# Alpha-1 Foundation Research Registry: Highlighting Pulmonary Manifestations Among Patients with Liver-Affected Alpha-1 Antitrypsin Deficiency in the USA

**Authors:** Alison Keaveny,[1] *Nadine Nuchovich,[1] Jennifer Illarramendi,[1] Randel Plant,[1] Jeanine M. D'armiento,[2] Monica P. Goldklang[2]

1. Alpha-1 Foundation, Coral Gables, Florida, USA
2. Columbia University Irving Medical Center, New York City, New York, USA

*Correspondence to nnuchovich@alpha1.org

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## BACKGROUND AND AIMS

Alpha-1 antitrypsin deficiency-associated liver disease (AATD-LD) is characterised by the accumulation of misfolded alpha-1 antitrypsin (AAT) protein in hepatocytes, causing cellular stress and inflammation.[1,2] This intracellular buildup damages hepatocytes, causing liver fibrosis and leading to severe hepatic disease, including cirrhosis and cancer.[3] Meanwhile, this backlog of mutated AAT protein results in reduced AAT protection in the lungs.[2] Consequently, individuals with dysfunctional alleles may be at risk for both AATD-LD and pulmonary disease due to subsequent low circulating AAT protein. Therefore, the authors aim to analyse patients with AATD with AATD-LD and describe concomitant pulmonary disease burden.[4]

## MATERIALS AND METHODS

The Alpha-1 Research Registry is an online database, supported by the Alpha-1 Foundation, of patients with AATD in the USA who answered a patient-reported questionnaire on health factors and comorbidities surrounding AATD. Among 3,569 patients who answered a liver disease burden questionnaire, the authors reviewed 1,776 liver-affected patients between June 2019–June 2026, who reported a positive history of abnormal liver function tests, liver symptoms, cirrhosis, metabolic dysfunction-associated steatohepatitis/metabolic dysfunction-associated steatotic liver disease, ascites, cholestasis, hepatopulmonary syndrome, portopulmonary hypertension, or bacterial peritonitis, and assessed for co-occurring pulmonary conditions.

## RESULTS

Liver-affected AATD participants identify largely as female (68.8%), white (97.3%), and have a mean age of 50.54 (±16.5 years). PiZZ genotype was most frequently reported (38.7%), followed by PiMZ (29.4%) and PiSZ (11.6%). Patients largely reported fatty liver (51.7%), cirrhosis (16.1%), and a history of childhood jaundice (30.5%). Even among those who were liver-affected, lung symptoms were the most reported reason for AATD testing (32.9%), followed by liver symptoms (21.4%).

Overall, 63.1% of patients who were liver-affected had obstructive pulmonary disease, including COPD (34.2%), adult asthma (36.8%), emphysema (25.4%), and bronchiectasis (17.8%). Patients also reported pulmonary symptoms occurring at least several days per week, including cough (48.5%), shortness of breath (44.8%), sputum production (33.0%), and wheezing (16.7%). More than two exacerbations in the previous year (defined as episodes requiring antibiotics or corticosteroids) were reported by 27.2% of patients.

Treatment for AATD lung disease (augmentation infusion therapy), either currently or in the past, was reported by 31.4%, with patients currently also on

corticosteroids (oral 9.7%, inhaled 33.0%), anticholinergics (14.3%), beta agonists (40.9%), and oxygen therapy (15.2%).

## CONCLUSION

A significant number of patients with liver-affected AATD also reported co-occurring lung involvement, symptoms, and impacted quality of life. Given the considerable multi-system overlap in patients with AATD, it is imperative patients with AATD be screened for both hepatic and pulmonary disease, and for hepatologist and pulmonologist to work collaboratively on patient care for those with AATD. Patient-led databases surveying the current scope of care for patients with AATD can also be utilised to analyse discrepancies in care and highlight avenues for strengthening interdepartmental collaboration.

### References

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