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Initiatives and Strategies for Tackling Asthma in Low and Medium-Income (LMIC) Countries

Every month, the West African Journal of Medicine provides a platform to focus on specific international health days that occur during that month. This initiative aims to raise awareness about various diseases and support global efforts to reduce their burden on society. One such event is the commemoration of World Asthma Day, which takes place on the first Tuesday of May each year. This global observance aims to promote awareness of asthma on a worldwide scale.[1] The theme for this year *Asthma Care for All,* is particularly apt as it addresses the disproportionate morbidity and mortality from asthma in low and medium-income (LMIC) countries.

Asthma is one of the major non-communicable diseases affecting adults globally and the most common chronic disease in children.[2] Although the overall burden of asthma has decreased globally with a 24% and 51.3% decrease in death since 1990, there is still a large inter-country variability.[3] Moreover, the prevalence, mortality, and disability-adjusted life years (DALYs) remain high.[3,4] Despite concerted efforts to minimize its impact and reduce the burden,[5–7] asthma continues to affect an estimated 339 million people worldwide,[8] and in 2019 alone, it caused the loss of 21.6 million DALYs and 461,069 deaths.[2,9] Reports from the Global Asthma Network Phase I study revealed that 1 in 10 children and adults have asthma symptoms, and 1 in 20 school-aged children have severe asthma symptoms.[10,11]

Nearly 90% of the burden of asthma is borne by people living in LMICs, and many African countries are affected. Asthma has been attributed to be a cause and effect of poverty in LMICs, where underdiagnosis, undertreatment, unaffordability, and prevailing myths still undermine successful asthma management.[10–12] The widening care gap between developed countries and LMICs is alarming, despite global cumulative successes. Several factors contribute to this gap, including the increase in tobacco use and the effects of urbanization and westernization on diet and lifestyle. Additionally, the burden of health financing falls on individuals due to unsubsidized health costs. Furthermore, the lack of availability and affordability of new and target-specific asthma medications further compounds the situation. [11,13] It is crucial to address these factors individually to bridge the care gap and improve asthma management in LMICs.[13]

This year, the Global Initiative for Asthma (GINA) advocates that resource-rich countries should execute all-inclusive asthma management programs with far-reaching outcomes and global impact to increase accessibility and availability of high-quality asthma care by all, irrespective of location. International respiratory communities are encouraged to collaborate with everyone involved in asthma care, including patients, to promote the development and implementation of effective asthma management programs in all resource countries.[1] A multifaceted approach involving asthma education, profile-raising, and fund-raising, geared towards improving asthma care with recommendations for environmental sustainability, is being promoted.[1]

Asthma is a complex heterogeneous disease that requires ongoing management to reduce the risk of exacerbations and hospitalizations, prevent fixed airflow limitation, reduce symptom burden, and improve quality of life.[14] In the management of asthma, especially in difficult-to-treat cases, poor control is usually linked to poor education about the disease, poor compliance with inhaled corticosteroids, incorrect inhaler technique, inappropriate use of rescue medications, and poor environmental control resulting in increased exposure to triggers. Furthermore, co-morbid conditions such as gastroesophageal reflux disease (GERD) and obesity can complicate asthma management, exacerbating the difficulty in achieving control. Effective treatment depends on a partnership between the patient and the healthcare provider, and patients should be encouraged to follow a self-management plan to ensure successful management.[15]

The pathophysiology of asthma is driven by airway inflammation, airway hyperresponsiveness, and airway obstruction, which produce the symptoms experienced by patients.[4,16] Inhaled corticosteroid (ICS) help to reduce airway inflammation and control asthma symptoms, while bronchodilators dilate the airways and provide relief of symptoms.[14,15] Treatment strategy in asthma is based on a control-driven cycle that requires regular assessment of patients, treatment adjustment, and response review.

Over the years, various national and international guidelines have been formulated for asthma management.[15,17] The Global Initiative for Asthma (GINA) guideline is prominent among these. Initially, the treatment of asthma focused on using short-acting beta-agonists as the first line of management in patients with mild asthma,[15] aiming to control symptoms rather than the background inflammation. However, a significant paradigm change occurred following the GINA Guideline review of 2019. This change came with the adoption of anti-inflammatory reliever therapy (Maintenance and Reliever Therapy – MART) at all stages of severity. The GINA Stepwise treatment guideline now has two tracks of asthma management: Track 1, with low-dose ICS-formoterol (a MART) as the reliever, is the preferred approach as it has been found to reduce the risk of exacerbations compared to using a short-acting bronchodilator reliever alone. Track 2 is an alternative approach in which Step 1 has been modified to recommend taking ICS whenever a short-acting bronchodilator is taken. Step 2 of this track remains regular, low-dose ICS with as-needed short-acting bronchodilators.[15]

While most patients achieve control using as-needed or daily combined long-acting bronchodilators and inhaled corticosteroids, there is still a concern for the 10% of adults and 2.5% of children who have severe asthma and are not controlled by these therapies.[18] These patients with severe asthma constitute a considerable burden of asthma morbidity and mortality and are the focus of biologic therapies. Severe asthma results in reduced quality of life, increased risk for airflow limitation, increased risk of exacerbations, psychosocial problems, frequent hospitalizations, and even death.[18–21]

Recent findings have identified different endotypes of asthma characterized by specific intracellular pathways. Asthma endotypes are divided into TH2-high (eosinophilic) and TH2-low (non-eosinophilic).[22] The knowledge about these pathways has led to the development of biologic therapies targeted to treat severe asthma.[23] Currently, six biologics are approved for the treatment of severe asthma. These agents are effective add-on therapies for uncontrolled severe eosinophilic asthma.

Biologic therapies specifically target the inflammatory pathways involved in the development of asthma, particularly in patients with Type 2 (T2) inflammation driven by specific endotypes.[18] These medications have been found to reduce asthma exacerbations, improve lung function, and decrease the need for oral corticosteroids. In addition, it has been reported that these therapies improve the quality of life in patients with asthma. The earliest biologic used in managing severe asthma was Omalizumab, an anti-immunoglobulin E therapy that targets downstream IgE. One of the earliest studies supporting its use was the landmark COCHRANE Review, a meta-analysis of twenty-five studies comparing Omalizumab with placebo or conventional therapy conducted over 25 years ago.[24] The review found that Omalizumab reduced asthma exacerbations and hospitalizations, with modest improvements in quality of life and lung function observed in adults and children.[24] However, it is essential to note that Omalizumab primarily focuses on severe allergic asthma and targets IgE, limiting its applicability to other asthma subtypes.

In the past decade, there have been significant advancements in developing newer therapies targeting specific cytokines involved in asthma pathogenesis. For instance, Mepolizumab (Anti-IL5) has shown promising effects in reducing annualized asthma exacerbation rates (AER) and improving forced expiratory volume in 1 second, as demonstrated in the MENSA and SIRIUS studies.[25,26] Similarly, Reslizumab (Anti-IL5), investigated in the Reslizumab BREATH Trial, has exhibited positive outcomes in reducing exacerbations and improving asthma control.[27] Another notable therapy is Benralizumab (Anti-IL5Rα), which has demonstrated efficacy in reducing exacerbation rates, improving lung function, and enhancing asthma control, as observed in the SIROCCO Study.[28] Dupilumab (Anti-IL4Rα), evaluated in the LIBERTY ASTHMA QUEST Trial, has also shown beneficial effects in reducing exacerbations, sparing oral corticosteroid use, and improving Asthma Control Questionnaire scores.[29]

However, recent research efforts have shifted towards targeting upstream epithelial alarmins involved in the immunologic heterogeneity of asthma.[19] These alarmins include IL-33, thymic stromal lymphopoietin (TSLP), and IL-25. As a result of this focus, a novel therapy called Tezepelumab (Anti-TSLP) has been developed. Tezepelumab works by blocking thymic stromal lymphopoietin and has demonstrated positive outcomes in reducing exacerba-tions, improving lung function, asthma control, and health-related quality of life (QoL) in the phase III NAVIGATOR trial.[30] These advancements in targeting specific cytokines and upstream alarmins offer promising avenues for addressing the immunological complexities of asthma and improving patient outcomes. However, further research and clinical trials are necessary to explore the full potential of these therapies and their suitability for different asthma subtypes.

Biologics are not without limitations, including the incomplete success of these therapies due to the overlap of different pathways in the pathogenesis of asthma and the high costs associated with their use.[18,19] Further research is needed to compare various biologics in head-to-head trials and explore their effectiveness in different patient populations. Access to these novel therapies remains challenging in low- and middle-income countries due to their high costs. Governments of these nations should strive to implement policies that promote healthcare and improve access to regular medications and novel therapies for asthma management.

As we await the availability of biologics for asthma therapies in low- and middle-income countries (LMICs), healthcare providers must continue to prioritize the optimal utilization of current management options and adapt existing guidelines to significantly enhance asthma care. Particular attention should be given to patients with severe asthma, given their lower survival probability and considerable healthcare resource consumption compared to the general population and individuals with controlled asthma.

In conclusion, the comprehensive management of asthma necessitates a multifaceted approach encompassing awareness-raising, improved accessibility to high-quality care, and the implementation of effective treatments. By addressing the challenges faced in LMICs and fostering collaboration among international respiratory communities, we can strive towards achieving *Asthma Care for All* and enhancing the overall well-being of individuals living with asthma worldwide.

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