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Asthma control in adults in the Middle East and North Africa: Results from the ESMAA study

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ABSTRACT

Background: Low levels of asthma control are reported in many countries worldwide. Improved knowledge of asthma control in the Middle East and Africa and predictive factors is needed to address this major public healthcare burden.

Objective: To assess the level of asthma control in patients attending a routine consultation for asthma in the Middle East and North Africa, and the relationship between level of control and patient and disease characteristics, adherence, and quality of life (QoL).

Methods: A large-scale cross-sectional epidemiological study (ESMAA: Assessment of Asthma Control in Adult Asthma Population in the Middle East and North Africa) was performed in adults suffering from asthma for at least 1 year and without an acute asthma episode within 4 weeks. Asthma control was assessed per the 2012 GINA guidelines and the ACT questionnaire. QoL and adherence were assessed with the SF-8 and Morisky questionnaires respectively. Predictive factors of asthma control were analysed with univariate and multivariate logistic regressions analyses.

Results: Overall 7236 eligible patients were included in 577 sites between June 2014 and December 2015 (median 10 patients/site). Mean age was 45 years (± 14), 57% were female, mean BMI was 28.5 kg/m^2 (± 6.0), and 11% were active smokers. Reliever medication was prescribed in 96% of patients with 65% having fixed-dose combined inhaled corticosteroid plus long-acting beta agonists. Good medication adherence was reported in 24% of patients. Among 7179 patients evaluable for GINA, asthma was controlled in 29.4% (95% CI, 28.4%–30.5%), partly controlled in 29.1% (95% CI, 28.1%–30.2%), and uncontrolled in 41.5% (95% CI, 40.3% to 42.6). The mean global ACT score was 17.8 (± 5.0), with 16% of patients considering their asthma as controlled. Poor medication adherence, active smoking, absence of medical insurance, lower level of education, or diagnosis at least 5 years earlier were significantly associated with uncontrolled asthma in multivariate analyses ($p < 0.001$).

Conclusions: Asthma control in the Middle East and North Africa is unsatisfactory with less than one-third of asthma patients having controlled disease, highlighting the need to improve treatment access and medication adherence, along with better follow-up and education among healthcare providers and patients.

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1. Introduction

In 2015, asthma was thought to affect as many as 385 million people of all ages and is reported in all parts of the world [1], creating a substantial burden not only to the individual but also to the public health care system. This is particularly the case in low- and middle-income countries, where avoidable asthma deaths are still occurring due to inappropriate disease management. The 2017 Global Initiative for Asthma (GINA) report, the "Global Strategy for Asthma Management and Prevention", defines asthma control according to two domains, symptom control and future risk of adverse outcomes [2]. The level of asthma control is defined as the extent to which the manifestations of asthma can be observed or have been reduced or removed by treatment. Several tools are available to measure asthma control.

Data reporting asthma control provide a reflection of asthma management and an indication of the costs to both the individual and the community. Asthma control has been evaluated in several regions including Europe, the USA, Latin America, and Asia-Pacific with poor levels of control reported by both physicians and patients in recent large-scale and prospective studies [3–7]. Sub-optimal asthma control ranges from approximately 55% in Europe, 71% in the USA, 87% in Australia to over 90% in most Asian and Latin American countries. Nonetheless there are large gaps in our current knowledge of asthma control in Africa and the Middle East. Available data are from up to a decade ago with a GINA-based assessment of asthma control for a number of Middle East countries, including the AIRGNE study in 1000 patients from Jordan, Kuwait, Lebanon, Oman, and the United Arab Emirates (UAE) [8], the AIRET study in 400 asthmatics from Turkey [9], and the AIRMAG study reported asthma control in 264 patients from Algeria, Tunisia and Morocco [10], and an ACT-based assessment was reported for 1000 asthmatic patients in Saudi Arabia [11].

Factors cited as impacting the level of asthma control are many and varied. They include access to guidelines, environmental and patient-related influences such as exposure to allergens, seasonal changes, active smoking, disease-related features (sleep conditions), comorbidities and cultural aspects, while treatment-related aspects as a whole, including poor adherence, inadequate therapy, poor efficacy, poor inhalation technique, poor tolerability play a major role [3,12–14] all of which vary inherently by region. The relationship between asthma control and quality of life has also been widely reported, with poor asthma control associated with a poorer quality of life [3,15,16].

There is an absence of large-scale clinical data in the Middle East and North African region for the level of asthma control and factors influencing it, both of which are essential elements for improving management of this disease. We report the results of an epidemiological study carried out in this region which was designed to establish the level of asthma control, according to physician assessment per GINA [17] in patients attending a public or private consultation for diagnosed asthma. Data on patient and disease characteristics, medication adherence and quality of life were collected and evaluated to identify potential predictive factors impacting the level of asthma control.

2. Methods

2.1. Study design

A cross-sectional epidemiological multicentre study (ESMAA: Assessment of Asthma Control in Adult Asthma Population in the Middle East and North Africa) was designed to assess asthma control levels in patients treated in public or private consultations. Asthma control was assessed by physicians according to the GINA 2012 classification which was in place at the time the study was designed [17]. The study was conducted in 11 Middle Eastern and North African countries: Algeria, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Qatar, Saudi Arabia, Tunisia, and the UAE. General practitioners and/or specialists (pulmonologists and/or allergists) were selected randomly from a regional database of asthma physicians with physicians selected according to their scientific level and willingness to participate. Each physician was planned to include approximately 10 eligible patients. The overall ratio of general practitioners to specialists was approximately 1:1. Patient data were obtained from a clinical evaluation and questionnaires completed during a single planned patient visit. Data for sociodemographic and disease and treatment characteristics were collected for all patients by the physician via direct questioning of the patient during the consultation. The ACT questionnaire (for asthma control), SF-8 questionnaire (quality of life), and the 4-item Morisky questionnaire (for treatment adherence) were completed by all patients. The protocol was approved in each country by a central or local ethics committee as per national requirements. All patients provided written informed consent.

2.2. Study population

To be eligible, patients had to be 18 years or more, diagnosed with asthma for at least one year prior to enrolment, and attending a routine consultation. Patients with other chronic respiratory diseases except for rhinitis [18] were excluded, as were patients participating in a clinical trial, patients who consulted for an asthma attack during the 4 weeks prior to enrolment, patients with a psychiatric disorder and pregnant patients.

2.3. Assessments

Asthma control was assessed as per the physician (GINA) and the patient (ACT, SF-8, and Morisky questionnaires). The GINA 2012 classification has two components: current asthma control based on the previous 4 weeks, and risk of future asthma events [17]. Current asthma control is based on the previous 4 weeks, according to the following definitions. Controlled asthma: no diurnal/nocturnal symptoms, no activity limitation and no exacerbation, β2 rescue no more than 2 times a week, and normal FEV/PEF; Partly controlled asthma: at least one of the following criteria present in any of the 4 weeks, diurnal symptoms more than 2 times a week, any activity limitation, any nocturnal symptoms, β2 rescue more than 2 times a week, and/or FEV/PEF < 80%; Uncontrolled asthma: at least three criteria of partly controlled asthma present any week or an exacerbation attack in any week. Risk of future asthma events is evaluated in terms of clinical control, exacerbations, hospitalisations, lung function, environment and treatments.

The ACT questionnaire [19] was used to determine patients' assessment of asthma control during the 4 weeks prior to physician consultation. It is a simple validated self-administered instrument, composed of four questions that assess asthma symptoms (frequency of shortness of breath), impact on daily life, use of rescue medication, and a fifth question of overall self-assessment of the patient's asthma control (as not controlled at all; very little controlled; little controlled; well controlled; totally controlled) [20,21]. The overall ACT score is the sum of scores for the five questions (each scored from 1 to 5) measuring the impact of the disease on daily life, with higher scores reflecting better control. Question 5 is a patient-derived assessment of disease control.

The validated four-item Morisky medication adherence scale (MMAS-4) was used to evaluate medication adherence [22,23]. It consists of four yes/no questions relating to reasons of medication underuse or omission, forgetfulness, carelessness, feeling better and feeling worse, with the total score ranging from 0 (highly adherent) to 4 (highly non-adherent).

Patients completed the short-form 8 (SF-8) questionnaire, a generic measure of health status based on the SF-36, as a measure of QoL. It consists of eight questions concerning the past four weeks covering physical activity, life and relationships, physical pain, perceived health, vitality, limitations due to mental status, and limitations due to physical and mental health. Results are expressed as a score from 0 to 100 (100

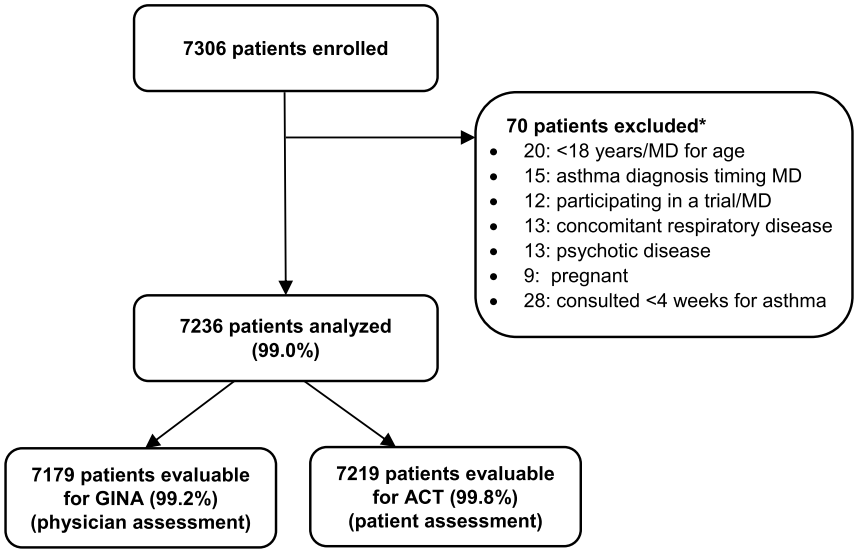

Fig. 1. Flow chart for patient inclusion and analysis.
*Patients could have more than one reason for exclusion; MD, missing data.

indicates the highest level of health) and two summarized scores, physical component score and mental component score, are calculated [24,25].

2.4. Statistical considerations

The number of patients required (N = 7245) was determined on a per-country basis, according to the level of good asthma control (p_0) and the associated accuracy. The following equation was used: $N = (1.96)^2\ p_0\ q_0/i^2$ where "p_0" is the percentage of patients with good asthma control, "q_0" is 1-p_0, and "i" is the accuracy degree. Accuracy was expected to be between 2% and 5%, and a 10% rate of non-exploitable/non-response questionnaire data was anticipated. For example in Algeria, a sample size of 894 produces a two-sided 95% confidence interval (95% CI) with a width equal of 6% (accuracy = 3%) and a good asthma control proportion of 30%. With the 10% rate of non-exploitable patients, 1000 patients need to be included in this country. The number of physicians required was determined according to this planned patient sample size on the basis that each physician was intended to enrol an average of 10 eligible patients, with the exception of Saudi Arabia (increased to 40 to 50 patients), and in the UAE and Kuwait (increased to 30 to 35 patients) to ensure recruitment.

The analysed population was composed of all enrolled patients without protocol deviations. Descriptive statistics were used and two-sided 95% CI were calculated using the Wilson method. ACT scores and SF-8 scores (8 items and 2 main composite scores) were calculated with Qualimetric Health Outcome Scoring Software version 4.5.

The relationship between asthma control (dependant variable) and explanatory independent variables was analysed by logistic regression. The following explanatory variables were tested using univariate logistic regressions: age ([18–35];]35–55]; > 55 years), gender, country, BMI (< 18 [18–25], > 25 kg/m^2), level of education, professional situation, medical insurance coverage, comorbidities of allergic rhinitis (yes/no), gastroesophageal reflux (yes/no), related chronic disease (yes/no), smoking status (current smoker/former smoker/non-smoker), regular physical exercise, time to asthma diagnosis in class (< 2 years, 2–5 years and > 5 years), history of the disease in the last six months (symptoms, exacerbations, night-time symptoms, spirometry), good compliance to asthma treatment according to Morisky questionnaire (i.e. score = 4) (yes/no), and asthma treatment in the past 6 months (yes/no for: inhaled corticosteroids, long acting bronchodilator, oral corticosteroids, fixed combination [ICS + LAB2], anti-leukotrienes, theophylline, anticholinergic bronchodilator, other medications). Univariate logistic regressions were performed to explain asthma controlled (optimal and acceptable levels, i.e. current clinical controlled or partly controlled) versus uncontrolled (non-acceptable level). The proportion of patients with an acceptable level of asthma control was calculated in each modality of each explanatory variable and odds ratio calculated with their 95% CI. Significant variables after univariate regression ($p < 0.10$) were entered in a backward multivariate model using a 0.10 significance level. ACT and SF8 scores were compared between asthma control levels using an ANOVA test. Good adherence (Morisky score = 4) were compared between asthma control levels using a Chi^2 test.

All analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, USA).

3. Results

3.1. Patient population

Overall, 7306 patients were included in a total of 577 sites (range, 8 to 97 sites per country) between 11 June 2014 and 30 December 2015. The proportion of included patients varied per country, between 2.7% of the study population from Qatar to 14.3% of the population from Egypt. A median of 10 patients were enrolled per site (range 1–240) with a similar median number between countries other than Saudi Arabia where a median of 91 patients were enrolled (as allowed for in the protocol), and Qatar and the UAE where a median of 20 patients were entered per site. Seventy patients (1.0%) were considered ineligible and were excluded from the analysis (Fig. 1).

Sociodemographic characteristics in the 7236 (99.0%) evaluable patients are presented by country in Table 1. Mean age was 45 years (± 14) with a 1.3 female:male ratio. Mean BMI was 28.5 kg/m^2 (± 6.0) with 34.1% of the population classified as obese (BMI > 30 kg/m^2), and 10.8% were active smokers. Over half the population (58.5%) had allergic rhinitis. Characteristics were mostly well balanced between countries: Jordan and Lebanon had higher rates of active smokers compared to the other countries; allergic rhinitis was more prevalent in Qatar, Algeria, and Kuwait while the lower rates reported in Iraq

Table 1
Patient socio-demographics by country.

	Algeria (N = 984)	Egypt (N = 1040)	Iran (N = 996)	Iraq (N = 699)	Jordan (N = 446)	Kuwait (N = 370)	Lebanon (N = 372)	Qatar (N = 197)	Saudi Arabia (N = 1009)	Tunisia (N = 600)	UAE (N = 523)	Total (N = 7236)
Age (years), mean (SD)	45.2 (14.6)	44.1 (13.9)	48.4 (14.5)	44.3 (14.4)	44.5 (14.2)	44.9 (13.0)	41.7 (15.6)	49.0 (14.6)	48.7 (15.9)	45.4 (14.6)	40.3 (13.6)	45.4 (14.7)
Male[a]	39.2%	47.8%	42.1%	44.6%	46.0%	47.8%	39.8%	51.3%	34.7%	40.8%	50.1%	42.9%
BMI (kg/m^2), mean (SD)[b]	26.8 (5.2)	29.4 (5.9)	27.2 (5.0)	28.8 (5.9)	27.9 (5.3)	30.1 (5.6)	26.6 (4.6)	30.5 (6.7)	30.7 (7.4)	26.9 (5.0)	29.0 (6.3)	28.5 (6.0)
Smoking status[c]												
Non-smoker	85.2%	76.5%	89.4%	81.8%	66.2%	76.7%	61.0%	75.8%	86.5%	77.2%	76.2%	80.1%
Past smoker	12.4%	4.9%	7.5%	9.6%	7.8%	7.5%	8.8%	18.8%	7.9%	13.7%	9.2%	9.1%
Active smoker	2.3%	18.6%	3.1%	8.6%	26.0%	15.9%	30.2%	5.4%	5.6%	9.0%	14.7%	10.8%
Allergic rhinitis	74.7%	49.0%	64.5%	40.5%	52.9%	73.2%	56.7%	77.2%	52.4%	67.8%	49.1%	58.5%
Professionally active[d]	48.9%	72.7%	62.4%	64.6%	64.3%	73.2%	69.7%	64.1%	38.3%	60.9%	76.5%	60.9%
Medical insurance[e]	87.2%	52.5%	95.0%	17.8%	54.8%	73.0%	71.4%	53.6%	66.2%	84.2%	90.2%	69.1%

[a] Missing data N = 1.
[b] Missing data N = 139.
[c] Missing data N = 321.
[d] Missing data N = 34.
[e] Missing data N = 40.

(40.5%), Egypt (49.0%) and the UAE (49.1%) were likely due to poor patient awareness of the diagnosis; and the proportion of patients with medical insurance was lower in Iraq and higher in the UAE and Iran.

3.2. Asthma characteristics

Characteristics of asthma, treatment and quality of life in the study population are presented in Table 2. Patients had been diagnosed a mean of 12.5 (± 10.1) years prior to study inclusion, with 70.0% of the population diagnosed for more than 5 years. Symptoms over the past 6 months occurred more than once a week in 46.9% of the population, including 14.5% with daily symptoms. Frequent night-time symptoms were reported in 10.3% of patients. Two-thirds of the population (66.4%) had a history of mild exacerbations, while 22.6% of patients reported an impact on daily activities and sleep. Some inter-country variations were seen, with patients from Qatar and Tunisia having a lower frequency of symptoms, while patients in Iraq had more exacerbations affecting activities and sleep.

Almost all patients (95.5%) had been prescribed reliever medications at the time of the consultation. The principal controller treatment was a fixed-dose combination of inhaled corticosteroid with a long-acting beta agonist, prescribed in 65.0% of the patients, including 38.0% of patients using it with another treatment. The proportion of patients receiving treatment was smallest in Lebanon and inter-country variations in the types of treatments administered were apparent.

Good medication adherence (a Morisky score of 4) was reported in less than one-quarter of the population (23.6%) with some variation between countries. Mean SF-8 scores for evaluation of quality of life were in the middle of the scale for both physical and mental summary scores, with minimal inter-country variation.

3.3. Asthma control

Overall, 7179 patients (99.2% of the eligible population) were assessable according to GINA 2012, providing a physician perspective of asthma control. In terms of current control, asthma was considered controlled in 29.4% of the overall population (95% CI, 28.4%–30.5%), partly controlled in 29.1% (95% CI, 28.1%–30.2%), and uncontrolled in 41.5% (95% CI, 40.3%–42.6%; Fig. 2A). Lower rates of controlled asthma were reported in Jordan (14.8%) and Iraq (17.5%), and higher rates in Kuwait (42.6%), Qatar (41.1%), and Tunisia (40.2%). All five parameters used in the GINA 2012 asthma control algorithm [17] were reported in at least one-third of patients having uncontrolled asthma, notably abnormal lung function reported in 54.3% and nocturnal symptoms in 46.6% (Table 3). Inter-country variations in the presence of contributing symptoms were coherent with the overall findings for frequency of controlled asthma. Assessment of future risk of asthma events (Fig. 2B) showed that 82.9% of the overall population had at least one risk factor for future exacerbations. Patients with GINA controlled asthma (N = 2111) were more likely to have no risk factors (36.1%) compared to patients with uncontrolled asthma (5.7%; N = 2977). The two main contributing factors were current poor control (35.5%) and exposure to cigarette smoke (34.0%).

Asthma control was evaluated from the patient perspective in 7219 patients using the ACT questionnaire. The mean global ACT score in the total population was 17.8 (± 5.0), and global scores were relatively consistent between countries with means ranging from 15.3 (± 5.3) in Iraq to 20.0 (± 4.3) in Qatar. Patient evaluation of their asthma control (as per question 5) is presented in Fig. 2C. When questioned how they rate their asthma control over the last 4 weeks, 15.9% of patients reported it as being completely controlled, 35.5% as well controlled, 27.0% as somewhat controlled, and 21.5% as poorly or not controlled.

The global ACT score, medication adherence and quality of life were associated with the level of GINA asthma control (Table 4). Significant differences between different levels of control ($p < 0.001$) were seen for all four parameters, with a mean ACT score of 21.8 (± 3.1) in

Table 2
Asthma history, treatment, and impact by country.

	Algeria (N = 984)	Egypt (N = 1040)	Iran (N = 996)	Iraq (N = 699)	Jordan (N = 446)	Kuwait (N = 370)	Lebanon (N = 372)	Qatar (N = 197)	Saudi Arabia (N = 1009)	Tunisia (N = 600)	UAE (N = 523)	Total (N = 7236)
Years since diagnosis, mean (SD)	15.1 (11.2)	12.1 (9.0)	9.6 (8.4)	11.7 (9.6)	10.0 (7.9)	12.5 (8.7)	13.3 (11.0)	14.0 (10.6)	13.2 (11.2)	14.3 (10.3)	12.8 (10.4)	12.5 (10.1)
Frequency of symptoms[a,b]												
< 1/week	66.7%	44.2%	49.2%	40.3%	39.4%	61.2%	44.8%	72.8%	54.2%	68.1%	55.6%	53.1%
> 1/week and < 1/day	25.1%	41.1%	31.7%	33.5%	40.3%	28.5%	36.4%	21.0%	33.4%	24.5%	33.5%	32.4%
Daily	8.2%	14.7%	19.1%	26.2%	20.4%	10.3%	18.8%	6.2%	12.3%	7.4%	10.9%	14.5%
Frequent night-time symptoms[a]	7.5%	12.8%	8.5%	15.3%	15.0%	7.6%	11.0%	2.5%	12.3%	7.7%	6.1%	10.3%
Exacerbation affecting activities and sleep[a]	20.3%	26.9%	21.8%	33.6%	29.6%	17.0%	26.9%	8.6%	18.5%	16.3%	19.9%	22.6%
Mild exacerbation[a]	68.5%	64.3%	71.9%	48.1%	59.6%	79.2%	57.8%	73.6%	65.7%	73.2%	73.8%	66.4%
Currently treated	92.2%	97.1%	97.8%	98.4%	92.5%	95.4%	81.8%	98.0%	97.1%	96.8%	97.1%	95.5%
Receiving asthma treatment: yes	92.2%	97.1%	97.8%	98.4%	92.5%	95.4%	81.8%	98.0%	97.1%	96.8%	97.1%	95.5%
Main asthma treatment [c]												
Fixed ICS + LABA with other treatment	27.6%	25.1%	48.3%	33.9%	34.9%	33.0%	27.3%	49.7%	62.7%	17.3%	53.6%	38.0%
Fixed ICS + LABA alone	28.1%	30.9%	29.9%	18.0%	30.3%	43.8%	25.6%	34.0%	13.6%	39.5%	19.5%	27.0%
Free ICS + LABA	6.7%	21.3%	8.5%	4.3%	5.5%	2.7%	3.6%	0%	1.9%	18.0%	1.7%	8.1%
Only ICS	16.1%	4.5%	4.5%	4.0%	2.1%	6.8%	2.8%	4.6%	1.7%	11.0%	1.3%	5.8%
SABA alone	1.2%	4.8%	1.1%	8.9%	8.2%	1.9%	3.6%	5.1%	5.4%	2.2%	10.6%	4.5%
Other	20.3%	13.4%	7.7%	30.9%	19.0%	11.8%	37.1%	6.6%	14.7%	12.0%	13.3%	16.6%
Good adherence (Morisky score = 4)[d]	27.2%	22.6%	22.5%	15.8%	16.3%	23.4%	30.9%	37.1%	22.9%	23.1%	29.7%	23.6%
SF-8 summary score[e]												
Physical, Mean (SD)	49.7 (9.0)	42.9 (9.9)	46.4 (9.9)	39.9 (10.1)	42.9 (9.7)	48.4 (8.9)	46.4 (9.3)	48.9 (7.8)	43.0 (9.2)	47.2 (9.3)	47.5 (8.5)	45.3 (9.9)
Mental, Mean (SD)	48.4 (10.2)	45.0 (10.6)	47.6 (10.3)	43.2 (10.4)	45.5 (9.7)	50.4 (9.5)	47.9 (9.7)	52.1 (7.7)	44.9 (9.9)	47.7 (9.5)	50.2 (9.2)	46.9 (10.2)

ICS, inhaled corticosteroids; LABA, long-acting β-agonist; SABA, short-acting β-agonist.

[a] During the 6 months prior to enrolment.

[b] Missing data N = 61.

[c] At the time of the consultation, Missing data N = 71.

[d] During the 4 weeks prior to enrolment, Missing data N = 33.

[e] Missing data N = 83. SF-8 summary score ranges from 0 to 100; 100 indicates the highest level of quality of life.

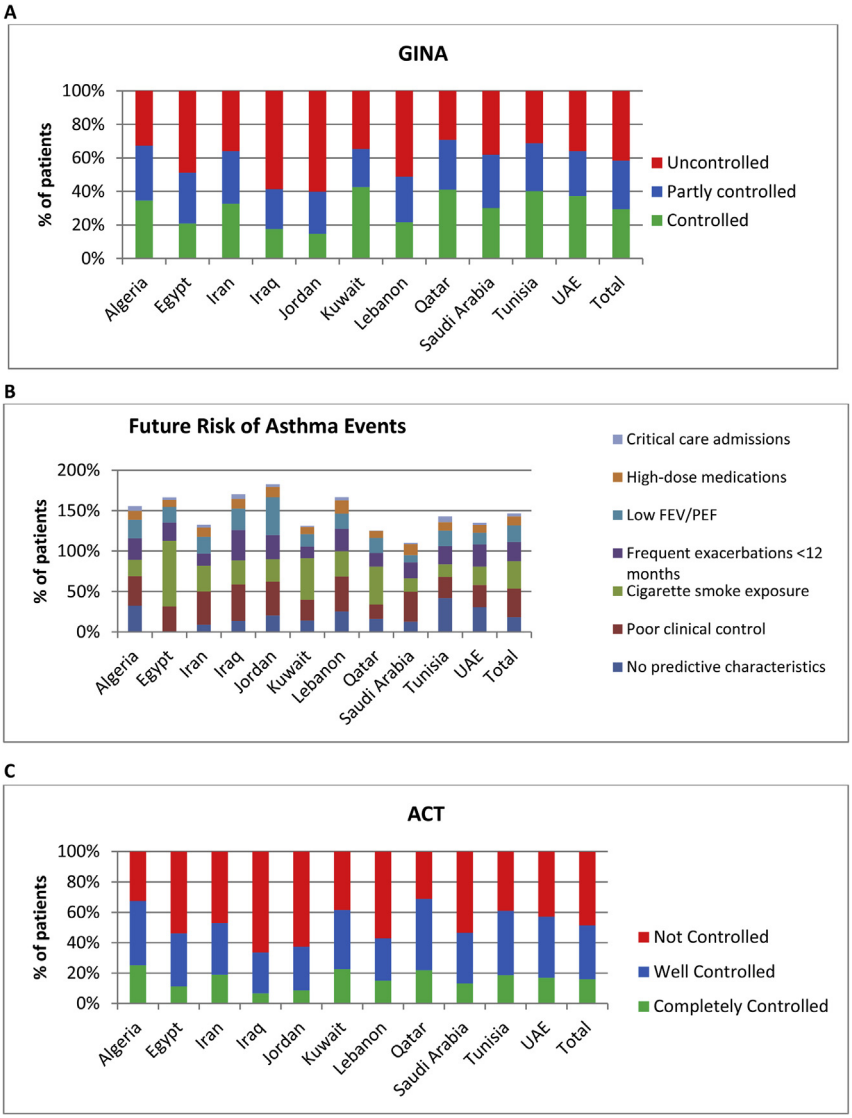

Fig. 2. Asthma control as assessed for each country and the overall population is shown according to the physician assessment per GINA 2012 (N = 7179) for (A) current control and (B) future risk (patients could have more than one factor so data are cumulative), and (C) according to the patient's assessment for the ACT Question 5 ("How would you rate your asthma control during the past 4 weeks?" where not controlled = somewhat controlled + poorly controlled + not controlled at all; N = 7219).

patients with GINA controlled asthma compared to 13.8 (± 4.0) in the uncontrolled group. Likewise, a 31.6% medication adherence rate was seen in the controlled group versus 17.8% in the uncontrolled group. Similar trends were seen for quality of life, with higher mean SF-8 scores for both components associated with better asthma control according to GINA classification (physical summary 52.2 [± 7.0] for controlled versus 38.6 [± 8.5]; mean mental summary 51.6 [± 8.5] versus 42.2 [± 10.1], respectively).

3.4. Factors predicting GINA asthma control

Univariate and multivariate analyses were performed to identify potentially predictive factors for the level of GINA asthma control. In the univariate analysis comparing the pooled completely/partially controlled population versus the uncontrolled population, most variables evaluated showed significant differences between different levels of asthma control, with the exception of the presence of allergic rhinitis and inhaled corticosteroid intake. Multivariate analysis identified several factors with a significantly higher likelihood of having uncontrolled asthma (Table 5). These included poor medication adherence (as per Morisky) (OR, 0.55 [95% CI, 0.49; 0.63]), active smoking (OR, 0.57 [95% CI, 0.48; 0.67]), absence of medical insurance (OR, 0.65 [95% CI, 0.58; 0.72]), or diagnosis at least 5 years earlier (OR, 0.73 [95% CI 0.62; 0.88]). Patients with a higher level of education were more likely to have controlled asthma (OR, 2.31 [95% CI 1.72; 3.09]). BMI, age, and professional status did not significantly influence asthma control in the multivariate model.

4. Discussion

Despite availability of effective treatments and international care recommendations, nationally representative surveys carried out over the last two decades report that asthma control worldwide continues to be suboptimal [3–7,26]. The current study in more than 7000 asthma patients confirms this to be the case in the Middle East and North Africa, with a physician assessment of asthma control (according to the GINA 2012 recommendations) showing that more than 40% of the asthma population has uncontrolled asthma. The 29.4% rate of controlled asthma in the overall population varied between countries, ranging from as low as 14.8% in Jordan to 42.6% in Kuwait. Overall,

Table 3
Factors contributing to uncontrolled asthma according to GINA 2012 (during the last 4 weeks).

	Algeria (N = 984)	Egypt (N = 1040)	Iran (N = 996)	Iraq (N = 699)	Jordan (N = 446)	Kuwait (N = 370)	Lebanon (N = 372)	Qatar (N = 197)	Saudi Arabia (N = 1009)	Tunisia (N = 600)	UAE (N = 523)	Total (N = 7236)
Daytime symptoms > 2/week[a]	28.8%	48.6%	38.3%	54.9%	59.0%	30.0%	50.3%	29.9%	36.7%	33.5%	35.8%	40.5%
Limitation of activities[b]	26.7%	41.2%	32.0%	55.2%	50.7%	26.5%	41.6%	18.3%	35.9%	28.0%	29.8%	35.9%
Nocturnal symptoms/awakening[c]	44.1%	54.1%	39.1%	64.8%	66.8%	39.7%	56.8%	26.9%	39.7%	37.7%	37.7%	46.6%
Reliever/rescue treatment > 2/week[a]	33.3%	41.8%	31.1%	51.8%	56.7%	35.7%	51.4%	30.5%	34.7%	28.6%	40.2%	38.7%
Lung function FEV/PEF < 80% predicted[d]	46.4%	68.6%	55.9%	70.5%	68.5%	37.8%	53.8%	47.6%	50.7%	42.8%	38.6%	54.3%

[a] Missing data N = 6.
[b] Missing data N = 6.
[c] Missing data N = 8.
[d] Missing data N = 95.

82.9% of patients had at least one factor for an increased risk of a future asthma event, primarily driven by current poor control or exposure to cigarette smoke. From the patient perspective, only 15.9% of all patients considered their asthma was completely controlled. Although this represented only half the physician-estimated rate, physician and patient assessment of asthma control were significantly correlated ($p < 0.001$).

Under-evaluation of symptoms by patients combined with sub-optimal adherence to prescribed treatments are known causes of sub-optimal asthma control [3,12–14]. This is clearly a driver of poor asthma control in our population, with less than one-quarter of our population self-reporting good adherence to their prescribed treatment. Coherent with this, poorer adherence was significantly associated with poorer GINA asthma control in our population ($p < 0.001$). Smoking, poor level of education, asthma-related comorbidities such as gastro-intestinal reflux disease were also associated with poorer control, confirming reports from smaller studies in this region [27,28]. As reported for other regions, higher quality of life was associated with better asthma control according to GINA classification for both physical and mental components [3,15,16,29].

Global ACT scores of 20–25 are classified as well-controlled asthma while 16–20 is not well-controlled and 5–15 as very poorly controlled asthma, with a minimum clinically important difference of 3 points [30]. Our results were coherent with this, supporting the value of the ACT questionnaire; patients with GINA controlled asthma had a mean ACT score of 21.8, patients with GINA partly controlled asthma had a mean ACT score of 19.4, and patients with GINA uncontrolled asthma had a mean ACT score of 13.8. A published cross-sectional survey in Europe and the USA comparing the ACT score and GINA classification of asthma control in nearly 3000 patients attending primary care physicians and specialists, reported that ACT scores of less than 19 correlated with patients having poorly controlled asthma according to the GINA definition [31]. In the AIRMAG study, the ACT questionnaire was considered a valid measure of asthma control in a North African context, although the authors reported its internal consistency was compromised by the 'use-of-rescue-treatment' item which they considered likely to be influenced by limited access to care and use of short-acting beta agonists [21]. A study performed in Jordan also confirmed the utility of the ACT questionnaire as a simple assessment tool to screen and categorize asthma control in this population [32].

While some data were available for asthma control in the Middle East and Maghreb at the time of our study [8–11], they are derived from multiple studies and include a total of less than 3000 patients. The current report is the most comprehensive and recent to date in this region, encompassing 11 countries and over 7000 patients. The profiles of the patient populations in the published studies in this region correlate broadly with those of our study in terms of age, sex, and smoking status. Our ACT assessment outcomes were largely coherent with those reported in the AIRGNE study in Jordan, Kuwait, Lebanon, Oman, and the UAE [8], and in a study in Saudi Arabia [11]. However the AIRMAG study in Algeria, Morocco, and Tunisia reported higher levels of patients with uncontrolled asthma (67%–75% with ACT score < 20) [10]. Small-scale country-specific studies emerging around the time our study was under preparation or since its initiation also reported poor levels of asthma control in Jordan, Saudi Arabia, and Qatar [32–34].

There are a number of methodological limitations associated with this study, implicating sources of potential bias and potential limitations in interpreting the data. Firstly, GINA recommendations are updated regularly with the current version dating from 2017. At the time the study was conceived and implemented, the GINA 2012 guidelines were in place and were thus used for data analysis. In the update published in May 2014, released around the time of study implementation, lung function was removed as a measure of symptom control (and the term "symptom control" was employed rather than "current clinical control"). This may mean that the outcome from the analysis reported here is worse compared to an analysis of the same

Table 4
Parameters varying significantly according to level of GINA asthma control.

	Asthma control according to GINA			
	Controlled (N = 2111)	Partly controlled (N = 2091)	Uncontrolled (N = 2977)	p-value
Global ACT score, Mean (SD)	21.8 (3.1)	19.4 (3.5)	13.8 (4.0)	< **0.001 (A)**
Missing data	13	10	17	
Good adherence (Morisky)	31.6%	24.1%	17.8%	< **0.001 (C)**
Missing data	15	4	14	
SF-8 Physical summary, Mean (SD)	52.2 (7.0)	47.9 (7.9)	38.6 (8.5)	< **0.001 (A)**
Missing data	20	25	38	
SF-8 Mental summary, Mean (SD)	51.6 (8.5)	48.5 (9.3)	42.2 (10.1)	< **0.001 (A)**
Missing data	20	25	38	

(A) Analysis of variance; (C) Chi-square test.
ACT global score ranges from 5 to 25; 25 indicates the highest level of asthma control.
SF-8 summary score ranges from 0 to 100; 100 indicates the highest level of quality of life.
Morisky score of 4 was considered as good adherence.

data with the GINA recommendations from 2014 or later. Secondly, with the methodology used, data obtained primarily from healthcare personnel reports along with patient self-reporting are associated with a level of subjectivity. In addition, spirometry data were lacking (not reported in patient records). As a cross-sectional observational study, cause and effect cannot be analysed. Finally, inter-country variations were seen for the number of patients per site (from 1 to 240 patients per site), proportion of the population included per country (from 2.7% to 14.3%), and number of sites per country (from 8 to 97) which may have impacted the results.

The study has several strengths, in particular the large sample size for an epidemiological study in this field, along with the nationwide sampling. The methodology used to assess asthma control in our population which involved direct patient interviews, differs from that of many published studies which often identify patients from a random sample of the general population using a standardized, computer-assisted telephone interview [10,26,35] or by using online surveys [4]. The choice of a face-to-face interview approach is considered beneficial in many settings, notably when dealing with patients with high asthma illiteracy, which is common difficulty faced in this region. The current study specifically targeted asthma patients attending a routine consultation, directly addressing general practitioners and/or specialists known to treat asthma patients. Efforts were made to balance patient recruitment between primary care and specialty care centres to match the countries' specific health systems. While this targeted approach excluded the collection of prevalence data, it has two advantages. Firstly, it rendered a relatively high response rate compared to random population-based studies. And secondly, it allowed collection of data from a physician perspective of the level of asthma control, which is somewhat less subjective than that obtained with the ACT questionnaire from the patient perspective.

This study highlighted a number of areas with the potential for improvement of asthma control. Patient education as to the importance of medication adherence and avoidance of smoking remain critical

Table 5
Parameters predictive of GINA asthma control (multivariate logistic regression).

Explanatory variable Interpretation	Asthma control according to GINA - pooled			
	Controlled or partly controlled (N = 4202)	Uncontrolled (N = 2977)	Odds ratio [95% CI][a]	p-value
Good adherence (Morisky)				< 0.001
Yes (reference)	1089 (69.2%)	484 (30.8%)	1.00	
No	2821 (55.4%)	2267 (44.6%)	0.55 [0.49; 0.63]	
Smoking status				< 0.001
No smoker (reference)	3200 (59.9%)	2142 (40.1%)	1.00	
Past smoker	358 (59.1%)	248 (40.9%)	0.86 [0.71; 1.03]	
Active smoker	352 (49.4%)	361 (50.6%)	0.57 [0.48; 0.67]	
Medical insurance				< 0.001
Yes (reference)	2866 (62.4%)	1729 (37.6%)	1.00	
No	1044 (50.5%)	1022 (49.5%)	0.65 [0.58; 0.72]	
Asthma diagnosis history (class)				< 0.001
≤2 years (reference)	412 (63.9%)	233 (36.1%)	1.00	
2–5 years	828 (62.1%)	505 (37.9%)	0.92 [0.76; 1.13]	
> 5 years	2670 (57.0%)	2013 (43.0%)	0.73 [0.62; 0.88]	
Sex				0.009
Male (reference)	1761 (61.1%)	1123 (38.9%)	1.00	
Female	2149 (56.9%)	1628 (43.1%)	0.85 [0.76; 0.96]	
Level of education				< 0.001
Cannot read and write (reference)	286 (44.1%)	362 (55.9%)	1.00	
Primary	806 (54.3%)	679 (45.7%)	1.47 [1.21; 1.79]	
Secondary school	1251 (57.9%)	909 (42.1%)	1.64 [1.35; 1.99]	
University degree	1331 (66.0%)	685 (34.0%)	2.27 [1.85; 2.79]	
Higher education	236 (67.0%)	116 (33.0%)	2.31 [1.72; 3.09]	
Gastro-oesophageal reflux				0.010
Yes (reference)	876 (54.9%)	721 (45.1%)	1.00	
No	3034 (59.9%)	2030 (40.1%)	1.17 [1.04; 1.31]	

Note: Symptom, exacerbation description and asthma medication questions were not included in multivariate model despite univariate pvalues < 1%.
[a] Higher likelihood of uncontrolled vs controlled.

issues (two areas receiving increasing attention in the updated GINA recommendations), although cultural barriers pose limitations to the latter. For physicians, it is important to be attentive to management of patients with long-term asthma diagnosis.

5. Conclusions

Asthma control was poor in all 11 Middle East and North African countries evaluated in the ESMAA study, with physicians judging that less than one-third of the asthma population has controlled asthma symptoms and four in five asthma patients have risk factors for future exacerbations. Asthma control remains unsatisfactory in the Middle Eastern and North African adult population. This can be addressed by improving access to appropriate treatments, encouraging better medication adherence and smoking avoidance, along with more proactive follow-up and better education among health care providers and patients.

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