing the discussions on current topics in COPD, Dr. Ramón Rojas clearly described how patients with COPD who continue to smoke represent a distinct phenotype from those who no longer smoke. The evidence presented left little doubt regarding the impact of ongoing tobacco use on morbidity and mortality in this patient population.

Addressing a topic that is frequently debated, the applicability of major COPD management guidelines was examined, focusing specifically on the discordance between guideline recommendations and real-world clinical practice. Dr. Gustavo Zabert presented the results of a survey conducted in the weeks preceding the meeting, highlighting clear examples of the discrepancy between ideal management and everyday practice. He then proposed a practical clinical scenario for discussion and analysis with the audience and session moderators.

The segment concluded with a presentation by the third international guest speaker, Dr. Antonio Anzueto, who provided an update on current concepts related to COPD exacerbations. He described exacerbations as a complex clinical challenge because of their multiple triggering factors and focused on one of the most significant contributors worldwide: poor treatment adherence.

ASTHMA MODULE 2

Addressing what has remained a persistent challenge without a clear solution over recent decades, Dr. Marcos Hernández reviewed the various tools available for the diagnosis of asthma. In a disease lacking a single definitive diagnostic test, how can lung volume measurements, impulse oscillometry, fractional exhaled nitric oxide (FeNO), and other complementary assessments be integrated to establish the diagnosis with maximal confidence?

At the closing of the day directed to specialists, the last two international guest speakers were presented. They discussed the management of the patient with non-T2 asthma, a complex topic that presents a challenge and an unmet obligation for the specialty. Dr. Vicente Plaza discussed the role of a promising new therapeutic tool, tezepelumab, as a biologic treatment for this group of patients, who have historically lacked targeted management strategies. Subsequently, Dr. Francisco de Borja García Cosío presented his experience and reviewed available evidence regarding an emerging approach for the phenotyping and in-depth evaluation of patients with severe asthma: endobronchial biopsy.

MODULE FOR CLINICIANS AND GENERAL PRACTITIONERS

The event concluded with a special "bonus track" session that welcomed internal medicine specialists, family physicians, and general practitioners interested in expanding their knowledge of the management of obstructive airway diseases. This space was created by the AAMR through the coordination of its immunology and obstructive diseases section as an opportunity to dialogue with those who manage a large number of patients with asthma and COPD, generally mild cases, who

have extensive contact with the first consultation and, therefore, are in the setting of initial diagnosis. Participants shared their experiences and discussed certain recommendations aimed at facilitating detection and eventual timely referral of these cases.

THE ROLE OF INDUSTRY SYMPOSIA

As in previous years, industry participation played an important role in the meeting. The sessions sponsored by the industry provided valuable updates on therapeutic tools in the area of obstructive diseases of the airway.

In the first industry space titled "New Strategies, Better Expectations. Advancing a More Ambitious Respiratory Medicine for Patients with COPD," Drs. María Eugenia Franchi and Marcos Hernández analyzed the benefits of triple therapy and biologic medications in patients with exacerbating COPD, focusing on those with underlying eosinophilic inflammation who are candidates for biologic treatments.

Continuing with the presentation of growing evidence on the role of biologic medications in obstructive diseases, Dr. Sebastián Gando discussed "Single Airway. Role of Tezepelumab in Severe Asthma and Chronic Rhinosinusitis with Nasal Polyposis."

The second day gave way to the presentation by Drs. Fernando Saldarini and Ignacio Zabert and the opportunity to address a novel and increasingly accepted viewpoint: "Asthma/COPD: Two Sides of the Same Coin." The inflammatory basis of obstructive diseases as a common point and therapeutic target.

CONCLUSIONS

A highlight of the meeting was the tribute paid to Dr. Figueroa Casas, a longstanding member of the AAMR, distinguished pulmonologist, and dedicated educator whose extensive contributions to the specialty left a lasting legacy through the many fellows, trainees, and students he mentored. The event was named in his honor.

The meeting spanned 2 full days, during which the scientific program provided a comprehensive overview of the most relevant topics. The course directors were Drs. Sebastián Ferreiro, Manuel Ibarrola, and Manuela Garro. The academic program was developed by the Scientific Committee, consisting of Drs. Miguel Penizzotto, Daniel Pascansky, Diego Litewka, Ana Stok, Gabriel García, Ricardo Del Olmo, Valeria Brichetti, Sebastián Wustten, Rosana Morales, Ana María López, and Fernando Saldarini.