

Challenges of treatment management in patients with asthma





- World Asthma Day (WAD) (May 3, 2022) is organized by the Global Initiative for Asthma, (GINA) (www.ginasthma.org), a World Health Organization collaborative organization founded in 1993. WAD is held each May to raise awareness of Asthma worldwide.
- Although asthma **cannot be cured**, it is possible to manage asthma to reduce and prevent asthma attacks, also called episodes or **exacerbations**.



- GINA has chosen '**Closing Gaps in Asthma Care**' as the theme for the **2022** World Asthma Day.
- There are a number of gaps in asthma care which require intervention in order to reduce preventable suffering as well as the costs incurred by treating uncontrolled asthma.

Asthma



- Asthma is a
- chronic inflammatory condition characterized by
- airway hyper-responsiveness to a variety of stimuli largely of allergic origin with
- reversible airflow limitation.
- The major clinical features of asthma are
 - wheezing,
 - shortness of breath,
 - and cough.
- It is a major cause of impaired quality of life with impact on work and recreational as well as physical activities and emotions.
- The goal of treatment is to achieve overall clinical control, which entails the achievement of symptom-free control and to minimize future risks.

Asthma



- **Current** (day-to-day) **control** of asthma include:
- **achievement of symptom relief,**
- reduction in the use of on **demand inhalers,**
- **improvement in activity,**
- **improvement in lung function.**
- Future risk minimization is achieved by ensuring the **absence of asthma exacerbations,**
- the prevention of **accelerated decline in lung function over time,**
- and **no side-effects from medications.**

Asthma



- World-wide, it is estimated that 300 million people are affected with bronchial asthma.
- The prevalence of asthma is variable.
- It is a disease that has been observed to be more prevalent in developed countries with higher rates seen in Australia, UK, and New Zealand.
- Sex ratio varies according to age: In childhood, asthma affects more boys than girls for unknown reasons, but by the third decade, the prevalence becomes equal and subsequently, more women than men are affected.
- Asthma prevalence is increasing despite recent advances being made in its management.
- Most patients with asthma can be controlled with currently available therapies.
- However, an estimated 3–5%, remain either poorly controlled or require high doses of corticosteroids .
- These patients manifest a significant morbidity and decreased quality of life from the disease and as a consequence of oral corticosteroids.
- Patients with severe asthma may also be at a higher risk of death

Asthma



- Enormous advances have been made in the understanding and **management of asthma** in the past 20 years.
- **These include;**
- understanding **the inflammatory** nature of the disease,
- **use of steroids,**
- add-on of **long acting bronchodilators** to steroids,
- use of **devices to deliver the medications** more appropriately/conveniently, and
- appreciation of the value of **self-management** education.

Asthma



- In managing asthma, health-care providers and the patients are often faced with lots of **challenges** and these challenges of asthma management include:
- challenges in **diagnoses**,
- challenges in the **treatment**,
- **follow-up** challenges, and
- **other general** challenges.

Challenges in diagnoses



- The major clinical challenge facing asthma diagnoses is that there is **no single satisfactory diagnostic test** for all asthmatic patients. As a result, physicians often use **different criteria** in making a bronchial asthma diagnosis.
- Other problems encountered in asthma management in this setting include **lack of standard diagnostic equipment** such as **peak flow meters**, and **spirometers**.
- **Skin allergy tests** test/allergen **specific IgE estimation**, equipment for **exhaled nitric oxide**, **histamine/methacholine challenge** tests are also lacking too. Even when the equipment are available,
- **physicians often are not conversant** with their use owing to lack of proper training on their use.
- The overall effect of these **diagnostic challenges** will lead to **under diagnoses**, **over diagnoses**, **misdiagnosis**.
- This will lead to increased **morbidity** and **mortality** due to asthma.

Challenges with follow-up



- There is often a **communication gap** between the **health-care providers** and the **patients**, Lack of patients **self-monitoring equipment**, and lack of **educational materials**.
- Follow-up challenges will lead to
- **lost** to follow-up,
- **poor** asthma control,
- **increased** frequency of asthma exacerbations and subsequent
- **frequent** emergency room visits.

General challenges



- There is often lack of will by the **government/hospital administrative** staff in the provision of basic infrastructure such as
 - **asthma clinics,**
 - **asthma clinic registers,**
 - **appointment and recall systems in the clinics,** and
 - **attendance of asthma care training courses** by doctors and nurses.
- Furthermore, there are very few **trained public health nurses**-who usually play a **major role** in ensuring quality care in asthma programs by periodically identifying staff needs and developing strategies to address asthma management challenges.

General challenges



- There is a poor medication purchase regulations as people are able to buy medications to wrongly treat asthma or even to trigger attacks.
- Purchase of over the counter medications such as NSAIDs and beta blockers are known to trigger attacks of asthma.

General challenges



- Other general challenges include;
- **failure to understand** the reason for increasing prevalence of asthma despite all efforts at the management,
- **failure to develop** a **meaningful primary preventive strategy** and high-cost of transport to a health facility. In addition, we need proper enclosure of industrial processes and adequate ventilation with a view to curtailing the influence of general atmospheric pollution as a trigger for asthmatic attacks.
- **Conflicting reports** from physicians and patients about levels of symptom and side-effects, awareness, and adherence to physician-recommended treatment regimens, point to poor communication as a **significant barrier** to **better asthma control**. Often these lead to differences between the **goals of professionals** and the **goals of the patient**.

General challenges



- Assumptions that physicians make about **how much their patients understand asthma symptoms** and **side-effects** frequently lead to **patient confusion** about their tolerability and success with treatment; consequently, patients often compromise their respiratory health by making their **own therapeutic decisions** resulting in **poor adherence to treatments**. Results from the Asthma Insights and Reality study have shown that many patients often settle for a quality of life considerably less than that achievable if recommended management practices and asthma treatments are used.
- **Improving patients' and physicians' expectations** of what can be achieved with asthma therapy may lead to improved overall asthma control.

General challenges



- To achieve goal, appropriate pharmacological treatment should be accompanied by optimum use of **non-pharmacological strategies** and **treatment of modifiable risk factors** regardless of the severity of the disease.
- These include, :
 - •**Education** of patients for self-management and providing a written asthma action plan
 - •**Teaching** correct inhaler technique
 - •**Environmental** control for airway irritants such as tobacco smoke
 - •**Environmental** control for specific allergens such as house dust mites, molds and animals
 - •**Weight loss** for overweight and obese
 - •**Treatment of co-morbidities** such as allergic rhinoconjunctivitis, psychosocial problems and reflux disease.

Challenges in treatment



- Treatment challenges include :
- a high-cost and unavailability of essential asthma medications.
- The unaffordability of inhaled corticosteroids as a potential barrier to treatment of asthma in developing countries.
- The Lack of essential devices like nebulisers, spacer devices that are used for effective medication administration constitute a strong challenge affecting correct management of asthma.
- Even when the devices are provided, poor technique of use of medication devices especially the inhalational drugs contribute to poor delivery of medications to the required site of action, poor asthma control, and the resultant increase in the health resource utilization.

Challenges in treatment



- The pressurized metered-dose inhaler (pMDI) is the most commonly used and the cheapest device, which may also be used in conjunction with a spacer device. The drug is dissolved or suspended in the propellant under pressure. When activated, a valve system releases a metered volume of drug and propellant.
- Other devices include breath-activated devices which incorporate a mechanism activated during inhalation that triggers the drugs.
- Dry powder inhalers, such as Turbohaler, Diskhaler, Diskus, Accuhaler, and Rotahaler, are activated by inspiration by the patient. The powdered drug is dispersed into particles by the inspiration.
- These devices require
 - careful,
 - repeated, and
 - sustained education of patients by the health-care providers to enable the patients benefit maximally from their use.
- These educations are not generally given to the patients leading to poor use.

Challenges in treatment



- Lack of **national/hospital protocol** or **guidelines** also contribute to the challenges.
- Furthermore, even when available these management protocols are **poorly implemented**.
- Another challenge of asthma treatment is that the **very newer asthma medications** are of limited benefit, for a small percentage of patients, and **often more expensive**, e.g., leukotrienes antagonist, omalizumab (monoclonal IgE antibody), thermoplasty etc., thereby making it **impossible for patients** with poor resources to benefit from them.

Asthma in smokers: challenges in treatment

- Smokers have more severe symptoms and are more likely to be admitted to hospital due to poorly controlled asthma compared with nonsmokers with asthma.
- Possible causes of reduced sensitivity to inhaled corticosteroids in smokers with asthma are
 - noneosinophilic airway inflammation,
 - impaired glucocorticoid receptor function, and/or
 - reduced histone deacetylase activity.
- Smoking cessation improves asthma control, but quit rates are low. The optimal drug therapy for smokers with asthma is not established due, in part, to the small number of clinical trials performed in these patients.
- Preliminary data, however, suggest that leukotriene-receptor antagonists may have a beneficial effect in smokers with mild asthma.



ACOS Management challenges

- General management
- Because patients with ACOS are generally excluded from randomized controlled trials for either asthma or COPD, their response to therapy is largely unknown. In principle,
- ACOS has similar goals of treatment as asthma and COPD:
 - control and relief of symptoms,
 - a reduction in the frequency of exacerbations,
 - a reduction in the rate of decline in lung function and limiting adverse effects from therapeutic treatments.
- Treatment may comprise the following components:
 - patient education,
 - smoking cessation,
 - allergen avoidance,
 - flu vaccination,
 - pulmonary rehabilitation and
 - management of any comorbidity.



ACOS Management challenges



- Individualized management
- To optimize the treatment outcome, each patient may require further investigation to detect features that would need specific interventions.
- As an example of individualized management, ICS may be considered in patients with ACOS with significant sputum eosinophilia (eosinophil count $\geq 3\%$). In a crossover trial, sputum eosinophilia predicts short-term clinical benefit from high-dose ICS treatment in COPD patients with eosinophilic bronchitis. Another study showed that the eosinophil count and the eosinophil cationic protein concentration in bronchoalveolar lavage fluid were significantly higher in responders to prednisone than in non-responders among patients with COPD.
- Another example of individualized management is that current smokers with ACOS may require a higher dose of ICS than ex-smokers with ACOS. A randomized, double blind, parallel group study showed that smokers with mild asthma had an impaired response to ICS at low doses. This insensitivity could be overcome by ICS given at a higher dose.
- Elderly patients with ACOS may need special attention and careful management. Although spirometry can be adequately performed in more than 90% of older patients with obstructive airway disease, when technicians are appropriately trained and rigorous quality control is used, it is still hampered by poor cooperation in this population. With the lack of lung function data, diagnosis or severity evaluation is often delayed in the elderly. Thus, the initiation of ICS and/ or LABA and follow-up monitoring to evaluate symptomatic improvement might be necessary. In addition, repetitive education and review of side effects should be performed because elderly patients usually have poor adherence to prescribed medications and more side effects due to interactions with medications prescribed for other comorbidities.

Challenges in Current Pediatric Asthma Treatment

- asthma in children has a **highly variable activity level** that is driven by **airway inflammation**, which is not addressed in step 1 treatment
- there is lack of understanding about the information related to the safety of SABA and LABA; this leads to lower use of LABA in children
- **parents' and caregivers' safety concerns regarding regular use of an ICS**
- there is poor perception of disease control by patients and/or parents and caregivers, which is fueled by underuse of validated control instruments and measurement of pulmonary function and airway inflammation.



Nasal polyps in patients with asthma: prevalence, impact, and management challenges

- The European position paper on rhinosinusitis and nasal polyps provides a specific treatment guideline for patients with CRSwNP with and without asthma.¹ On the basis of available evidence, medical therapy for CRSwNP should begin with daily application of a topical ICS in conjunction with high-volume saline irrigation, and subsequent therapies are based on the patient's polyp status, severity of symptoms, and/or QoL impairment. Regarding the question about how sinus surgery and medical CRSwNP treatment may modify the course of bronchial asthma, different authors^{38,39} have concluded that the weight of evidence suggests a beneficial effect. A recent systematic review⁴⁰ analyzed the effect of upper airway intervention in the subpopulation of patients with coexisting CRSwNP and asthma and did not find marked differences between outcomes after endoscopic sinus surgery (ESS) or medical treatment with montelukast, omalizumab, or erythromycin.



Challenges in the Management of Asthma in the Elderly

- Many challenges in management of asthma in the elderly are apparent.
- Not only asthma management issues, but also **comorbid conditions** impose significant burdens on the elderly . Despite the significance of comorbidities, very little clinical evidence is available on the efficacy of controlling comorbidities in the elderly; previous trials have rarely focused on elderly patients.
- Several other practical issues must be considered, including the role of a **caregiver**, **health literacy**, and **cognitive functioning**. Thus, management of asthma in the elderly should be multifaceted, and the recent growth in reports on elderly health is encouraging. We anticipate that an evidence-based management strategy for asthma and multiple comorbidities in the elderly will be forthcoming.



Asthma symptoms in obese adults: The challenge of achieving asthma control

- Obese patients with asthma have, an **altered response to asthma therapy**, including controller medication.
- In general, obese patients with asthma symptoms seem to be **less responsive to asthma medication** than non-obese patients with asthma.
- On the other hand, the '**obesity-related asthma**' phenotype is characterized by
 - **altered lung volumes,**
 - **increased work of breathing,**
 - **no association with atopic status,**
 - **increased systemic inflammation** and
 - **less eosinophil airway inflammation,** and
 - **a much weaker association between clinical expression of asthma and level of airway responsiveness.**
- Furthermore, weight loss in obese patients with asthma symptoms results in an improvement in respiratory symptoms, medication needs, lung function, airway responsiveness and markers of airway inflammation. Asthma-like symptoms in the obese adult may, therefore, represent a subtype of asthma or even a different disease than asthma, which makes it of outmost importance always to diagnose asthma in an obese patient by objective measures of airway function. In line with this, assessment of disease control and effect of pharmacological therapy should be examined carefully.
- In conclusion, asthma symptoms in obese adults are likely to represent a **distinct disease entity** or even another disease than asthma based on response to pharmacological therapy and effect of weight reduction. Instead of attempts to achieve best possible disease control by pharmacological asthma therapy alone, more focus should be on tailoring the management strategy to the individual patient, as weight reduction is likely to be at least as important as pharmacological therapy in obese adults with asthma symptoms.

Challenges in the Management of Asthma and Adherence to therapy

- Adherence to therapy and compliance with physician recommendations are other important components of successful asthma management.
- Many factors contribute to level of adherence to controller therapy for asthma, including
 - beliefs about the benefits of treatment,
 - concerns about potential adverse effects of treatment,
 - perceived asthma severity,
 - and duration of asthma.
- In addition, cultural factors may influence beliefs about medications.
- Reported factors influencing adherence among adolescents also include
 - cognitive difficulties,
 - lack of social support,
 - lack of self-efficacy,
 - denial or distrust, and
 - peer and family issues.



The Challenge of asthma in adolescence

- The adolescents with asthma are a distinct group of patients with different problems and needs compared to **children and adults**. Specific issues of asthma in adolescence are the variability of the clinical spectrum, the presence of particular risk factors for the persistence of symptoms, underdiagnosis and undertreatment of the disease.
- Refusal of the **sick role**,
- **denial of symptoms**,
- **carelessness about dangerous inhalation exposure**,
- erratic self-medication,
- overexertion without taking precautions against exercise-induced asthma, and
- a poor relationship between patients, their families, and often doctors are the main obstacles to successful management of asthma in this critical age. There are also major problems of **compliance for these patients**.

Challenges faced in managing adult asthma: A perspective from Asian countries

- **CHALLENGES IN OPTIMIZING ASTHMA CARE IN ASIAN COUNTRIES**
- In Asia, barriers to asthma care range from stigma of asthma diagnosis to preference of oral over inhaled therapy, prevailing misconceptions regarding steroid inhalers, belief in ultimate cure of asthma or alternate therapies, suboptimal treatment goals, inability to identify warning signs and non-adherence to treatment. These factors contribute to suboptimal asthma care, resulting in progressive airflow obstruction.¹⁰



Challenges faced in managing adult asthma: A perspective from Asian countries

- Stigma of asthma diagnosis
- The taboo about asthma may hamper social life and professional performance, and leads to significant morbidity and reduction in quality of life.
- Stigmatization of the diagnosis of asthma definitely impairs asthma control. In some parts of Asia, asthma stigmatization is greater in populations with a lower literacy rate.
- The stigma of an asthma diagnosis is higher in the paediatric age group.
- There is however a decline in the perception of this stigma, as noted in a solitary study from India where the rates of discontinuation of asthma medication due to stigmatization have come down from 58% to 6% over a decade. In the same study, it was observed that the acceptance of a diagnosis of asthma has increased in recent times (42%) as compared to a decade ago (30%).
- Nevertheless, stigma is still a major concern in rural populations with lower socio-economic status, which may lead to a preference of oral medication over inhalation therapy.

Challenges faced in managing adult asthma: A perspective from Asian countries

- Preference of oral/alternate therapy over inhaled therapy in Asia
- Psychological effects of asthma such as depression and embarrassment contribute to the overall burden. Results from the Asia Pacific Asthma Insights in Management (AP-AIM) study revealed that almost 42% of patients reported a 'feeling of embarrassment' in using their inhalers. Similar findings have been observed in the REALISE study where almost half of the recruited patients felt that using or even carrying an inhaler was considered as an impediment in their social lives.
- Even in the Indian context, use of inhalers has been thought to be a major barrier for marriage prospects, especially for females.
- Similarly, preference of oral therapies over inhaled medications has been a significant obstacle in achieving ultimate control of asthma. Even in a modern healthcare system like Korea, prescription of oral corticosteroids (OCS) without inhaled corticosteroids (ICS) was found in about 30% of all asthmatic patients in the analysis of the Korean Health Insurance Review and Assessment Service (HIRA).
- Among Asian asthmatic patients, Taiwanese parents and patients reported the highest rate of steroid phobia. Concerning statistics from the Indian arm of the AP-AIM study revealed that almost 70% of asthmatic patients used oral medications as controllers, whereas only 36% of patients used inhalers.¹⁵
- In a study of 98 Chinese asthma patients from Hong Kong, almost 80% admitted using Chinese herbal remedies.
- As recently as 2013, up to 62% of Indian asthmatic patients had tried alternative medicine techniques to 'cure' their asthma.
- These therapies include 'saintly therapy', herbal medicine, fish therapy and acupuncture. Such therapies not only add to the economic burden of asthma, but also lead to further worsening of asthma due to the delay in diagnosis, risk of potential drug interactions and postponement of appropriate treatment.

Challenges faced in managing adult asthma: A perspective from Asian countries

- Suboptimal treatment methods
- In a large questionnaire-based survey on asthma from eight Asian countries, it was found that patients' expectations regarding asthma control were low and patients' perception of controlled asthma was not consistent with the Global Initiative for Asthma (GINA) definitions of asthma control. This disassociation was seen as a result of **patients' perception** that asthma control is generally focused on **management of exacerbations** and not on **symptom control** and **prevention of such exacerbations**.
- Across the low-income regions of Asia, suboptimal clinical practices such as preference of reliever therapy over maintenance therapy are rampant. A study evaluating asthma prescriptions from the Indian pulmonology fraternity revealed that the **combination of ICS + long-acting beta-agonist (ICS + LABA)** was prescribed to asthmatic patients in only **41%** of cases.
- A study performed in South Korea revealed that prescriptions of **ICS** were lower as compared to other modalities of asthma management.
- Fortunately, countries such as **Japan** have reported prescription rate of ICS or ICS + LABA reaching **99%** in adult **asthmatic** patients receiving treatment from allergologists and respirologists in Japan.

Challenges faced in managing adult asthma: A perspective from Asian countries

- Oral steroid use and asthma phenotype in Asia
- Chronic OCS maintenance in severe asthma is associated with subsequent complications and increased mortality.
- In Asian countries, given the higher preference of oral medications to inhalers, a large number of severe asthma patients take OCS as a maintenance treatment.
- The Indian arm of the AP-AIM study revealed that 89% of asthmatic patients had used OCS in the previous year. Average annual use of oral steroids has been estimated at 10.5 treatment episodes per patient. In the Korean Severe Asthma Registry, chronic OCS use was found to be 18% among those in GINA step 4 or 5 treatment levels as compared to Taiwanese severe asthmatic patients, where the rate of OCS prescriptions in the previous year reached almost 50%. While robust data regarding the ongoing use of OCS is lacking, it can be safely concluded that the burden of OCS use in our population is high. Such conditions warrant the need for phenotype-guided therapy and prescription of steroid-sparing medications in asthma.
- In non-eosinophilic asthma, there has been a recent surge in evidence regarding the use of macrolides. The efficacy is based on the anti-inflammatory effect of macrolides rather than the antibiotic effect. In the Asian context, a meta-analysis from China and a trial from Taiwan demonstrated the efficacy of macrolides in terms of reduction of exacerbations but failed to improve any lung function parameters.

Challenges in treatment



- Thus, treatment challenges highlighted could lead to
- under-treatment,
- unnecessary treatments and
- poor control.
- It will also lead to increased
- adverse drug reactions,
- increased morbidity and
- mortality, and
- poor quality of life.

