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Alpha-1-antitrypsin deficiency in children: a single-centre retrospective study

Niedobór alfa-1-antytrypsyny u dzieci – analiza retrospektywna pacjentów jednego ośrodka

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Abstract

Introduction and objective: Alpha-1-antitrypsin deficiency is a common inherited metabolic disorder. Deficiency of this serine protease inhibitor predisposes to progressive tissue damage, primarily affecting the lungs and liver. In children, the clinical presentation is heterogeneous and may extend beyond classical organ involvement. The aim of this study was to assess the relationship between serum alpha-1-antitrypsin levels and individual clinical manifestations in children with confirmed alpha-1-antitrypsin deficiency. **Materials and methods:** A retrospective analysis of medical records was performed in 18 patients (nine girls, nine boys) aged 1–17 years. In all cases, serum alpha-1-antitrypsin concentration was measured, and *SERPINA1* genotyping was performed. Clinical data, liver enzyme activity (aspartate aminotransferase, alanine aminotransferase), and family history were analysed. **Results:** The PIMZ genotype was identified in 94.4% and the PISZ genotype in 5.6% of patients. The median serum alpha-1-antitrypsin concentration was 79.0 mg/dL (range 61–96 mg/dL). The most common clinical features in the study group were recurrent respiratory tract infections (72.2%), inhalant allergy (61.1%), recurrent otitis media (38.9%), and food allergy (33.3%). Hepatic manifestations were observed in 27.8% of patients, and asthma in 22.2%. Lower alpha-1-antitrypsin levels correlated with early-onset asthma (67.5 vs. 80.0 mg/dL; $p = 0.017$). A positive family history was reported in seven patients (38.9%). **Conclusions:** Alpha-1-antitrypsin deficiency in children is characterised by a heterogeneous clinical presentation, with predominant respiratory and hepatic involvement. It should therefore be considered in the differential diagnosis of children presenting with atypical or recurrent respiratory or hepatic disorders. Although atopic conditions were frequently observed, their relationship with alpha-1-antitrypsin deficiency remains unclear and warrants further investigation.

Keywords: children, asthma, neonatal cholestasis, alpha-1-antitrypsin, AAT deficiency

Streszczenie

Wprowadzenie i cel: Niedobór alfa-1-antytrypsyny jest jedną z najczęstszych chorób metabolicznych o podłożu genetycznym. Deficyt tego inhibitora proteaz serynowych prowadzi do postępującego uszkodzenia tkanek, głównie płuc i wątroby. U dzieci obraz kliniczny jest zróżnicowany i często nieswoisty. Celem pracy była ocena manifestacji klinicznych oraz ich związku ze stężeniem alfa-1-antytrypsyny u dzieci z potwierdzonym niedoborem. **Materiał i metody:** Przeprowadzono retrospektywną analizę dokumentacji 18 pacjentów (9 dziewcząt, 9 chłopców) w wieku 1–17 lat. U wszystkich oznaczono stężenie alfa-1-antytrypsyny w surowicy oraz wykonano badania genetyczne genu *SERPINA1*. Analizowano dane kliniczne, aktywność aminotransferazy asparaginianowej i aminotransferazy alaninowej oraz wywiad rodzinny. **Wyniki:** Genotyp PIMZ

stwierdzono u 94,4% pacjentów, a PISZ u 5,6%. Mediana stężenia alfa-1-antytrypsyny wynosiła 79,0 mg/dl (zakres wartości 61–96 mg/dl). Najczęstszymi chorobami współistniejącymi z niedoborem alfa-1-antytrypsyny w badanej grupie były nawracające infekcje dróg oddechowych (72,2%), alergia wziewna (61,1%), nawracające zapalenia ucha środkowego (38,9%) oraz alergia pokarmowa (33,3%). Objawy wątrobowe występowały u 27,8% dzieci, a astma wczesnodziecięca u 22,2%. Stężenie alfa-1-antytrypsyny było istotnie niższe u pacjentów z astmą (67,5 ± 6,2 *vs* 80,0 ± 7,7 mg/dl; $p = 0,017$). Dodatni wywiad rodzinny stwierdzono u 38,9% badanych (7 dzieci). **Wnioski:** Niedobór alfa-1-antytrypsyny u dzieci charakteryzuje się zróżnicowanym obrazem klinicznym z dominującym zajęciem układu oddechowego i wątroby. W badanej populacji choroby atopowe współwystępowały z niedoborem alfa-1-antytrypsyny. Aspekt ten wymaga jednak dalszych badań. Należy uwzględniać niedobory alfa-1-antytrypsyny w diagnostyce różnicowej dzieci z nawrotowymi lub nietypowymi objawami ze strony układu oddechowego i wątroby.

Słowa kluczowe: dzieci, astma, cholestaza noworodkowa, alfa-1-antytrypsyna, niedobór AAT

INTRODUCTION

Alpha-1-antitrypsin deficiency (AATD) is one of the most common inherited monogenic disorders, with an estimated prevalence of 1:1,500–1:3,000 live births. Despite this, it remains underdiagnosed, largely due to its heterogeneous and often nonspecific clinical presentation. As a result, diagnosis is frequently delayed, with a typical interval of 6–10 years between symptom onset and confirmation of the disease[1–3].

Alpha-1-antitrypsin (AAT) is a glycoprotein produced mainly by hepatocytes and belongs to the serine protease inhibitor (serpin) superfamily. It is encoded by the *SERPINA1* gene on chromosome 14q32.1 and plays a key role in maintaining protease–antiprotease balance in peripheral tissues by inhibiting neutrophil elastase released during inflammation. This function protects the extracellular matrix from excessive degradation and helps preserve normal tissue architecture[1,4].

More than 120 allelic variants of the *SERPINA1* gene have been described. The normal genotype is designated PI*MM, while the most clinically relevant variants include the Z and S alleles. The Z allele, in either the homozygous (PI*ZZ) or heterozygous (PI*MZ) state, leads to protein misfolding and intracellular polymerisation within hepatocytes, resulting in a substantial reduction in circulating AAT levels. In individuals with the PI*ZZ genotype, serum AAT levels are typically reduced by 85–90%, whereas carriers of the PI*MZ genotype show an approximate 50% reduction[5,6]. The S allele is associated with a milder decrease (around 40%), mainly due to accelerated intracellular degradation, with the PI*SZ genotype corresponding to serum levels of approximately 37–45% of normal[7].

The clinical presentation of AATD is heterogenous and influenced by genotype, environmental factors, and likely additional genetic and epigenetic modifiers[8,9]. In adults, the disease most commonly manifests as early-onset pulmonary emphysema. In children, however, liver involvement is usually the first clinical manifestation and may include prolonged neonatal jaundice, cholestasis, hepatitis of infancy, and, in some cases, progressive fibrosis or cirrhosis[6,10,11].

In recent years, growing attention has been directed toward individuals with heterozygous *SERPINA1* variants, particularly the PI*MZ genotype. Although previously considered clinically insignificant, accumulating evidence suggests that even partial AATD may be associated with an increased risk of disease, especially in the presence of additional environmental or genetic factors[1,12]. There is also increasing recognition that the clinical spectrum of AATD may extend beyond the classical pulmonary and hepatic manifestations, particularly in children.

Despite these observations, the full clinical spectrum of AATD in paediatric populations remains insufficiently defined. In particular, non-classical manifestations are still poorly characterised and may contribute to delayed diagnosis. A better understanding of these early and often subtle features is important for improving disease recognition. Therefore, the aim of the present study was to characterise the clinical spectrum of AATD in a paediatric cohort and to assess the relationship between serum AAT levels and selected clinical manifestations.

MATERIALS AND METHODS

This retrospective study was conducted at the Department of Paediatrics, Paediatric Nephrology and Allergology, Military Institute of Medicine – National Research Institute, Warsaw, Poland. Between 2022 and 2024, serum AAT levels were measured in 1,784 hospitalised patients based on clinical indications. Reduced serum AAT concentrations were identified in 20 patients. In 18 of them, AATD was confirmed. In the remaining two patients, repeat AAT testing and genotyping were normal.

The study group therefore consisted of 18 patients with confirmed AATD. Eligibility required both a decreased serum AAT concentration measured by immunoturbidimetry (reference range 90–200 mg/dL) and detection of a pathogenic *SERPINA1* variant by RT-PCR (reverse transcription polymerase chain reaction) performed on dried blood spot samples. In one patient, genetic testing was undertaken despite a normal serum AAT concentration because of a positive family history of AATD.

Medical records were reviewed retrospectively in detail. The following variables were collected: age, sex, serum AAT

concentration (mg/dL), and AAT genotype. Clinical data included recurrent respiratory tract infections (>2 lower respiratory tract infections per year and/or >8 upper respiratory tract infections per year), chronic rhinosinusitis (duration >3 months), recurrent urinary tract infections (≥2 episodes of acute tubulointerstitial nephritis, 1 episode of upper urinary tract infection plus ≥1 episode of lower urinary tract infection, or ≥3 episodes of lower urinary tract infection), recurrent otitis media (≥3 episodes), skin disease, inhalant allergy, food allergy, adenoidal hypertrophy, hepatic manifestations [prolonged neonatal jaundice, cholestasis, hepatomegaly, or elevated aminotransferase activity (aspartate aminotransferase, alanine aminotransferase – AST and ALT)], autoimmune disease, chronic diarrhoea, abdominal pain, early childhood asthma, family history of AATD, and other chronic conditions.

Statistical analysis

Statistical analyses were performed in Python using the pandas and SciPy libraries. Continuous variables are presented as mean ± standard deviation (*SD*) or, where distribution was non-normal, as median and interquartile range (IQR). Categorical variables are reported as absolute numbers and percentages. Serum AAT concentrations were compared between patients with and without specific clinical manifestations using the Mann–Whitney *U* test for independent samples. The association between age and serum AAT concentration was assessed with Spearman's rank correlation coefficient. A two-sided p value <0.05 was considered statistically significant. Because only one patient had the PI*SZ genotype, comparisons between PI*MZ and PI*SZ were descriptive only.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki. Under local regulations, ethics committee approval was not required for this retrospective analysis.

RESULTS

Study population

The analysis included 18 patients: nine girls (50.0%) and nine boys (50.0%). Age ranged from 1 to 17 years (median 7.0 years; IQR 3.25–10.75; mean 7.7 ± 5.0 years). The PI*MZ genotype was identified in 17 patients (94.4%), while one patient (5.6%) carried the PI*SZ genotype. None of the patients had the PI*ZZ genotype.

Median serum AAT concentration was 79.0 mg/dL (IQR 71.0–83.0; range 61–96 mg/dL; mean 77.2 ± 9.0 mg/dL). The lowest value (61 mg/dL) was observed in the patient with the PI*SZ genotype, whereas the highest (96 mg/dL) was recorded in a patient with the PI*MZ genotype.

Serum AAT levels did not show a statistically significant correlation with age (Spearman's $r = 0.424$; $p = 0.079$). Detailed clinical characteristics of individual patients are presented in Tab. 1.

Clinical manifestations and comorbidities

Recurrent respiratory tract infections were the most common clinical feature, observed in 13 patients (72.2%). Inhalant allergy was the second most frequent finding, affecting 11 patients (61.1%). Recurrent otitis media was reported in seven patients (38.9%), while food allergy was present in six (33.3%).

Chronic rhinosinusitis was diagnosed in five patients (27.8%). The same proportion was observed for recurrent urinary tract infections, skin disorders, and hepatic manifestations. Skin involvement included atopic dermatitis in four patients and seborrhoeic dermatitis in one. Early-onset asthma was identified in four patients (22.2%), and adenoidal hypertrophy in three (16.7%). Chronic diarrhoea or recurrent abdominal pain was reported in two patients (11.1%). No autoimmune diseases were identified in the study group.

Hepatic involvement was observed in five of 18 patients (27.8%). Reported manifestations included prolonged neonatal jaundice with subsequent hepatic steatosis at the age of 5 years ($n = 1$), isolated prolonged neonatal jaundice ($n = 1$), neonatal cholestasis with elevated aminotransferase activity ($n = 1$), isolated elevation of aminotransferases without cholestasis ($n = 1$), and hepatomegaly ($n = 1$). ALT activity ranged from 13 to 162 U/L (median 16 U/L for the entire cohort), and AST from 19 to 100 U/L (median 37.5 U/L). Detailed characteristics of patients with hepatic involvement are presented in Tab. 2.

Other comorbidities included systemic mastocytosis ($n = 1$) and cystitis cystica ($n = 2$).

The relationship between serum AAT concentration and individual clinical manifestations was assessed using the Mann–Whitney *U* test; the results are summarised in Tab. 3. A statistically significant difference was observed only for early-onset asthma. Patients with asthma had significantly lower serum AAT levels compared with those without asthma (67.5 ± 6.2 vs. 80.0 ± 7.7 mg/dL; $p = 0.017$).

No significant differences in AAT concentration were found for any of the remaining clinical variables.

A positive family history of AATD was documented in seven patients (38.9%), including three with affected siblings, two with both maternal and sibling involvement, and one patient (PI*SZ genotype) with both parents affected.

DISCUSSION

The predominance of the PI*MZ genotype (94.4%) in this cohort is consistent with data from European populations, where heterozygous carriers of the Z allele constitute the majority of clinically identified cases[1,7]. Serum AAT levels in these patients were within the expected range for the PI*MZ genotype, reflecting a moderate degree of deficiency, which may explain the relatively mild clinical presentation observed in this group.

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No.	Age [years]	Sex	AAT [mg/dL]	AAT genotype	Recurrent respiratory tract infections	Chronic rhinosinusitis	UTI	Recurrent otitis media	Skin disease	Inhalant allergy	Food allergy	Adenoidal hypertrophy	Hepatic manifestations	AST [U/L]	ALT [U/L]	Early-onset asthma	Family history
1	5	M	70	MZ	Yes	Yes	Yes	No	Eczema	Yes	Yes	No	Neonatal jaundice, hepatic steatosis	38	21	Yes	No
2	5	F	74	MZ	No	No	No	Yes	Eczema	No	No	Yes	No	42	19	No	No
3	3	M	64	MZ	Yes	No	No	No	No	Yes	Yes	No	No	49	88	Yes	No
4	9	M	83	MZ	No	No	No	Yes	No	Yes	Yes	No	No	24	11	No	No
5	9	M	80	MZ	Yes	No	No	No	No	Yes	No	No	No	32	24	No	No
6	11	F	77	MZ	Yes	Yes	No	No	Eczema	No	No	No	Neonatal jaundice	24	15	No	No
7	15	F	75	MZ	Yes	Yes	No	No	No	No	No	No	No	52	17	Yes	No
8	4	F	67	MZ	No	No	Yes	No	No	No	No	No	No	41	21	No	No
9	3	M	61	SZ	Yes	No	No	Yes	No	Yes	No	No	No	50	49	Yes	Yes (both parents)
10	8	F	84	MZ	Yes	No	Yes	Yes	Eczema	Yes	No	Yes	No	30	11	No	No
11	6	M	66	MZ	Yes	Yes	No	Yes	No	No	No	No	No	37	16	No	No
12	2	M	83	MZ	Yes	No	No	Yes	No	Yes	No	No	No	46	29	No	No
13	2	F	80	MZ	Yes	Yes	No	No	No	No	No	No	Cholestasis, ↑ aminotransferases	98	112	No	Yes (mother, brother)
14	1	M	80	MZ	No	No	No	No	No	No	No	No	↑ Aminotransferases	100	162	No	Yes (mother, sister)
15	10	M	86	MZ	Yes	No	No	Yes	No	Yes	Yes	Yes	No	31	19	No	Yes (sister)
16	12	F	78	MZ	Yes	No	No	No	No	Yes	Yes	No	Hepatomegaly	24	13	No	Yes (brother)
17	16	F	86	MZ	Yes	No	Yes	No	Eczema	Yes	Yes	No	No	19	10	No	Yes (sister)
18	17	F	96	MZ	No	No	Yes	No	No	Yes	No	No	No	14	16	No	Yes (sister)

↑ – elevated values; **AAT** – serum alpha-1-antitrypsin concentration (mg/dL); **ALT** – alanine aminotransferase; **AST** – aspartate aminotransferase; **F** – female; **Family history** – positive family history of AAT deficiency; **M** – male; **UTI** – recurrent urinary tract infections; **Yes/No** – presence/absence of the feature.

Tab. 1. Clinical characteristics of the study patients

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Age [years]	Sex	AAT [mg/dL]	Genotype	Hepatic manifestations	AST [U/L]	ALT [U/L]
5	M	70	MZ	Prolonged neonatal jaundice, hepatic steatosis	38	21
11	F	77	MZ	Prolonged neonatal jaundice	24	15
2	F	80	MZ	Neonatal cholestasis, ↑ aminotransferases	98	112
1	M	80	MZ	↑ Aminotransferases	100	162
12	F	78	MZ	Hepatomegaly	24	13

↑ – elevated values; **AAT** – serum alpha-1-antitrypsin concentration (mg/dL); **ALT** – alanine aminotransferase; **AST** – aspartate aminotransferase.

*Tab. 2. Characteristics of patients (*n *= 5) with hepatic manifestations*

The single patient with the PI*SZ genotype had the lowest AAT level and presented with early-onset asthma and recurrent respiratory infections, consistent with previously described clinical patterns[7,9]. Although based on a single case, this finding supports the concept that lower AAT levels may be associated with a more pronounced clinical phenotype.

Respiratory manifestations and atopy

Respiratory involvement was the most common clinical feature, with recurrent infections affecting more than two-thirds of patients. This is consistent with previous reports and reflects the role of AAT in protecting the airways from protease-mediated injury[1,8,13]. Reduced AAT activity allows insufficient control of neutrophil elastase, leading to epithelial damage and increased susceptibility to infection[4]. Upper airway manifestations, including recurrent otitis media and chronic rhinosinusitis, were also frequent. Although not always emphasised in the literature, these findings suggest that AATD may affect both the upper and lower respiratory tract, contributing to persistent mucosal inflammation[8,12].

The high prevalence of inhalant allergy is another notable finding. The proportion observed in this cohort exceeded that reported in the general paediatric population, suggesting a possible link between AATD and atopy. Beyond its antiprotease function, AAT exerts immunomodulatory properties on mast cells, eosinophils, T lymphocytes, and Th2-related cytokines[1,12]. Disruption of these mechanisms may promote allergic responses.

However, the available evidence remains inconsistent. Some studies report an increased frequency of allergic disease in AATD[1], whereas others do not confirm this association[11]. At the same time, data from paediatric cohorts suggest that atopy may be more common than previously assumed[12]. The high rates of inhalant and food allergy observed in the present cohort are in line with this possibility, although they should be interpreted with caution and verified in larger studies. Whether allergic diseases and asthma represent genuine manifestations of AATD or conditions that merely co-occur with it remains a matter of debate. Most published data suggest a co-occurrence rather than a direct causal relationship, and the design of the present study does not allow us

Clinical manifestation	*n* (%)	AAT [mg/dL] (mean ± *SD*), symptom present	AAT [mg/dL] (mean ± *SD*), symptom absent	*p*
Respiratory tract				
Recurrent respiratory tract infections	13 (72.2)	76.2 ± 8.4	80.0 ± 10.8	0.656
Chronic rhinosinusitis	5 (27.8)	73.6 ± 5.6	78.6 ± 9.8	0.199
Recurrent otitis media	7 (38.9)	76.7 ± 9.9	77.5 ± 8.9	0.892
Atopic disease				
Inhalant allergy	11 (61.1)	79.2 ± 10.4	74.1 ± 5.7	0.146
Food allergy	6 (33.3)	77.8 ± 9.1	76.9 ± 9.4	0.639
Early-onset asthma	4 (22.2)	67.5 ± 6.2	80.0 ± 7.7	0.017*
Skin disorders (eczema/dermatitis)	5 (27.8)	78.2 ± 6.7	76.8 ± 10.0	0.805
Hepatic and gastrointestinal				
Hepatic manifestations	5 (27.8)	77.0 ± 4.1	77.3 ± 10.5	0.767
Chronic diarrhoea/abdominal pain	2 (11.1)	78.0 ± 11.3	77.1 ± 9.1	0.778
Other manifestations				
Recurrent urinary tract infections	5 (27.8)	80.6 ± 12.0	75.9 ± 7.8	0.299
Adenoidal hypertrophy	3 (16.7)	81.3 ± 6.4	76.4 ± 9.4	0.312
Autoimmune diseases	0 (0.0)	–	–	–

* $p < 0.05$ – statistically significant difference. **AAT** – serum alpha-1-antitrypsin concentration; ***SD*** – standard deviation. Values are expressed as mean ± *SD*. Mann–Whitney *U* test for independent samples was used.

Tab. 3. Serum AAT concentration (mg/dL; mean ± SD*) according to the presence of clinical manifestations*

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causal interference. The referral pattern of the study site – a paediatric allergology department – may also have contributed to the high observed frequency of atopic conditions through selection bias. These considerations should be borne in mind when interpreting the results.

An additional finding was the lower serum AAT concentration in patients with early-onset asthma compared with those without asthma. Although based on a small number of cases, this finding suggests that the severity of AATD may influence the development of an asthma phenotype. A possible mechanism involves increased protease activity in the airways, leading to epithelial damage and bronchial hyperresponsiveness[1,12]. Asthma is not consistently described as a distinct manifestation of AATD in children and is often included within broader categories of obstructive airway disease[8,13].

From a clinical perspective, early-onset asthma – particularly when accompanied by recurrent infections or an atypical course – may warrant consideration of underlying AATD, particularly in patients with a suboptimal response to standard treatment.

Hepatic manifestations

Hepatic involvement was observed in 27.8% of patients and typically presented in the neonatal or early infancy period, most often as prolonged jaundice, cholestasis, or elevated aminotransferase activity[6,11,14]. This pattern reflects the underlying pathophysiology of AATD, in which accumulation of misfolded Z protein in hepatocytes leads to endoplasmic reticulum stress and progressive liver injury[4].

One patient with the PI*MZ genotype presented with neonatal cholestasis and markedly elevated aminotransferases, while a sibling showed isolated elevation of liver enzymes. Although liver involvement is less common in PI*MZ than in PI*ZZ, it is well documented and should not be considered exceptional[7,15]. Previous studies indicate that even moderate AATD may be associated with clinically relevant liver disease in children[15].

Long-term outcomes appear to depend more on markers of liver injury than on the initial clinical presentation. Data from the cohort reported by Costa et al. suggest that elevated AST and higher APRI (Aspartate Aminotransferase-to-Platelet Ratio Index) at diagnosis are associated with progression to portal hypertension, whereas cholestatic jaundice alone is not an independent predictor[15]. Overall, the course of liver disease in AATD is variable and likely influenced by multiple factors.

Hepatic steatosis, observed in one patient with the PI*MZ genotype, represents a less commonly reported feature. Although not routinely described in paediatric AATD, disturbances in intracellular protein processing may interfere with lipid metabolism and contribute to steatosis[4,16].

Serum AAT levels did not differ between patients with and without liver involvement, suggesting that factors other than the degree of deficiency – such as genetic modifiers or environmental influences – may play a key role in the development of liver disease[17].

Less common manifestations

Recurrent urinary tract infections were observed in more than one-quarter of patients, representing a relatively high proportion. This association is not well characterised and may reflect local antiprotease imbalance in the urinary tract, although this remains speculative[8].

Cystitis cystica was identified in two siblings with the PI*MZ genotype. This condition has not previously been linked to AATD; however, impaired protease regulation in chronic urothelial inflammation cannot be excluded.

Skin disorders, mainly atopic or seborrhoeic dermatitis, were also relatively frequent. Although cutaneous involvement in AATD is typically associated with panniculitis, AAT exerts broader anti-inflammatory effects in the skin. Its deficiency may contribute to both impaired barrier function and increased inflammation, although current evidence remains limited[1].

Systemic mastocytosis, observed in one patient, is most likely incidental, although AAT is known to inhibit mast cell proteases, and its deficiency could potentially influence disease activity.

No autoimmune diseases were identified in this cohort. This finding should be interpreted with caution, as AATD has been associated with ANCA-associated vasculitis, particularly granulomatosis with polyangiitis[2]. The absence of such conditions is likely related to the young age of the patients, as these diseases typically present later in life.

Gastrointestinal symptoms were reported in a small number of patients. Although not well defined, AATD may affect intestinal mucosal integrity and has been linked to inflammatory bowel disease in some studies[8,17].

Family history

A positive family history of AATD was identified in 38.9% of patients, supporting the need for targeted screening of first-degree relatives in newly diagnosed cases.

LIMITATIONS

This study has several limitations, including a small sample size, single-centre design, and retrospective data collection. The presence of only one patient with the PI*SZ genotype precluded meaningful comparisons between genotypes. Furthermore, the patient profile at the study site – a department specialising in paediatric allergology and nephrology – may have influenced the spectrum of clinical presentations. Patients with predominant respiratory or allergic symptoms are more likely to be referred to this setting, which may partly explain the relatively low proportion of hepatic manifestations compared with cohorts from hepatology-focused centres. Additionally, because this was

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a retrospective analysis, it was not always possible to definitively exclude concurrent conditions as alternative or contributing explanations for the clinical features observed. Some symptoms – particularly atopic disease and recurrent infections – may have been driven partly or entirely by conditions unrelated to AATD, and this possibility cannot be excluded based on available data.

Despite these limitations, the study provides a detailed overview of the clinical spectrum of AATD in children and highlights features that may be under-recognised in routine practice.

CONCLUSIONS

1. AATD in children from the studied cohort presents with a heterogeneous clinical picture, most commonly characterised by recurrent respiratory infections and a high frequency of co-occurring atopic conditions.
2. Lower serum AAT levels were significantly associated with early-onset asthma, suggesting that the degree of deficiency may influence the respiratory phenotype.
3. Hepatic manifestations may occur even in patients with moderate AATD (PI*MZ genotype) and warrant regular biochemical and imaging follow-up.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

Author contribution

Original concept of study; writing of manuscript: AB. Collection, recording and/or compilation of data: AB, NG, KM, MŚ, DG, AŁ, AZ, SW. Analysis and interpretation of data: AB, MŚ, AŁ. Critical review of manuscript; final approval of manuscript: AB, AT, AR.

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