



Impact of the GINA asthma guidelines 2019 revolution on local asthma guidelines and challenges: special attention to the GCC countries

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Abstract

The Global Initiative for Asthma (GINA) provides the most comprehensive and frequently updated guidelines for the management of asthma. The primary aim of guidelines is to bridge the gap between research and current medical practice by presenting the best available evidence to aid clinical decision-making, thereby improving patient outcomes, quality of care, and cost-effectiveness. Guidelines are particularly useful in situations where scientific evidence is limited, multiple treatment options exist, or there is uncertainty about the best course of action. However, due to variations in healthcare system structures, many countries have developed their own local guidelines for the management of asthma. Adoption of GINA recommendations into local guidelines has been uneven across different countries, with some embracing the changes while others continue to follow older approaches. This review article will explore the impact of the noteworthy changes in GINA guidelines, particularly in the 2019 version, on local guidelines and some of the challenges associated with implementing them.

Keywords

Asthma, Global Initiative for Asthma (GINA), national asthma guidelines, international asthma guidelines, adherence to guidelines, implementation of guidelines

Introduction

Asthma is a heterogenous respiratory disease characterized by chronic airway inflammation, obstruction, and hyperresponsiveness [1]. Over the last few years, various guidelines at both national and international levels have been created and revised with the aim of enhancing the diagnosis and management of asthma.

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Among these guidelines, the Global Initiative for Asthma (GINA) [1] has emerged as one of the most influential and broadly accepted international documents for the care of individuals with asthma. Over the years, the GINA guidelines have undergone significant revisions in response to new research and advancements in asthma management.

The impact of the GINA guidelines on local asthma guidelines [2–10] and management has been substantial. Many countries and healthcare organizations have adopted the GINA guidelines as the basis for their own guidelines and have tailored them to their specific needs and resources. This has led to greater standardization and consistency in asthma care across different regions, which can ultimately improve patient outcomes [11].

In this review, the impact of the GINA asthma guidelines revolution on local asthma guidelines and management will be explored. Specifically, we will assess the extent to which the GINA guidelines have influenced the development and revision of local guidelines, as well as the implications of these changes for healthcare providers and patients.

Asthma burden at a global and local scale

Asthma is estimated to affect 357 million people worldwide [12]. At a local level in the Gulf Cooperation Council (GCC) countries, the prevalence of asthma ranges from 4.7% to 32% [13], which translates to 2.9 to 17 million affected. In Saudi Arabia, the estimated prevalence is 14.2%, and almost a third of them are affected by severe asthma symptoms [14]. In fact, 70% of all asthmatics in Saudi Arabia are labeled to have partially controlled to uncontrolled asthma [15]. Globally, the reported mortality rate associated with asthma is 5.8 per 100,000 [16]. In Kuwait, the asthma mortality rate was reported to be 0.9 per 100,000 in 2000 [17]. It has a significant economic impact in the GCC countries, ranging from 23 million to 208 million US dollars annually [13].

Overview of GINA guidelines

Global and local guidelines [1–10] have been established to standardize asthma diagnosis and management. Among these guidelines, the GINA guideline has become one of the most influential and widely adopted international documents for asthma care. GINA was established in 1993 as a collaboration between the National Heart, Lung, and Blood Institute, the National Institutes of Health, and the World Health Organization. Since its inception, 21 iterations have been published. GINA aims to reduce asthma morbidity and mortality by developing and disseminating evidence-based guidelines for asthma management. The GINA guidelines include recommendations for the diagnosis, assessment, and monitoring of asthma, as well as treatment strategies based on the severity and control of the disease. The establishment of GINA guidelines has led to a global standardization of asthma care and hence improvement in asthma symptoms and control both globally [18] and locally [19].

Summary of the local asthma guidelines and their importance

Numerous national and local guidelines exist for the assessment and management of asthma. Local guidelines are customized to meet the specific needs of a particular region, encompassing aspects such as treatment decisions, criteria for initiating certain therapies (e.g., biologics), diagnostic procedures, and strategies for addressing unique challenges at the country or local level.

A few examples of these local and national guidelines can be found in Table 1. In the “Why asthma still kills” report [20] conducted by the Royal College of Physicians on behalf of the Health Quality Improvement Partnership in the UK, it was argued that “There were potentially avoidable factors related to non-implementation of the current UK British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) asthma guidelines in 89 (46%) out of the 195 deaths”. This speaks of the importance of having a national unified asthma guideline and the proper application of these guidelines.

Table 1. Examples of local asthma guidelines and their modifications in contrast to GINA changes, if any

Guidelines	Country	Latest update	Measure of asthma severity	Implemented new GINA changes	Presence of the preferred track	Start with inhaled corticosteroids (ICS)/formoterol as needed PRN for mild intermittent asthma	Short-acting β 2-agonists (SABA) alone as an option in mild intermittent asthma	Maintenance-and-reliever therapy (MART) as an option in any step	ICS for mild persistent asthma
GINA [1]	Global	2022	Symptoms	N/A	Yes	Yes	No	Yes	Alternative option
BTS/SIGN [4]	UK	2019	Symptoms plus exacerbation history in the past 2 years	No	No	No	Yes	Yes	Preferred
Saudi Initiative for Asthma (SINA) [6]	Saudi Arabia	2021	Asthma Control Test (ACT)	Yes	No (although ICS to be given when SABA is used as needed is considered as an alternative option)	Yes	No	Yes	Yes
Ministry of Health Asthma Pocket Guide for health care professionals [21]	Saudi Arabia	2020	ACT symptoms	Yes	No, but clear recommendation to use ICS/formoterol as the first choice and alternative use of ICS whenever SABA used	Yes	No	Yes	No (use ICS/formoterol)
Manejo Integral del Asma (MIA), Comprehensive Asthma Management Guidelines for Mexico [7]	Mexico	2021	Symptoms plus exacerbation and hospitalization	Yes	Yes	Yes	No	Yes	Yes
Spanish Asthma Management Guidelines (GEMA) [9]	Spain, Portugal, and Latin America	2022	Symptoms and exacerbation	Partial	No	Yes	Yes	Not specifically	Preferred
Japanese guidelines for adult asthma [8]	Japan	2020	Symptoms and frequent exacerbation for severe persistent only	No	No	No	No (low dose ICS to be used regularly)	No	Preferred
Canadian Thoracic Society (CTS) [10]	Canada	2021	Symptoms, exacerbation, and inflammatory markers	No	No	Yes	Yes	Yes	Preferred
Qatar National Clinical Guidelines [5]	Qatar	2019	Symptoms	No	No	No (low dose ICS)	No	Yes	Preferred

Table 1. Examples of local asthma guidelines and their modifications in contrast to GINA changes, if any (*continued*)

Guidelines	Country	Latest update	Measure of asthma severity	Implemented new GINA changes	Presence of the preferred track	Start with inhaled corticosteroids (ICS)/ formoterol as needed PRN for mild intermittent asthma	Short-acting β 2-agonists (SABA) alone as an option in mild intermittent asthma	Maintenance-and-reliever therapy (MART) as an option in any step	ICS for mild persistent asthma
Abu Dhabi Department of Health guidelines [2]	Abu Dhabi, United Arab Emirates (UAE)	2018	Symptoms	No	No	No	Yes	Yes, for steps 3 and 4	Low dose ICS
Dubai Department of Health guidelines [3]	Dubai, UAE	2018	Symptoms	No	No	No	Yes	Yes	Low dose ICS

N/A: not applicable

Currently, at the level of the GCC countries, there are published nationwide asthma guidelines for only two Gulf countries, Saudi Arabia [6] and Qatar [5]. In 2008, as a subsidiary of the Saudi Thoracic Society (STS), the SINA group was founded to develop guidelines for diagnosing and managing asthma for adults and children. The mission of SINA is to develop up-to-date and easy-to-use asthma guidelines for all healthcare individuals in Saudi. The SINA 2021 is the fifth and latest version of the SINA guidelines.

Both Department of Health in Abu Dhabi [2] and Dubai [3], UAE, published guidelines for diagnosing, managing, and monitoring asthma in their perspective areas in 2018. These two guidelines used multiple guidelines including GINA, the National Asthma Education and Prevention (NAEP), and other guidelines. In addition, these guidelines were customized to fit Abu Dhabi and Dubai's local culture, healthcare system, and the context of the Emirate.

The “fundamental” changes to GINA guidelines in 2019

Over more than ten years, the GINA guidelines recommendations based on disease severity as measured by the history of daytime and nighttime asthma symptoms, exacerbation, and lung function [forced expiratory volume in one second (FEV1) and peak expiratory flow rate (PEFR)] to assess and monitor asthmatic patients. However, significant revisions of the GINA report have occurred over the years based on the best and updated evidence-based knowledge [22]. Due to concerns about its oral version's significant side effects, daily ICSs were slowly and carefully introduced into the guidelines [23]. Another concern was developed around β 2-agonist risk in asthma, especially against long-acting β 2-agonists (LABAs). This led to recommendations against using LABA as only asthma treatment; however, SABA alone as needed remained the mainstay therapy for mild asthma. ICS is recommended for patients with frequent symptoms.

SABA is inexpensive and relieves symptoms quickly, and it has been recommended as a reliever and treatment for mild asthma for many years. However, treatment of asthma with SABA alone is associated with an increased risk of asthma exacerbation and related death [24]. Three or more canisters of SABA per year is associated with an increasing risk of severe asthma exacerbations and mortality. This may be because SABA alone leads to downregulation of the beta-2 receptors which would result in the development of tolerance of its bronchodilator effect and possibly rebound bronchoconstriction once SABA alone is stopped as suggested by Hancox and colleagues [25]. By contrast, clinical trials in mild asthma showed that as-needed ICS-formoterol decreases the risk of severe

exacerbations significantly compared with SABA alone [26–30]. This could be related to the fact that the addition of ICS increases the expression of beta-2 receptors [31] which possibly counteract the above-described effect of SABA. Additionally, ICS reduces inflammation in the airways which is the cardinal feature of asthma.

Prior to 2019, GINA guidelines recommend starting treatment with a low-dose ICS for patients with mild persistent asthma and increasing the ICS dose or adding a LABA for patients with more severe or poorly controlled asthma. SABA alone as needed was recommended as therapy for mild intermittent asthma and rescue therapy for all severity categories. The guidelines also recommend the use of add-on therapies such as leukotriene receptor antagonists (LTRAs) or theophylline for patients with persistent symptoms despite treatment with ICS and LABA.

GINA strategy report witnessed “the most fundamental change in asthma management in over 30 years” in its 2019 revision [32]. The critical change in the GINA 2019 report was SABA reliever therapy alone is no longer recommended as a starting treatment of asthma. In this edition, there was a clear recommendation against using SABA alone. To reduce the risk of severe exacerbations and control symptoms, the GINA report recommended that mild intermittent asthmatics should be treated with an ICS, either daily or driven by symptoms [33]. The following year, during the coronavirus disease 2019 (COVID-19) pandemic, GINA suggested the same management reported in GINA 2019. Still, it was recommended against spirometry and nebulization during COVID-19 times. It also recommended having a written asthma action plan for asthmatics [34].

GINA has updated its guidelines in 2021 to reflect the latest evidence on asthma management. There are two recommended treatment tracks, with track 1 being the preferred approach. This track uses low-dose ICS-formoterol as a reliever. Compared to SABA reliever, this therapy led to a reduced risk of exacerbation and stable asthma symptoms and lung function. Track 2 is an alternative approach that uses SABA as the reliever if track 1 is not possible or not preferred by the patient and they have had no exacerbations on their current controller therapy [35].

For individuals with mild asthma, a combination of ICS-formoterol can be taken regularly or as needed for symptom relief, while MART using ICS-formoterol is recommended for those with moderate-severe asthma. However, the guidelines emphasize the importance of individualized assessment, adjustment, and review of treatment plans, as asthma treatment is not a one-size-fits-all approach [36].

Impact of the GINA 2019 significant changes on the local guidelines

Based on these fundamental changes in GINA post-2019, only a few local guidelines have adopted them in their post-2019 versions based on the best available evidence-based medicine. The changes in some of the local guidelines in comparison to the GINA modifications are shown in [Table 1](#).

On a global level, four country-level guidelines were published in 2019 onward: the Mexican [7], Japanese [8], Spanish [9], and Canadian [10] guidelines. The Mexican guidelines which were updated in 2021 implemented the preferred track with ICS/formoterol as needed for patients with mild intermittent asthma. They kept SABA and ICS as alternative options for such patients. The Japanese guidelines, updated in 2020, did not recommend a preferred track for ICS/formoterol. In fact, they still recommend using low-dose ICS for their steps 1 and 2, and SABA alone is not recommended in mild intermittent asthmatics. The CTS guidelines, revised in 2021, still adopt the SABA alone as the needed approach in mild intermittent asthma and suggest low-dose ICS in step 2, resembling the old GINA approach. The GEMA revisited their stance in 2022, and they had a hybrid approach between the 2018 and the GINA post-2019 recommendations. On the one hand, they recommend using ICS/formoterol in mild intermittent asthma, but they still suggest using SABA alone as needed in this category. For patients with mild persistent asthma, GEMA recommends using low-dose ICS, and alternatively, ICS/formoterol can be used for patients with low adherence to inhalers.

Similar to the GINA pre-2019 guidelines, SINA 2016 guidelines recommended using SABA as needed for step 1 (mild intermittent asthma). The rest of the steps in their guidelines were almost identical to the GINA 2018 guidelines. In their most recent iteration, SINA updated its guidelines to match the changes in GINA 2019. For controlled patients with ACT \geq 20, SINA recommends using an anti-inflammatory reliever therapy comprising a combination of ICS and formoterol on an as-needed basis for asthma management initiation. An alternative option is to use a combination of SABA and low-dose ICS on an as-needed basis. They have also recommended using maintenance daily low-dose ICS in particular situations, such as for patients with symptoms more than twice a week and risk factors for acute attack (severe attacks in the past 12 months or prior history of admission to an intensive care unit; especially if intubated) or evidence of fixed airway obstruction. They do not recommend using SABA alone as needed for controlled patients. SINA did not label any of these options as preferred, albeit they named ICS/SABA as an alternative. This is quite similar to the changes in GINA 2019 steps 1 and 2, with no preference for one therapy *versus* the other. For partially controlled patients with ACT between 16 and 19, they suggested low-dose ICS and labeled formoterol/ICS combination on an as-needed basis as an alternative option which is a slight deviation of the GINA step 3, which mandates a low-dose ICS/formoterol as controller and reliever in the preferred track or low dose ICS/LABA in the alternative one. In patients with ACT $<$ 16 labeled as uncontrolled in SINA guidelines, it is recommended to start a combination of regular low-dose ICS and LABA as maintenance treatment, like GINA guidelines, albeit at a lower dose of ICS.

Similar to GINA recommendations, SINA has adopted a recommended and alternative approach for asthma treatment adjustment and maintenance. They preferred using ICS/formoterol over SABA together with low-dose ICS on an as-needed basis for patients in step 1. For step 2, they preferred a daily low-maintenance dose ICS with as-needed SABA over a combination of ICS/formoterol on an as-needed basis, a deviation from the GINA guidelines suggestion. For the following steps 3–5, they did not have a preference for ICS/formoterol. They followed the alternative track from GINA, with their reliever option being SABA for non-ICS/formoterol regimen or ICS/formoterol as needed when used as maintenance therapy.

Guidelines for asthma management in Dubai [3] and Abu Dhabi [2] were published in 2018, before the GINA 2019 guidelines were released. As a result, these guidelines did not incorporate the changes introduced by the GINA 2019 guidelines.

However, in 2022, a group of asthma specialists from Kuwait, Oman, the UAE, and Qatar published their expert review and recommendations for the diagnosis and management of asthma in adults [13]. They incorporated the changes introduced by the GINA guidelines post-2019, including the recommendation for initiating treatment of mild intermittent asthma with ICS/formoterol and using ICS/SABA as needed as an alternative. Their overall approach to asthma management closely aligns with the GINA guidelines, with only minor deviations.

Another paper [37] was published by the Middle East and Africa (MEA) asthma experts examining recommendations and challenges for the management of asthma in the region. They listed different challenges in the MEA when dealing with asthma patients' management, including overreliance on SABA and the fact that the local guidelines are old and outdated. The expert panel recommended adapting the new changes in the latest GINA into the local guidelines, including avoiding SABA alone in mild intermittent asthmatics and following the same preferred and alternative tracks.

Challenges in implementing these changes on a local level

Although recent changes to the local guidelines based on the GINA recommendations can potentially improve asthma management, their full impact has yet to be fully realized. Further studies are needed to assess the extent to which these changes reduce annual asthma exacerbations, enhance asthma control, decrease healthcare costs, and potentially improve survival. Nonetheless, implementing these changes expressed in the local guidelines into real-world daily practice can be challenging, even if they have been published.

Physicians' knowledge of asthma guidelines

Yousef et al. [38] conducted a cross-sectional study in Saudi Arabia reviewing the asthma knowledge of general practitioners (GPs). SINA or GINA was only utilized by 33.7% of the study's surveyed physicians. The mean asthma knowledge score was used in this study to test the knowledge of GPs of asthma which had questions about asthma diagnosis, control management, and inhaler technique. This knowledge score was statistically better in those who used guidelines than in those who did not. Abuzakouk and others [39] examined the understanding of GINA guidelines in their local hospital in the UAE. They found that 65.3% of asthmatics were misclassified as severe asthma patients, which was related to the poor understanding of the physicians of the GINA guidelines. Nguyen et al. [40] showed similar results, with only 22% of their surveyed physicians having a correct understanding of the GINA guidelines.

This highlights the importance of continued education at all healthcare professional levels, including GPs, pulmonologists, and other allied healthcare individuals. Awareness of the local and international guidelines with ease of access to them needs to be prioritized by policymakers to ensure that they are well informed about the most recent evidence-based recommendations.

Adherence to guidelines and recommendations

Adherence to guidelines and recommendations is crucial in optimizing asthma management. Unfortunately, it has been shown that compliance with GINA guidelines among healthcare professionals is far from ideal. Baldacci and colleagues [11] examined the adherence to GINA guidelines in an Italian cross-sectional study among GPs. They found poor adherence to GINA guidelines among GPs, with only 28% being compliant with the proper GINA guidelines recommendations. Consequently, it showed that there is overtreatment of mild intermittent and mild persistent asthma among GPs with ICS/LABA maintenance therapy, which does not follow GINA guidelines. This study revealed that adherence to GINA guidelines with respect to drug prescription led to improved asthma control. At the same time, non-adherence could result in either overtreatment or undertreatment, potentially affecting patient outcomes. It is, therefore, crucial to encourage healthcare providers to adhere to the latest guidelines and recommendations consistently, as this can help enhance asthma control and reduce healthcare costs.

As previously discussed in this article, non-adherence to the guidelines leads to asthma exacerbation-related death which can be avoidable with proper compliance with the recommendations made in the local guidelines.

Adopting new changes and poor patient education

Chapman and others [41, 42] conducted two studies to investigate how current clinical practice in various countries around the globe relates to the latest GINA recommendations, APPaRENT1 [41] and APPaRENT2 [42]. In APPaRENT1, the study team recruited patients and GPs from Australia, Canada, China, and the Philippines. They were invited to complete an online survey about their asthma management. Even though the significant changes to GINA were published at least a year before this study was recruited, 66–81% of patients reported using regular maintenance therapy with or without an as-needed reliever. About 14 percent of them were using MART. In fact, 9–29% of patients and 24–45% of physicians were unaware of MART, although this is the preferred track set by GINA. Interestingly, among those who prescribed MART, 80–95% prescribed an additional (non-ICS) as-needed reliever, which is counterintuitive to the point of the MART approach.

In APPaRENT2, patients were recruited from Argentina, France, Italy, Brazil, and Mexico, and in this study, both GPs and pulmonologists were involved in the survey. It showed that most pulmonologists (75%) and GPs (57%) preferred a regular dose of ICS over the MART approach, contrary to the GINA 2019 changes. Similar to the previous study, 85% of patients in the MART track were prescribed SABA as needed. Interestingly, SABA was added in 67% of these patients based on their request.

Fostering a culture of shared decision-making and patient education can help ensure the successful implementation of updated guidelines and ultimately improve asthma management and patient outcomes in the long term.

Conclusions

The substantial revisions introduced in the GINA guidelines post-2019 have significantly impacted asthma management globally. Based on the latest evidence-based medicine, these changes aim to improve patient outcomes and reduce asthma exacerbations. However, adopting these recommendations into local guidelines has been uneven, with some countries embracing the changes while others continue to follow older approaches.

The challenges in implementing these paradigm-shifting recommendations into local guidelines are multifaceted. On the other hand, more studies are needed to examine the long-term impact of the changes and their expansion into the local guidelines.

Abbreviations

ACT: Asthma Control Test

GCC: Gulf Cooperation Council

GEMA: Spanish Asthma Management Guidelines

GINA: Global Initiative for Asthma

GPs: general practitioners

ICS: inhaled corticosteroids

LABAs: long-acting β 2-agonists

MART: maintenance-and-reliever therapy

SABA: short-acting β 2-agonists

SINA: Saudi Initiative for Asthma

UAE: United Arab Emirates

Declarations

Author contributions

RA and HALJ: Conceptualization, Investigation, Writing—original draft, Writing—review & editing. Both authors read and approved the submitted version.

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The authors declare that they have no conflicts of interest.

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