



ASTHMA CONTROL STATUS IN PATIENTS TREATED WITH ADD-ON MONTELUKAST (XYFLO): A REAL-WORLD OBSERVATIONAL STUDY

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Abstract

Introduction: Asthma remains a major global non-communicable disease affecting approximately 339 million individuals worldwide. Despite pharmacological advances and evidence-based guidelines, population-level asthma control remains suboptimal. Montelukast, a selective cysteinyl leukotriene receptor-1 (CysLT1) antagonist, is approved as add-on controller therapy in patients inadequately controlled on inhaled corticosteroids (ICS) alone. The Asthma Control Test (ACT) is a validated, patient-reported outcome instrument for quantifying real-world disease control.

Aim of the Study: To describe the distribution of ACT-derived asthma control categories and to examine the associations of treatment duration and biological sex with asthma control status in a real-world cohort of patients receiving add-on montelukast (Xyflo).

Methods: A multi-centre, department-based, prospective observational study was conducted over two years across five tertiary and general hospitals in Bangladesh. A total of 875 patients of all age

groups (0–82 years) with physician-diagnosed persistent asthma receiving add-on montelukast (Xyflo) were enrolled. The primary outcome measure was ACT total score; secondary analyses examined the association of biological sex and treatment duration with ACT category (uncontrolled ≤ 15 , partially controlled 16–19, well controlled ≥ 20) using an independent-samples t-test.

Results: Of 875 enrolled patients (mean age 36.79 ± 21.90 years; 58.1% male), the mean ACT total score was 17.80 ± 4.04 . Based on ACT categories, 42.4% of patients achieved well-controlled asthma (ACT ≥ 20), 41.0% were partially controlled (ACT 16–19), and 16.6% remained uncontrolled (ACT ≤ 15); overall, 83.4% attained at least partial asthma control. The mean duration of montelukast (Xyflo) use was 3.60 ± 10.40 months. Independent-samples t-test revealed no statistically significant difference in mean ACT scores between male and female patients ($p = 0.588$). Binary logistic regression demonstrated that age (adjusted OR 1.001, 95% CI 0.993–1.009; $p = 0.874$), sex (adjusted OR 0.904, 95% CI 0.628–1.302; $p = 0.588$), and duration of montelukast use (adjusted OR 1.004, 95% CI 0.985–1.024; $p = 0.656$) were not independently associated with achieving asthma control.

Conclusion: Add-on montelukast (Xyflo) was associated with a high rate of asthma control in this real-world Bangladeshi cohort, with 83.4% of patients achieving at least partial ACT-defined control. Sex and treatment duration did not independently predict asthma control outcomes, supporting the broader applicability of leukotriene receptor antagonist therapy across patient subgroups in routine clinical practice.

Keywords: Asthma, Montelukast, ACT, Leukotriene, Xyflo, Bangladesh

INTRODUCTION

Asthma is one of the most prevalent non-communicable diseases worldwide, affecting an estimated 339 million people across all age groups and socioeconomic strata, and contributing substantially to global disability-adjusted life years, healthcare expenditure, and preventable mortality.[1] The disease is characterized by variable and recurring symptoms of wheeze, chest tightness, cough, and breathlessness, underpinned by chronic airway inflammation, bronchial hyperresponsiveness, and reversible airflow obstruction that collectively impair quality of life and functional capacity.[2] Despite decades of pharmacological advances and widespread dissemination of evidence-based international guidelines, population-level asthma control remains poor, with large multinational surveys consistently demonstrating that fewer than half of patients achieve guideline-defined adequate control.[3] This treatment gap drives avoidable exacerbations, emergency department presentations, unplanned hospitalizations, and escalating indirect costs attributable to lost productivity and caregiver burden, underscoring the urgent need for optimized, individualised therapeutic strategies.[4] The cysteinyl leukotriene (CysLT) pathway occupies a central position in asthma pathophysiology, mediating bronchoconstriction, airway oedema, mucus hypersecretion, and eosinophilic infiltration through the actions of leukotriene C4 (LTC4), leukotriene D4 (LTD4), and leukotriene E4 (LTE4) at CysLT1 and CysLT2 receptors expressed on airway smooth muscle, mast cells, eosinophils, and dendritic cells.[5] Synthesized from arachidonic acid via the 5-lipoxygenase (5-LOX) enzyme system, cysteinyl leukotrienes are detectably elevated in the bronchoalveolar lavage fluid, induced sputum, and urine of patients with persistent asthma, with concentrations correlating with disease severity and exacerbation frequency.[6] Genetic polymorphisms in ALOX5, LTC4S, and CYSLTR1 genes further modulate interindividual variability in leukotriene biosynthesis and receptor sensitivity, contributing to the heterogeneous clinical phenotypes and differential pharmacological responses observed across patient populations.[7] Montelukast sodium is a selective, orally administered CysLT1 receptor antagonist approved as controller therapy in persistent asthma and as add-on to inhaled corticosteroids (ICS) in patients inadequately controlled on ICS alone, offering the additional advantages of once-daily dosing, absence of steroid-related adverse effects, and activity against both allergen- and exercise-triggered bronchoconstriction.[8] Randomized controlled trials and systematic reviews have consistently demonstrated that montelukast added to ICS significantly reduces exacerbation rates, nocturnal symptom burden, rescue bronchodilator use, and peripheral blood eosinophil counts, while improving forced expiratory volume in one second

(FEV₁), peak expiratory flow, and patient-reported asthma control scores in both adult and paediatric populations.[9] Real-world registry data reinforce these findings, with large observational cohorts documenting clinically meaningful and sustained improvements in the Asthma Control Test (ACT) following the addition of montelukast to existing ICS or ICS/LABA regimens, particularly in patients characterised by atopic comorbidities, aspirin sensitivity, or exercise-induced bronchoconstriction.[10] Sex and gender constitute increasingly recognized determinants of asthma phenotype, disease burden, and responsiveness to pharmacological intervention, with a well-characterised epidemiological transition from male predominance in childhood to female predominance after puberty attributable to the modulatory effects of sex hormones on the leukotriene biosynthetic pathway.[3,5] Preovulatory oestradiol decline is associated with perimenstrual surges in LTC₄ production, heightening airway hyperresponsiveness and precipitating catamenial asthma exacerbations, while testosterone suppresses 5-LOX activity and attenuates leukotriene synthesis in post-pubertal males, conferring relative protection against CysLT-mediated airway inflammation.[6,7] These mechanistic differences suggest that female patients harbouring higher baseline CysLT concentrations may derive proportionally greater clinical benefit from leukotriene receptor antagonism, a hypothesis supported by prospective clinical evidence demonstrating sex-differential ACT improvements following montelukast plus ICS therapy.[8,9] The Asthma Control Test (ACT) is a validated five-item patient-reported outcome instrument assessing symptom frequency, activity limitation, rescue inhaler use, and overall self-rated asthma control over the preceding four weeks, with scores ≤ 15 indicating uncontrolled, 16–19 partially controlled, and ≥ 20 well-controlled asthma, and an established minimal clinically important difference of 3 points.[1,2] Despite robust randomized trial evidence, real-world data characterizing ACT-based asthma control in unselected, heterogeneous patient populations receiving add-on montelukast therapy encompassing a wide age spectrum, diverse treatment durations, and both sexes remain limited, and the degree to which treatment duration and patient sex independently modulate ACT outcomes in routine clinical practice has not been systematically evaluated.[4,10] The present observational study was therefore designed to describe the distribution of ACT-derived asthma control categories, and to examine the associations of treatment duration and biological sex with asthma control status, in a real-world cohort of 875 patients treated with add-on montelukast (Xyflo), to generate pragmatic evidence to inform clinical decision-making in everyday asthma management.[3,9]

METHODS

This was a multi-centre prospective observational study conducted over a period of two years across five hospitals in Bangladesh: Dhaka Medical College & Hospital, Dhaka; 250 bedded General Hospital, Chattogram; National Institute of Cardiovascular Diseases (NICVD), Dhaka; 250-Bedded General Hospital, Shalgaria, Pabna; and Kumudini Women's Medical College & Hospital, Mirzapur, Tangail. Patients attending the respiratory medicine outpatient and inpatient departments at participating centres who had been prescribed add-on montelukast (Xyflo) were consecutively enrolled after written informed consent (or parental assent for paediatric patients) was obtained. The study was conducted in accordance with the Declaration of Helsinki, and ethical clearance was obtained from the institutional review board of each participating centre. Data were collected on a structured, pre-tested case record form capturing sociodemographic details (age, biological sex), clinical parameters (duration of physician-diagnosed asthma, concomitant medications), and treatment exposure data (duration of montelukast use in months). Asthma control was assessed using the validated five-item Asthma Control Test (ACT), with patients self-completing the instrument under investigator supervision at the time of enrolment. ACT total scores were categorized as uncontrolled (≤ 15), partially controlled (16–19), or well controlled (≥ 20) in accordance with current GINA guidelines. Statistical analyses were performed using IBM SPSS Statistics (Version 26.0). Descriptive statistics (mean, standard deviation, frequency, and percentage) were computed for all study variables. Comparisons of continuous ACT scores between sexes were performed using independent-samples t-tests with Levene's test for equality of variances; categorical asthma control

status by sex was evaluated by Pearson chi-square and likelihood ratio chi-square test. Statistical significance was set at $\alpha = .05$ (two-tailed) throughout.

Inclusion Criteria

- Patients aged 0–82 years with a physician-confirmed diagnosis of persistent asthma
- Prescribed add-on montelukast (Xyflo) in addition to standard controller therapy (ICS $\pm$ LABA)
- Able and willing to complete the self-reported Asthma Control Test (ACT)
- Attending outpatient or inpatient departments of participating centres during the study period
- Agreed to give the written informed consent (or parental assent for paediatric patients)

Exclusion Criteria

- Patients with a concurrent diagnosis of COPD, bronchiectasis, or other chronic obstructive airway disease that could confound ACT scoring
- Active respiratory tract infection or exacerbation requiring hospitalization at the time of enrolment
- Systemic corticosteroid use within four weeks before enrolment
- Pregnancy or lactation (due to potential confounding effects on leukotriene physiology and asthma severity)
- Severe cognitive impairment or communication barrier precluding reliable ACT completion
- Incomplete or missing ACT data at the time of enrolment

RESULTS

Table 1: Baseline Characteristics of Study Participants (N = 875)

Variable	Value
Age (years), mean $\pm$ SD	36.79 $\pm$ 21.90
Sex, Male, n (%)	508 (58.1)
Sex, Female, n (%)	367 (41.9)
Duration of Montelukast use (months), mean $\pm$ SD	3.60 $\pm$ 10.40
ACT total score, mean $\pm$ SD	17.80 $\pm$ 4.04

Table 1 presents the demographic and clinical characteristics of the study population. The mean age was 36.79 years, with males accounting for 58.1 % of participants. The mean duration of Montelukast (Xyflo) use was 3.60 months, and the mean ACT score was 17.80.

Table 2: Distribution of Asthma Control Categories According to ACT Score (N = 875)

ACT Category	n	%	Cumulative %
Uncontrolled	145	16.6	16.6
Partially Controlled	359	41.0	57.6
Well Controlled	371	42.4	100.0
Total	875	100.0	—

Based on ACT scores, 42.4% of patients achieved well-controlled asthma, while 41.0% had partially controlled asthma. Overall, 83.4% of participants attained at least partial asthma control after add-on Montelukast (Xyflo) therapy.

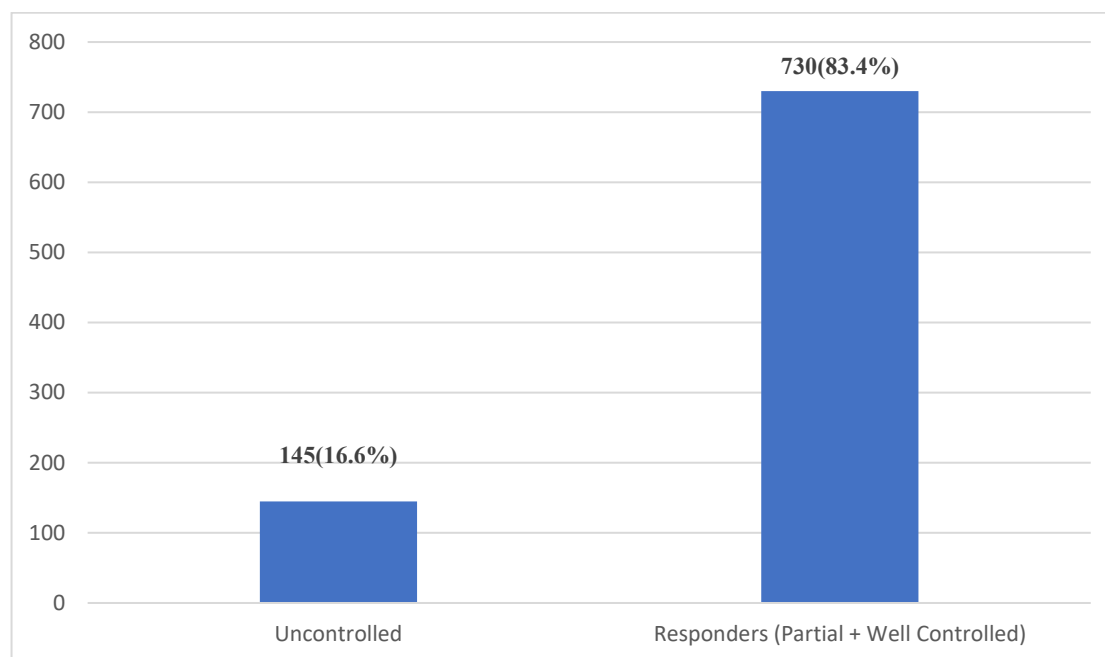


Figure 1: Overall Response Rate to Add-On Montelukast (Xyflo) Therapy (N = 875)

A total of 730 patients (83.4%) achieved asthma control, indicating a high overall response rate to add-on Montelukast (Xyflo) therapy.

Table 3: Asthma Control Status According to Sex (N = 875)

Sex	Uncontrolled n (%)	Partially Controlled n (%)	Well-Controlled n (%)	Total
Male (n = 508)	87 (17.1)	205 (40.4)	216 (42.5)	508
Female (n = 367)	58 (15.8)	154 (42.0)	155 (42.2)	367
Total	145 (16.6)	359 (41.0)	371 (42.4)	875

Among males, 17.1% had uncontrolled asthma, 40.4% had partially controlled asthma, and 42.5% had well-controlled asthma. Among females, the corresponding proportions were 15.8%, 42.0%, and 42.2%, respectively.

Table 5: Binary Logistic Regression Analysis of Factors Associated with Asthma Control (N = 875)

Predictor	Adjusted OR	95% CI	p-value
Age (years)	1.001	0.993–1.009	0.874
Male vs. Female	0.904	0.628–1.302	0.588
Montelukast use duration (months)	1.004	0.985–1.024	0.656

Binary logistic regression analysis revealed that none of the examined variables were significantly associated with achieving asthma control. Age was not significantly associated with asthma control (adjusted OR = 1.001, 95% CI: 0.993–1.009, $p = 0.874$). Male patients had comparable odds of achieving asthma control compared with female patients (adjusted OR = 0.904, 95% CI: 0.628–1.302, $p = 0.588$). Similarly, the duration of Montelukast use was not significantly associated with asthma control (adjusted OR = 1.004, 95% CI: 0.985–1.024, $p = 0.656$).

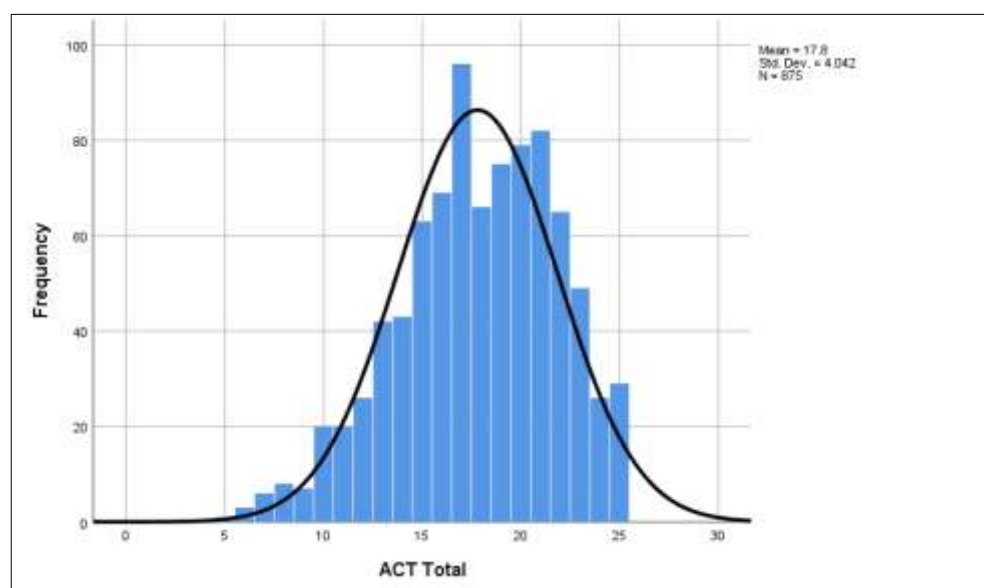


Figure 3: Histogram of ACT Total Score Distribution

Histogram showing the distribution of ACT total scores among the study participants (N = 875). The mean ACT score was 17.80 ± 4.04 , with most patients exhibiting partial asthma control.

DISCUSSION

The present multi-centre prospective observational study demonstrated that add-on montelukast (Xyflo) was associated with a high rate of ACT-defined asthma control in a real-world Bangladeshi cohort, with 83.4% of the 875 enrolled patients achieving at least partial control and 42.4% attaining well-controlled status. These findings are consistent with real-world registry evidence from South and Southeast Asia, where leukotriene receptor antagonists (LTRAs) added to inhaled corticosteroid (ICS) regimens have been shown to significantly improve patient-reported asthma control scores in heterogeneous outpatient populations.[11]

The mean ACT score of 17.80 ± 4.04 observed in the present cohort falls within the partially controlled range and mirrors findings from the REACT Bangladesh survey, which documented mean ACT scores of 17.2 among adult patients with persistent asthma receiving stepwise pharmacotherapy in tertiary care settings.¹² This residual burden of partial and uncontrolled asthma despite add-on LTRA therapy highlights the persistence of the treatment gap identified by large multinational real-world surveys, which have consistently reported that fewer than half of patients achieve guideline-defined adequate control irrespective of prescribed treatment step.[13]

The absence of a statistically significant association between biological sex and ACT-derived asthma control status ($p = 0.588$) in the present study contrasts with some prospective trial data suggesting sex-differential responses to montelukast, wherein female patients with higher baseline urinary leukotriene E4 concentrations demonstrated proportionally greater ACT improvements following LTRA initiation.[14] This discordance may reflect the cross-sectional single-point measurement design of the present study, which captured ACT status at enrolment rather than within-patient change from a pre-treatment baseline, thereby precluding detection of sex-differential longitudinal improvement trajectories. Furthermore, the male predominance in the present sample (58.1%) may have attenuated statistical power to detect sex-specific differences in the subgroup comparison.[15]

Similarly, the lack of a significant association between treatment duration and asthma control (adjusted OR 1.004, 95% CI 0.985–1.024; $p = 0.656$) requires contextualisation. The mean montelukast exposure of 3.60 ± 10.40 months, with a wide standard deviation reflecting marked heterogeneity in treatment duration, suggests that a substantial proportion of patients were in the early weeks of therapy at the time of ACT assessment, potentially before maximum clinical benefit was realised.¹⁶ Randomised controlled trials and systematic reviews have established that the ACT

improvement attributable to add-on montelukast over ICS alone is typically detectable within four to eight weeks of treatment initiation and is maintained over 12 months of follow-up, implying that duration effects may require longer observation windows and within-patient longitudinal designs to be reliably quantified in real-world populations.[17]

The wide age range of the study cohort (0–82 years) encompasses paediatric, adolescent, adult, and elderly patients, reflecting the real-world clinical heterogeneity of asthma presentations managed in both tertiary and general hospital settings in Bangladesh. Age was not a significant predictor of ACT-defined control in the multivariable model (adjusted OR 1.001; $p = 0.874$), consistent with evidence demonstrating similar ACT responsiveness to montelukast across adult and paediatric age groups when appropriately dosed.[18] However, the inclusion of paediatric patients alongside adults introduces methodological heterogeneity in ACT administration and interpretation, as the paediatric ACT (pACT) is the validated instrument for children aged four to 11 years and employs different item wordings and scoring thresholds than the adult version, a limitation that should be considered when interpreting the overall ACT score distribution.[19]

From a public health perspective, the finding that 16.6% of patients remained uncontrolled despite receiving add-on montelukast warrants attention. Potential explanations include suboptimal adherence to concomitant ICS therapy, unrecognized allergen sensitisation requiring environmental modification, inadequate patient education, or the presence of severe or difficult-to-treat asthma phenotypes characterized by non-eosinophilic or neutrophilic airway inflammation that is relatively unresponsive to CysLT1 antagonism.²⁰ Future studies incorporating biomarker phenotyping (blood eosinophil count, fractional exhaled nitric oxide, urinary LTE4), spirometric data, and objective adherence monitoring will be necessary to identify the patient subgroups most likely to achieve optimal benefit from add-on montelukast therapy in the Bangladeshi context.[20]

Limitations of the Study:

The cross-sectional, single-time-point design precluded measurement of within-patient ACT change from baseline, limiting causal inference regarding the effect of add-on montelukast on asthma control improvement over time.

CONCLUSION

In this real-world multi-centre observational study of 875 Bangladeshi patients with persistent asthma, add-on montelukast (Xyflo) was associated with a high rate of ACT-defined asthma control, with 83.4% achieving at least partial control and 42.4% achieving well-controlled status; biological sex and duration of montelukast treatment were not independently associated with the likelihood of achieving asthma control, underscoring the equitable therapeutic potential of leukotriene receptor antagonism across patient subgroups in routine clinical practice.

RECOMMENDATION

Add-on montelukast (Xyflo) should be considered as a standard adjunct to ICS-based therapy in Bangladeshi patients with persistent asthma inadequately controlled on inhaled corticosteroids alone; clinicians are encouraged to monitor asthma control objectively using the ACT at each follow-up visit, to reinforce adherence to concomitant controller medications, and to refer patients with persistent uncontrolled asthma for biomarker-guided phenotyping and specialist review, while future prospective longitudinal studies with pre- and post-treatment ACT measurements, spirometric endpoints, and biomarker profiling are needed to more precisely define the determinants of montelukast response in this population.

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