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Clinical impact of Aspergillus fumigatus in children with cystic fibrosis

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Background

The clinical relevance of Aspergillus fumigatus (Af) in cystic fibrosis (CF) is controversial. Aim of the study was assessing whether allergic bronchopulmonary aspergillosis (ABPA) and sensitization to Af affected lung function, body mass index (BMI) and exacerbation rate.

Methods

Over the year 2020, demographic data, BMI and lung function of patients with CF aged 6-18 years followed in the CF Centre of Parma (Italy) were recorded. According to total IgE, specific Af IgE, Af precipitins and sputum culture, patients were classified as:

- non-Af
- Af sensitized *(positive prick test or specific IgE for Af)*
- Af colonized *(2 positive sputum cultures for Af)*
- ABPA
- Aspergillus bronchitis *(precipitating Ab and clinic)*

Most recent chest CT images were reviewed and scored by Bhalla system by a radiologist blinded to clinical information.

Diagnostic Criteria
Obligatory (both needed)
Type 1 *Aspergillus* skin test positive or elevated IgE against *A. fumigatus*
Elevated total IgE levels (>1000 IU/mL unless all other criteria are met)
Other (≥2 out of 3):
Presence of IgG antibodies against *A. fumigatus* or precipitating antibodies
Presence of fleeting or fixed pulmonary opacities on chest X-ray
Eosinophil count >500 cells/μL in steroid-naïve patients

Diagnostic criteria for **Allergic Bronchopulmonary Aspergillosis (ABPA)** according to the ISHAM Working Group.

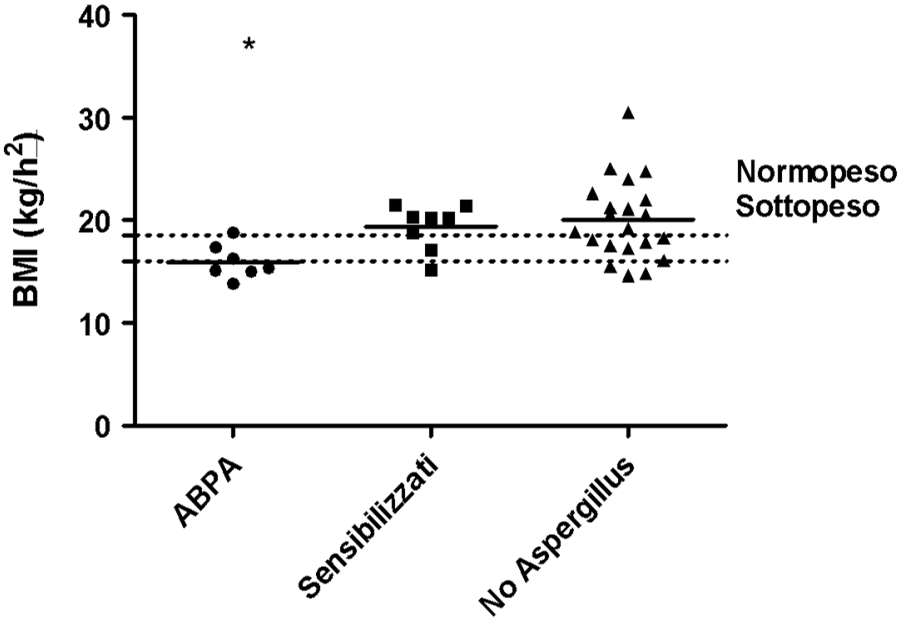
Results

Tot. 38 pz	No signs of Af n. 21 (55%)	Af sensitization n. 8 (21%)	ABPA n. 7 (18%)	Af colonization n. 1 (3%)	Aspergillus Bronchitis n. 1 (3%)
Eosinophil count	0,24±0,20	0,31±0,17	0,55±0,37	0,16±0,04	0,24±0,09
Total IgE	91,58±101,71	214,68±182,52	918,42±509	27,83±6,62	110,10±56,15
Specific IgE for Aspergillus fumigatus	0±0,01	1,10±1,48	12,51±6,56	<0,01	0,12±0,11
Aspergillus specific precipitating antibodies	17,44±140,88	42,42±240,29	64,97±340	44,33±4,04	>100
Af in sputum, n (%)	0 (0)	4 (50)	4 (57)	1 (100)	0 (0)

Results

	No signs of Af (n 21)	Af sensitization (n 8)	ABPA (n 7)	Af colonization (n 1)	Af Bronchitis (n 1)	p-value
Age, mean±SD	12.9 ± 4.3	14.6 ± 2.9	13.4 ± 2.5	17.7	16.2	ns
Sex	11 M- 10 F	5 M - 3 F	5 M- 2 F	1 M	1 M	ns
BMI (kg/m^2) mean±SD	20.36 ± 3.61	19.79 ± 2.48	16.1 ± 1.56	19.6	17.6	<0.005
Pancreatic insufficiency, n (%)	5 (24)	5 (62.5)	6 (86)	1 (100)	1 (100)	<0.001
CFTR gene mutation, n (%)						<0.001
Homo-F508del	2 (9.5)	3 (37.5)	2 (28.5)	1 (100)	1 (100)	
Hetero-F508del	15 (71.5)	3 (37.5)	2 (28.5)	-	-	
Others	4 (19)	2 (25)	3 (43)	-	-	
FEV$_1$ % predicted	91.3 ± 18.9	96.8 ± 22.3	62 ± 25.9	71.9	95.3	<0.001
FEV$_1$ change over 3 years (%)	-3.7 ± 10.2	+9.14 ± 14.1	-27 ± 19.1	-14.9	-39	
Diabetes, n (%)	1 (4.7)	2 (25)	0	0	1	ns
CT score	22.2 ± 2.8	17.1 ± 5.8	14 ± 3.6	-	-	<0.005
Exacerbations in last 12 months	0.9 ± 1.26	3.50 ± 3.25	4.43 ± 2.44	1	6	<0.005
Sputum culture						
Pseudomonas aeruginosa, n (%)	9 (42.9)	1 (12.5)	3 (42.8)	0 (0)	1 (100)	<0.005
Aspergillus, n (%)	0 (0)	2 (25)	1 (14.3)	0 (0)	0 (0)	ns
P. aeruginosa AND *Aspergillus*, n (%)	0 (0)	2 (25)	3 (42.8)	1 (100)	0 (0)	0.011
Multi-resistant bacteria, n (%)	4 (19)	2 (25)	2 (28.6)	1 (100)	1 (100)	ns

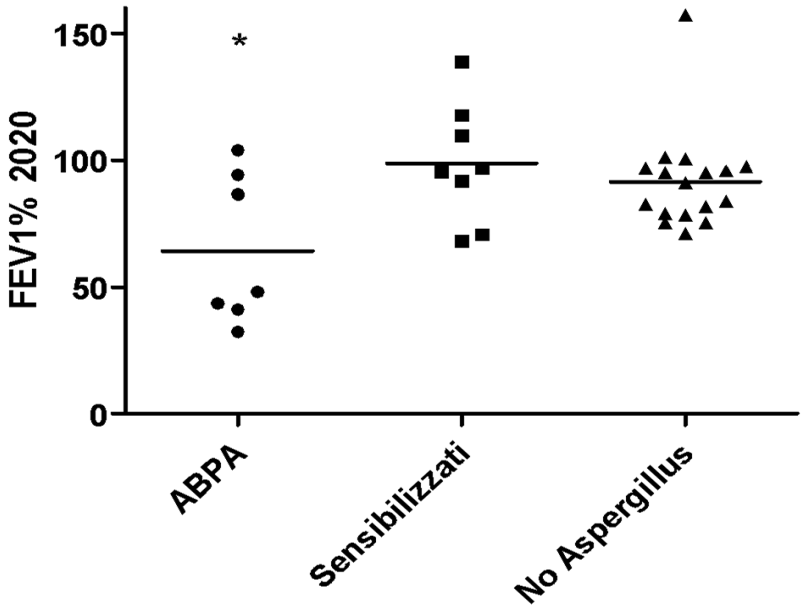
Results - BMI



Compared to non-ABPA patients, patients with **ABPA had lower BMI** (16.1 ± 1.56 vs 19.7 ± 3.4, p <0.005),

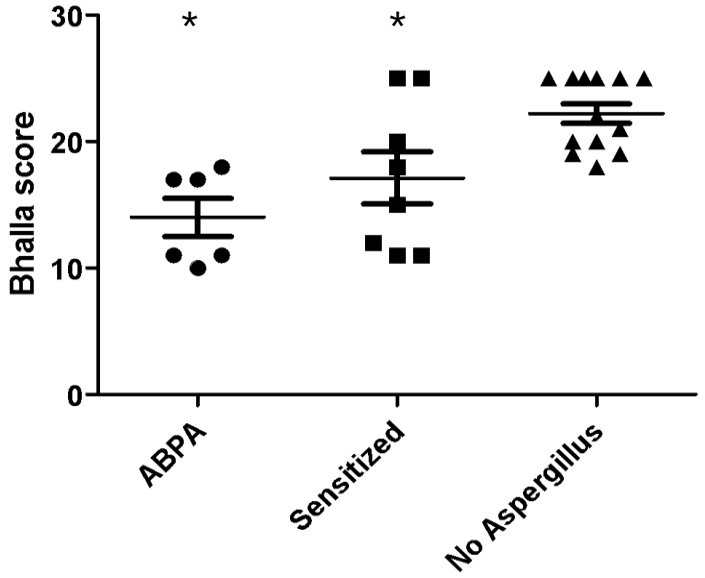
Results- FEV1

Compared to non-ABPA had
lower lung function
(FEV1 62 ± 25.9% predicted vs 92.2 ± 19.3% predicted, p 0.005).



ABPA patients showed a FEV1 decline of 27 ± 19.1% over the last three years (vs -2 ± 14% in the rest of the cohort) (p <0.001).

Results -CT scores



Compared to patients with no signs of Af, **ABPA & sensitized patients had more abnormalities at chest CT scan** (Bhalla scores: ABPA 14±3.6 vs Af sensitization 17.1±5.8 vs non-Af patients 22.2±2.8; p <0.005).

Results - exacerbations

Patients with ABPA had **higher number of exacerbations/year** (4.43 ± 2.44 vs 1.74 ± 2.33, p <0.005).

Patients with Af sensitization showed more exacerbations/year than non-Af patients (3.5 ± 3.2 vs 0.9 ± 1.2, p <0.005).

Discussion and conclusions

- **ABPA** patients had lower BMI, greater FEV1 decline, higher exacerbation rate and more lung abnormalities.
- While maintaining normal lung function, **patients sensitized to Af** have more lung abnormalities and exacerbations than children with no signs of Af.
- Not only ABPA but also **Af sensitization may have relevant clinical impact on children with CF**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