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Authors' Affiliation:

¹Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Lahore University of Biological & Applied Sciences, Lahore, Pakistan
²Research Student, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Lahore University of Biological & Applied Sciences, Lahore, Pakistan

*Corresponding Author

Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Lahore University of Biological & Applied Sciences, Lahore, Pakistan
Email: drmmziqbal@gmail.com

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A systematic review of prescription patterns and cost of treatment in Asthma management in Asian countries

Sara Shahid¹, Sumbal Rafique², Afshan Abdul Shakoor², Muhammad Sheraz², Ramsha Aamir², Maryam Safder Butt², Aqsa Malik², Eman Javed², Samar Zia², Aliza Amjad², Sakeena Amir², Hassan Fayyaz², Ayesha Zulfiqar², Muhammad Zahid Iqbal^{1*}

ABSTRACT

Background: Asthma, a chronic disease of airways is associated with recurring episodes of dyspnea and wheezing that vary in intensity and frequency among individuals. Effective management of Asthma is crucial to manage symptoms and decrease the economic burden associated. **Objective:** The present review is aimed to find out prescription pattern trends for asthma treatment and to measure the cost for treating asthma in Asian countries. **Methodology:** Following PRISMA flow statement guidelines, the present systematic literature-review that was conducted by utilizing keywords that were related to Asthma prescription patterns and economic burden in Asia, focusing on original research published from 2002-2023. Databases like Google Scholar, PubMed, Scopus were employed to extract data. The ZEE tool was utilized to minimize the risk of bias among extracted cross-sectional studies. Inclusion criteria encompassed studies involving asthmatic patients of all ages from Asian countries, focusing on prescription patterns and asthma treatment costs. **Results:** Out of 33 extracted studies, 30 met the inclusion criteria. Prescription trends across Asia vary, with some regions prefer short-acting beta-agonists and anticholinergics for acute attacks. While, others emphasize inhaled-corticosteroids along with the long-acting beta-agonists. Notably, economic burden of disease management remains significant, particularly in Japan, for severe asthma patients. **Conclusion:** The systematic literature review comprehensively analyzes asthma prescription patterns and the economic impact of its management in Asia. Despite advancements in treatment, there remains a need to harmonize practices with global guidelines for improving clinical results and decreasing the economic burden associated with Asthma.

Keywords: Asthma, Asia, ZEE tool, Beta agonist, Corticosteroids, Cost of treatment, Prescription Pattern.

1. INTRODUCTION

The Global Initiative for Asthma (GINA) defines Asthma as follows: "A heterogeneous disease, that is usually characterized by the chronic airway inflammation", which contributes to mortality as well as morbidity worldwide. Variable expiratory airflow restriction and a history of respiratory symptoms like chest tightness, wheezing, shortness of breath and cough that varies over time are the characteristics of asthma (Shahid et al., 2022). The majority of the time, asthma symptoms appear in early infancy as the result, Asthma's fundamental processes remain poorly understood (Iqbal, 2020). Roughly 50% of individuals suffering from asthma have underlying allergic mechanisms, whereas the remaining 50% have non-allergic mechanisms; the latter group is more prevalent in low- and middle-income countries as compared to developed high-income countries (Mubarak et al., 2019).

Physicians identify a variety of symptoms as suggestive of asthma, such as wheezing, chest tightness, dyspnea, and coughing with or without phlegm. Wheezing is the most significant symptom among them for diagnosing asthma in epidemiological studies (Ali et al., 2021). The incidence and severity of asthma are rising even though there are efficient therapies available, due to the chronic nature of asthma, daily treatment is often necessary for the best possible management in many cases. Asthma is estimated to affect 300 million people globally. 10% of youngsters in 2011—nearly 25.9 million Americans—had asthma. A rise in atopic sensitization and other allergy illnesses including rhinitis and eczema has been linked to the rising prevalence of asthma.

As the percentage of people living in cities is expected to rise from 45% to 59% by 2025, there will probably be a noticeable rise in the global asthma epidemic. By 2025, it's predicted that there may be 100 million more asthmatics worldwide. Numerous poor nations in South Asia are home to a large population of asthmatics who lack access to basic asthma drugs and medical care. According to recent general population statistics, the total incidence rate of asthma in children under the age of five was 23/1,000 per year; however, in teens aged 12–17, the incidence rate dropped to 4.4/1,000 per year. The incidence of adult female asthma was 1.8 times higher than that of adult male asthma (4.9/1000 vs. 2.8/1000, respectively). According to a recent assessment on chronic respiratory disorders, 84% of disability-adjusted life years (DALY) and 96% of fatalities attributable to asthma occur globally in low- and middle-income countries.

Many Asian cultures, especially those in low- and middle-income countries, also frequently employ herbal and alternative medicines, which might complicate asthma diagnosis and cause patients to stop taking maintenance medication (Chokhani et al., 2021). Recent data from the USA demonstrated unequivocally that, when compared to medical expenses of individuals without asthma, those with indicators of uncontrolled illness had considerably greater medical costs owing to asthma. A therapeutic response that is not at its best is the result of inadequate adherence to treatment standards (Chokhani et al., 2021). For quick symptom alleviation, the majority of patients use short-acting beta agonists and hence overuse of Short acting beta-agonists (SABA) raises the risk of hospitalization, mortality. Different nations have different prescribing practices for asthma. Patient education about medication adherence and self-management has enhanced treatment efficiency in several countries (Shahid et al., 2022).

A report on all asthma risk factors is required in order to accurately quantify the burden of asthma in various nations. The socioeconomic load decreased people's quality of life, moreover the asthma prevalence was higher in nations with lower sociodemographic indices. Moreover, a high body mass index is considered to be the primary risk factor for asthma. Asthma has distinct features in Asian countries compared to Western ones, presenting that the population of Japan, which is located closest to Korea in Asia, has a higher incidence of asthma but a lower prevalence of severe asthma. Therefore, the National Asthma Education and Prevention Program (NAEPP) and Global Initiative for Asthma (GINA) recommendations diverge significantly from the Japanese Pediatric Guideline (JPGL) approach.

In Korea, children have a higher prevalence of asthma than adults do. This is a serious issue as it raises pediatric hospital admissions and death. The prescription pattern, financial strain, and children's low adherence and compliance responsible and recommendations for treatment by examining prescription patterns in the national health insurance database, it is possible to predict compliance and prevent asthma in children. The current systematic-review is designed to estimate the cost of treating asthma and determine prescription pattern trends. This review specifically focuses on Asian people with established asthma. The study's observations will aid in comprehending the most often prescribed medications, the overuse of specific medications, the use of alternative asthma medications in various nations, the expense of treatment for various age groups in various Asian regions.

2. METHODOLOGY

Study Design

The conducted systematic review protocols were according to recommendations of the PRISMA flow guidelines. The key words being used to extract related data for this review was “Prescription pattern of asthma in Asia”, “Economic burden of Asthma- Asia”, “Asthma management in Asia”, “Cost of Asthma management- Asia”. For current systematic review, the electronic data bases such as; Google Scholar, Scopus, PubMed etc. were used for literature search. The cross-sectional studies in the language “English” and conducted over the time capsule 2002-2023 were included in the current review.

The information regarding this search obtained from different sources in different Asian countries i-e HIRA database, Hospital records, Prescriptions, Korean NHI claims, questionnaire, GBD Database, JMDC database etc. Age of asthmatics included in this review is 0-90 years old. Out of 33 studies obtained, there was no duplicate study. After screening of these 33 studies, 2 studies were excluded i.e., one was a review article and one study was published before 2002. Then full text articles were accessed for eligibility and accessed through ZEE tool. A total of 30 studies that were in accordance with the inclusion criteria were included in the present review.

Inclusion criteria

The following were the inclusion criteria:

Target study population was asthmatic patients of all ages, including children and adults from Asian countries.

The studies involved the prescription patterns and the cost of asthma treatment.

The studies published and available in the language “English”.

The original research studies published from the year 2002 to 2023.

Exclusion criteria

The following were the exclusion criteria:

The research studies conducted in areas other than Asian countries

The studies which do not include the prescription pattern and the cost of asthma treatment

The research studies published and available in language other than “English”

The studies published before 2002

Data Extraction

The information that was extracted from the included studies include: Author detail, year of the publication, country of study, age of included patients, study-design, sample-size, study-population, study duration, gender of participants, data collection source, medicines prescribed, cost of treatment, prescription pattern trends and prevalence of asthma. The data was obtained and reviewed without any biasness. The possibility of biasness was eliminated by using the “ZEE tool” for risk assessment.

Data Synthesis and Analysis

The prescription pattern and economic burden of asthma was reviewed in all included studies. The competency and incompetency of prescription and reason for incompetency of prescription was also assessed. Competency of prescription was reviewed by comparing it with the international guidelines e-g GINA guidelines, SINA guidelines, Chinese guidelines, Japanese Pediatric Guidelines (JPGL). Reason for economic burden of asthma was assessed.

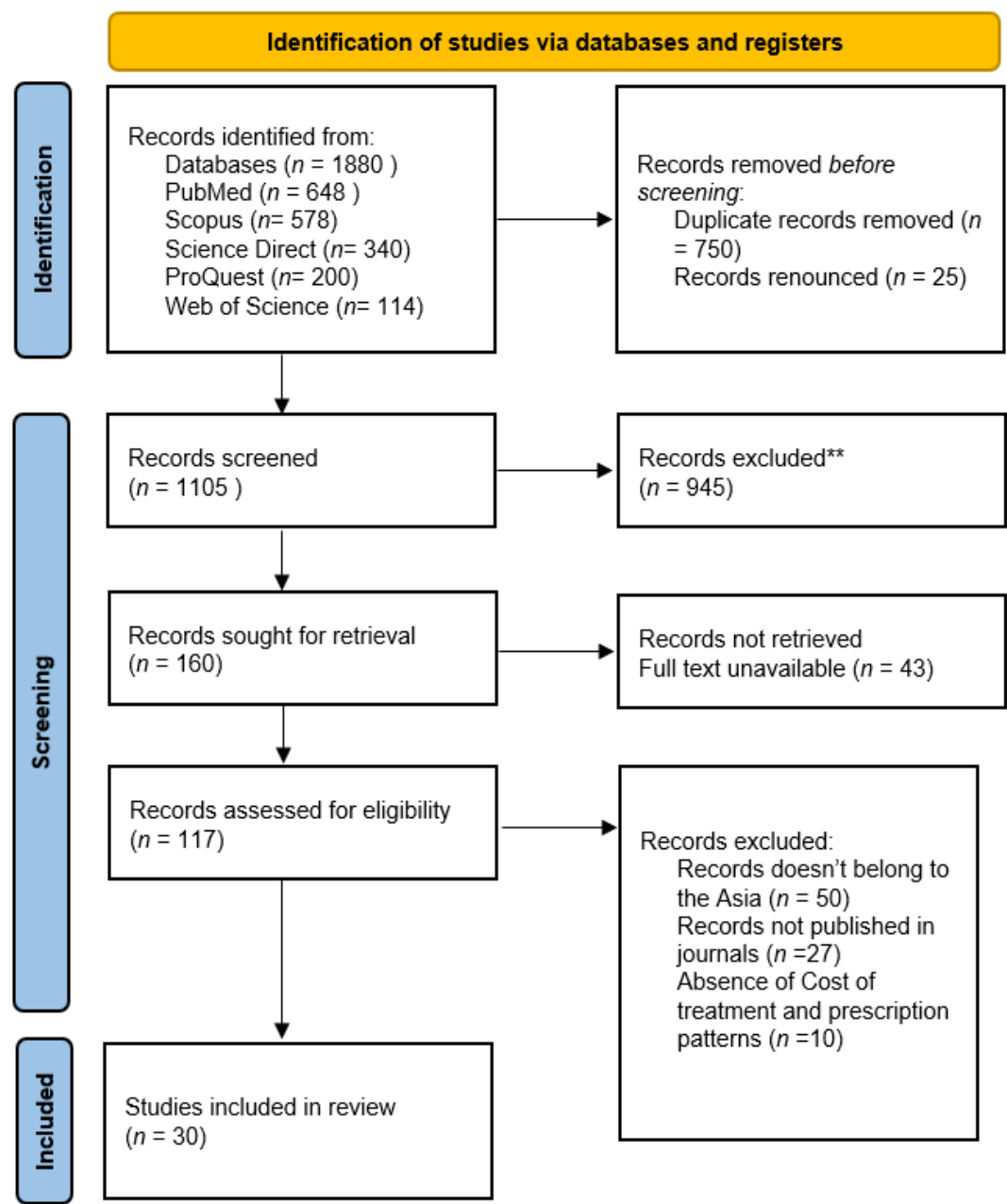
3. RESULTS

Thirty-three original research studies were extracted using search engines; all of the original research articles were examined following the removal of duplicate records. Two records were eliminated from the 33 examined research studies that did not meet the inclusion criteria. Ultimately, thirty papers that satisfied the inclusion criteria were extracted and assessed for the systematic review. The PRISMA flow diagram describes the specifics in (Figure 1). Cross-sectional studies can be assessed using various tools like the Newcastle-Ottawa scale, NIH-QAT, JBIC, AXIS tool/AXIS 20 and ZEE tool which are tailored for specific studies (Table 1). Analysis was done on the study design, sample size, data collecting time period, and target population’s nation. All of the included studies most

of the prescription pattern trends of the studies followed GINA guidelines while two studies did not mention the prescription pattern trends.

All of the studies published year were above 2000 between 2002 to 2023. All of the studies defined target /reference population that is asthmatic children/patients. All of the studies were recruited among Asian countries, 2 studies were recruited from South Korea, 3 studies were recruited from Korea, 3 studies were from turkey, 2 studies were from Taiwan, 1 study from Malaysia, 2 were from Saudi Arabia, 2 studies from Thailand, 2 studies from India, 2 studies from China and 1 from Tehran, UAE Dubai, Philippines, northern Jordan, Indonesia, Singapore and Japan (Table 2). 1 study recruited data from 5 countries (Nepal, Malaysia, Myanmar, Morocco and Lebanon), 1 study retrieved data from overall Asia. Most of the studies included cost of the treatments except some of them not mentioned the treatment cost. All of the studies focused on the impact of prescription pattern on the cost of treatment in the management of asthma in Asian countries.

The results of the studies included; South Korea was observed to prescribe oral medications more frequently as compared to the inhaled medications that resulted in suboptimal asthma management. The present study highlights the need to reduce oral corticosteroid medications. Most of the studies concluded that prescription of steroids and SABA+ anticholinergic prescribed as main drug of choice in acute asthma attack. Moreover, it is observed that the total asthma treatment cost has decreased with the effective usage of medicines in recent decades. Also, the outpatient management cost has the largest share of direct cost of asthma. Inhalations route is most preferred one for asthma. Salbutamol was the most popular for quick relieve, while budesonide was the most favored for childhood asthma management.



The PRISMA 2020 statement: an updated guideline for reporting systematic reviews.
For more information, visit: <http://www.prisma-statement.org/>

Figure 1 PRISMA flow diagram for systematic review

Table 1 Appraisal tool for included studies (ZEE tool)

30	(Shin et al., 2020)	✓	✓	✓	✓	✓	✓
29	(Shantakumar et al., 2018)	✓	✓	✓	✓	✓	✓
28	(Lee et al., 2017)	✓	✓	✓	✓	✓	✓
27	(Chen et al., 2016)	✓	✓	✓	✓	✓	✓
26	(Tan et al., 2016)	✓	✓	✓	✓	✓	✓
25	(Inoue et al., 2019)	✓	✓	✓	✓	✓	✓
24	(Gupta and Awasthi, 2016)	✓	✓	✓	✓	✓	N / A
23	(Suh et al., 2017)	✓	✓	✓	✓	✓	N / A
22	(Finkelstein et al., 2021)	✓	✓	✓	✓	✓	N / A
21	(Yorgancıoğlu et al., 2022)	✗	✓	✓	✓	✗	✗
20	(Bao et al., 2022)	✓	✓	✓	✓	✓	✓
19	(Singh, 2005)	✓	✓	✓	✓	✓	✓
18	(Wang et al., 2023)	✓	✓	✓	✓	✓	✓
17	(Wiyono et al., 2022)	✓	✓	✓	✓	✓	✓
16	(Altawalbeh et al., 2021)	✗	✓	✓	✓	✓	✓
15	(Diaz et al., 2023)	✓	✓	✓	✓	✓	✓
14	(Sekereş et al., 2020)	✓	✓	✓	✓	✓	✓
13	(Wu et al., 2020)	✓	✓	✓	✓	✓	✓
12	(Chokhani et al., 2021)	✓	✓	✓	✓	✓	✓
11	(Ali et al., 2021)	✓	✓	✓	✓	✓	✓
10	(AIOlayvan et al., 2021)	✓	✓	✓	✓	✓	✓
9	(Fahmy et al., 2016)	✗	✓	✓	✓	✓	✓
8	(Rostanzadeh et al., 2018)	✓	✓	✓	✓	✓	✓
7	(Sol et al., 2019)	✓	✓	✓	✓	✓	✓
6	(Yimsawad et al., 2016)	✓	✓	✓	✓	✓	✓
5	(Liam, 2015)	✗	✓	✓	✓	✓	✗
4	(Kaur et al., 2020)	✓	✓	✓	✓	✓	✓
3	(Türktaş et al., 2010)	✓	✓	✓	✓	✓	✓
2	(Theerakitikul et al., 2023)	✓	✓	✓	✓	✓	✓
1	(Choi et al., 2018)	✓	✓	✓	✓	✓	✓
Introduction							
Are study objectives specific?							
Methods							
Is study design suitable for aims?							
Is study sample size justified?							
Is study population specified?							
Is study data taken from the appropriate population that was under investigation?							
Was the selection process likely to select subjects that were representat							

[illegible]

[illegible]

Discussion																											
Are discussion & conclusions justified by results?	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Were the limitations of the study discussed?	✓	✗	✗	✗	✗	✓	✓	✗	✗	✗	✓	✓	✗	✓	✗	✓	✗	✗	✓	✗	✗	✓	✓	✗	✓	✓	✓
Other																											
Is there any conflict of interest that might affect study findings?	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗
Is ethical approval attained?	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓	✗	✗	✓	✓	✓	✓

Table 2 Study characteristics of the included studies

No.	Study	Year	Country	Study design	Study sample size	Study duration	Gender	Age	Data Collection source	Medicines prescribed	Cost of Treatment	Prescription pattern guidelines	Prevalence	Results
1	(Choi et al., 2018)	2018	South Korea	Retrospective Cohort Study	2427446	Jan 2013 to Dec 2016	Both: Male + Female	>18 years	HIRA database	ICS, LABA, oral LTRA, theophylline	N.G	Follow GINA guidelines	Increased from: 4944-5707 patients per 100000 adults	Suboptimal asthma management & the need to reduce oral corticosteroid prescription
2	(Theerakitkul et al., 2023)	2023	Thailand	Observational cross-sectional	389	Nov 2019 to Jan 2020	Both: Male + Female	>12 years	Existing medical records	SABA monotherapy ICS monotherapy ICS /LABA, Antibiotics	N.G	Follow GINA guidelines	Ranks eighth in asthma mortality rates	28.3% of patients were over prescribed to SABA in the previous 12 months
3	(Türktaş et al.,	2010	Turkey	Retrospective study	294	N.G	Adult Female	18 - 90	Hospital	SABA, Ipratropium	N.G	Follow GINA	3-4 million	Prescription of

	2010)						s	years	records	, Salbutamol, Steroids Theophyllin e, anticholinergics		guidelines		steroids as main drug of choice in acute asthma attack
4	(Kaur et al., 2020)	2020	India	Observational, Cross-sectional Non-interventional study	300	Nov 2017 to Feb 2019	Children, Both: Male + Female	1 -17 years	Prescriptions	SABA, inhaled, oral corticosteroids, LABA, LTRA Antibiotics antihistamines	N.G	Follows GINA guidelines	Prevalent in 6-10 years of age, males. 43.33% had intermittent asthma	Per prescription average drugs were 2.7. Inhalational route was preferred.
5	(Liam, 2015)	2020	Malaysia	Pilot cross-sectional survey	101 bronchial asthma patients	6 months	Adults + children of both gender	1-65 years	Medical records + Prescriptions + Questionnaire	ICS, SABA, LABA, and alternative therapy + herbal medication, followed by mineral supplements, vitamins	Monthly direct cost of asthma treatment = US\$ 22.97 for adults & US\$ 15.56 for children.	Follows GINA guidelines.	N.G	Along with pharmacological treatment, alternative therapy and herbal medications are also being used.
6	(Yimsawad et al., 2016)	2016	Thailand (Bangkok)	Descriptive study	74	1 year Jan-Dec 2012	Both: Male + Female	15-65 years	Prescriptions + Questionnaire	SABA + LABA + ICS leukotriene modifiers	Average cost/month: US\$ 86/patient. Direct medical cost for quick-relief medications = 11.91% and control medications = 36.85%	Follows GINA guidelines	Prevalent in 46-65 years of age	Loss of work and productivity caused by acute asthma exacerbations, was the major indicator of non-medical costs
7	(Sol et al., 2019)	2019	South Korea	Retrospective population-based study	1,172,807 patients (in 2010) + 1,590,228 patients (in 2014)	4 years Jan 2010-Dec 2014	Children, Both: Male + Female	1- 18 years	Korean NHI database for outpatient prescriptions	LTRAs + LABA + ICS + Xanthine derivatives	Average cost/year: US\$ 366/patient in 2011. reduced to US\$ 275 in 2014.	Not mentioned	Asthma in 1,172,807 children in 2010 increased to 1,590,228 in 2014. Asthma prevalence decreased	Pediatric asthma prevalence increased annually but decreased with age and the individual treatment cost in

													with increasing age.	children decreasing trend in Korea.
8	(Rostamzadeh et al., 2018)	2018	Iran (Tehran)	Descriptive study	100 Out-patients	1 year 2014-2015	Children, Both: Male + Female	1-14 years	Medical records + Prescriptions + Interviews	Salbutamol + ICS+ LABA + LTRA + Antihistamine + steroid nasal spray	Average cost/year: US\$= 159.3±19 per patient	Not mentioned	Prevalent in children of age 6.9±0.3 years. More prevalent in males	Outpatient asthma management cost has largest share of direct cost.
9	(Fahmy et al., 2016)	2016	UAE (Dubai)	Observational study	154 Out-patients	4 months Sep-Dec 2012	Both: Male + Female	1-70 years	Prescriptions + Questionnaire	SABA+LABA+ Xanthine+ Leukotriene modifiers + Oral, IV, Inhaled corticosteroids+ Antibiotics	N.G	N.G	Prevalent in age group 0-10 years	Most of the patients were smokers with family history of asthma. Prescribed combination drug therapy.
10	(AlOlayan et al., 2021)	2021	Saudi Arabia (Qassim)	cross-sectional hospital-based-retrospective study	3319 pediatric patients	9 years 2010-2019	Children, Both: Male + Female	0-14 years	Prescriptions	SABA+ LABA+ ICS+ Antibiotics + Herbal medication (Ivy leaf extract)	N.G	N.G	Prevalent in age group 0-9 years	Pediatric emergency room physicians prescribed more antibiotics than pediatricians
11	(Ali et al., 2021)	2021	Saudi Arabia	Retrospective cross-sectional study	9404 patients	1 year Jan-Dec 2019	Children, Both: Male + Female	0-12 years	Prescriptions	SABA+ LABA+ ICS+ LTRA+ anticholinergic drugs+ oral corticosteroids	Average cost/month of ICS: US\$ 53/ patient.	Follows SINA (Saudi initiative of asthma) guidelines	More prevalent in male children	ICS (budesonide) was the most preferred for asthma management followed by Salbutamol.
12	(Chokhani et al., 2021)	2021	Nepal, Malaysia, Lebanon, Myanmar, Morocco	Observational study	816 Asthmatics+ Healthcare providers	1-2 months	Both: Male + Female	>18 years	Prescriptions + Questionnaire	SABA+ LABA+ ICS+ oral corticosteroids	not mentioned	Follows GINA guidelines	N. G	Patient Non-adherence, Incorrect inhaler technique was observed. cost

			cco											remained a challenge to achieve good asthma control
13	(Wu et al., 2020)	2020	China	Cross-sectional descriptive study	Asthmatic children	3 years	Children, Both: Male + Female	0-14 years old	2015 version of CHIRA Database in China	N. G	Per capital direct medical cost was about (US \$75),	Follows Chinese Guidelines and GINA guidelines	More prevalent in male before puberty (15 years) and more common in females after puberty	Economic burden of childhood asthma is low in China. Antibiotics misuse is observed in asthma management
14	(Şekerel et al., 2020)	2020	Turkey	Observational study	Sample size not specified, asthmatic children	2016-2019	Children, Both: Male + Female	5-18 years old	Questionnaire	N. G	Total per patient annual direct cost for pediatric asthma= \$1,232.53	N. G	prevalence of pediatric asthma in turkey is 7.4%	Managing patient with pediatric asthma pose a considerable burden to health economics in Turkey
15	(Diaz et al., 2023)	2020	Philippines	Observational cross sectional	245 asthmatic patients	May 2019 to January 2020	Both: Male + Female	>12 years	Prescriptions	ICS+ SABA+ LABA + OCS	Not mentioned	Follows GINA guidelines	36.7% patients had mild asthma and 63.3% had moderate to severe asthma	A higher proportion of patients were enrolled by pulmonologists, pediatricians, than by primary care physicians
16	(Altawalbeh et al., 2021)	2021	Northern Jordan	Retrospective Cohort Study	761, 87	1 year	Both: Male + Female	≥18 years	Medical records of patients and pharmacy data	Not Mentioned	Not mentioned	Not mentioned	Not mentioned	Asthma-COPD overlap syndrome has higher disease severity compared to asthma and COPD patients

17	(Wiyono et al., 2022)	2022	Indonesia	Cross-sectional study	219 Out-patients	6 months	Both: Male + Female	≥12 years old	Prescriptions	SABA, ICS	Not mentioned	Follows GINA guidelines	Prevalence of asthma in Indonesia is 2.4%	SABA over-prescription occurs in one third of patients with asthma
18	(Wang et al., 2023)	2023	Asia	Cohort study design	262.41 million cases	29 years 1990-2019	Both: Male + Female	0-84 years	Databases, Questionnaires from surveys	ICS + SABA	Not mentioned	Not mentioned	Burden of asthma prevalence is 3.6%	Number of prevalent cases and deaths of asthma continues to increase and burden remains severe.
19	(Singh, 2005)	2005	Asia (38 countries)	ISAAC questionnaire-based survey conducted	257800 children aged 1-12 463801 children aged 13 to 14 years	Not mentioned	Both: Male + Female	1-14 years	Questionnaires	ICS+ steroid inhalation therapy	Not mentioned	Not mentioned	Prevalence Nepal-1.5% Hong Kong-6.2% China-3.91% India-3% Pakistan-4.3% Bangladesh-3.8% Sri Lanka-5.5%	This survey inferred that there have been certain improvements in accuracy of diagnosis and in the practice of steroids inhalation therapy by pediatricians in different cities
20	(Bao et al., 2022)	2022	China	Observational, Cross sectional study	498	6 months Mar-Aug 2020	Both: Male + Female	>12 years	Prescriptions	SABA+ ICS+ LABA+ LTRA	Not included	Follow GINA guidelines	Prevalence of asthma is 4.2%	Patients received ICS/LABA prescription experienced annual exacerbation than those prescribed SABA add on
21	(Yorgancıoğlu et al., 2022)	2022	Turkey	Cohort study design	579	6 months Sep 2019 -	Both: Male + Female	>12 years	Prescriptions	SABA, ICS/LABA oral corticosteroids	Not mentioned	Follow GINA guidelines	Not mentioned	Turkish cohort of the SABINA 3

						Jan 2020				ds				study indicated SABA over prescription in nearly a quarter of all patients. SABA over prescription is a public health issue in Turkey.
22	(Finkelstein et al., 2021)	2021	Singapore	Cross-sectional online survey	521	2020	Adults + children of both gender	4-65 years old	Questionnaire	Not mentioned	Total cost= SGD 1.74 billion (for adults) and SGD 0.35 billion (for children)	Follow GINA guidelines	Not mentioned	Poorly-controlled asthma implants a notable economic burden upon Singapore's healthcare cost.
23	(Suh et al., 2017)	2017	South Korea	Descriptive study	840	3 months Sep-Nov 2013	Children of both gender	less than 6 years	Prescriptions	Not Mentioned	Not mentioned	Follow GINA and JPGL	Not mentioned	Management strategies preference toward LTRA rather than (ICS) alone or add-on LABA
24	(Gupta and Awasthi, 2016)	2016	India	Cross sectional study	250	August 2008 to August 2011	Children of both gender	Less than 12 years	Questionnaire	SABA, LTRA or ICS, corticosteroids	Not mentioned	Not mentioned	Not mentioned	Prescription pattern does not correspond to GINA guidelines recommendation
25	(Inoue et al., 2019)	2019	Japan	Retrospective cohort Study	54,433	7 years April 2009 to march 2015	Both male and female	> 16 years	JMDC database	Not Mentioned	Total annual cost= US\$ 4345 ± 11,104	Not mentioned	3 million people suffer from asthma	The burden is significantly and disproportionately concentrated in Japanese severe

														asthma patients, suggesting clinical failure to achieve adequate disease control
26	(Tan et al., 2016)	2016	Singapore	Longitudinal Study	939	2004-2013	Both male and female	<16 years to > 65 years	Data recorded in database at the time of prescription refill	Fluticasone/salmeterol, budesonide/formoterol, budesonide, montelukast, theophylline ICS	10-year average annual asthma cost was GBP 341 per patient	Follow GINA guidelines	Chinese accounted for nearly 60%, followed by Malay (20%), Indian (14%) and others (6%). About half of the patients had intermittent asthma	The 10-year average annual asthma cost was GBP 341 per patient. Medications and consultation fees were main drivers of costs of asthma. Use of combined inhaled Drugs increased
27	(Chen et al., 2016)	2016	Taiwan	Retrospective Cohort study	282	5 years 2007-2011	Both male and female	Mean age of 51.3 ± 17.2 years	Taiwan National Health Insurance Research Data base (NHIRD)	ICS, SABA, ICS+LABA, OCS, Omalizumab	The cost of medical expenses decreased from NTD 3934 at 2 months to NTD 2860 at 12 months.	Not mentioned	Not mentioned	Patients who received omalizumab for over 4 months were more likely to decrease the use of other medications.
28	(Lee et al., 2017)	2017	South Korea	Descriptive study	Sample size not specified, asthmatic patients	1 year Jan-Dec2014	Both male and female	> 18 years	National Patient Sample data from South Korean Health Insurance Service	Not Mentioned	Not mentioned	Follow GINA guidelines	Not mentioned	In patients with severe asthma, the relative cost ratio in South Korea were higher than

														other countries
29	(Shantakumar et al., 2018)	2018	Taiwan	Retrospective Cohort Study	Sample size not specified, asthmatic patients	Not mentioned	Both male and female	≥40 years old	Taiwan National Health Insurance Research Data base (NHIRD)	Not Mentioned	Total cost of asthma was recorded \$227 per patient	Not mentioned	Not mentioned	Cost for asthma management in Taiwan is not higher than the other respiratory diseases
30	(Shin et al., 2020)	2020	Korea	Descriptive Study	26052 asthmatic children	1 January 2014 to 31 December 2016	Both male and female children	2-17 years	HIRA database	Budesonide inhalation suspension and montelukast	Cost measured in Korean won using consumer price index for medical goods and services	Not mentioned	Prevalence of asthma estimated 358 million people	Montelukast patients had better adherence a longer time to loss of persistency and less likely to experience exacerbation

4. DISCUSSION

The review's overall conclusions provide a vivid image of the Korean prescription system favoring oral over inhalation medicine. Similarly, oral therapy was more frequently administered than inhalers in retrospective observational research carried out in South Korea, which involved 2386 adult patients with asthma who were over the age of 18 and had been monitored by asthma specialists in 13 university hospitals for more than 13 years (Choi et al., 2018). These results, however, are in line with a similar study conducted in Korea, where 16804 institutions and 831613 individuals were included. The findings indicated that internal medicine physicians prescribed ICS to asthmatic patients more frequently than other physicians (>80%). Our findings may be explained by the patient's adherence to oral treatment.

The review's subsequent conclusions show that SABA is most frequently given in Thailand, Turkey, Indonesia, and India to treat asthma, and that this overprescription is having a negative impact on these nations' health (Wang et al., 2023). Likewise, a retrospective study conducted in Turkey demonstrating the overprescription of SABA for the treatment of asthma was carried out. The results of this study of mostly asthmatic patients receiving specialized care show that at least one in four individuals had SABA overprescription, which is linked to unfavorable clinical outcomes. Cross-sectional research including asthma patients (over the age of 12) found that inadequate treatment of asthma symptoms is linked to the overprescription of short-acting β2-agonists i.e., 85.7% of the 1389 patients (mean age, 46.7 years; 69.5% female) had moderate-to-severe asthma, and 88.7% of them received specialized treatment.

In the last year, 51.3% of patients reported having at least one severe asthma exacerbation, and 58.2% reported having partially or completely uncontrolled asthma (Al-Zaabi et al., 2022). Our findings are the outcome of an evaluation of SABA's efficacy. Another conclusion from our assessment is that patients who were prescribed ICS or LABA had yearly exacerbations (Iqbal, 2020). Similarly, patients who had at least two exacerbations or one hospitalization as a result of an exacerbation were the subjects of another medication usage study. The exacerbation frequency after 12, 24, 36, and 48 months of follow-up was used to stratify the study population into groups based on the use of ICS, long-acting β2-agonists (LABA), long-acting anticholinergics (LAMA), and combinations of these (Iqbal, 2020).

The necessity for the creation and application of de-escalation techniques in clinical practice is highlighted by the widespread use of ICS and the comparatively high adherence to ICS-containing regimens in patients who saw a reduction in the frequency of exacerbations. The concurrent use of ICS and LABA is linked to exacerbation, which explains this outcome. The second conclusion of our evaluation is that using Omalizumab reduces hospital stays and exacerbations. In a related trial, 346 patients received omalizumab treatment for a duration of more than 16 weeks. The study demonstrated that Omalizumab is linked with reduced use of oral corticosteroids (OCS) in patients with severe asthma. The research showed that for the majority of individuals with severe asthma, omalizumab is not cost-effective. Omalizumab estimated cost-effectiveness ratios may be within a positive range if its price drops considerably.

This outcome is due to the fact that omalizumab usage lowers treatment costs, hospital stays, and exacerbations. The review's subsequent conclusions state that the primary medications of choice for treating an acute asthma attack are SABA and anticholinergics. In a similar vein, a UK investigation revealed that several recommendations from earlier national guidelines suggested that SABA and anticholinergics be provided as the preferred medication in cases of severe asthma attack (Sato et al., 2019). These results, however, run counter to those of nine randomized controlled trials involving 576 participants, which found that formoterol administered via dry powder inhaler provides a quick and efficient bronchodilation comparable to high dose salbutamol and should be the drug of choice for patients experiencing an acute asthma attack who have SABA tolerance (Nagase et al., 2020). Our findings might be explained by the medications being provided in accordance with professional recommendations.

The inhalation approach is more preferred for asthma, according to the review's subsequent conclusions. In a similar way, research detailing the use of inhaled asthma medications from the last 50 years revealed that inhaled therapy is the recommended treatment for asthma. These results, however, conflict with those of a cross-sectional observational study that used an ad hoc 13-item questionnaire to gather data. The study included 150 patients who met the inclusion criteria and who completed the questionnaire, and the results showed that some patients preferred the intravenous administration routes. This is dependent on the patient's desire, convenience, and confidence in the medication's efficacy (Sun and Ko-Huang, 2008). Our findings may be explained by the lack of oral medicine and the rapid relief provided by inhalers.

The review's subsequent conclusions show that severe asthma sufferers in Japan bear a disproportionately large burden of the condition. In a similar vein, a retrospective analysis including 16,107 asthmatic patients found that 2.4% of asthmatic patients in Japan had severe asthma, and that individuals with severe asthma who are receiving high-intensity therapy have a notable disease burden (Hon et al., 2014). These results, however, are at odds with research carried out in Japan that included 10579 asthma patients, of whom 7.8% had severe asthma and 5.3% had severe uncontrolled asthma, reported that a large-scale analysis utilizing a health insurance claims database was used to determine the percentages of patients with severe uncontrolled asthma and severe asthma patients who are continually treated in Japan, therefore reducing the burden of the disease (Lajqi et al., 2015). Our findings might be explained by Japan's higher levels of pollution or pollen allergies.

The review's subsequent conclusions state that Taiwan's asthma treatment costs are comparable to those of other respiratory conditions. Similarly, a prospective cohort study was carried out in Taiwan with 70 asthmatic patients, of whom 55 completed the questionnaire and 45.5% completed the asthma diary chart. The study's findings indicated that managing asthma can be reasonably priced when pharmacists intervene and prevent the need for expensive medical care. These results, however, run counter to another study carried out in Taiwan that found that the cost of asthma is 2.7 times more than that of other respiratory disorders. The study used the National Health Insurance Research Database and provided population-based prospective studies (Lee et al., 2017).

Our findings might be the consequence of using more affordable alternatives to prescription drugs. The review's subsequent conclusions show that patients on montelukast had greater adherence, were more effective, and were less likely to develop exacerbations than those on budesonide. Comparably, research that comprised case control studies, big case studies, and randomized controlled trials came to the conclusion that montelukast was a useful substitute for corticosteroids with minimal side effect risks and a decrease in medical visits brought on by exacerbations. Alternatively, research using body plethysmography to measure lung function parameters and a sample size of 12 people with bronchial asthma found that budesonide outperformed montelukast due to its stronger bronchodilator effect (Wang et al., 2023). Our findings may be explained by montelukast's higher effectiveness and lower occurrence of adverse effects.

The cost of an acute asthmatic exacerbation is more expensive in Korea than in other nations, according to the study that follows this review. In a similar vein, a prospective study carried out in Korea to ascertain the degree to which recall bias influenced

questionnaire responses revealed that among chronic respiratory disease, Asthma is a notable contributor to health-care costs in the country, with costs rising as asthma severity increased. The study included 660 asthmatic patients from 31 institutions. On the other hand, retrospective research carried out in Korea on 124 patients with severe asthma revealed that omalizumab, an alternative medication, is probably a more affordable choice for treating severe asthma in Korea than conventional treatment alone, with a 53.2% reduction in asthma exacerbations. Our findings might be explained by the weak economy in Korea.

The cost of treating asthma has dropped in recent decades due to the effective use of medications, according to the following article in this evaluation. Comparably, a retrospective study carried out in Canada revealed that 10% of asthmatic patients account for more than 50% of the expenses and suggests that costs might be decreased by enhancing patient education initiatives, therapeutic intervention, and pharmaceutical usage that is efficient. On the other hand, a prospective study that included 108 patients, 73.8% of whom were women, and whose direct costs accounted for 82.3% of the estimated total cost came to the conclusion that asthma medication, environmental control measures, and long-term health leaves had the greatest potential to influence overall cost variation in certain countries. Our findings might be explained by the fact that treatment alternatives are more affordable.

The second conclusion drawn from this analysis is that in North Jordan, asthma, and COPD are associated with a significant financial and clinical burden. Another cross-sectional observational study with higher disease severity was carried out in Greece, Vietnam, Uganda, and Kyrgyzstan using validated questionnaires among patients (total N = 1040) with COPD and/or asthma diagnosed by spirometry. This study also showed a correlation between chronic lung diseases and socioeconomic burden. This outcome is the result of an investigation of the respiratory diseases that are linked to both clinical and financial burden (Zar and Levin, 2012). Our review's second conclusion is that pediatricians' diagnostic, inhalational therapy, and diagnostic methods have improved in Asian nations; a second cross-sectional study carried out in Turkey also showed improvements in practitioner therapeutic techniques (Zar and Levin, 2012).

On the other hand, a different study showed that in many low- and middle-income nations, childhood asthma is the most prevalent chronic illness. Childhood asthma is becoming more common in these environments and is linked to serious illness. In these situations, it might be difficult to provide the best care possible for children with asthma. These include the underdiagnosis of children asthma, the lack of access to care, the capacity of medical professionals to manage asthma, the accessibility and cost of inhaled medication, the management of possible triggers in the environment, public and healthcare provider education, and linguistic or cultural barriers. Although national and international standards have been developed for childhood asthma, there are still significant implementation challenges. This outcome is the result of an evaluation of the advancement in inhalation therapy.

Our review's second finding is that the primary causes of cost were consultation fees and asthma medication. This is supported by a different study that examined and discussed differences in asthma management across various nations and areas, including access to pharmaceuticals and medical personnel as well as the inability to develop effective control and preventative measures due to limited financial resources. The purpose of this report is to identify the primary factors influencing the expense of treating asthma. The second conclusion of our evaluation is that inadequately managed asthma significantly increased Singapore's economic burden. In a similar vein, a study carried out in Indonesia found that noncompliance with clinical recommendations and inadequate asthma control raise the financial burden of asthma (Wiyono et al., 2022). This outcome can be attributed to the correlation between inadequate management of asthma and financial strain.

Enhancing asthma control lowers the average cost of asthma therapy, according to another research we conducted. Through random digit dialing, adults and adolescents suffering from asthma were enlisted. A total of 517 people (average age 48.9, 65.8% female) with mild-to-moderate asthma who had contributed 2033 follow-up visits were included in the final sample. Asthma control as defined by GINA and the utilization of healthcare resources were evaluated at baseline and three-monthly visits up to one year. Asthma was symptomatically managed in 598 visits (29.4%), moderately controlled in 809 visits (30.9%), and uncontrolled in 626 visits (30.8%). In this population-based sample of mostly mild-to-moderate asthmatics, a significant portion had uncontrolled symptoms. A decrease in direct expenses was linked to the achievement of symptom management. This outcome is due to the fact that better patient compliance and asthma management lower the cost of asthma therapy.

Our analysis also revealed that 54% of patients were prescribed more than one medication to treat their asthma; nonetheless, two drug therapy is the most prevalent course of treatment. at a similar vein, a prescription auditing procedure was used to examine 100 patients at three renowned hospitals in Gorakhpur, India. Two months of data collection from patients visiting the outpatient department using a chance random sample approach showed that two-drug treatment is most frequently prescribed. On the other

hand, an investigation revealed that the most popular and efficient form of medication therapy is triple combination therapy, with increasing data supporting the value of treating asthma with this combination of ICS, long-acting β_2 -agonist (LABA), and long-acting muscarinic antagonist (LAMA). The purpose of this outcome was to assess the efficacy of dual medication therapy in the management of asthma.

The review's second finding is that there isn't much of an economic burden associated with childhood asthma. A study carried out in the United States revealed that the cost of treating childhood asthma isn't too high; the survey's main data source was the 2008–2013 household component of the Medical Expenditure Panel Survey (Nagase et al., 2020). In contrast, different research that examined the financial impact of pediatric asthma in the US was carried out there. The results indicated that the financial burden of treating pediatric asthma is higher and that treatment costs are quite high. These findings presents that the economic impact of childhood asthma might be minimal.

Our review's second conclusion is that ICS and LABA are the most often given medications for asthma in Korea. Combination treatment with ICS and LABA is safe and effective for individuals with more severe asthma who are not adequately managed with ICS alone (Nagase et al., 2020). Furthermore, it is linked to a notable decrease in the quantity of asthma flare-ups. When combined with ICS maintenance medication, the extra anti-inflammatory properties of LABAs may account for some of the combination therapy's positive results. However, the analysis of data from RCTs revealed that fatalities were uncommon with SABA reliever monotherapy and that rates of SAEs and DAEs were similar across SABA reliever and ICS treatment groups (Türkta et al., 2010). This result is due to the fact that it lists the most often recommended medications for asthma.

5. CONCLUSIONS

The pattern of asthma prescriptions and the financial burden of managing asthma in Asia are examined in the systematic literature review. It is found that the inhalation method is more favored for treating asthma, and that SABA is most frequently given for asthma in Asian nations. Omalizumab therapy for asthma lowers the risk of hospitalization and exacerbation. Additionally, it is determined that using ICS and LABA concurrently is linked to exacerbation. Medication for asthma and consultation fees are the primary sources of expense in asthma care.

Additionally, it has been discovered that improved asthma control reduces the average cost of therapy, but poor control is associated with a financial burden. Effective medication use enhanced therapeutic interventions, and patient education initiatives all help to minimize the cost of treating asthma. Additionally, it is assumed that compared to budesonide patients, montelukast patients had higher adherence, were more effective, and were less likely to develop exacerbations. Anticholinergics and SABA are typically used as the first line of therapy for acute asthma attacks.

Abbreviations

Global Initiative for Asthma (GINA); disability-adjusted life years (DALY); Short acting beta-agonists (SABA); National Asthma Education and Prevention Program (NAEPP); Global Initiative for Asthma (GINA); Japanese Pediatric Guideline (JPGL); SINA guidelines (Saudi initiative of asthma guidelines); Health Insurance Review and Assessment Service (HIRA) database; Inhaled corticosteroids (ICS); Oral corticosteroids (OCS); Long-acting beta agonist (LABA); Leukotriene receptor antagonists (LTRA); Long-acting anticholinergics (LAMA); Chronic Obstructive Pulmonary Disease (COPD); Accountable Care Organization (ACO)

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Limitations of the study

The current study is a systematic review of prescription patterns and cost of treatment for Asthma management from the regions of Asia. Therefore, it lacks the worldwide prospective.

Authors' Contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Informed Consent

Not applicable.

Ethical Approval

The current systematic review was conducted after getting ethical approval from the university's ethical review board with ethical protocol number: ERB-PHRMD-DPP/4733-A.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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