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The real-world "ControL'Asma" study: a nationwide taskforce on asthma control in children and adolescents

Maria Angela Tosca[a], Gian Luigi Marseglia[b], Giorgio Ciprandi[c]*, "ControL'Asma" Study Group[†]

[a]*Pediatric Allergy Center, Istituto Giannina Gaslini, Genoa, Italy*
[b]*Pediatrics Clinic, Pediatrics Department, Policlinico San Matteo, University of Pavia, Pavia, Italy*
[c]*Allergy Clinic, Casa di Cura Villa Montallegro, Genoa, Italy*
[†]*The "ControL'Asma Study Group" members: Elisa Anastasio, Ilaria Brambilla, Carlo Caffarelli, Federica Caricato, Loredana Chini, Riccardo Ciprandi, Valentina De Vittori, Marzia Duse, Maria Elisa Di Cicco, Sara Esposito, Viola Giovinazzo, Ahmad Kantar, Maddalena Leone, Amelia Licari, Viviana Moschese, Roberta Olcese, Diego G Peroni, Angela Pistorio, Mayla Sgrulletti, Michela Silvestri, Valeria Talarico.*

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Abstract
Background: Asthma control is the goal of asthma management. A nationwide study on this aspect was launched by the Italian Society of Paediatric Allergy and Immunology (ControL'Asma study).
Objective: To define variables associated with different asthma control grades in a nationwide population of asthmatic children and adolescents.
Methods: This cross-sectional real-world study included 480 asthmatic children and adolescents (333 males, median age 11.2 years) consecutively enrolled in 10 third level pediatric allergy clinics. According to the Global Initiative for Asthma (GINA) document, history, medication use, perception of asthma symptoms assessed by visual analog scale (VAS), clinical examination, lung function, childhood asthma control test (cACT)/asthma control test (ACT), and asthma control level were evaluated.
Results: Considering GINA criteria, asthma was well controlled in 55% of patients, partly controlled in 32.4%, and uncontrolled in 12.6%. Regarding cACT/ACT, asthma was uncontrolled in 23.2%. Patients with uncontrolled asthma had the lowest lung function parameters and VAS scores, more frequent bronchial obstruction and reversibility, and used more oral and inhaled corticosteroids (CS).
Conclusions: The ControL'Asma study, performed in a real-world setting, showed that asthma in Italian children and adolescents was usually more frequent in males. Asthmatic patients had an early onset and allergic phenotype with very frequent rhinitis comorbidity. Uncontrolled and partly controlled asthma affected about half of the subjects, and the assessment of asthma symptom perception by VAS could be a reliable tool in asthma management.

*Corresponding author: Giorgio Ciprandi. Via P. Boselli 5, 16146, Genoa, Italy. *Email address:* gio.cip@libero.it

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Introduction

Asthma is a severe global health problem, and its prevalence is increasing, mainly in children.[1] Asthma is one of the most common chronic diseases of childhood and adolescence.[2] Therefore, asthma management is a daily challenge in pediatric practice. Variability of symptoms and airflow limitation is an asthma characteristic that may vary over time and in intensity. Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation.[1] To define clinical, functional, and immunopathological patterns allows asthma phenotypes and endotypes to be identified.[3] In this regard, the allergic asthma phenotype is the most common in childhood and is defined when asthma symptoms and airway inflammation are associated with inhalation of the sensitizing allergen.[4]

Asthma management should include the assessment of asthma control, as suggested by many guidelines.[1,5-7] GINA identifies three levels of asthma control: well-controlled, partly controlled, and uncontrolled.[1] The level of asthma control is recognized by the frequency and intensity of symptoms and functional limitations. It is associated with the underlying severity, responsiveness to treatment, and adequacy of asthma care and management.[8] From a clinical point of view, the treatment is tailored to severity and adjusted based on the level of control. Many factors may affect asthma control, including socioeconomic and environmental factors, poor adherence to treatment, suboptimal treatment, or unresponsiveness to treatment.[9-11] Uncontrolled asthma is the leading risk factor for exacerbations and leads to impaired quality of life and increased health care use.[12-14] Therefore, assessing asthma control and medication use is fundamental in evaluating the effectiveness of the current treatment. Indeed, the current asthma guidelines recommend a control-based approach to management. However, achieving control can be elusive in asthmatic children. Therefore, new strategies are searched for to implement pragmatic asthma management. For this purpose, the Italian Society of Pediatric Allergy and Immunology recently established a perspectival study ("ControL'Asma") to investigate asthma control in children and adolescents managed in clinical practice.

The present study aimed to compare the asthma control levels in a group of children and adolescents suffering from asthma and recruited in a real-world setting, such as third level asthma clinics.

Ethical disclosures

Protection of human subjects and animals in research

The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and with those of the World Medical Association and the Helsinki Declaration.

Patients' data protection

Confidentiality of data
The authors declare that they have followed the protocols of their work center on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in the study.

Right to privacy and informed consent
The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Materials and methods

Patients

This cross-sectional study included a series of children and adolescents consecutively visited across 10 Italian Pediatric Allergy centers. All patients were currently treated according to the GINA guidelines based on the asthma control level.

The visit included careful history, mainly concerning asthma duration, current use of asthma medications, including inhaled corticosteroids dosage (ICS) expressed as beclomethasone equivalence, oral corticosteroids (CS) use, rhinitis, and allergy comorbidity. Clinical examination, lung function testing (including bronchodilation testing), self-administration of the childhood asthma control test (c-ACT) questionnaire, or asthma control test (ACT) for adolescents, asthma control level according to the GINA guidelines were also evaluated.[1] The inclusion criterion was a documented asthma diagnosis, based on the history of intermittent wheezing, breathlessness, cough, and chest tightness combined with reversibility to bronchodilators and/or positive response to bronchial methacholine challenge. The exclusion criteria were: history of lung disease other than asthma; recent asthma exacerbation; the presence of acute (in the last 4 weeks) or chronic upper and/or lower respiratory infections. Patients discontinued the use of long-acting and short-acting bronchodilators, respectively, for 12 and 4 h before measurement of lung function.

The Ethics Committee of the Istituto Giannina Gaslini of Genoa initially approved the procedure (code number: 22253/2017; in the context of the Italian Project "ControL'Asma" promoted by the Italian Society of Pediatric Allergy and Immunology). All the other Review Ethics Committees further approved the study procedure and written informed consent was obtained from all parents.

Clinical data were recorded by an electronic case report form designed especially for this study.

Functional assessment

Spirometry was performed using a computer-assisted spirometer (Pulmolab 435-spiro 235, Morgan, England – predictive values ECCS 1993), with an optoelectronic whirl flow meter. According to the guidelines, this spirometer fulfills the ATS/ERS standards, and it was performed as stated by the European Respiratory Society.[15,16]

Asthma control level

Asthma control level was assessed according to the GINA criteria: patients were classified as having well-controlled, partly controlled, or uncontrolled asthma.[1]

Asthma control test

Asthma control test and cACT questionnaire consisted of five questions with five possible responses, exploring the patient's perception of his/her asthma control.[17] The result could range between 0 and 25 or 27, where 25 or 27 is, respectively, the optimal asthma control.

Rhinitis

Rhinitis was considered if there was a history of typical nasal symptoms, such as itching, sneezing, watery rhinorrhea, and nasal obstruction apart from the common cold.

Allergy

The diagnosis of allergic rhinitis was made if the symptom occurrence was consistent with the exposure to the sensitizing allergen. In patients with seasonal conditions, the demonstration was simple. Instead, in patients with persistent conditions, children were asked if they developed symptoms when approaching a pet. Alternatively, when they exposed themselves to dust (opening a closet, doing housework, opening old books), they had symptoms.

Visual analog scale (VAS)

The visual analog scale (VAS) consisted of one ruler asking for asthma symptoms perception.[18] In this study, the VAS was a 10-cm vertical line on which 0 implied the most severe respiratory symptoms, while 10 corresponded to no respiratory symptom. Initially, patients (or parents or doctors) were instructed to a mark on the line indicating their symptom perception. Thus, the lower the numerical score marked by the patient was, the higher the perceived symptom severity was. With a movable marker, the subject could mark any point on the 10-cm segment that best described his/her perception. No interval marker was visible on the line. A value >6 was considered normal.

Statistical methods

Descriptive statistics of the study patients were firstly calculated; qualitative data were reported in terms of absolute frequencies and percentages; quantitative data were reported in terms of medians, first and third quartiles (1st-3rd q). The normality of distributions was evaluated using the Shapiro-Wilk test. A comparison of frequencies was performed by the Chi-square test or Fisher's Exact test (in case of expected frequencies less than 5). Quantitative data of three groups were analyzed using the non-parametric analysis of variance (Kruskal-Wallis test). Bonferroni's correction was used as a *post hoc* test to avoid multiple comparisons error, and whenever applied indicated as P_B. All statistical tests were two-sided, and a P-value of less than 0.05 was considered statistically significant. The statistical software "Statistica" (version 9, StatSoft Corporation, Tulsa, OK, USA) was used for all the bivariate analyses, and the software "Stata" (version 11, Stata Corporation, College Station, TX, USA) was used to calculate the Shapiro--ilk and the Fisher's Exact test (in case of 2 by n cross-tabulations).

Results

The clinical and demographic characteristics of the sample are shown in Table 1. There were 333 (69.4%) males

Table 1 Description of the study patients (n=480).

	N (%)
Gender:	
Male	333/480 (69.4%)
Female	147/480 (30.6%)
Age at enrollment:	
<12 years (children)	270/471 (57.3%)
≥12 years (adolescents)	201/471 (42.7%)
Age at enrollment (years)	11.2 [8.9-13.7] [n=471]
Asthma duration (years)	5 [3-8] [n=374]
Rhinitis duration (years)	5 [3- 8] [n=311]
VAS (patient)	8 [7-9] [n=476]
VAS (parent)	8 [7-9] [n=430]
VAS (physician)	8 [7-9] [n=474]
VAS (patient) ≥ 6, n/N (%)	422/476 (88.7%)
VAS (parent) ≥ 6, n/N (%)	385/429 (89.7%)
VAS (physician) ≥ 6, n/N (%)	422/473 (89.2%)
FVC - at baseline (% pred.)	98.5 [90-108] [n=434]
FEV1 - at baseline (% pred.)	96 [87-106] [n=434]
FEV1/FVC - at baseline	99 [92-105] [n=434]
FEF 25-75 - at baseline (% pred.)	86 [69-102] [n=389]
Delta FVC (% pred.)	1.2 [-2-7.9] [n=289]
Delta FEV1 (% pred.)	6 [2-13] [n=288]
Delta FEV1/FVC	5.5 [2-10] [n=279]
Delta FEF 25-75 (% pred.)	20 [7.1-35] [n=281]
Bronchial reversibility (Δ% FEV1 > 12%)	67/287 (23.3%)
Bronchial obstruction (FEV1-< 80% pred.)	55/434 (12.7%)
Rhinitis	423/480 (88.1%)
Allergy	452/476 (95.0%)
Asthma control (GINA):	
Well-controlled	263/478 (55.0%)
Partly controlled	155/478 (32.4%)
Uncontrolled	60/478 (12.6%)
cACT/ACT - *median* [1st - 3rd q]	22 [19-24] [n=474]
Asthma control (cACT/ACT):	
Well-controlled/partly controlled (cACT/ACT ≥ 20)	336/474 (70.9%)
Uncontrolled (cACT/ACT < 20)	138/474 (29.1%)
OCS (at least one course)	97/419 (23.2%)
High dose ICS	14/473 (3.0%)
Omalizumab	5/459 (1.1%)

Figures represent median values (unless otherwise specified) and figures in square brackets represent 1st and 3rd quartiles.

and 147 (30.6%) females; the median age was 11.2 years, 270 (57.3%) were children and 201 (42.7%) adolescents. The median VAS was 8 for patients, parents, and doctors; considering the subjects reporting a normal VAS value (>6), there were 422 (88.7%) patients, 385 (89.7%) parents, and 422 (89.2%) doctors. As concerns lung function, the median values were in the normal range; there were bronchial reversibility in 67 (23.3%) patients and bronchial obstruction in 55 (12.7%). Rhinitis comorbidity was present in 423 (88.1%) and allergy in 452 (95%). Asthma was controlled in 263 (55%) patients, partly controlled in 155 (32.4%), and uncontrolled in 60 (12.6%). The median cACT/ACT value was 22, subdividing patients into two subgroups: 336 (70.9%) had well-controlled/partly controlled asthma and 138 (29.1%) uncontrolled asthma. As regards treatment, 97 (23.2%) took at least a course of oral corticosteroids, 14 (3%) used high dose inhaled corticosteroids, and five (1.1%) used omalizumab.

Table 2 reports the comparison between asthma control levels and other characteristics. There were significant differences concerning VAS reported by patients, parents, and doctors, considering the categorization for normal values: the highest median values were reported in the well-controlled asthma subgroup. Lung function parameters were significantly lower in the uncontrolled subgroup, even though the median values were in the normal range. There was a significantly higher rate of bronchial obstruction in the uncontrolled subgroup and bronchial reversibility. The median cACT/ACT values were significantly lower in the uncontrolled subgroup. Categorizing cACT/ACT, the well-controlled/partly controlled asthma perception was more frequent in the well-controlled subgroup. As concerns

Table 2 Comparison among the three groups of patients: controlled, partially controlled, and not controlled according to GINA guidelines.

	Asthma control (GINA)			
	Well-controlled [N = 263]	Partly controlled [N = 155]	Uncontrolled [N = 60]	##P
Gender: Male, n/N (%)	186/263 (70.7%)	103/155 (66.5%)	43/60 (71.7%)	0.61
Age at enrollment: <12 years (children), n/N (%)	139/260 (53.5%)	94/153 (61.4%)	36/56 (64.3%)	0.15
Age at enrollment (years)	11.5 [9.2-13.8] [n=260]	10.9 [8.6-13.8] [n=153]	10.8 [9.4-12.7] [n=56]	0.32
Asthma duration (years)	5 [3-8] [n=206]	5 [3-8] [n=132]	5 [3-8] [n=36]	0.87
Rhinitis, n/N (%)	231/263 (87.8%)	137/155 (88.4%)	53/60 (88.3%)	0.98
Rhinitis duration (years)	5 [3-8] [n=174]	5 [3-8] [n=104]	5 [3-8] [n=33]	0.98
Allergy, n/N (%)	248/259 (95.8%)	144/155 (92.9%)	58/60 (96.7%)	0.38
VAS (physician)	9 [7.5-9] [n=260]	8 [6-9] [n=154]	7 [6-8.5] [n=59]	<0.0001
VAS (patient)	9 [7.5-9] [n=261]	8 [7-9] [n=154]	8 [6.5-9]	<0.0001
VAS (parent)	8.5 [8-9] [n=242]	8 [7-9] [n=136]	7 [5.5-8.5] [n=51]	<0.0001
VAS[a] (patient) ≥6, n/N (%)	240/261 (92%)	131/154 (85.1%)	50/60 (83.3%)	0.039[#]
VAS[a] (parent) ≥ 6, n/N (%)	228/242 (94.2%)	119/136 (87.5%)	38/51 (74.5%)	<0.0001[#]
VAS[a] (physician) ≥ 6, n/N (%)	249/260 (95.8%)	127/154 (82.5%)	46/59 (78%)	<0.0001[#]
FVC - at baseline (% pred.)	98 [91-106.5] [n=236]	102 [91-109.4] [n=143]	94 [85-103] [n=55]	0.018
FEV_1 - at baseline (% pred.)	97 [88.5-107] [n=236]	96 [88.1-106] [n=143]	90 [78-101] [n=55]	0.002
Bronchial obstruction				
(FEV_1 - <80% pred.), n/N (%)	25/236 (10.6%)	14/143 (9.8%)	16/55 (29.1%)	0.0005
FEV_1/FVC - at baseline	100 [93-105] [n=236]	99 [92-107] [n=143]	97 [88.8-103] [n=55]	0.07
FEF 25-75 - at baseline (% pred.)	88 [71-107] [n=217]	90 [70-106] [n=123]	70 [56-88] [n=49]	0.0003
Delta FVC (% pred.)	0 [-2-4.3] [n=157]	3 [-1-9.5] [n=94]	5.7 [1-20] [n=38]	0.0003
Delta FEV_1 (% pred.)	5 [2-9] [n=156]	8.1 [3-16.5] [n=94]	8 [4-25.8] [n=38]	0.003
Bronchial reversibility				
(Δ% FEV_1 > 12%), n/N (%)	27/155 (17.4 %)	23/94 (24.5 %)	17/38 (44.7 %)	0.002
Delta FEV_1/FVC	5 [2-9.1] [n=152]	7 [2-15] [n=91]	4 [2.5-10] [n=36]	0.28
Delta FEF 25-75 (% pred.)	19 [8.2-29.3] [n=153]	23.1 [4-39] [n=90]	21 [10-66] [n=38]	0.24
cACT/ACT	24 [22-25] [n=259]	20 [18-22]	17 [13-18] [n=59]	<0.0001
Well-controlled/partly controlled asthma (cACT/ACT ≥ 20), n/N (%)	233/259 (90%)	92/155 (59.4%)	10/59 (16.9%)	<0.0001
OCS (at least one course)	29/232 (12.5%)	45/135 (33.3%)	23/51 (45.1%)	<0.0001[#]
High dose ICS	2/259 (0.8%)	4/152 (2.6%)	8/60 (13.3%)	<0.0001[§]
Omalizumab	2/252 (0.8%)	2/146 (1.4%)	1/59 (1.7%)	0.54[§]

Figures represent median values (unless otherwise specified) and figures in square brackets represent 1st and 3rd quartiles; figures in round brackets represent column percentages; [#]P: Chi-square test; [§]P: Fisher's Exact test; [##]P: Kruskal-Wallis test.
[a]VAS: the higher the score the less severe the symptom is.

Table 3 Comparison between two groups of patients: well-controlled versus partly controlled according to GINA guidelines (Post hoc analysis).

	Asthma control (GINA)		
	Well-controlled [N = 263]	Partly controlled [N = 155]	PB
VAS (physician)	9 [7.5–9] [n = 260]	8 [6–9] [n = 154]	<0.0001
VAS (patient)	9 [7.5–9] [n = 261]	8 [7–9] [n = 154]	0.0002
VAS (parent)	8.5 [8–9] [n = 242]	8 [7–9] [n = 136]	0.0001
VAS[a] (patient) ≥ 6, n/N (%)	240/261 (92%)	131/154 (85.1%)	0.08
VAS[a] (parent) ≥ 6, n/N (%)	228/242 (94.2%)	119/136 (87.5%)	0.07
VAS[a] (physician) ≥ 6, n/N (%)	249/260 (95.8%)	127/154 (82.5%)	<0.0001
FVC – at baseline (% pred.)	98 [91–106.5] [n = 236]	102 [91–109.4] [n = 143]	0.65
FEV1 – at baseline (% pred.)	97 [88.5–107] [n = 236]	96 [88.1–106] [n = 143]	0.99
Bronchial obstruction			
(FEV1 – <80 % pred.), n/N (%)	25/236 (10.6 %	14/143 (9.8%)	0.99
FEF25–75 – at baseline (% pred.)	88 [71–107] [n = 217]	90 [70–106] [n = 123]	1.00
Delta FVC (% pred.)	0 [-2–4.3] [n = 157]	3 [–1–9.5] [n = 94]	0.030
Delta FEV1 (% pred.)	5 [2–9] [n = 156]	8.1 [3–16.5] [n = 94]	0.033
Bronchial reversibility			
(Δ% FEV1 > 12%), n/N (%)	27/155 (17.4%)	23/94 (24.5%)	0.45
cACT/ACT	24 [22–25] [n = 259]	20 [18–22]	<0.0001
Well-controlled/partly controlled asthma			
(cACT/ACT ≥ 20), n/N (%)	233/259 (90.0%)	92/155 (59.4%)	<0.0001
OCS (at least one course)	29/232 (12.5%)	45/135 (33.3%)	<0.0001
High dose ICS	2/259 (0.8%)	4/152 (2.6%)	0.49

Figures represent median values (unless otherwise specified) and figures in square brackets represent 1st and 3rd quartiles; figures in round brackets represent column percentages.
PB: P-value adjusted according to Bonferroni's correction.
[a]VAS: visual analog scale – the higher the score the less severe the symptom is.

treatment, the use of oral CS was significantly more frequent in uncontrolled patients as well as the high dose ICS. The biologic omalizumab was used in two well-controlled patients, two partly controlled, and one uncontrolled.

Tables 3, 4, and 5 report the *post hoc* analysis comparing well-controlled versus partly controlled, well-controlled versus uncontrolled, and partly controlled versus uncontrolled, respectively.

Discussion

The current study, promoted by the Italian Society of Pediatric Allergy and Immunology, evaluated the real situation of asthma control in asthmatic children and adolescents. Therefore, a nationwide study was designed to pursue this objective, involving 10 third level pediatric allergy clinics across Italy. The results revealed a real-world situation of asthma control in the country. Notably, increasing attention is presently paid to real-world studies as they may provide information more adherent to the daily practice than randomized controlled trials that involve selected patient populations which rarely mirror the real situation.[18,19]

This real-life study provided interesting findings that may, therefore, faithfully mimic the daily medical activity on asthmatic pediatric outpatients. Moreover, these 10 centers are representative of the Italian pediatric population as they are distributed homogenously across Italy and are tertiary level centers placed in hub hospitals.

The primary outcome showed that there was a relative prevalence of asthmatic males, of about 70%; this finding is surprisingly conflicting with data obtained on asthmatic adults in whom female prevalence is higher.[20,21] This discrepancy mainly depends on different hormonal patterns over the lifetime. There was a slight prevalence of children even though the median age was 11.2 years, but the median asthma duration was 5 years: this means that the asthma onset was rather early, at about 6 years. Asthma seems to onset very early and affects mainly males. Another interesting outcome was the perception of asthma symptoms assessed by VAS. This issue has been scarcely investigated in childhood. Two studies showed that asthma symptom VAS could fairly predict bronchial obstruction and bronchial reversibility.[22,23] VAS assessment could be very fruitful to achieve a quick idea of actual airflow in clinical practice.

Interestingly, the current study also included the parents' and doctors' perceptions of asthma symptoms to obtain a complete assessment of the subjective asthma experience. The median and categorized VAS results were high in patients, parents, and doctors. Rhinitis was a very frequent comorbidity, as almost 90% of asthmatics also had upper airway involvement. This finding underlines the close association between asthma and rhinitis and the concept

Table 4 Comparison between two groups of patients: well-controlled versus uncontrolled according to GINA guidelines (Post hoc analysis).

	Asthma control (GINA)		
	Well-controlled [N = 263]	Uncontrolled [N = 60]	PB
VAS (physician)	9 [7.5–9] [n = 260]	7 [6–8.5] [n = 59]	<0.0001
VAS (patient)	9 [7.5–9] [n = 261]	8 [6.5–9]	0.003
VAS (parent)	8.5 [8–9] [n = 242]	7 [5.5–8.5] [n = 51]	<0.0001
VAS[a] (patient) ≥ 6, n/N (%)	240/261 (92%)	50/60 (83.3%)	0.12
VAS[a] (parent) ≥ 6, n/N (%)	228/242 (94.2%)	38/51 (74.5%)	<0.0001
VAS[a] (physician) ≥ 6, n/N (%)	249/260 (95.8%)	46/59 (78%)	<0.0001
FVC – at baseline (% pred.)	98 [91–106.5] [n = 236]	94 [85–103] [n = 55]	0.06
FEV1 – at baseline (% pred.)	97 [88.5–107] [n = 236]	90 [78–101] [n = 55]	0.002
Bronchial obstruction (FEV1 – <80% pred.), n/N (%)	25/236 (10.6%)	16/55 (29.1%)	0.001
FEF25–75 – at baseline (% pred.)	88 [71–107] [n = 217]	70 [56–88] [n = 49]	0.0002
Delta FVC (% pred.)	0 [−2–4.3] [n = 157]	5.7 [1–20] [n = 38]	0.0005
Delta FEV1 (% pred.)	5 [2–9] [n = 156]	8 [4–25.8] [n = 38]	0.010
Bronchial reversibility (Δ% FEV1 > 12%), n/N (%)	27/155 (17.4%)	17/38 (44.7%)	0.001
cACT/ACT	24 [22–25] [n = 259]	17 [13–18] [n = 59]	<0.0001
Well-controlled/partly controlled asthma (cACT/ACT ≥ 20), n/N (%)	233/259 (90%)	10/59 (16.9%)	<0.0001
OCS (at least one course)	29/232 (12.5%)	23/51 (45.1%)	<0.0001
High dose ICS	2/259 (0.8%)	8/60 (13.3%)	<0.0001

Figures represent median values (unless otherwise specified) and figures in square brackets represent 1st and 3rd quartiles; figures in round brackets represent column percentages.
PB: P-value adjusted according to Bonferroni's correction.
[a]VAS: visual analog scale – the higher the score the less severe the symptom is.

that the evaluation of the upper airways deserves adequate attention in all asthmatics.[24] Consistently, allergy was present in 95% of patients. In other words, the allergic phenotype is predominant in childhood and adolescence and confirms the clinical relevance of type 2 inflammation in asthma pathogenesis.[25] In this regard, the use of more aggressive therapy, such as systemic corticosteroids, is relatively frequent, affecting about one-quarter of patients.

On the contrary, high dose ICS are very rare, concerning only 3%. Biologic use is still minimal, as only 1% was treated with omalizumab. These findings are substantially conflicting with the asthma control level observed in the current study. Well-controlled asthma was achieved in 55% of patients, but 32.4% had partly controlled and 12.6% uncontrolled. These outcomes are consistent with literature data showing that it is challenging to obtain good control of asthma.[26–28] Many factors may be involved in partly uncontrolled asthma, including severe pheno-endotypes, comorbidity, poor adherence, emotional disorders. In this regard, asthma control perception may be an intriguing issue. The asthma control questionnaire revealed that about 30% of patients perceived uncontrolled asthma. This outcome conflicts with the GINA asthma control level that is considerably lower (12.6%). It may, however, depend on different factors, as recently reported.[29]

Comparing the three subgroups analyzed by the asthma control level, the uncontrolled patients had, as expected, the lowest spirometry parameters (including bronchial obstruction and reversibility) and cACT/ACT scores as well as VAS values (including parents and doctors), and more use of corticosteroids (both oral and inhaled). These significant differences also remained in the *post hoc* analysis. However, allergy and rhinitis comorbidity did not affect the differences among subgroups. It could mean that type 2 inflammation is a pivotal sign of asthma in childhood and adolescence. Thus, tailored treatment should target airway eosinophilic infiltrate using anti-inflammatory drugs, namely CS or biologics in severe asthma. However, high dose ICS are barely used, whereas systemic CS is more frequently used. Probably, this might depend on low adherence issues or inadequate follow-up, also considering the time interval.

The current study confirmed the literature data but has added some interesting information. The assessment of asthma symptom perception may be a valuable parameter for an immediate idea concerning the asthma trend, including clinical and functional aspects.

The main limitation of this study was the cross-sectional design, but a detailed longitudinal study is still ongoing. Another limitation was the presence of some missing data, but it was compatible with a real-world study. On the other hand, the study's strength was the nationwide size that provides generalizability of the outcomes. Moreover, this study reinforced the difference between the different scores used in the assessment of asthma control.

Table 5 Comparison between two groups of patients: partly controlled versus uncontrolled according to GINA guidelines (Post hoc analysis).

	Asthma control (GINA)		
	Partly controlled [N = 155]	Uncontrolled [N = 60]	P_B
VAS (physician)	8 [6-9] [n=154]	7 [6-8.5] [n=59]	0.38
VAS (patient)	8 [7-9] [n=154]	8 [6.5-9]	0.99
VAS (parent)	8 [7-9] [n=136]	7 [5.5-8.5] [n=51]	0.10
VAS[a] (patient) ≥ 6, n/N (%)	131/154 (85.1%)	50/60 (83.3%)	0.98
VAS[a] (parent) ≥ 6, n/N (%)	119/136 (87.5%)	38/51 (74.5%)	0.09
VAS[a] (physician) ≥ 6, n/N (%)	127/154 (82.5%)	46/59 (78%)	0.84
FVC - at baseline (% pred.)	102 [91-109.4] [n=143]	94 [85-103] [n=55]	0.020
FEV_1 - at baseline (% pred.)	96 [88.1-106] [n=143]	90 [78-101] [n=55]	0.008
Bronchial obstruction			
(FEV_1 - <80% pred.), n/N (%)	14/143 (9.8%)	16/55 (29.1%)	0.002
FEF_{25-75} - at baseline (% pred.)	90 [70-106] [n=123]	70 [56-88] [n=49]	0.0009
Delta FVC (% pred.)	3 [-1-9.5] [n=94]	5.7 [1-20] [n=38]	0.33
Delta FEV_1 (% pred.)	8.1 [3-16.5] [n=94]	8 [4-25.8] [n=38]	0.78
Bronchial reversibility			
(Δ% FEV_1 > 12%), n/N (%)	23/94 (24.5%)	17/38 (44.7%)	0.06
cACT/ACT	20 [18-22]	17 [13-18] [n=59]	<0.0001
Well-controlled/partly controlled asthma			
(cACT/ACT ≥ 20), n/N (%)	92/155 (59.4%)	10/59 (16.9%)	<0.0001
OCS (at least one course)	45/135 (33.3%)	23/51 (45.1%)	0.36
High dose ICS	4/152 (2.6%)	8/60 (13.3%)	0.015

Figures represent median values (unless otherwise specified) and figures in square brackets represent 1st and 3rd quartiles; figures in round brackets represent column percentages.
PB: P-value adjusted according to Bonferroni's correction.
[a]VAS: visual analog scale - the higher the score the less severe the symptom is.

On the other hand, a study exploring the possible correlation between the different instruments is ongoing.

In conclusion, the ControL'Asma study showed that asthma in Italian children and adolescents was usually more frequent in males, had an early onset and allergic phenotype with very frequent rhinitis comorbidity; uncontrolled and partly controlled asthma affected about half of subjects; and the assessment of asthma symptom perception by VAS could be a reliable tool in asthma management.

Conflict of interest

All authors declare that there is no conflict of interest.

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