Original Article

Evaluation of Drug Utilization Pattern for Patients of Bronchial Asthma in a Government Hospital of Saudi Arabia

MM Rafeeq, HAS Murad

Department of Pharmacology, Faculty of Medicine, Rabigh Campus, King Abdulaziz University, Jeddah, Saudi Arabia

Abstract

Background: Bronchial asthma is a social and economic healthcare burden. Drug utilization studies are important tools to assess current prescription practices against standard guidelines and help in rationalizing the management. **Materials and Methods:** This retrospective cross-sectional study was designed to evaluate the pattern of drug utilization in bronchial asthma patients in a government hospital of Saudi Arabia. Retrospective prescribing information of patients of all ages and both sexes diagnosed with bronchial asthma being treated with at least one of the anti-asthmatic medications was utilized. Demographic details, brand/generic name, indication, route, dosage, frequency, and date of starting the drug were recorded. Prescriptions were examined for order, number, and therapeutic class of drugs in addition to poly-pharmacy and appropriateness. Patients having other respiratory disorders such as chronic obstructive pulmonary disorder (COPD), bronchitis, emphysema, or any comorbidity such as diabetes, hypertension, and peptic ulcer were excluded. The Statistical Package for the Social Sciences was used for statistical analysis. **Results:** A total of 380 prescriptions were studied. Patients were aged from 4 months to 79 years, with 55.3% males and 44.7% females. Pediatric prescriptions were 47.4%. Bronchodilators followed by steroids were the most common drug groups. Salbutamol and budesonide were the most common from each group, respectively. 89.5% of the patients were having at least two drugs. Number of drugs per prescription averaged 3.18 ± 1.22, however, no correlation was found between different age groups and number of drugs. 61.3% drugs were administered by inhalational route and 34.8% by oral route. Approximately 77.2% prescriptions were found to be appropriate. **Conclusion:** Prescription pattern was mainly in accordance with standard guidelines with some knowledge and technical gaps in prescription writing methodology.

Keywords: *Airway, pharmaco-epidemiology, pharmacy, public health, survey*

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Introduction

Bronchial asthma is a worldwide health issue affecting more than 150 million people worldwide and causing 180,000 deaths annually.[1] People of different age groups are affected with an increasing prevalence in children. Saudi Arabia also carries a large burden of adult and pediatric asthmatic patients, and prevalence among adolescents is increasing due to environmental issues, lifestyle changes, and rapid industrialization. There is also regional variation in the prevalence pattern.[2-4] A study by Bener *et al*. documented an asthma prevalence of 13.9% and 8%, respectively, among Saudi school children in industrial and nonindustrial areas.[5] Another study reported significantly higher prevalence of allergy symptoms among Saudi and urban children than non-Saudi and rural children, respectively.[6,7] In addition, a study by Donques and Nooh 2007 revealed a prevalence of 15% in school age children;

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Address for correspondence: Dr. MM Rafeeq, Department of Pharmacology, Faculty of Medicine, Rabigh Campus, King Abdulaziz University, Jeddah, Saudi Arabia.
E-mail: marafeeq@kau.edu.sa

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they considered this a major cause of nonappearance in schools.[8] Overall, based on past three decades, the reported asthma prevalence in pediatric population from Saudi Arabia ranged from 8% to 25%.[9] Adolescents' prevalence is also high but still within the world-wide reported ranges.[10]

Bronchial asthma is a chronic inflammatory condition of the respiratory tract associated with bronchial hyper-reactivity and airflow restriction due to airway smooth muscle contraction often leading to difficulty in breathing and hypoxia.[11] The pathogenesis of asthma involves mast cell activation, eosinophil, and T helper 2 (TH 2) lymphocytes infiltration, IgE formation by B lymphocytes, and release of other inflammatory mediators, chemokines, and growth factors by airway epithelium.[12] On allergen exposure, the asthmatic patients show an early phase characterized by sudden onset of bronchoconstriction, and then a late phase occurring 8–24 hour post exposure. The late phase is characterized with influx of inflammatory cells into the airways and airway hyper-responsiveness to nonspecific stimuli.[13,14] Proper drug therapy is one which controls both phases. Asthma produces a substantial economic and social burden on families and generally requires long-term treatment and patient cooperation to achieve clinical control.[15] The main pharmacological approach includes bronchodilators, corticosteroids, leukotriene modifiers, mast cell stabilizers, antihistamines, and mucolytics, often using a combination of these drugs.

Drug utilization studies aim at evaluation of appropriateness of drug therapy. WHO defines them as "marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences."[16] These studies intend to identify whether the patterns of prescribing, dispensing, and use of medications in a specified health care set-up are reliable against standard guidelines.[17] The WHO[18] emphasized the use of drug utilization studies as a management tool in healthcare infrastructure as well as a measuring tool to assess the outcome of a therapeutic intervention. Other advantages of these studies include (1) creation of a comprehensive medico-socio-economic background for decision-making in healthcare, (2) rationalization of drug use, (3) detection and prevention of drug interactions, adverse effects and toxicity, (4) provision of performance feedback to physicians and other stake holders, and (5) designing educational programs that would eventually lead to improvement in prescription and drug use.[16] The inappropriate medication use patterns in the form of irrational prescribing, unwarranted multidrug regimens, and disproportionate dosage decreases the effectiveness of therapy, increases incidence of the adverse effects, and heightens cost of the medical care.[19,20] Therefore, it is imperative to assess the prescribing pattern of physicians periodically to identify any defects and undertake effective corrective measures. Asthma drug evaluation studies are rare in Saudi Arabia. Two recent studies highlighted some lacunae regarding the management of asthma. Al-Kabbaa *et al*. 2002 reported that merely 39% primary care physicians adhered to the standard guidelines in asthma management.[21] They also found a low overall awareness level regarding national guidelines among physicians. Another study revealed that only a small fraction of patients were fully controlled, nearly one-third partially controlled, and about half were uncontrolled.[22]

This study intends to evaluate the drug utilization patterns of anti-asthmatic drugs in asthmatic patients and to evaluate whether the drug utilization pattern is deviated or in accordance with international guidelines for management of asthma.

Material and Methods

Study design: Retrospective cross sectional study.

Inclusion criteria: Patients of all ages and both sexes diagnosed with bronchial asthma being treated with at least any one of the anti-asthmatic medications at Rabigh general hospital.

Exclusion criteria: Patients having other respiratory disorders like COPD, bronchitis, emphysema or any comorbidities such as diabetes, hypertension, peptic ulcer, etc.

The protocol of the study was approved by the King Abdulaziz University Research Ethics Committee (KAU-REC). Retrospective prescribing information was utilized and patient medical records were entered by a systematic random sampling. The study duration was 6 months. Prescriptions of patients who visited the chest clinic during the last 1 year counting from the start of the study were included. In addition to patient demographic details, the following details of each prescribed drug were noted: (1) name (brand/generic), (2) indication, (3) route, (4) dosage, (5) frequency, and (6) date of starting the drug. The prescriptions were examined for order, number and therapeutic class of the drugs in addition to poly-pharmacy and appropriateness.[23]

The prescriptions were classified as "appropriate" when the prescribed drugs have full relationship to diagnosis, "partially appropriate" when the drugs are partially related to diagnosis, "inappropriate" when there is no relationship between the prescribed drugs and the diagnosis, and "difficult to comment" when either the

diagnosis is missing or the prescription not written clearly.[24] Assessment of deviations from the Global Initiative for Asthma (GINA)/Saudi Initiative for Asthma (SINA) guidelines was done accordingly.[25,26]

Statistical analysis

Creative Research Systems 1709 Schaeffer Road Sebastopol, CA 95472 Descriptive analysis was used for all variables. Pearson's test was used to assess for any correlation between age group and number of drugs prescribed. Numeric values were placed as mean values ± SD. A value of $P < 0.05$ was considered statistically significant.

Results

A total of 380 prescriptions were studied. Figure 1 shows the flowchart of patient medical records included for evaluation. The age range was from 4 months to 79 years. Table 1 shows the demographic characteristics of the studied population. Pediatric prescriptions were 47.4%. There were 55.3% males and 44.7% females.

Figure 2 shows the prescription pattern of anti-asthmatic drugs. When analyzed according to the percentage of prescriptions containing a particular drug or combination, most common individual drug category present in the maximum number of prescriptions were bronchodilators, of which albuterol (beta-agonist) in the inhalational form was the most common followed by anticholinergic drug ipratropium. Approximately 78.9% prescriptions were found to contain albuterol (aka salbutamol). The next most prescribed class of drugs was steroid led by budesonide present in 28.9% of the prescriptions. Further analysis based on the usage of individual classes of drugs also revealed bronchodilators as the leading group (32.63%) followed by steroids (21.84%), as depicted in Table 2, which shows the usage of individual classes of drugs.

Figure 3 shows the total number of drugs for each prescription according to different age groups (Mean ± SD). The average total number of drugs in each prescription (all groups combined) was (3.18 ± 1.22; CI:

Table 1: Demographic characteristics of the study population

Age group (years)	Percent
1–10	47.4
11–20	10.5
21–30	5.3
31–40	15.8
41–50	13.2
51–60	2.6
61–70	2.6
>70	2.6
Total	100.0

Table 2: Usage of individual classes of drugs

Drug Class	Percentage (n)
Bronchodilators	32.63 (124)
Beta-agonists	19.47 (74)
Anticholinergics	7.89 (30)
Methylxanthines	5.26 (20)
Steroids alone	21.84 (83)
Steroids + Beta-agonists	9.74 (37)
Leukotriene Modifiers	4.21 (16)
Antihistaminics	9.74 (37)
Mucolytics / Antitussives	8.68 (33)
Miscellaneous	13.16 (50)

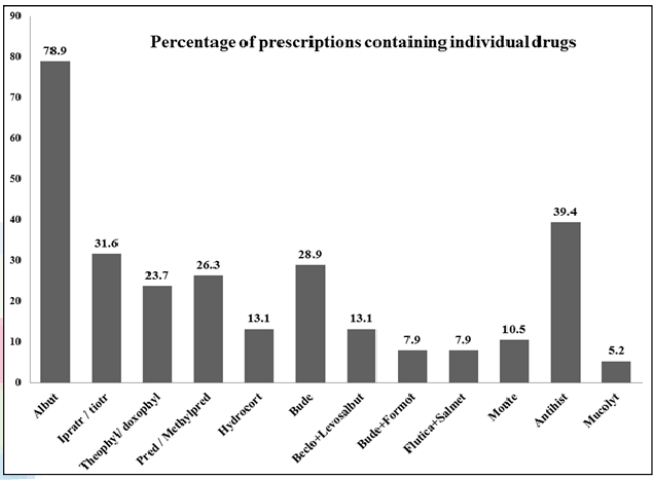

Figure 1: Flowchart of patients' medical record screened for evaluation. *N* = total number of patients in a particular category

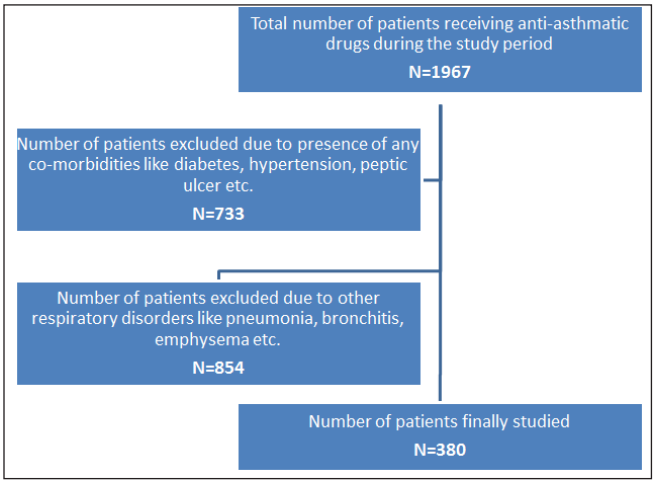

Figure 2: Prescription pattern of anti-asthmatic drugs. Albut = Albuterol or Salbutamol; Ipratr = Ipratropium; Tiotr = Tiotropium; Theophyl = Theophylline; Doxophyl = Doxophylline; Pred = Prednisolone; Methylpred = Methylprednisolone; Hydrocort = Hydrocortisone; Bude = Budesonide; Beclo = Beclomethasone; Levosalbut = Levosalbutamol; Formot = Formoterol; Flutica = Fluticasone; Salmet = Salmeterol; Monte = Montelukast; Antihist = Antihistamines; Mucolyt = Mucolytics

Table 3: Percentage of patients and the total number of drugs prescribed

Percentage of patients	Number of drugs per prescription
10.5	01
15.8	02
34.2	03
26.4	04
13.1	>04

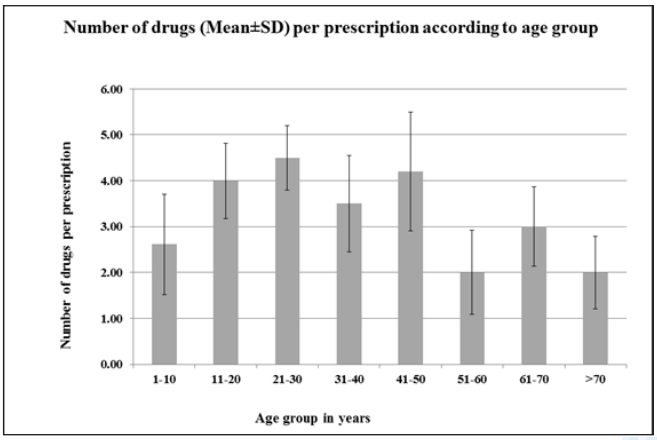

Figure 3: Total number of drugs for each prescription according to different age groups (Mean ± SD). Average number of drugs was 3.18 ± 1.22 with all the groups combined. There was no correlation between the age groups and number of drugs prescribed

2.78–3.53). Young adults (21–30) and middle aged (41–50) were having the maximum number of medications, approximately ≥4 drugs per prescription. There was no significant correlation between age groups and number of drugs prescribed (R = 0.23, P = 0.18).

Table 3 shows the percentage of patients and the total number of drugs prescribed. As depicted in Table 3, most of the patients (89.5%) were given a combination therapy, whereas only 10.5% patients received a single drug. Approximately 13.1% prescriptions were having more than four drugs (indicating poly-pharmacy).

Figure 4 shows the percentage of route of drug administration. Inhalational route was the most common (61.3%) followed by oral route (34.8%), whereas injectables were given only in a minority of patients. None of the prescriptions contained injectables more than one-third of the total number of drugs.

Figure 5 shows the appropriateness of prescriptions. Approximately 77.2% prescriptions were appropriate, 4.4% were partially appropriate, and 18.4% were "difficult to comment" (diagnosis missing). In general, the treatment prescribed were having SABA, LABA, ICS, etc., as advocated in GINA document and were in accordance with GINA guidelines.

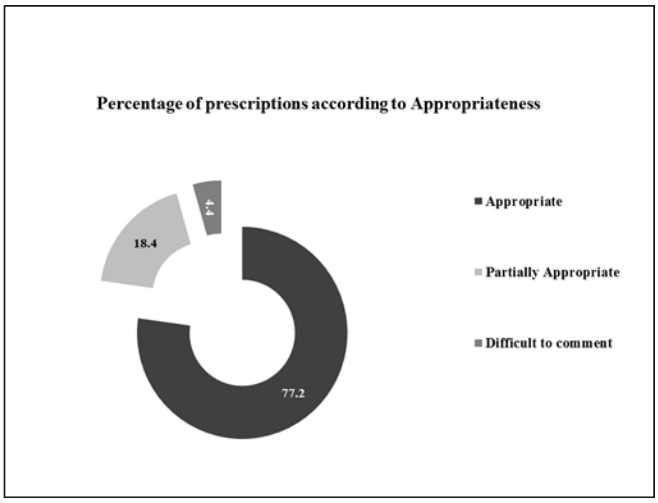

Figure 4: Route of drug administration. Inhalation route was most common. Inh = Inhalation; Neb = Nebulization; IV = Intravenous

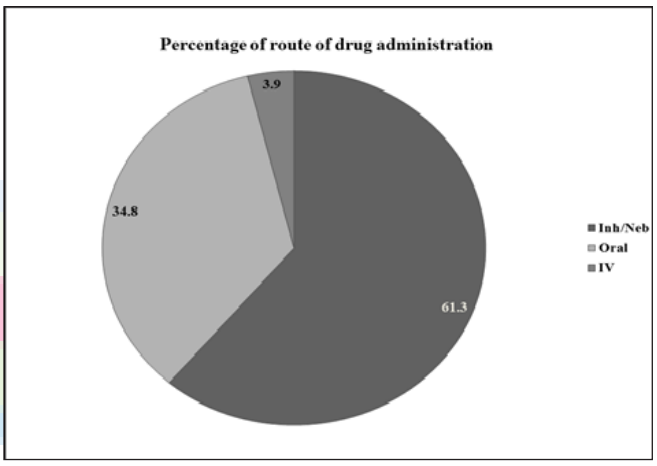

Figure 5: Appropriateness of prescriptions. Majority (77.2%) of the prescriptions were appropriate

Discussion

Drug utilization studies are an important tool to assess the current therapeutic practices and serve as a background for modification and rationalization of disease management to decrease economic and social healthcare burden. The present study was conducted in Rabigh general government hospital which caters to a population of approximately 200000. The demographic characteristics show a large number of patients (47.4%) in the pediatric age group. This is anticipated as Rabigh is becoming a heavy industrial city and pollution producing units are gradually coming closer to the city. These facts are further reinforced by a similar study in Saudi Arabia.[5] On the other hand, less number of adult and geriatric patients may be attributed to underreporting and gradual progression to COPD, which was an exclusion criterion in this study.

Prescription pattern shows that maximum number of patients (78.9%) were prescribed beta-agonists,

more specifically albuterol (salbutamol), making it the preferred choice for asthma management. This finding is further reinforced by some previous studies in other countries.[27,28] It is from the group Short Acting Beta Agonist (henceforth SABA), and the main reason for its use is rapid onset and low cost. In addition, albuterol does not increase exacerbation rates and provides instant symptomatic relief.

Anticholinergics were present in approximately 31.6% of the prescriptions and individually they are just given in 7.89% of the patients. There is limited role of anticholinergics alone in asthma; they are mostly used for COPD patients though there is some benefit when they are used in combination with SABA. Furthermore, the side effects of anticholinergic such as dryness of mouth and urinary retention may further limit their use.[29-31] Methylxanthines are also less preferred (5.26%) as solo agents due to their cardio and neurotoxicity profile, therapeutic window phenomenon, and zero order kinetics. A previous study in Malaysia also revealed similar figure for methylxanthines use.[32]

In our study, steroid consist the second largest prescribed drugs. This finding is reinforced by a similar study from India.[33] Corticosteroids (inhaled and oral) are one of the mainstay therapies for asthma. In addition to reduction of severity and exacerbation, they reduce airway hyper-responsiveness. They also help in reducing inflammation by inhibiting the activation and recruitment of T cells, macrophages, and dendritic cells, by decreasing mast cells survival, and by inhibiting the release of inflammatory mediators.[34] In addition, they reduce hospitalization, improve quality of life, and reduce overall mortality and morbidity.[35] A recent systematic review established the myriad benefits of systemic steroids in the management of asthma.[36]

Previous studies reported equivocal results regarding comparative efficacy of different steroids by various route of administration, as discussed below. Budesonide has shown better pharmacological profile as compared to prednisolone,[37] however, prednisolone is cheap and available for oral administration. Another study documented the preference of budesonide over prednisolone in pediatric acute moderate asthmatic attacks.[38] However, a study by volovitz *et al*. reported comparable efficacy for budesonide and prednisolone.[39]

There are equivocal results regarding the route of administration for steroids, for example, prednisolone oral versus hydrocortisone intravenous showed similar efficacy.[40] However, a trial studying comparison of sequential therapy discovered that PEF, FEV1, and asthma scores are far better in the group prescribed IV methylprednisolone after oral methylprednisolone compared to the group given IV hydrocortisone after oral methylprednisolone.[41] In another study, oral prednisolone and IV methylprednisolone were found equally efficacious in children.[42]

There are also well established reports concerning the superiority of combination of Inhalational Corticosteroids (henceforth ICS) and Long Acting Beta Agonist (hereafter LABA) against individual therapy. A study in Brazil concluded that a combination of budesonide + salbutamol is better than oral prednisolone.[43] Cochrane review database also supports these reports.[44,45] However, mutual comparison between different ICS and LABA combinations revealed equivocal results.[46]

Recently introduced SMART (Single Inhaler Maintenance And Reliever Therapy) or SiT (Single Inhaler Therapy) approach has produced good results regarding the quality of life and dose reduction of both ICS and LABA as compared to ICS alone,[47,48] however, there are few incidences of flare ups in children; hence, a controversy is ongoing regarding the long-term benefits, especially in pediatric age group.[49] However, a systematic review found fewer exacerbations but associated poor symptom control,[50] which was supported by two other studies advocating its use based on cost effectiveness and achievement of greater asthma control.[51,52] Still trials are going on to establish the superiority of single inhaler treatment on "as needed" basis.[53] In our study, most of the patients were on more than two drugs but subanalysis revealed that ICS+LABA SiT were restricted to few and that too mainly in adult population. This is in accordance with recent updates.

Our results indicated that a small fraction of patients were prescribed montelukast, a leukotriene receptor antagonist as compared to other previous studies. It may be partially explained by a better asthma control with already prescribed ICS and SABA. Another reason may be a slightly higher cost. Montelukast improves PEF, FEV1, and other parameters, reduces nocturnal symptoms, and may decrease the concomitant doses of ICS and SABA/LABA.[54]

Antihistamines, expectorants, and mucolytics were not so much prescribed. Average drugs per prescription was 3.16, which is far less than a previous study from India, indicating better therapeutic practices and adherence to guidelines.[55] Further, most of the patients (89.5%) were on ≥2 drugs which are required for better control of asthma.

Inhalational route is the choice for asthmatic patients as it delivers the maximum amount of drug with minimal systemic side effects. A previous study showed similar

percentage.[55] However, medication by oral route becomes essential in case of inability to use the inhaler efficiently in an appropriate manner, especially in pediatric and geriatric population. They may not be able to coordinate the inspiration timing with inhaler puff. One solution is provided by nebulization that does not require coordination and works with normal tidal respiration but it is needs longer periods and mainly used in emergency for termination of acute attack. Oral medications do not depend on the technique, and a study reported a higher compliance of tablets than inhaled medications for asthma.[56] IV route also produces quick relief with 100% bioavailability and less airway irritation. Few studies have compared the efficacy of these regimens,[40-42] however, there is a need for well-designed studies to explore the issue of route further.

In our study, the polypharmacy was found to be 13.1%. The definition of polypharmacy is very ambiguous. Nevertheless, polypharmacy predisposes to drug-related problems but a standard number of drugs (as a cut-off of polypharmacy), which actually predisposes to this is not validated. It is further complicated by major and minor polypharmacy.[57-59] Some reports advocate two categories of polypharmacy; i.e., >5 drugs/day and >7 drugs/day;[60] the percentage of polypharmacy increased markedly (54.1 to 79%) as the number of drugs defined for polypharmacy decreased, as reported previously.[61]

Polypharmacy is also defined by clinically inappropriate use of drug.[62] A study by Bushardt *et al* used two definitions of polypharmacy (>6 drugs or potentially inappropriate drug). They also summarized different definitions and criteria for polypharmacy and a possible tool to evaluate polypharmacy.[63] Another study also found that polypharmacy defined conventionally (4 or 5 or more drugs) is not a good indicator for assessment of drug-related problems, however, drug interactions and side effects are directly proportional to a gradual increase in number of drugs in addition to comorbidities and age. They advocated that no cut-off should be put as a risk marker to predict an increase or decrease in drug related problems.[64]

In addition, even after taking into account ≥4 drugs as polypharmacy, in our study, this is still not a significant concern as a previous study reported similar results (41%) with ≥5 drugs.[65] Thus, a polypharmacy of 13.1% in our study by the criteria of more than 4 drugs is not alarming, however as discussed above, this percentage will increase to 40% if we take the definition of polypharmacy as ≥4 drugs and even more if we consider minor polypharmacy criteria. However, majority of the studies have taken polypharmacy as ≥5 drugs. It is also worth mentioning that no study was found mentioning polypharmacy of anti-asthamitic drugs specifically and more scientific data is required for a precise definition of asthma polypharmacy.

Concerning the prescription appropriateness, majority (77.2%) were appropriate. Even some from the "difficult to comment" category may be appropriate but the diagnosis was missing. Partially appropriate prescriptions were mainly those having miscellaneous drugs for symptomatic treatment like antitussive, antipyretics, and analgesics. Moreover, dosage schedule, duration, proper address, and legible writing were some other issues.

Limitations

Possible limitations of this study include (1) single study site, (2) inability to register records due to missing diagnosis in almost one-fth (18.4%) of the population, and (3) no follow-up due to time constraints.

Conclusion

Our study revealed that prescription pattern is mainly in accordance with standard guidelines. Polypharmacy was detected but within acceptable limits depending on our criteria of 5 or more drugs. Physicians seem to be aware of recent guidelines in the management of asthma. This may be partially attributed to mandatory CMEs, protocol based treatment, and impact of extensive asthma education campaign.[66] However, there are some knowledge and technical gaps in prescription writing methodology such as dosage schedule, duration, patient particulars, and legible writing.

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Conflicts of interest

There are no conflicts of interest.

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