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Original Article

The implementation of global initiative for asthma (GINA) guidelines and Its Impact on asthma control in Ethiopia: A Longitudinal Study

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Abstract

Background: *Asthma is one of the common chronic respiratory illnesses that affect approximately 339 million people in the world. This study aimed to assess asthmatic patients' usage of short-acting beta-2 agonist (SABA) medication and Asthma control with GINA recommended asthma management guidelines.*

Methods: *A longitudinal study of data set from the Ethiopian African Severe Asthma Project (ASAP) at Tikur Anbessa Specialized Hospital was used as a data source. The ASAP project was a prospective, multicentered, cohort study designed to investigate the prevalence and clinic characteristics of severe asthma in three African countries. Socio-demographic, comorbid conditions, and medication usage were extracted from the database. Descriptive statistics and binary logistic regression were used in data analyses.*

Results: *A total of 203 asthmatics were included in this analysis; 124 (61.1%) were females and 55 (27.1%) were age group 50-59 years. At baseline, 190 (93.6%) had uncontrolled asthma. Most 110(54.2%) were using only SABA medication. Of those patients using SABA alone, 108 (98.18%) had uncontrolled asthma. After enrollment in ASAP, GINA management guidelines were followed, inhaled corticosteroids (ICS) and long-acting beta-agonist (LABA) medications were the most frequently prescribed medications 182(89.7%), and usage of SABA medication decreased from 54.2% to 29.6%. Asthma control level significantly improved (P<0.0001) at six and twelve months of therapy as compared to baseline. Combination therapies were frequently prescribed at six months 172(84.2%). The frequency of controlled asthma at baseline, six, and twelve months was 6.40%, 65.02%, and 71.92%, respectively.*

Conclusion: *Implementation of GINA guidelines significantly improved asthma control. For a better outcome of asthma treatment, we are highly recommended the adoption of the GINA guideline in the national treatment guideline of Ethiopia.*

Keywords: Short-acting beta agonist, Asthma control, Asthma guidelines

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Introduction:

According to the Global Initiative for Asthma (GINA), asthma is a complex disease defined by chronic airway inflammation and a history of respiratory symptoms such as wheezing, shortness of breath, and chest tightness. Asthma is one of the most common chronic respiratory illnesses that affects 339 million people in the world and causes a significant burden of disease in people of all ages, including early mortality and poor quality of life [1-6].

According to a worldwide cross-sectional survey on asthma, prevalence is expected to rise to 400 million by 2025 [7-10]. According to the most recent WHO statistics, which were published in 2020, there were 4,484 asthma-related deaths in Ethiopia in 2020 or 0.80% of all deaths. Ethiopia was ranked 71st in the world with an age-adjusted death rate of 8.13 per 100,000 people [11].

Asthma's long-term management focuses on symptom control and risk reduction, including lessening the overall health burden as well as exacerbations, airway damage, and medication side effects [6, 12, 13]. Proper implementation of GINA guidelines on the best preventive and management strategies for mild to severe asthma has improved asthma outcomes [12].

In Ethiopia, most asthmatics use short-acting beta agonist (SABAs) medication for asthma treatment due to the lack of availability and high cost of other better controller therapies [14]. Many studies have suggested that asthma control is inadequate with SABA treatment alone [15-18].

One post hoc analysis study showed that the use of only SABA treatment for two weeks led to severe exacerbation of asthma resulting in hospital admission [19]. In 1992, it was reported that the use of SABA was associated with a risk of fatal and nearly fatal asthma, as well as death [20]. The US National Review of Asthma Deaths (NRAD) identified high prescription of SABA treatment as a key factor in over 40% of deaths [21]. Today, the controversy is not only focusing on SABA but also included long-acting beta-agonist (LABA) [15-17, 22].

The Ethiopian Asthma Management Guideline still advocates SABA (salbutamol) for the treatment of acute asthma attacks and severe persistent asthma. However, in high-resource countries, SABA medications have largely been replaced by low-dose inhaled corticosteroid (ICS) and LABA combination therapy for better asthma control [12, 23]. For this reason, we aimed to assess the SABA usage pattern and asthma control of participants in the Ethiopian component of the African Severe Asthma Project (ASAP) using the GINA guideline.

Methods

Study design

This was a longitudinal study of a database from the Ethiopian ASAP project at Tikur Anbessa Specialized Hospital. ASAP Project was a prospective cohort study conducted from August 2016-May 2018 in three African countries; Ethiopia, Uganda, and Kenya [24]. This longitudinal study was done from 2018 to 2019 at Tikur Anbessa Specialized Hospital database archive of the ASAP project.

Source data

The source data was from ASAP Project which was a research project. severe asthma in East Africa. The study sites include of three teaching and national referral hospitals in Kenya (Kenyatta Hospital), Uganda (Mulago Hospital) and Ethiopia (Tikur Anbessa Hospital).

The inclusion criteria for ASAP project were patients with chronic respiratory symptoms (more than 8 weeks) with Physician diagnosed asthma based on symptom, Skin prick test and spirometry and age above or equal to 18 years and below 70 years. For the current analysis the Ethiopian site data was used as the original data for this study, with 419 participant records serving as source data [24].

Based on the data-sharing agreement, the ASAP project data at Tikur Anbessa Hospital, Addis Ababa, Ethiopia was retrieved and reviewed. The extracted information for this study included sociodemographic, comorbid conditions, risk factors, and medications. The severity of asthma, its control, and the medications given and utilized by the patients were the primary factors examined before enrollment, six-month, and during the 12-month treatment period. The study inclusion criteria were $\geq$18 years of age, confirmed asthma diagnosis, and Addis Ababa residents. The exclusion criteria were any missing data on important factors that might impact the primary goal of the study, such as spirometry findings, asthma severity, and control status. (Figure 1).

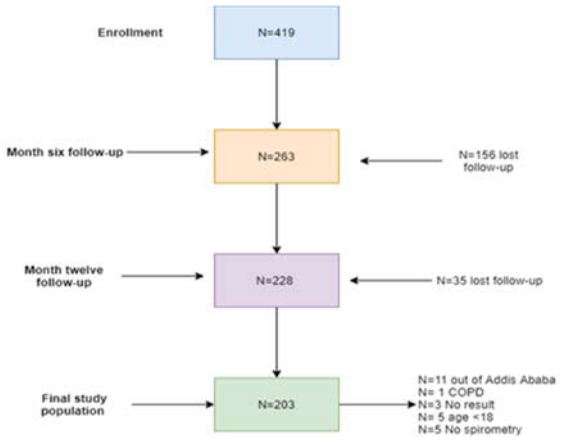

Figure 1: Flow chart for final participant selection from the original dataset for this study.

Operational definitions

The severity of asthma was defined based on the American Thoracic Society (ATS)/European Respiratory Society (ERS) definition [25].

Procedures

At the start of the study, medications use as well as asthma control and severity were evaluated for each subject. The participants were then given standard care asthma medicines based on their asthma severity and control level at baseline following GINA and Expert Panel 3 guidelines [8,12].

Those who received standard asthma medications continued to use it for the next six months. At six months, asthma severity and control were again assessed. Based on these findings, the management of asthma was modified for the next six month. After 12 months from enrollment, asthma control and severity were again reassessed (Figure 2).

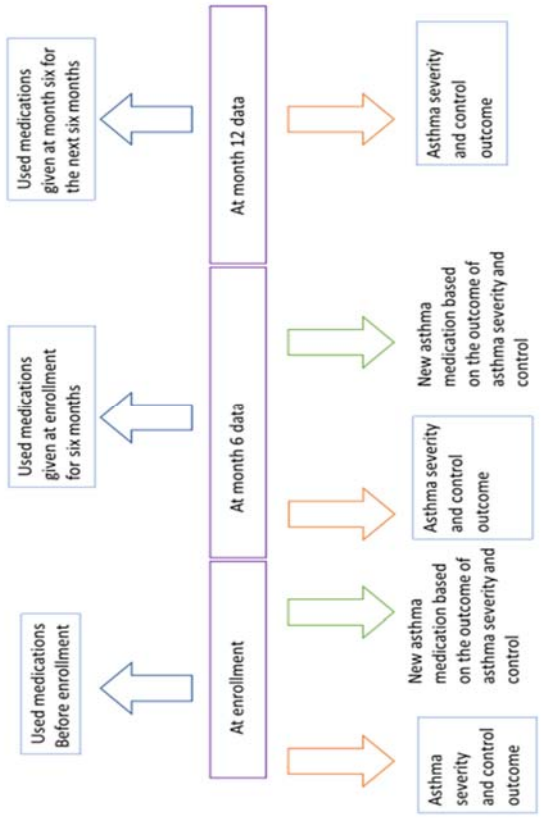

Figure 2: Exposure to asthma medications and the respected outcome related to the exposed medications.

Statistical analysis

Based on the original research case recording forms (CRF) dummy code, data from the baseline, six months' and twelve months' were imported into the STATA software version 15.0 code. In a table, continuous variables were summarized using means (standard deviations). All categorical variables were summarized using percent for the various categories and displayed as bar graphs, pie charts, dot charts, or tables. When comparing two categorical data sets, chi-square test was used while Fisher's exact tests were used when the expected cells were less than 5.

The Cochran Q test was used to compare the result at three distinct periods since our data was matched (Paired), having more than two datasets and it was nominal independent data set. Each pair of independent groups was likewise subjected to the McNamara test.

For numerous comparisons across groups, the p-value is taken as individual comparison alpha = (Overall Alpha)/c = 0.05/3 = 0.01667 for the Cochran Q test. To predict the relationship between different medicines and asthma control status, a binary logistic regression was used. Statistical significance was defined as a p-value of less than 0.05.

Ethical considerations

All participants in the original ASAP research gave their written consent to participate in the study.

The study was authorized by CDT Africa's scientific and ethics committee, as well as the Institutional Review Board at Addis Ababa University College of Health Sciences.

RESULTS

Table 1 summarizes socio-demographic data. There were 203 (48.5%) study participants; 124 (61.1%) were females and 55 (27.1 %) were between the ages of 50 - 59 years. A total of 40 individuals (19.7%) did not have formal education, while 58 (28.6%) started but did not complete elementary school. Most participants (67.2%) were married; 42 (20.7%) were jobless, and 58 (28.6%) were housewives.

At baseline, 114 subjects (56.2%) had severe persistent asthma and 190 (93.6%) had uncontrolled asthma (115, 92.7% women and 75 (94.9%) men). The age of first asthma attack and disease severity differed significantly in proportion (P=0.038).

One hundred and eighty-eight (92.6%) of the participants were nonsmokers. Ten (66.7%) of the 15 smokers had uncontrolled asthma, whereas one (6.67%) had controlled disease. Most of the participants, 148 (72.9%), claimed to have been exposed to biomass smoke, and many of them suffered from uncontrolled asthma. All the smoking-related exposures were not statistically significant (P > 0.05) (Table 2).

The most common co-morbidity was hypertension 28 (13.8%), followed by gastro-esophageal reflux disease 17 (8.4 %). The majority (n=17, 60.7%) of individuals with hypertension had uncontrolled asthma, whereas 2 (7.4%) had well-controlled asthma. Eight (47.1 %) of those with gastro-esophageal reflux had poorly or partially controlled asthma, none of whom had controlled asthma. There were 8 (3.9%) and 10 (4.9%) with rhinosinusitis and eczema/dermatitis, respectively, and both co-morbidities were significantly related to asthma severity (P=0.011 and P=0.018, respectively) (Table 3).

Table 1: Table 1. Shows the descriptive statistics of eligible participants based on their asthma control at Baseline.

Measures	**Overall N=203**	**Asthma severity N (%)**			**Asthma control level N (%)**		
		Severe	Non-severe	P-value	Well controlled	Not controlled	P-value
Sex n (%)							
Male n (%)	79 (38.92)	46 (58.23)	33(41.77)	0.635	4(5.06)	75(94.94)	0.533
Female n (%)	124 (61.08)	68 (54.84)	56(45.16)		9(7.26)	115(92.74)	
Total	203(100)	114(56.16)	89(43.84)		13(6.40)	190(93.60)	
Age n (%)							
18-29	8(3.94)	3(37.50)	5 (62.50)	0.157	0(0.00)	8(100)	0.244
30-39	24 (11.82)	8(33.33)	16(66.67)		4(16.67)	20(83.33)	
40-49	52(25.62)	29(55.77)	23(44.23)		1(1.92)	51(98.08)	
50-59	55(27.09)	34(61.82)	21(38.18)		4(7.27)	51(92.73)	
60-69	43(21.18)	27(62.79)	16(37.21)		3(6.98)	40(93.02)	
>=70	21(10.34)	13(61.90)	8(38.10)		1(4.76)	20(95.24)	
Education level n (%)							
None	40(19.70)	23(57.50)	17(42.50)	0.603	2(5.00)	38(95.00)	0.610
Incomplete Primary	58(28.57)	32(55.17)	26(44.83)		2(3.45)	56(96.55)	
Complete Primary	17(8.37)	7(41.18)	10(58.82)		2(11.76)	15(88.24)	
Incomplete Second-ary	21(10.34)	15(71.43	6(28.57)		1(4.76)	20(95.24	
Complete Second-ary	23(11.33)	13(56.52)	10(43.48)		3(13.04)	20(86.96)	
Tertiary	44(21.67)	24(54.55)	20(45.45)		3(6.82)	41(93.18)	
Marital status n (%)							
Single	19 (9.45)	9(47.37)	10(52.63)	0.299	2(10.53)	17(89.47)	0.661
Married	135(67.16)	77(57.04)	58(42.96)		9(6.67)	126(93.33)	
Separated	14 (6.97)	11(78.57)	3(21.43)		0(0.00)	14(100.00)	
Widowed	32(15.92)	17(53.13)	15(46.88)		1(3.13)	31(96.88)	
Child	1 (0.50	0(0.00)	1(100.00)		0(0.00)	1(0.53)	
Occupation n (%)							
Unemployed	42(20.69)	27(64.29)	15(35.71)	0.542	3(0.932)	40(93.02)	0.299
Housewife	58(28.57)	31(53.45)	27(46.55)		5(8.62)	53(91.38)	
Teacher/ Lecturer	6(2.96)	3(50.00)	3(50.00		1(16.67)	5(83.33)	
Lawyer	2(0.99)	1(50.00)	1(50.00		0(0.00)	2(100.00)	
Armed forces	1(0.49)	1(100.00)	0(0.00)		0(0.00)	1(100.00)	
Student	1(0.49)	0(0.00)	1(100.00)		0(0.00)	6(100.00)	
Factory Worker	7(3.45)	2(28.57)	5(71.43)		1(14.29)	6(85.71)	
Allied Health Worker	2(0.99)	1(50.00)	1(50.00)		0(0.00)	2(100.00)	
Manager	4(1.97)	3(75)	1(25.00)		0(0.00)	3(100.00)	
Clerical Worker	2(1.97)	0(0.00)	1(100.00)		0(0.00)	2(100.00)	
Other	78(37.50)	45(57.69)	33(42.31)		3(3.85)	75(96.15)	
Age asthma Occurs n (%)							
<15	15 (7.39)	7(46.67)	8(53.33)	0.038	1(6.67)	14(93.33)	0.922
15-24	40 (19.70)	29(72.50)	11(27.50)		2(5.00)	38(95.00)	
25-34	82 (40.39)	44(53.66)	38(46.34)		7(8.54)	75(91.46)	
35-44	36 (17.73)	24(66.67)	12(33.33)		1(2.78)	35(97.22)	
45-54	17 (8.37)	5(29.41)	12(70.59		1(5.88)	16(94.12)	
55-64	10 (4.93)	4(40.00)	6(60.00)		1(10.00)	9(90.00)	
>64	3 (1.48)	1(33.33)	2(66.67)		0(0.00)	3(100.00)	

Note: The age of the participants was categorized based on the eligibility criteria but the age that asthma occurred is not necessary to consider any age limit. The age of asthma occur is statistically significant with the severity of asthma $P<0.05$

Table 2: Shows Cigarette smoking, Biomass, and kerosene exposure vs asthma control level

Exposure Measures	Overall N=208	Asthma severity No (%)		P-value	Asthma control level No (%)		P-value
		Severe	Not severe		Well-controlled	Not con-trolled	
Smoking history No (%)							
Current/ Former Smoker	15 (7.39)	10(66.67)	5(33.33)	0.394	1(6.67)	14(93.33)	0.966
Never smoker	188(92.61)	104(55.32)	88(44.68)		12(6.38)	176(93.62)	
Biomass smoking history No(%)							
Yes	148(72.91)	85(57.43)	63(42.57)	0.548	10(6.76)	138(93.24)	0.736
No	55 (27.09)	29(52.73)	26(47.27)		3(5.45)	52(94.55)	
Kerosene Exposure No (%)							
Yes	41(20.20)	24(58.54)	17(41.46)	0.731	4(9.76)	37(90.24)	0.326
No	162(79.80)	90(55.56)	72(44.44)		9(5.56)	153(94.44)	

Note: The smoking habits to cigarette, biomass, and kerosene is not statistically significant P >0.05

Table 3: Co-morbidities associated with asthmatic patients grouped versus severity and control level of asthma

Medication changes from enrollment to month 12 of the study are shown in Table 4.

Comorbidities	Overall N=203	Asthma severity		P-value	Asthma control level No (%)		P-value
		Severe n=114	Not severe n=89		Well-controlled	Not con-trolled	
Rhino sinusitis	8(3.94)	1(12.50)	7(87.50)	0.011	0(0.00)	8(100.00)	0.450
Nasal polyps	3(1.48)	2(66.67)	1(33.33)	0.712	0(0.00)	3(100.00)	0.648
Eczema/dermatitis	10(4.93)	2(20.00)	8(80.00)	0.018	0(0.00)	10(100.00)	0.396
Depression	1(0.49)	1(0.49)	0(0.00)	0.430	0(0.00)	1(100.00)	0.793
Gastroesophageal re-flux disease	17(8.37)	8(47.06)	9(52.94)	0.430	0(0.00)	17(100.00)	0.260
Obstructive sleep apnea	2(0.99)	0(0.00)	2(100.00	0.108	0(0.00)	2(100.00)	0.710
HIV	3(1.48)	3 (100.00)	0(0.00)	0.123	0(0.00)	3(100.00)	0.648
COPD	0(0.00)	0(0.00)	0(0.00)		0(0.00)	0(0.00)	
Heart failure	0(0.00)	0(0.00)	0(0.00)		0(0.00)	0(0.00)	
Hypertension	28 (13.79)	17 (60.71)	11(39.29)	0.601	2(7.14)	26(92.86)	0.863
Other diseases	29 (14.29)	19 (65.52)	10(34.48)	0.273	2(6.90)	27(93.10)	0.907

Table 4: The medication used by participants at different points in the study visits and the level of asthma control that corresponds with asthma.

Before enrollment	N=203 n (%)	Asthma control at base line		P-value	N=203 n (%)	Asthma control at six month		P-value	N=203 n (%)	Asthma control at twelve month		P-value
		Well Controlled	Not controlled			Well Controlled	Not controlled			Well Controlled	Not controlled	
SABA only	110 (54.)	2(1.82)	108 (98.1)	0.004	60 (29.56)	41 (68.33)	19 (31.67)	0.522	2 (0.99)	2 (100.0)	0 (0.00)	0.375
ICS only	7 (3.45)	3 (42.86)	4 (57.14)	0.000	3 (1.48)	1 (33.33)	2 (66.67)	0.246	1 (0.49)	1 (100.0)	0 (0.00)	0.531
SA-BA+ICS	20 (9.85)	3 (15.00)	17 (85.00)	0.098	15 (7.39)	8 (53.33)	7 (46.67)	0.324	24 (11.8)	15 (62.5)	9 (37.50)	0.274
ICS+LABA	28 (13.7)	2(7.14)	26 (92.86)	0.863	182 (89.6)	119 (65.3)	63 (34.62)	0.752	171 (84.2)	124 (72.)	47 (27.4)	0.664

SABA-only medications were taken by 110 (54.2%) individuals before enrollment, but this number dropped to 60 (29.56%) once the severity of asthma was assessed at the beginning of the study and patients started with GINA based treatment regimen. Similarly, over the next six months of the study, the use of SABA medicines by study participants decreased significantly (n=2, 0.99 %). In contrast to the baseline, the usage of ICS+SABA and ICS+LABA medicines use significantly increased.

The proportion of asthma control at each visit was substantially different from baseline to month twelve (P= 0.0001), according to the Cochran Q

During the six-month follow-up visit, 132 (65.0%) had controlled asthma and by the end of twelve month, 146 (71.92%) had controlled asthma while 57 (28.08%) of participants had uncontrolled asthma.

Multiple comparison tests were evaluated with the McNemar test where the absolute smallest difference predicted was 12.9%; alpha = (Overall Alpha)/c = 0.05/3 = 0.01667 for individual comparisons. Baseline and six-month asthma control levels, as well as baseline and twelve-month asthma control levels, were substantially different from each other, with absolute differences of 58.6 % and 65.5 %, respectively. The difference in P-value at baselines and six-month as well as baseline and twelve-month was statistically significant (P<0.0001). There was no statistically significant

Table 5: shows the Cochran Q test between the outcome of asthma control following the medication at three different times and the McNamara test between each group pair.

			Cochran's Q	Multiple Comparisons using Minimum Required Absolute Difference				Multiple Comparisons using the McNamara Test
Group Variables	Asthma Control outcome		P-value	Comparison of each group	Absolute difference (π_i (%)-π_j (%)	Minimum required absolute difference	Reject Ho with the overall α*	P-value
	Controlled	Not controlled						
Test at Baseline	13(6.40%)	190 (93.6%)	0.0000	Test at Baseline Vs Test at Month six	(93.60 - 34.98) 58.62	12.88	Yes	0.00000
Test at 6 month	132 (65.0%)	71 (34.98%)		Test at Baseline Vs Test at month twelve	(93.60 - 28.08) 65.52	12.88	Yes	0.00000
Test at 12 month	146 (71.92%)	57 (28.08%)		Test at Month six Vs Test at month twelve	(34.98-28.08)6.90	12.88	No	0.17967

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The proportion of asthma control at each visit was substantially different from baseline to month twelve (P= 0.0001), according to the Cochran Q paired group test. At the start of the study, 190 (93.6%) of the patients had uncontrolled asthma.

During the six-month follow-up visit, 132 (65.0%) had controlled asthma and by the end of twelve month, 146 (71.92%) had controlled asthma while 57 (28.08%) of participants had uncontrolled asthma.

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Test at 6 month	132 (65.0%)	71 (34.98%)		Test at Baseline Vs Test at month twelve	(93.60 - 28.08) 65.52	12.88	Yes	0.00000
Test at 12 month	146 (71.92%)	57 (28.08%)		Test at Month six Vs Test at month twelve	(34.98-28.08)6.90	12.88	No	0.17967

A binary logistic regression was employed to examine SABA-only medication users, ICS-only medication users, ICS plus SABA as needed medication users, and ICS plus LABA medication users at baseline to predict the effects on the odds of observing Asthma control. The binary logistic regression analysis showed that ICS-only medication users were 10.07 times more likely to control their asthma than non-users (OR = 10.071, CI = 1.683, 60.275, P = 0.011).

Discussion

Our study clearly demonstrates the role of controller medication (ICS or ICS+LABA) in improving asthma control. At baseline, most of the asthmatic individuals were using SABA alone therapy and had uncontrolled asthma. After enrollment in ASAP and starting on GINA guideline-based management, there was gradual and significant improvement in asthma control with ICS and LABA medications. This gradual improvement in asthma control shown over a year of appropriate treatment was also associated with less use of SABA- alone therapy.

Our findings are consistent with previous study findings. Numerous studies, mostly in high-resource countries, have shown that ICS use lessens asthma exacerbations and increases asthmatic quality of life [24, 26-29]. Long -term use of SABA-only medications has been linked to severe asthma exacerbation and inflammation in other studies [21, 30-32]. Furthermore, a post-hoc analysis study published in 2015 found that long-term usage of SABA before admission to the hospital resulted in severe asthma exacerbation [19].

In 2019, GINA reviewed 231 prospective articles and proposed an evidence-based recommendation that SABA-only treatment for asthma in adults and adolescents should no longer be used [12]. For as-needed controller therapy in mild asthma, evidence-based alternatives are offered, with low dosage controllers being preferred for Step 1 and Step 2. If needed, ICS-formoterol can be given as needed for symptom alleviation and before exercise [8,12].

In 2014, the Ethiopian Asthma Management Guidelines proposed first-line therapy for persistent moderate to severe persistent asthma should be ICS + SABA as required. Other drugs, such as OCS and methylxanthines, could be used as a backup. Alternative treatments such as ICS+LABA medicines were mentioned but not recommended [14]. The 2019 GINA guideline, on the other hand, consider ICS to be a major controller and reliever, while SABA is an option, and does not advocate ICS+SABA as first-line therapy [12].

There were two other important study findings. Environmental exposures to cold weather, dust, vehicle fumes, and strong odors played a key role in triggering asthma [33-35]. Avoidance of these environmental triggers may also improve asthma control in our cohort as shown in other studies [36-38].

In our analysis, similar to other studies, comorbidities were common in our study population. Proper management of comorbidities may also improve asthma control [39].

Conclusion :

In Ethiopia, a low-resource country, use of GINA guidelines significantly improved asthma control. The use of SABA medication to control and alleviate asthma symptoms was shown to be ineffective. Furthermore, it was discovered that ICS was the most effective first-line treatment. Societies and regulatory body should advocate for the availability of reasonably priced asthma medications including ICS and LABA for disease control as recommended by current asthma management guidelines.

Limitation of the study

Because we used secondary data that was originally obtained for other purposes, generalization is questionable. But this study clearly showed that guideline-based asthma management improved asthma control.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could potentially influence the work reported in this paper

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OF, GY, EM developed the draft manuscript from ASAP data, GM, AB, TH, YB, AM, involved in primary ASAP data generation and EKE reviewed the paper and included all comments from others. All authors contributed to the draft and finalization of the manuscript

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Consent for publication
Not applicable.

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Reference

1. The Global Asthma Report 2018. Auckland, New Zealand: Global Asthma Network, 2018. www.globalasthmanetwork.org
2. Chimeddamba O, Peeters A, Walls HL, Joyce C. Noncommunicable Disease Prevention and Control in Mongolia : A Policy Analysis. 2015;15.
3. Chan M. Global status report on noncommunicable diseases. World Health Organ. 2010.
4. Alberto Papi , Adel H Mansur , Tetyana Pertseva,el.at. Long-Term Fluticasone Propionate/Formoterol Fumarate Combination Therapy Is Associated with a Low Incidence of Severe Asthma Exacerbations . J Aerosol Med Pulm Drug Deliv
2016 Aug;29(4):346-61. doi: 10.1089/jamp.2015.1255. Epub 2016 Apr 22.
5. World Health Organization. (.(2014Global status report on non-communicable diseases 2014. World Health Organization. https://apps.who.int/iris/handle/10665/148114
6. Reddel HK. The Impact of the Global Initiative for Asthma (GINA): Compass , Concepts , Controversies and Challenges. BRN Rev.2019;5(1):4–18.
7. Forum of International Respiratory Societies. The Global Impact of Respiratory Disease – Second Edition. Sheffield, European Respiratory Society, 2017.5-42.
8. 2018 Clinical Practice Guidelines. National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program, Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007. http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf
9. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global asthma prevalence in adults : findings from the cross-sectional world health survey. *BMC Public Health* [Internet]. 2012;12 (1):204. Available from: http://www.biomedcentral.com/1471-2458/12/204
10 WHO. Global Asthma Network The Global Asthma Report. Auckland, New Zeal [Internet]. 2018;92. Available from: http://www.globalasthmanetwork.org
11. WORLD HEALTH ORGANIZATION 2020. WORLD LIFE EXPECTANCY COM. Available from: https://www.worldlifeexpectancy.com/ethiopia-asthma
12 GLOBAL INITIATIVE FOR ASTHMA. ASTHMA MANAGEMENT AND PREVENTION for adults and children older than 5 years .A POCKET GUIDE FOR HEALTH PROFESSIONALS Updated 2019.
13. Dotan Y, So JY, Kim V. Chronic bronchitis: where are we now? *Chronic Obstr Pulm Dis.* 2019;6(2):178-192. doi: https://doi.org/10.15326/jcopdf.6.2.2018.0151
14. FEDERAL DERAL DEMOCRATIC REPUBLIC OF ETHIOPIA MINISTRY OF HEALTH. Guidelines on Clinical and Programmatic Management of Major Non Communicable Diseases.2016 .Addis Ababa
15. Smucny J, Ca F, La B, Glazier R. Beta2-agonists for acute bronchitis (Review). 2006;(1). National Center for Biotechnology Information. Cochrane Database Syst Rev . 2006 Oct 18;(4):CD001726. doi: 101002/14651858.CD001726.pub3.

16. Moore RH, Khan A, Dickey BF. Long-acting Inhaled β2-Agonists in Asthma Therapy. Chest [Internet]. 1998;113(4):1095–108. Available from: http://dx.doi.org/10.1378/chest.113.4.1095
17. Bisgaard H. Effect of Long-Acting β2 Agonists on Exacerbation Rates of Asthma in Children. Pediatr Pulmonol. 2003;36(5):391–8.
18. Hull SA, Mckibben S, Homer K, Taylor SJC, Pike K, Grif C. Asthma prescribing , ethnicity and risk of hospital admission : an analysis of 35 , 864 linked primary and secondary care records in East London. NPJ Prim Care Respir Med . 2016 Aug 18;26:16049. doi: 10.1038/npjpcrm.2016.49.
19. Patel M, Pilcher J, Hancox RJ, Sheahan D, Pritchard A, Braithwaite I, et al. The use of β 2 -agonist therapy before hospital attendance for severe asthma exacerbations : a post-hoc analysis. Nat Publ Gr [Internet]. 2015;(August 2014). Available from: http://dx.doi.org/10.1038/npjpcrm.2014.99
20. Walter O. Spitzer,Samy Suissa,Pierre Ernst, et al. The Use of β-Agonists and the Risk of Death and near Death from Asthma. N Engl J Med 1992; 326:501-506. DOI: 10.1056/NEJM199202203260801
21. Mckibben S. " Tossing a coin : " defining the excessive use of short-acting beta 2 -agonists in asthma — the views of general practitioners and asthma experts in primary and secondary care. 2018;(February):2018–20.
22. Suissa S, Blais L, Ernst P. Patterns of increasing β -agonist use and the risk of fatal or near-fatal asthma. 1994;1602–9.
23. Food , Medicine and Healthcare Administration and Control Authority of Ethiopia Standard Treatment Guidelines For General Hospital Diseases Investigations Good Prescribing & Dispensing Practices for Better Health Outcomes. Thrid Edition, Stg. 2014;
24. Kirenga B, Chakaya J, Yimer G, Nyale G, Haile T, Muttamba W, et al. Phenotypic
25. characteristics and asthma severity in an East African cohort of adults and adolescents with asthma: findings from the African severe asthma project. BMJ open Respir Res. 2020 Feb;7(1).
26. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS / ATS guidelines on definition , evaluation and treatment of severe asthma. *Eur Respir J* 2014; 43: 343–373 | DOI: 10.1183/09031936.00202013 .
27. Bf C, Chartrand C, M NC, Sj M, Fm D. Addition of long-acting beta 2 -agonists to inhaled corticosteroids for chronic asthma in children .Intervention Review Review .. Evidence-Based Child Health: A Cochrane Review Journal, 2015;(11).
28. O'Byrne P, Fabbri LM, Pavord ID, Papi A, Petruzzelli S, Lange P. Asthma progression and mortality: the role of inhaled corticosteroids. Eur Respir J. 2019 Jul;54(1).
29. Cj C, Schmidt S, Ferrer M, Sayer B, Waterson S. Inhaled steroids with and without regular salmeterol for asthma : serious adverse events. Cochrane Database Syst Rev . 2018 Dec 3;12(12):CD006922. doi: 10.1002/14651858.CD006922.pub4.
30. Takeuchi M, Kano H, Takahashi K, Iwata T. Comparative effectiveness of inhaled corticosteroids for paediatric asthma: protocol for a systematic review and Bayesian network meta-analysis. BMJ Open. 2015 Oct;5 (10):e008501.
31. Magee JS, Pittman LM, Jette-kelly LA. Paradoxical Bronchoconstriction with Short- Acting Beta Agonist. Am J Case Rep . 2018 Oct 9;19:1204-1207. doi:10.12659/AJCR.910888..
32. Zeiger RS, Schatz M, Li Q, Solari PG, Zazzali JL, Chen W. Real-time asthma outreach reduces excessive short-acting β2-agonist use: a randomized study. J allergy Clin Immunol Pract. 2014;2(4):445–56, 456.e1-5
33. Martin MJ, Harrison TW. Is it time to move away from short-acting beta-agonists in asthma management? Eur Respir J [Internet]. 2019 Apr 1;53(4):1802223. Available from: http://erj.ersjournals.com/content/53/4/1802223.a
34. Takaro TK, Krieger JW, Song L. Effect of environmental interventions to reduce exposure to asthma triggers in homes of low-income children in Seattle. J Expo Anal Environ Epidemiol. 2004;14 Suppl 1:S133-43.
35. Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R 3rd, et al. Results of a home-based environmental intervention among urban children with asthma. N Engl J Med. 2004 Sep;351(11):1068–80.
36. Janssens T, Ritz T. Perceived triggers of asthma: key to symptom perception and management. Clin Exp Allergy [Internet]. 2013 Sep;43(9):1000–8. Available from: https://pubmed.ncbi.nlm.nih.gov/23957335
37. Prabhakaran L, Yap CW, Neo L, Gan C, Tham L, Wong W, et al. Effectiveness of the eCARE Programme: A Short Message Service (SMS) for Asthma Monitoring. Ann Acad Med Singapore. 2018 Jun 1;47:233–6.
38. Cockcroft DW. Environmental Causes of Asthma. Semin Respir Crit Care Med. 2018 Feb;39(1):12–8.
39. Strachan DP. The role of environmental factors in asthma. Br Med Bull. 2000;56(4):865–82.
39. Boulet L-P, Boulay M-È. Asthma-related comorbidities. Expert Rev Respir Med. 2011 Jun;5(3):377–93.