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Severe asthma in adult, inner-city predominantly African-American and Latinx population: demographic, clinical and phenotypic characteristics

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ABSTRACT

Introduction: The burden of asthma morbidity with co-existing atopy among the racial/ethnic minorities in the socio-economically disadvantaged NYC borough of the Bronx is unusually high. The multidisciplinary Montefiore Asthma Center (MAC) provides guideline-based treatment to this high-risk population through the joint efforts of Allergists/Immunologists, Pulmonologists, and on-site health educators.

Methods: The objective of this prospective, observational study was to define the demographic and clinical characteristics of severe asthma, evaluate improvement in asthma severity and lung function through the course of treatment at the MAC, and describe the asthma phenotypes of the patients managed at the MAC. Adults with severe asthma receiving treatment at the MAC were followed from their first to their last visit at the MAC. Patient demographics, along with asthma severity and co-existing allergies, were assessed. Possible phenotypes were defined (based on presence or absence of atopy, age at asthma onset, and blood eosinophil counts).

Results: 227 patients were included in the final analysis, of which 55.5% were Hispanic and 33.9% identified as non-Hispanic Black. Ninety-one percent (91%) of our cohort was found to be atopic and allergic rhinoconjunctivitis (ARC) was the most commonly identified co-existing allergic condition (86.3%). Mean Asthma Control Test (ACT) scores improved from 11.1 ($\pm$ 4.9) at the initial visit to 14.8 ($\pm$ 6.1) at the last visit. The spirometric values did not improve despite treatment at MAC.

Conclusion: A multidisciplinary severe asthma center is an ideal setting to phenotype patients and offer personalized guideline-based management and education to adults with severe asthma.

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Introduction

Asthma imposes a substantial burden on the New York State (NYS) healthcare system. The prevalence of asthma among adults in NYS is 10.1% as compared to 7.7% in the rest of the United States (1). The borough of the Bronx in New York City exhibits disproportionately high asthma rates, especially when compared to NYS and national averages. In 2016, among adults 18–64 years old, there were 18 202 asthma related emergency department (ED) visits in the Bronx at a rate of 198.6 per 10 000 as compared to 68.9 per 10 000 for NYS (2). With regards to asthma-related hospitalizations, for adults 18–64 years old, the Bronx has a hospitalization rate of 26.4 per 10 000 as compared to 7.0 per 10 000 for NYS (3).

Furthermore, the highest asthma-related mortality in NYS was reported in the Bronx with an age-adjusted asthma death rate of 43.5 per 1 million (4). A closer look at the racial make-up of the affected population reveals striking racial disparities. Adults with asthma who identified as non-Hispanic black and Hispanic had higher rates for asthma-related ED visits (15.5 per 100 and 8.5 per 100, respectively) compared to non-Hispanic whites (3 per 100) in NYS (4). These numbers demonstrate the heavy burden of asthma in the Bronx. Possible causes of this excess morbidity include poverty (5), outdoor and indoor pollution and high pollen concentrations, suboptimal access to healthcare, lack of patient knowledge regarding proper medication use, and patients' difficulty adhering to medical regimens (6–8).

Montefiore Medical Center (MMC), the largest health care system in the Bronx, serves approximately 40 000 adults and children with asthma through its inpatient and outpatient facilities. Most patients receiving care at MMC are from the inner city, and predominantly African American and Latinx individuals. The Montefiore Asthma Center (MAC) was established in June 2011 to address the need for multidimensional and patient-centered interventions to improve patient education and asthma outcomes in this vulnerable population. The MAC offers patients with severe asthma a unique team-based approach that combines close collaboration between Allergists/Immunologists, Pulmonologists, respiratory technicians, and asthma educators. Each year, the MAC evaluates nearly 700 patients, many of whom have refractory and poorly controlled asthma.

The present report describes the characteristics of the adult patients with severe asthma treated at the MAC from 2011–2015. We present the demographic, clinical, and laboratory characteristics and describe the co-existing allergies in this cohort. We also classified this cohort into phenotypes based on clinical and inflammatory characteristics and compared the asthma severity among the described phenotypes.

Methods

Study design and participants

We conducted a prospective, observational, 5-year study (2011–2015) of patients with severe or refractory asthma who received care at the MAC. The study included patients 18 years of age and older with severe asthma, defined as having at least one emergency department visit, one hospitalization or having received oral corticosteroids at least once for an asthma exacerbation during the previous year. A total of 227 patients were followed-up in the MAC from the time of their first visit until the final documented MAC visit. No experimental intervention was involved, and participants continued to receive medications for their asthma as decided by the treating MAC physician (Allergist/Immunologist, Pulmonologist, or both). The design and protocol of this observational, minimal risk study was approved by the Institutional Review Board.

Data collection

The MAC team developed an electronic health record template that facilitated the collection of clinical outcome measures including the Asthma Control Test

(ACT) (9), a validated 5-item survey of asthma control and the Patient Health Questionnaire-9 (PHQ-9) (10), a validated 9-item questionnaire used to assess depression severity. At the time of the patient encounter, these measures were collected for all visits by the nursing staff and MAC physicians. The following information was collected at the initial patient visit: age, sex, race/ethnicity, preferred language, health insurance type, smoking history, correctness of metered dose inhaler (MDI) technique (assessed by a MAC physician), body mass index, ACT score, PHQ-9 score, absolute eosinophil count, serum total immunoglobulin E (IgE) measured by Radioallergosorbent test (RAST), environmental allergy skin testing (SPT), pulmonary function testing (PFT) values, and age at asthma onset. Clinical data collected at the final MAC visit included ACT (9), PHQ (10), absolute eosinophil count, serum total IgE, and PFT. Additional information was also recorded, including, strongyloides IgG, ever having received allergen immunotherapy (either before the first visit or anytime during MAC treatment), allergen-specific serum IgE levels, and co-existing allergies (allergic rhinoconjunctivitis, eczema, and food allergies). Strongyloides IgG was collected since studies have shown an association between helminth exposure and asthma and allergic diseases, and also since parasitosis is a contraindication to biologic therapy (11) (MAC patients are considered for asthma biologics). Also, information on the number of controller medications the patients were taking in the year before their first visit to MAC as well as the number of courses of oral corticosteroids (OCS) received over the course of treatment at MAC were collected. The different types of controller medications included inhaled corticosteroids (ICS), ICS combined with long-acting beta-agonists (ICS/LABA), leukotriene inhibitors, long-acting muscarinic antagonists, and maintenance OCS. Well controlled asthma was defined as an ACT score of > 19 while an ACT score of ≤ 19 indicated poorly controlled asthma. An elevated blood eosinophil count was defined as ≥ 300 cells/ μ L and a count of < 300 cells/ μ L was considered normal.

Evaluation of subjects' atopic status

Patients with at least one positive skin prick test (SPT) or allergen-specific Ig E (≥ 0.35 kU/L) to any single allergen or both were categorized as atopic. SPTs for common aeroallergens (tree, grass, weed, plantain and ragweed pollens, dust mite, feathers, cat, dog, cockroach, three different mixtures of mold extracts, A.

fumigatus and mouse) were performed in the office using a ComforTen applicator (Hollister-Stier Laboratories, Spokane, WA). The allergenic extracts were applied on the anterior forearm in patients who had not received antihistamines for at least 1 week. Histamine (10 mg/mL) and physiologic saline solution were used as positive and negative controls, respectively. Skin reactions were evaluated after 15 min of application. A positive reaction was characterized as a wheal response at least 3 mm larger in diameter than the negative control (12,13).

To measure co-existing allergic conditions, data were collected on a history of eczema (self-reported or diagnosed by the physician), allergic rhinoconjunctivitis (self-reported or diagnosed by a physician), and food allergies (self-reported or identified via SPT).

Statistical analysis

Descriptive statistics were used to summarize participants' characteristics. Results were reported as either the mean $\pm$ standard deviation [SD] or as the median $\pm$ interquartile range (IQR), based on the distribution of the data. Demographic and clinical characteristics were analyzed and compared in the entire cohort, which was also stratified by age groups (19–39 years, 40–59 years, 60–85 years), gender, atopic status, the presence of eosinophilia, and early (< 12 yrs) versus late onset of asthma ($\geq$ 12 yrs). To assess change in asthma control between the first and the last visit at MAC, t-tests were used to compare ACT scores in a subset of patients who had ACT scores available from both the initial as well as the last visit at MAC. A p values < 0.05 was considered statistically significant.

Results

Demographic, clinical and laboratory characteristics of the entire cohort

A total of 227 eligible patients with severe asthma treated at the MAC were included in the study. The demographic and clinical characteristics for the 227 patients are shown in Table 1. Of the entire cohort, 82.3% were female, the majority were Hispanic (55.5%), with patients who identified as Black non-Hispanic being the next most common at 33.9%, while only 3% were white. Most patients had private insurance (48.4%), 37% had Medicaid, and 4.4% had Medicare. Overall, 59.9% of the patients were obese (BMI $\geq$ 30) and 28.2% were overweight (BMI 25–30).

60.7% of the cohort had never smoked, 24.6% were former smokers who had quit and 14.1% were current smokers. The mean ACT score at the initial visit was 11.1 ($\pm$ 4.9), and 7.4% of the cohort had well controlled asthma (ACT >19) while 85.4% had poorly controlled asthma (ACT $\leq$ 19). 20.7% had mild depressive symptoms (PHQ-9 score of 5–9) while 9.7% had moderate symptoms (PHQ-9 score of 10–14). Patients had a median of 6 ($\pm$ 9) MAC visits and were followed for a mean 16.7 ($\pm$ 14.4) months by both the Allergist and the Pulmonologist together at the MAC. The technique for inhaler use was correct in 25.5% of the patients and incorrect in 47.1% at the initial visit, which improved to 52.4% using the correct technique, while only 14.9% demonstrated an incorrect technique at the last MAC visit. 51.1% had never received immunotherapy (either at MAC or another center), while 22.5% had received immunotherapy at some point in their lifetime, with the data not available in 26.4%.

Laboratory characteristics for the cohort, stratified by age group are presented in Table 2. The median serum total IgE for the 168 patients in whom the data was available at the first visit was 222 ($\pm$ 487.45) IU/mL. Of these, 58.9% patients had elevated IgE while 41.0% had normal levels. For the patients in which the data were available, 37.3% had elevated blood eosinophil counts while 62.7% had normal counts at the initial visit ($n=185$), with similar numbers of 38.8% with elevated counts and 61.2% with normal counts at the final visit ($n=121$). Strongyloides IgG was positive in 9.2% and negative in 90.8%, of those tested ($n=98$). eTable1 details the baseline characteristics in the cohort stratified by gender.

Co-existing allergic conditions

In the study population, 90.7% (206/227) of the patients suffered from at least one of the assessed allergic co-morbidities. Allergic rhinoconjunctivitis (ARC) was the most common condition (86.3%, 196/227) and 42.3% of the cohort (96/227) had a concomitant food allergy with asthma, while 9.3% (21/227) had concomitant eczema at some point in their lifetime. (Figure 1) In the entire cohort, 4.4% (10) had all three allergic co-morbidities (food allergy, eczema, and ARC) with asthma, while 9.3% (14) did not have any co-morbid conditions. Co-existing food allergy and ARC were present in 34.4% (78) of the study population, eczema and ARC in 7.9% (15), while 4.8% (11) patients had eczema and food allergy, with asthma.

Table 1. Demographic and clinical characteristics of the cohort at baseline (stratified by age).

	Entire cohort (n=227)	Entire cohort		
		19- 39 yrs	40-59 yrs	60-85 yrs
No. of patients, n (%)	227 (100)	50 (22.0)	120 (52.8)	57 (25.1)
Race/ Ethnicity, n (%)				
Hispanic	126 (55.5)	25 (50)	67 (55.8)	34 (59.6)
Black	77 (33.9)	18 (36)	46 (38.3)	13 (22.8)
White	7 (3.0)	2 (4.0)	3 (2.5)	2 (1.6)
Asian	4 (1.7)	1 (2.0)	0 (0.0)	3 (2.5)
Others/ NA	13 (5.7)	4 (8.0)	4 (3.3)	5 (8.7)
Insurance, n(%)				
Medicare	10 (4.4)	0 (0.0)	3 (2.5)	7 (12.2)
Medicaid	84 (37.0)	17 (34.0)	41 (34.1)	26 (45.6)
Private	110 (48.4)	26 (52)	65 (54.1)	19 (33.3)
Others/ NA	23 (10.1)	7 (14)	11 (9.1)	5 (8.7)
BMI				
Mean $\pm$ SD	33.5 $\pm$ 9.0	31.7 $\pm$ 10.2	34.7 $\pm$ 8.9	32.5 $\pm$ 8.1
<18.5 (Underweight), n (%)	1 (0.4)	0 (0.0)	0 (0.0)	1 (1.7)
18.5 - < 25 (Healthy weight), n (%)	24 (10.5)	13 (26)	6 (5.0)	5 (8.7)
25 - < 30 (Overweight), n (%)	64 (28.2)	10 (20)	35 (29.1)	19 (33.3)
$\geq$ 30 (Obese), n (%)	136 (59.9)	26 (52)	79 (65.8)	31 (54.3)
N/A	2 (0.8)	1 (2.0)	0 (0)	1 (1.7)
Smoking history				
Current smokers, n (%)	32 (14.1)	8 (16)	20 (16.6)	4 (7.0)
Former/ Quit, n (%)	56 (24.6)	10 (20)	31 (25.8)	15 (26.3)
Never smoked, n (%)	138 (60.7)	32 (64)	68 (56.6)	38 (66.6)
N/A, n (%)	1 (0.004)	0 (0.0)	1 (0.8)	0 (0.0)
ACT, at initial visit				
Mean $\pm$ SD	11.1 $\pm$ 4.9	10.8 $\pm$ 4.9	10.7 $\pm$ 4.8	12.3 $\pm$ 5.2
ACT > 19, n (%)	17 (7.4)	3 (6.0)	10 (8.3)	4 (7.0)
ACT $\leq$ 19, n (%)	194 (85.4)	46 (92)	106 (88.3)	42 (73.6)
N/A, n (%)	16 (7.0 %)	1 (2.0)	4 (3.33)	11 (19.3)
ACT, at last visit				
Mean $\pm$ SD	14.8 $\pm$ 6.1	15.2 $\pm$ 6.9	14.4 $\pm$ 6.3	15.5 $\pm$ 4.9
ACT > 19, n (%)	35 (15.4)	8 (16)	19 (15.8)	8 (14)
ACT $\leq$ 19, n (%)	95 (41.8)	18 (36)	53 (44.1)	24 (42.1)
N/A, n (%)	97 (42.7)	24 (48)	48 (40)	25 (43.8)
PHQ, at Initial visit				
Mean $\pm$ SD	3.8 $\pm$ 3.6	3.60 $\pm$ 3.8	3.9 $\pm$ 3.7	3.7 $\pm$ 3.3
0-4 (Minimal or none), n (%)	132 (58.1)	30 (60)	75 (62.5)	27 (47.3)
5-9 (Mild), n (%)	47 (20.7)	9 (18)	23 (19.1)	15 (26.3)
10-14 (Moderate), n (%)	22 (9.7)	4 (8.0)	14 (11.6)	4 (7.0)
15-19 (Moderately severe), n (%)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)
20-27 (Severe), n (%)	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)
N/A, n (%)	26 (11.4)	7 9(14)	8 (6.6)	11 (19.2) [†]
Number of visits in MAC (Allergy and pulmonary visits)				
Median $\pm$ IQR	6.00 $\pm$ 9	4 $\pm$ 5	6 $\pm$ 9	8 $\pm$ 9
Data unavailable, n	3 (1.3)	2 (4)	1 (0.8)	0 (0.0)
No. of months followed by allergist and pulmonologist together				
Mean $\pm$ SD	16.7 $\pm$ 14.4	14.3 $\pm$ 12.1	16.5 $\pm$ 12.7	19.0 $\pm$ 14.6
Data unavailable, n	34 (14.9)	12 (24)	13 (10.8 %)	9 (15.7)
Inhaler use technique correct at initial visit				
Yes, n (%)	58 (25.5)	21 (42)	32 (26.6)	5 (8.7)
no, n (%)	107 (47.1)	15 (30)	61 (50.8)	31 (54.3)
Not assessed/ Not documented, n (%)	62 (27.3)	14 (28)	27 (22.5)	21 (36.8)
Inhaler use technique correct at last visit				
Yes, n (%)	119 (52.4)	25 (50)	67 (55.8)	27 (47.3)
no, n (%)	34 (14.9)	5 (10)	20 (16.6)	9 (15.7)
Not assessed/ Not documented, n(%)	74 (32.5)	20 (40)	33 (27.5)	21 (36.8)
Ever Received Immunotherapy?				
Yes	51 (22.5)	7 (14)	27 (22.5)	17 (29.8)
No	116 (51.1)	28 (56)	65 (54.1)	23 (40.3)
N/A	60 (26.4)	15 (30)	28 (23.3)	17 (29.8)

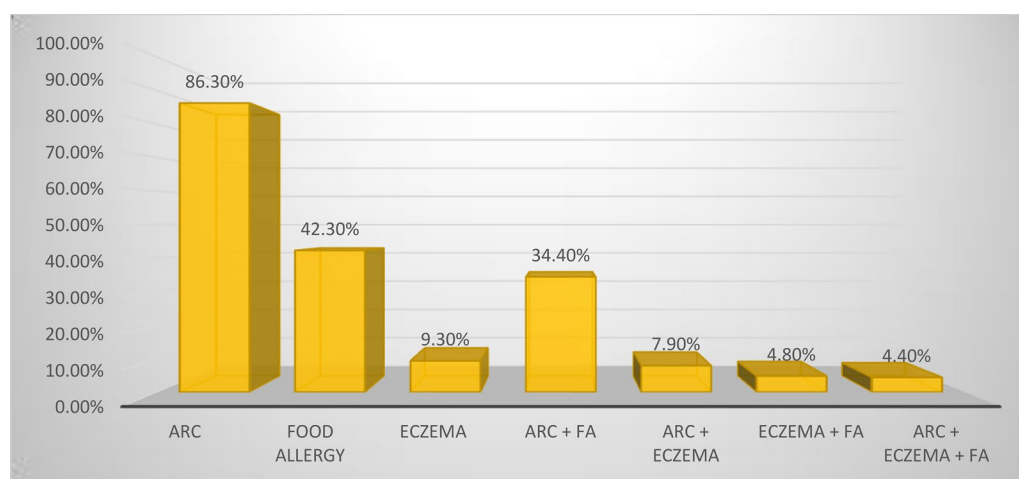
Change in asthma control during treatment at MAC

121 patients had ACT scores recorded at both the initial and the last visit. In this subset, mean ACT

improved from 11.1 $\pm$ 4.9 at the initial visit to 14.8 $\pm$ 6.1 at last visit ($p < 0.001$). The percentage of patients with ACT score >19 more than doubled from 7.4% at the initial visit to 15.4% at the last visit. Similar improvements in ACT scores were observed in all patients

Table 2. Laboratory characteristics of the cohort at baseline (stratified by age).

	Entire cohort	Entire cohort (n=227)		
		19- 39 yrs	40-59 yrs	60-85 yrs
Total serum IgE level, initial visit (n=168)				
Median $\pm$ IQR	211 $\pm$ 487.45	220.1 $\pm$ 515.9	211.5.0 $\pm$ 487.23	212.0 $\pm$ 479.15
Elevated IgE (≥ 150 U/ml), n (%)	99 (58.9)	19 (63.3)	59 (60.2)	21 (52.5)
IgE (< 150 U/ml)	69 (41.0)	11 (36.7)	39 (39.8)	19 (47.5)
Absolute eosinophil count, initial visit (n=185)				
Mean $\pm$ SD,	285.5 $\pm$ 336.1	251.9 $\pm$ 332.2	295.7 $\pm$ 345.4	290.0 $\pm$ 323.6
≥ 300 cells/ μ L, n (%)	69 (37.3)	12 (32.4)	41 (40.2)	16 (34.8)
< 300 cells/ μ L, n (%)	116 (62.7)	25 (67.5)	61 (59.8)	30 (65.2)
Absolute eosinophil count, at last visit (n=121)				
Mean $\pm$ SD, or	383.5 $\pm$ 1220.4	157.9 $\pm$ 150.2	513.3 $\pm$ 1608.5	258.8 $\pm$ 260.7
≥ 300 cells/ μ L, n (%)	47 (38.8)	5 (26.3)	31 (45.6)	11 (32.4)
< 300 cells/ μ L, n (%)	74 (61.2)	14 (73.7)	37 (54.4)	23 (67.6)
Strongyloides IgG (n=98)				
Positive	9 (9.2)	0 (0.0)	4 (7.4)	5 (16.1)
Negative	89 (90.8)	13 (100)	50 (92.6)	26 (83.9)

**Figure 1.** Proportion of the cohort with allergic co-morbidities.

stratified by age and gender - females ($p=0.008$) and males ($p=0.004$).

Pulmonary function testing in the cohort

The majority of the patients had abnormal pulmonary function tests at the initial visit. Impaired FEV1 ($< 80\%$ predicted) was reported in 74.8% (146/195) and an abnormal FEV1/FVC in 65.2% (126/193) patients, at the initial visit. (Table 3) Despite the improvements in the ACT scores, there was no significant improvement in pulmonary function test results between the first and last MAC visits. 75.7% (81/107) had an impaired FEV1 and 66.3% (71/107) had an impaired FEV1/FVC at the last visit (Table 3 and Figure 2).

Medication use in the year before first visit and during treatment at MAC

In a subset of the cohort ($n=43$), in which the medication data were consistent and verifiable, at the

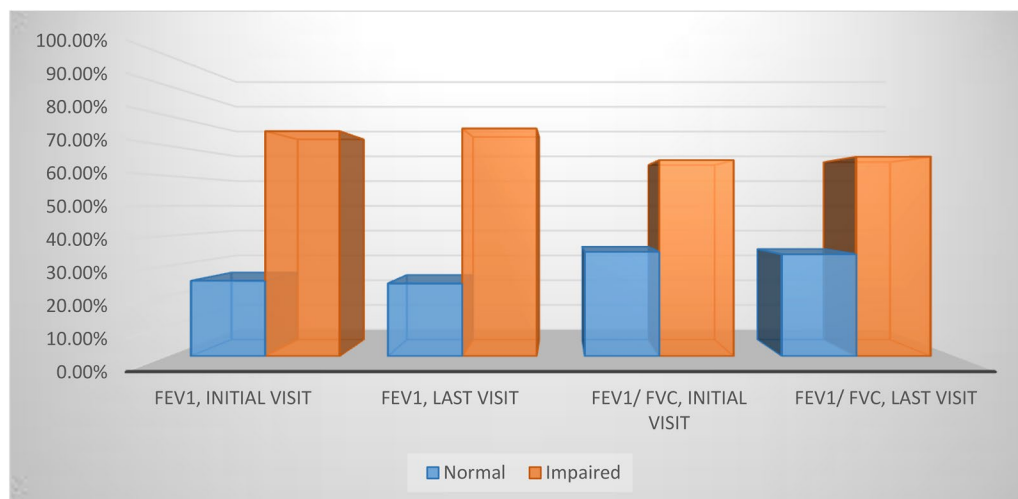
initial visit, patients were using a median of 2 (± 1) controller medications. Requirements for oral corticosteroids during the study period varied considerably between patients. Of the 31 patients for whom the data on OCS use was available, 11 (35.4%) did not take any oral corticosteroids between the first and last visit at MAC, while 10 (32.2%) took 1 course, 6 (19.4%) took 2 courses, 1 (3.2%) took 3 courses, 2 (6.4%) took 4 courses and 1 patient was on daily oral corticosteroids (as controller medication).

Comparison of clinical characteristics of patients with different asthma phenotypes

Of the cohort, 91.1% was atopic (defined as SPT and/or allergen specific IgE positive) while 8.9% was non-atopic (Table 4). Non-atopic patients tended to be older than atopic patients (61.7 years vs 49.8 years). Initial visit ACT scores between atopic and non-atopic patients were similar (11.0 vs 10.8, respectively). However, at the last visit, ACT scores in the atopic

Table 3. Pulmonary function in the cohort.

	Entire Cohort	Female	Male
FEV1, initial visit (<i>n</i> =195 with available data)	195	159	36
Normal ($\geq 80\%$ predicted), <i>n</i> (%)	49 (25.1)	43 (27.0)	6 (16.7)
Impaired ($< 80\%$ predicted), <i>n</i> (%)	146 (74.8)	116 (73.0)	30 (83.3)
FEV1, last visit 9 (<i>n</i> =107 with available data)	107	88	19
Normal ($\geq 80\%$ predicted), <i>n</i> (%)	26 (24.2)	24 (27.7)	2 (10.5)
Impaired ($< 80\%$ predicted), <i>n</i> (%)	81 (75.7)	64 (72.7)	17 (89.5)
FEV1/ FVC, initial visit (<i>n</i> =193 with available data)	193	157	36
Normal (≥ 0.80), <i>n</i> (%)	67 (34.7)	61 (38.8)	6 (16.7)
Impaired (< 0.80), <i>n</i> (%)	126 (65.2)	96 (61.2)	30 (83.3)
FEV1/ FVC, last visit (<i>n</i> =107 with available data)	107	88	19
Normal (≥ 80), <i>n</i> (%)	36 (33.9)	34 (38.6)	2 (10.5)
Impaired (< 80), <i>n</i> (%)	71 (66.3)	54 (61.3)	17 (89.5)

**Figure 2.** Proportion of the cohort with normal vs impaired PFT at initial and last visit.

patients had significantly improved to 15.3 while the non-atopic patients had remained essentially the same (11.1).

Among the patients in which the data on absolute eosinophil counts were available at the initial visit (*N*=185), 62.7% had non-eosinophilic asthma (< 300 cells/ μ L) and 37.2% had eosinophilic asthma (≥ 300 cells/ μ L). Their ACT scores were comparable at the first visit (10.9 ± 5.0 vs 11.2 ± 4.8) with similar improvements in both groups by the last visit (13.9 ± 6.2 vs 15.5 ± 6.1).

Age of asthma onset was available in 224 of the patients. Of the cohort, 39.3% had early onset asthma (< 12 yrs age) while 60.7% had late onset asthma (≥ 12 yrs) (Table 4). Mean ACT scores at the initial visit were similar between the early and late onset asthma groups (10.6 ± 4.8 vs 11.4 ± 4.9) Both groups showed similar improvements in ACT scores at the last visit (14.3 ± 6.5 vs 15.2 ± 5.8)

Discussion

In the present study, we describe the demographic, clinical, and laboratory characteristics of a predominantly minority, poor, severe asthma population in

the Bronx, NY. Patients in our cohort were followed by Allergy/Immunology and Pulmonary specialists for an average of 16 months at an Asthma Center staffed with health educators dedicated to patient education on medications and MDI technique, within our urban, academic tertiary care hospital. The group was predominantly female and had increased BMI. The female predominance observed in our cohort was not reported in a previously published study on severe asthma where patients were recruited from distinct centers (16). However, our results are in line with a recent study reporting shifting gender preponderance of asthma toward females after puberty (17) and with results from a European cohort (18). A high average BMI has been associated with severe asthma (19) and almost 90% of our cohort was either overweight or obese. Although mechanisms linking both conditions are still poorly understood, there is evidence that obesity impairs clinical control of asthma (18). Previous work in this field studying inflammatory pathways in obese asthmatics found obese patients with early-onset asthma to have more atopic disease, higher IgE levels, and greater bronchial hypersensitivity (15); while there is concurrent evidence of

Table 4. Demographic and clinical characteristics of the cohort divided by subgroups/ phenotypes.

	Atopic (SPT and /or RAST positive) n = 174 (91.1 %)	Non atopic n = 17 (8.9 %)	Eosinophilic asthma (≥ 300 cells/ μ L, initial visit) n = 69 (37.2%)	Non Eosinophilic asthma (< 300 cells/ μ L, initial visit) n = 116 (62.8%)
Age (Mean +/- SD)	49.8 $\pm$ 14.4	61.7 $\pm$ 10.1	52.3 $\pm$ 14.2	50.9 $\pm$ 14.1
Gender (% female)	82.2	82.3	73.9	88.7
ACT, initial visit				
Mean $\pm$ SD	11.0 $\pm$ 4.9	10.8 $\pm$ 4.5	10.9 $\pm$ 5.0	11.2 $\pm$ 4.8
ACT ≥ 19 , n (%)	18 (10.3)	2 (11.7)	7 (10.2)	13 (11.2)
ACT < 19, n (%)	145 (83.3)	13 (76.5)	53 (76.8)	98 (84.4)
N/A	11 (6.4)	2 (11.8)	9 (13)	5 (4.4)
ACT, last visit				
Mean $\pm$ SD	15.3 $\pm$ 6.10	11.1 $\pm$ 5.7	13.9 $\pm$ 6.2	15.5 $\pm$ 6.1
ACT ≥ 19 , n(%)	38 (21.8)	1 (5.9)	11 (16.0)	23 (19.8)
ACT < 19, n (%)	75 (43.2)	10 (58.8)	29 (42.0)	45 (38.8)
N/A	61 (35)	6 (35.3)	29 (42.0)	48 (41.4)

non-atopic Th1 inflammation in children and adults with obesity and asthma (20,21), which are all likely contributors to poorly controlled disease. About 30% of our cohort reported mild to moderate depressive symptoms. This could be attributed to a poorly controlled disease that impacts the patients' lives physically and emotionally causing increased levels of anxiety and depression. Previous studies have reported anxiety and depression as common and relevant comorbidities in asthmatic outpatients and associated with uncontrolled asthma and lower ACT scores (14,22,23).

Our cohort had concomitant atopy and several allergic co-morbidities. A striking 91% of our asthmatic cohort was found to be atopic with 4.4% suffering from all three types of allergic disorders (food allergy, eczema, and ARC) along with asthma. One possible explanation for this higher prevalence of atopy as compared to the normal population may be related to increased exposure to automobile pollution, since the Bronx is crossed by three, heavily trafficked, major highways - the Major Deegan, the Bruckner, and the Cross Bronx expressways. Previous studies suggest that air pollution increases IgE levels (24), as well as atopy (25).

According to the 2019 Global Initiative for Asthma (GINA) guidelines, allergic asthma is a phenotype that commences in childhood, and is associated with a past and/or family history of allergic disease such as eczema, allergic rhinitis, or food or drug allergy (11). The World Allergy Organization (WAO) reported 10%-30% of the adult population in the United States suffers from one or more allergic diseases (26). One study in African American teens with moderate to severe persistent asthma found that despite guideline directed therapy, there was a significant association between poorly controlled asthma and sensitization to aeroallergens, particularly seasonal outdoor allergens (27). Several epidemiologic studies observed that approximately 80% of asthma patients have allergic

rhinitis and 10–40% of allergic rhinitis patients also have asthma (28–33). Uncontrolled allergic rhinitis is known to worsen asthma symptoms, increase bronchial hyperactivity, and reduce lung function (32). Other longitudinal studies have shown that approximately half of eczema patients will develop asthma, particularly patients with severe eczema (34). A study by Roberts et al. reported that children with food allergies are nearly 6 times more likely to suffer from severe asthma later in life than children who did not have food allergies, while Priftis et al. showed that approximately 40% of children who were diagnosed with an egg and/or fish allergy in the first three years of their life reported asthma symptoms at school age (35,36). These findings from our study (91% prevalence of atopy) underscore the need for physicians to assess the allergic triggers of asthma and related exacerbations among their patients.

ICS use as a controller medication for all cases of persistent asthma reduces asthma symptoms, attenuates lung function deterioration, improves quality of life, and reduces the risks of exacerbation, asthma-related hospitalizations, and death (37–40). The MAC's health educator teaches patients on the importance of adhering to the national asthma guidelines including controller medication adherence and proper inhaler technique. 85.4% of the cohort had ACT scores ≤ 19 at the initial visit indicative of poorly controlled disease, with values in the range of 5–10 in 111 of the total 227 patients – nearly half the cohort. A majority of these patients were not on inhaled corticosteroid therapy when first evaluated at MAC and among those who were, many either never filled their inhaler prescription or did not have correct inhaler technique.

The natural progression of asthma to a more severe disease over time is not well understood. One possibility, within our patient cohort, is that the absence of routine asthma treatments for extended periods

contributed to the development of fixed airway obstruction by chronic inflammatory remodeling of the patients' airway. This is reflected in abnormal spirometric values in our cohort that did not improve despite guideline-based treatment at the MAC. This might also be because of other reasons such as the presence of co-existing chronic obstructive pulmonary disease (COPD) in a portion of this asthmatic cohort. Along these lines, 26.5% of patients with asthma have asthma-COPD overlap syndrome (ACOS) (41).

This study's clinical and laboratory findings reiterate that the MAC cohort was particularly atopic. As is typical of an asthmatic population, these study patients had substantially high IgE levels. However, the median IgE in our study group was an exceptionally high – 211 IU/ml as compared to an estimated average IgE in the general U.S. population of approximately 30 IU/mL (42,43). The cohort demonstrated no change in the percentage of patients with elevated absolute eosinophil count between the initial visit and the last visit. Previous studies have reported a suppression in blood eosinophil counts with the use of OCS in the presence of concomitant ICS use (44,45). However, the mean blood eosinophil count in the study cohort increased from 285.5 ± 336.1 at the first visit to 383.5 ± 411.4 at the last visit. This may be because only 64.4% of the patients got one or more doses of OCS while receiving treatment at MAC and due to challenges in data collection in an outpatient setting, causing some outliers to skew the mean peripheral eosinophil count. Measurement of sputum eosinophilia might help to better identify patients with severe eosinophilic asthma which might be especially useful in the current era of emerging biologic therapies for asthma (46). Most studies of severe asthma have identified the age of asthma onset and atopy as two of the most consistently reproducible clinical phenotypes (16,47). We identified these clinically defined asthma phenotypes in our cohort.

This study has several limitations. Our cohort includes patients with severe asthma from a single center, with a disproportionately high number of females with high BMI, thus results may not be generalizable, and a multicenter study across various centers may be warranted. Despite the EHR template designed to collect clinical outcome measures, only a little more than half (121 of 227) of our patients had their ACTs collected at both the initial and the last visits. The data on IgE and SPT is incomplete, and thus we were unable to analyze agreement between them. We recognize the gaps in our data due to the inevitable challenges in extensively, uniformly and consistently collecting several clinical and

laboratory parameters within the context of the outpatient setting. We acknowledge that self-reporting might have contributed to the high food allergy rate. In-office spirometry only yielded FEV1 and FEV1/FVC, and we evaluated lung volumes, but not pre- and post-bronchodilator response. The study lacks a control group and future studies would benefit from a comparative group. The data presented in the study spans from 2011 to 2015 and we did not collect data in the more recent years. Lastly, treatment adherence was not assessed during the study period, which could have affected outcome measures.

Conclusion

Appropriate medication and education are two important factors that influence the successful prevention of asthma exacerbations, especially in vulnerable populations throughout the country. Guideline-based asthma and allergy care at dedicated multidisciplinary asthma centers, and improving patient adherence by providing comprehensive asthma education, can improve asthma control. This in turn can prevent asthma ED visits, hospitalizations and OCS usage, thereby decreasing the massive economic burden this disease puts on the healthcare system and our vulnerable populations.

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Author contributions

Savneet Kaur, M.B.B.S. - conducted secondary research and literature for the topic, did data analysis, wrote a significant portion of the manuscript including formatting and presentation of data, provided final approval for publication, agrees to be accountable for all aspects of work related to accuracy and integrity as submitting author.

David Rosenstreich, MD- collected outcome measures in the clinic as a MAC physician, contributed to manuscript, reviewed manuscript critically for intellectual content, provided final approval for publication, agrees to be accountable for all aspects of work related to accuracy and integrity.

Krystal L. Clevon, MD - collected outcome measures in the clinic as a MAC physician, reviewed

manuscript critically for intellectual content, provided final approval for publication, agrees to be accountable for all aspects of work related to accuracy and integrity.

Simon Spivack, MD, MPH - collected outcome measures in the clinic as a MAC physician, reviewed manuscript critically for intellectual content, provided final approval for publication, agrees to be accountable for all aspects of work related to accuracy and integrity.

Joseph Grizzanti, DO - collected outcome measures in the clinic as a MAC physician, reviewed manuscript critically for intellectual content, provided final approval for publication, agrees to be accountable for all aspects of work related to accuracy and integrity.

Marina Reznik, MD, MS - reviewed manuscript critically for intellectual content, provided final approval for publication, agrees to be accountable for all aspects of work related to accuracy and integrity.

Sunit P Jariwala, MD - facilitated study design, decided outcome measures leading to acquisition of data, decided data analysis measures, coordinated study funding, made significant contribution to manuscript, reviewed manuscript critically for intellectual content, provided final approval for publication, agrees to be accountable for all aspects of work related to accuracy and integrity.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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