Evaluation of Inhaled Corticosteroids use and Associated Local Adverse Reactions in Respiratory Disease Patients at a Tertiary Care Teaching Hospital in Nepal

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Abstract

Background: Bronchial asthma and Chronic Obstructive Pulmonary Disease (COPD) are major respiratory diseases in Nepal, with an increasing prevalence. Inhaled corticosteroids (ICS) are the cornerstone of treatment, reducing exacerbations and mortality. However, local adverse reactions such as oropharyngeal candidiasis, dysphonia, and throat irritation can impact medication adherence and patient quality of life.

Materials and Methods: This cross-sectional descriptive study was conducted at a tertiary care teaching hospital in Nepal over a period of six months. Patients diagnosed with asthma or COPD and prescribed inhaled corticosteroids were included. Data on demographic characteristics, ICS usage, their dosage duration and severity of adverse drug reactions were collected through structured questionnaires. Those adverse drug reactions were observed and preventive measures taken by patients to counteract adverse drug reactions were included. Statistical analysis was performed using SPSS version 22, with chi-square tests applied to assess associations between variables.

Results: Among 138 patients, 81 (58.7%) reported at least one ICS-related adverse reaction, with a higher prevalence in females ($p<0.001$) and illiterate patients ($p<0.001$). The most commonly used Inhaled Corticosteroids was fluticasone (33.3%), and frequently reported adverse effects included tooth decay (35.8%), throat irritation (20.99%), and tongue abrasion (19.75%). Higher Inhaled corticosteroids dosages (200 mcg) and twice-daily regimens were significantly associated with increased adverse reactions ($p<0.001$). Self- management strategies included salt and water gargling (30.9%), use of antifungal cream (22.2%), and mouthwash use (21%).

Conclusion: ICS-related local adverse effects are common and influenced by demographic and drug related factors. Proper inhaler techniques, patient education, and preventive measures can help mitigate those effects and enhance treatment adherence.

Key words: Inhaled corticosteroids, adverse drug reactions, oral candidiasis, dysphonia

Introduction

Bronchial asthma is a chronic inflammatory disease that typically begins in childhood characterized by dyspnea, chest tightness, cough and recurrent episodes of wheezing. Chronic obstructive pulmonary disease (COPD) is marked by an enhanced chronic inflammatory response that distorts lung architecture, causing progressive irreversible airflow limitation. Both are major respiratory diseases with significant health concerns in Nepal (1). Diagnosis relies on clinical history, physical examination, chest x-ray and spirometry, the gold standard for confirmation (2).In Nepal the prevalence of respiratory diseases is increasing day by day in which the prevalence of asthma ranges from 4.2%to 8.9% and that of COPD varies between 1.67% to 14.3% (3).

Current guidelines recommend inhaled medications as the first line of treatment, including bronchodilators and inhaled corticosteroids. Bronchodilators help in dilation of constricted bronchioles for the flow of air in the obstructed airways: inhaled corticosteroids reduce exacerbations, inflammatory reaction and decrease mortality rates (4). Systemic adverse reactions of ICSs have been extensively studied, which are more common compared to infrequent local adverse reactions. Oro-pharyngeal candidiasis, dysphonia, pharyngitis, tongue abrasion, choking, tongue burning and cough are generally considered as common local adverse reactions which are more clinically significant and affect patient's quality of life by hampering daily food intake, compliance with medication and also mask symptoms of more serious diseases (5,6).

Local adverse reaction also depends on the drug formulation, dose, duration of use, regimen, characteristics of the inhaler device, intrinsic inflammation of the upper airways in respiratory disease patients, mechanical irritation caused by cough and concomitant inflammatory environmental factors (air pollution) and occupational exposure to chemical irritants. Similarly patients' related factors like physical disability, ageing, dementia, and difficulties in cognition leading to incorrect use of devices are major factors so careful attention to proper use of metered dose inhaler (MDI), and usage of spacer device are important factors to reduce local adverse reactions (7).
This study aims to find out various local adverse reactions on patients using inhaled corticosteroids on respiratory diseases and their management in order to prevent the further serious complications. Selection of better inhaled corticosteroids with appropriate doses for required duration are utmost important steps to prevent adverse drug reactions. It also helps in identifying proper use of inhaler device, spacers to prevent local adverse reactions and also helps in identification of various methods to manage the local adverse reactions.

Methods

This cross sectional descriptive study was designed to assess the prevalence, types and management of local adverse reactions associated with inhaled corticosteroids (ICS) among patients with respiratory diseases at a tertiary care teaching hospital. The study was conducted from August 2024 to 2025 for a period of six months after obtaining ethical approval from Institutional Review Committee (IRC) of Kathmandu Medical College (Ref:05082024/06).The study included patients diagnosed with respiratory diseases (e.g. Asthma, COPD) who are under treatment with inhaled corticosteroids (ICS) after taking informed verbal/written consent in the department of Internal Medicine.

Inclusion Criteria:
• Patients aged 18 years or older.
• Diagnosed with respiratory diseases such as asthma or COPD.
• Currently using ICS therapy.
• Capable of understanding study objectives and providing informed consent.
Exclusion Criteria:
• Pregnant or lactating women.
• Patients with mental health issues, cancers, or other terminal illnesses.
• Patients who are unable to provide informed consent.
• Uncooperative or unwilling participants

Data were collected using structured questionnaires in which demographic characteristics like (age, sex, occupation, education, and associated disease were included along with types of ICS used and their dose, and duration;) similarly types and frequency of local adverse effects were recorded along with measures taken to manage local adverse effects. A systematic random sampling method was used to calculate the sample size.

Sample size:

$n = z^2pq/e^2$

. Z = 1.96 (for 95% confidence level),

p = 0.10

(expected local adverse reactions)

e = 0.05 (desired precision),

N = 5000 (population size).

$$n = \frac{(1.96)^2 . 0.10 . (1-0.10) . 5000}{(0.05)^2 \quad 5000+1}$$

$$n = \frac{3.8416 . 0.10 . 0.90 . 0.9998}{0.0025}$$

n = 138.29. 0.9998

n = 138

Descriptive statistics (mean, standard deviation, frequency and percentage) were used to summarize patient characteristics and prevalence of adverse reactions. Chi square test was used to identify the effect of demographic and drug related factors with adverse reactions and their management. Data were analyzed using SPSS program, version 22.The study aimed to provide insights into optimizing ICS therapy and improving patient outcomes by enhancing understanding and management of local adverse reactions in this population.

Results

Out of 150 enrolled patients 138 patients participated in the study. The socio-demographic characteristics of patients are given in Table 1.There were 59(42.8%) from the age group below 60 years and 79(57.2%) were from age group more than 60 years. The number of male patients were 66(47.8%) and female 72(52.2%) respectively. On the basis of residence 58(42%) were residing in a village whereas 80(58%) were residing in the city. The Majority 52(37.7%) had obtained school level of education whereas 38(27.5%) were illiterate. On the basis of occupation 58(42%) were house builders, 31(22.5%) were office workers and 15(10.9%) were drivers. More than 70(50.7%) were suffering from respiratory diseases for more than 5 years and 68(49.3%) had been suffering from respiratory diseases less than 5 years duration. On the basis of associated diseases 88(63.8%) had respiratory disease along with other systemic diseases whereas 50(36.2%) were suffering from only respiratory disease. Chronic kidney disease followed by heart disease, diabetes mellitus and skin lesion disease are the other associated diseases.

Table 1: Socio-demographic characteristics of patients (n=138)

	Frequency	Percent
1.1 Age		
≤ 60 years	59	42.8
>60 years	79	57.2
Total	138	100.0
1.2 Sex		
Male	66	47.8
Female	72	52.2
Total	138	100.0
1.3 Residence		
Village	58	42.0
City	80	58.0
Total	138	100.0
1.4 Education		
Illiterate	38	27.5
School level	52	37.7
College level	39	28.3
University level	9	6.5
Total	138	100.0
1.5 Occupation		
Farmer	16	11.6
House builder	58	42.0
Office worker	31	22.5
Driving	15	10.9
Other	18	13.0
Total	138	100.0
1.6 Duration of disease		
≤5 years	68	49.3
> 5 years	70	50.7
Total	138	100.0
1.7 Associated other diseases		
Heart disease	23	26.1
Diabetes mellitus	20	22.7
Chronic kidney disease	27	30.7
Skin diseases	16	18.2
Other diseases	2	2.3
Total	138	100.0

On the basis of used of inhaled corticosteroids for the treatment of respiratory diseases (33.33%) had used Fluticasone followed by combination Salmeterol+Fluticasone (23.91%), Budesonide(22.46%) and Beclomethasone (20.29%).

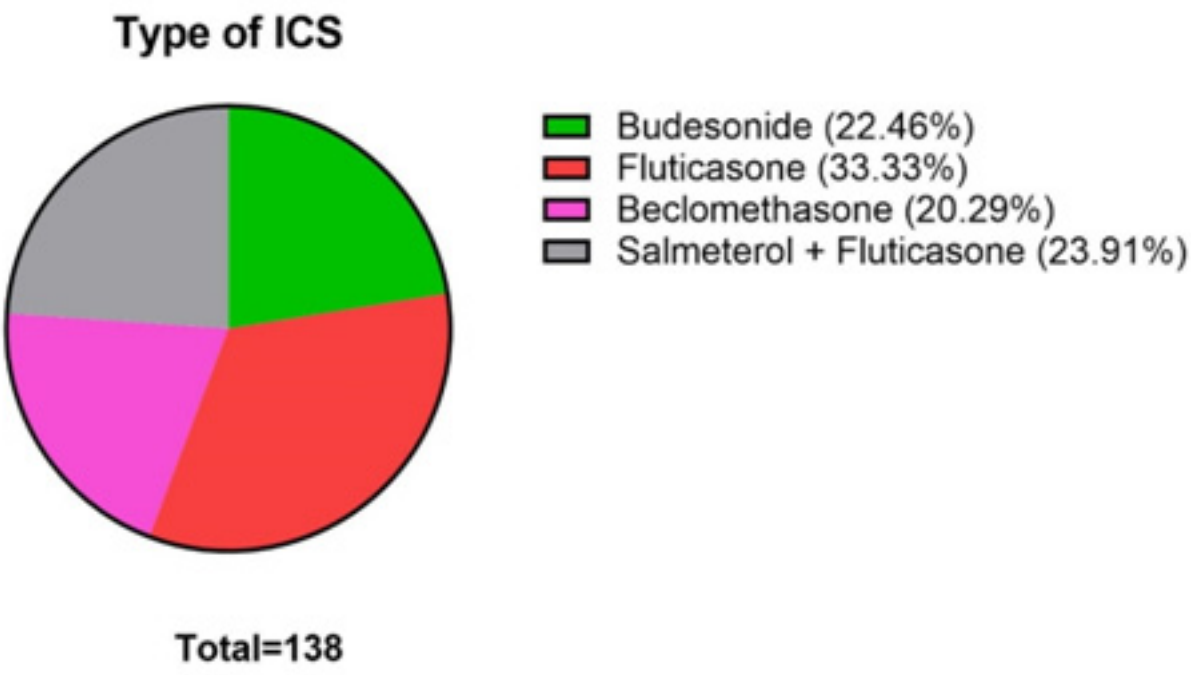

Figure 1: Types of inhaled corticosteroids used by the patients

Among 138 patients using inhaled corticosteroids for respiratory disease like asthma, chronic obstructive pulmonary disease 81 (58.7%) were found/ reported to have one or more signs of adverse drug reactions whereas 57(41.3) had not reported any adverse drug reaction.

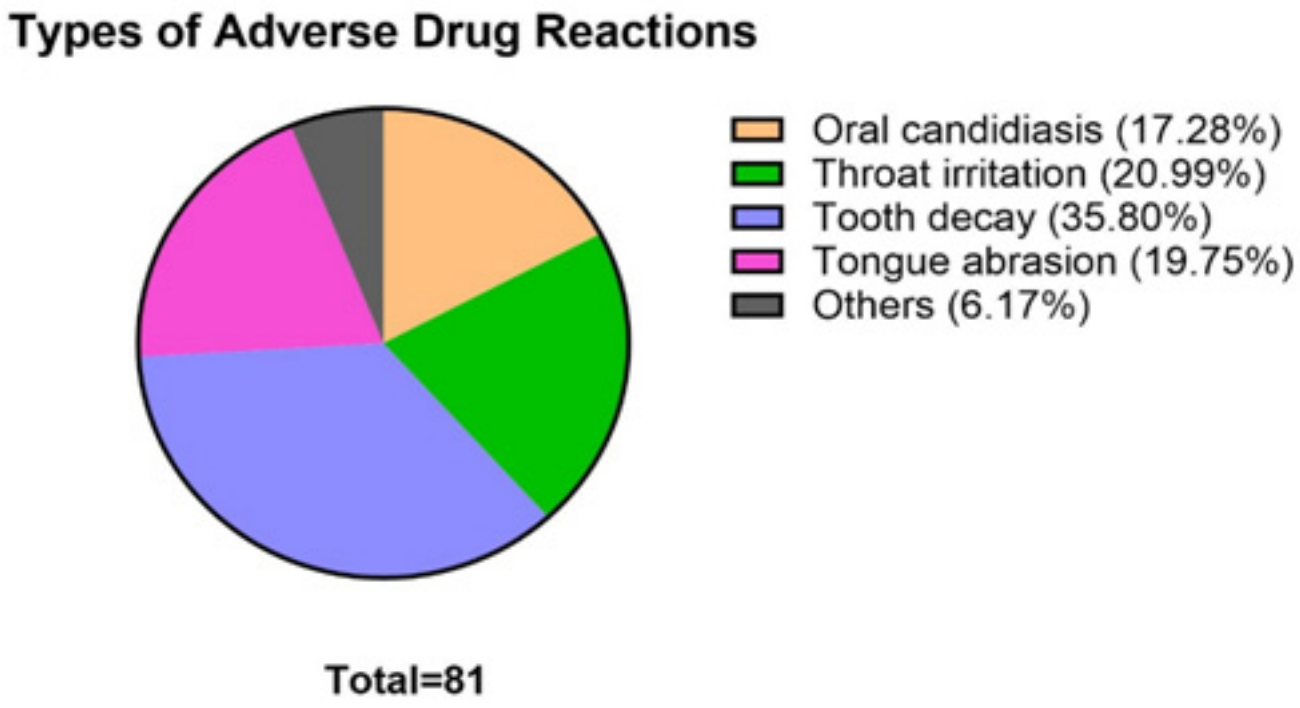

Figure 2: Types of adverse drug reactions from objective assessment

There was no significant difference in adverse reaction occurrence observed between age groups (p=0.37).On the basis of gender higher incidence was found in the female population which was significant (p<0.001).Similarly on the basis of education illiterate patients experienced more adverse drug reaction compared to educated (p<0.001).House builder reported more adverse effects compared to farmer and office worker in the context of occupation (p<0.001).

Table 2: Effect of demographic characteristics on adverse drug reactions (n=81)

Demographic feature	Frequency	Percent	Chi-square value (df)	p-value
Age			0.80 (1)	0.37
≤ 60 years	36	44.4		
>60 years	45	55.6		
Sex			10.86 (1)	<0.001
Male	39	48.1		
Female	42	51.8		
Education			27.17 (3)	<0.001
Illiterate	27	33.3		
School level	27	33.3		
College level	18	22.2		
University level	9	11.2		
Occupation			23.57 (4)	<0.001
Farmer	22	27.1		
House builder	35	43.2		
Office worker	9	11.1		
Driving	10	12.3		
Other	5	6.1		

Patients with disease duration ≤5 years reported more adverse effects compare to >5years (p=0.005).Similarly based on co-morbidities patients with diabetes mellitus were found with more adverse effects significantly (p=0.01).On the basis of dosage and its relation with adverse effects patients with 200mcg dosage had more adverse effects (p<0.001). Those patient who took twice daily dose (BID) were associated with higher incidence of adverse effects compare to single dose taking patients (p<0.001).

Table 3: Effect of asthma, other diseases and corticosteroid dosage on adverse drug reactions (n=81)

Variable	Frequency	Percent	Chi-square value (df)	p-value
Duration of disease			7.82 (1)	0.005
≤5 years	42	51.8		
>5 years	39	48.1		
Co-occurrence of other disease			10.59 (3)	0.01
Heart disease	21	25.9		
Diabetes mellitus	27	33.3		
Kidney disease	17	20.9		
Skin disease	16	19.7		
Type of ICS drug			3.85 (3)	0.28
Budesonide	17	20.9		
Fluticasone	23	28.3		
Beclomethasone	23	28.3		
Salmeterol+ Fluticasone	18	22.2		
Dosage of ICS drug			22.13 (2)	<0.001
100 mcg	12	14.8		
200 mcg	44	54.3		
250 mcg	25	30.8		
ICS dosage frequency			14.28 (1)	<0.001
OD	26	32.0		
BID	55	68.0		

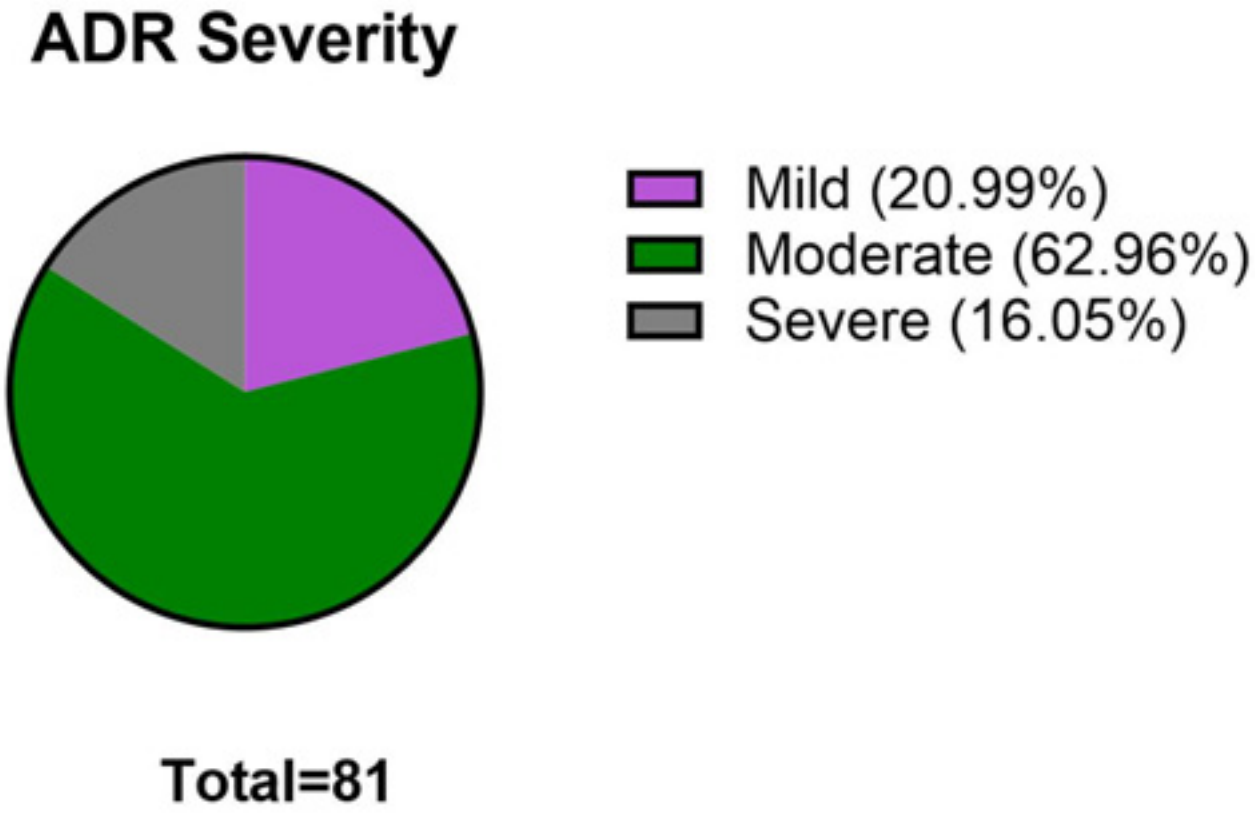

Figure 3: Severity of adverse drug reactions in the patients

Among 81 patients with adverse drug reactions, 16.0%had an episode almost every day, 56.8% at least once a week and 27.2% had it at least once a month. About 68 % of the patients had an adverse drug reaction onset after a month while 32% developed within a week of use of inhaled corticosteroids.

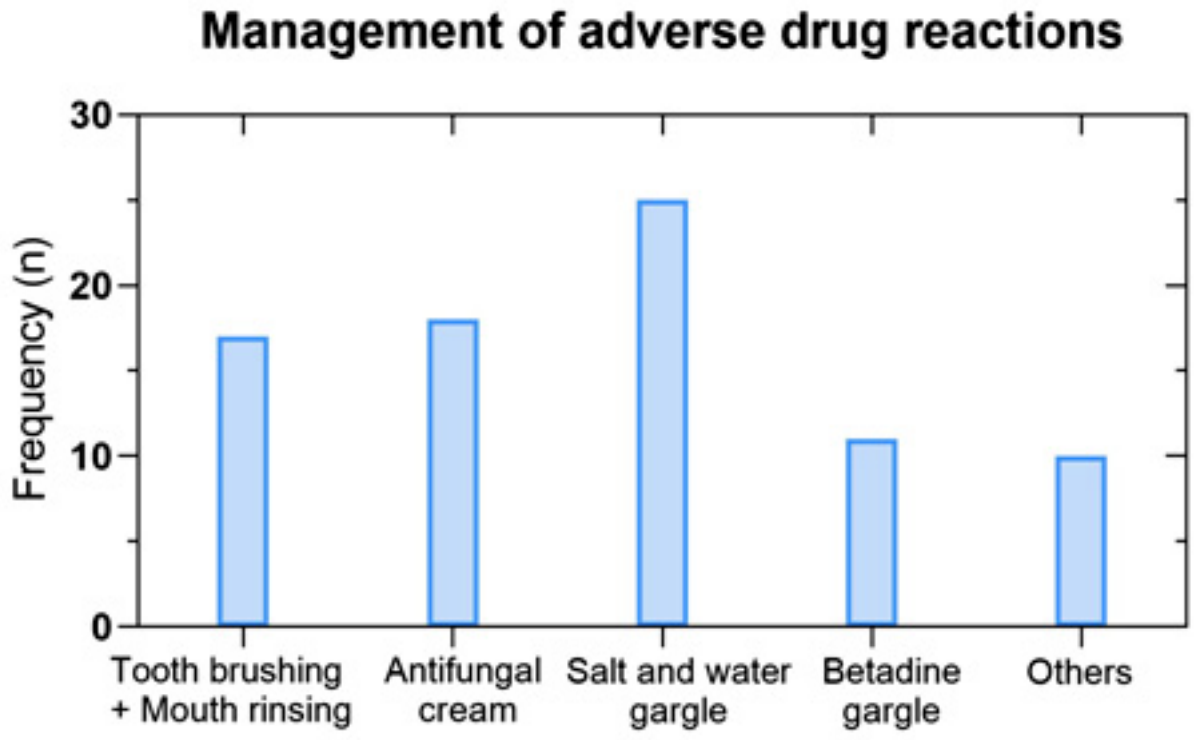

Figure 4: Management of adverse drug reactions adopted by the patients

For the management of adverse drug reaction 25(30.9%) had used salt and water gargle. Similarly 18(22.2%) had used antifungal cream for the treatment of oral candidiasis, 17(21%) had used mouthwash for rinsing and regular tooth brushing, 11(13.6%) had used Betadine gargle for the management whereas 10(7.2%) had used other methods like using oral ointments for the management of adverse reaction.

Discussion

This study provides a comprehensive analysis of the socio-demographic characteristics and adverse drug reactions associated with inhaled corticosteroids (ICS) therapy in patients with respiratory diseases and their management at tertiary care teaching hospital. Among 138 diagnosed respiratory disease patient using inhaled corticosteroids the majority of them 79 (57.2%) were over 60 years of age which is similar with the study conducted by Cooper et al which might be due to age related changes in drug metabolism (8).Another similar study found that asthma was more prevalent in children and COPD was more prevalent in older patients (9).Sex-based differences were also notable, with 66 (47.8%) male and 72 (52.2%) female participants which is similar with the study conducted in Nepal by Adhikari et al in which 54% of the patients were female and also Cooper had similar findings which might be due to variations in hormone levels and differences in immune system (1).

Regarding residence, 58 (42%) of the patients were from rural areas, while 80 (58%) resided in urban settings which is similar with the findings of a study done in Nepal which could be linked to increased environmental pollution, lifestyle factors, and greater healthcare access leading to more frequent prescriptions (10).Education level significantly influenced ADR occurrence. Among participants, 38 (27.5%) were illiterate, 52 (37.7%) had attained school-level education, 39 (28.3%) held a bachelor's degree, and 9 (6.5%) had a university-level education. Lower educational attainment has been associated with improper medication use and poor adherence, thereby increasing the risk of ADRs (11). Occupational based analysis showed that 58(42%) were house builders,31(22.5%)were office workers,15(10.9%) were drivers,16(11.6%)were farmers and 18(13%) were involved in other professions which is similar with the study conducted on a brick kiln in Nepal which clarify occupational factors contributing to respiratory disease, particularly in construction workers exposed to dust, chemicals and other irritants (12).Comorbid conditions were present in 88 (63.8%) patients, with chronic kidney disease (30.7%), heart disease (26.1%), diabetes mellitus (22.7%), and skin diseases (18.2%) being the most prevalent which is similar with the findings of Augusti et al which might lead to alteration in drug metabolism and enhanced susceptibility to adverse drug reaction requiring careful monitoring for the patient (13, 14).

Among the use of types of Inhaled corticosteroids in respiratory diseases fluticasone was more commonly prescribed followed by salmetorol+Fluticasone, budesonide and Beclomethasone which is similar with the study conducted in Finland where patients were prescribed with long acting bronchodilator followed by inhaled corticosteroids which is effective in reducing inflammatory reaction and bronchodilatation (15).

On the basis of reported local adverse drug reaction 81 (58.7%) reported experiencing one or more adverse drug reaction which is similar with the study in which 58% of the patient had complained of local adverse effects (16).The significant association of ADRs with gender ($p < 0.001$), education level ($p < 0.001$), and occupation ($p < 0.001$) suggests that these demographic factors influence the likelihood of experiencing Inhaled corticosteroid related adverse effects. Female patients and illiterate individuals reported a higher incidence of ADRs which is similar with the finding of Liu et al which may be due to biological differences in drug metabolism and a lack of awareness regarding proper Inhaled corticosteroids use, respectively. Additionally, house builders were found to be more affected than farmers and office workers, which could be attributed to occupational exposures that may exacerbate respiratory conditions (11, 17).

The study also examined the effect of disease duration and co-morbidities on adverse drug reaction occurrence. Patients with disease duration of ≤5 years had a significantly higher prevalence. Additionally, individuals with diabetes mellitus reported more ADRs ($p = 0.01$), which is similar with the study done by See KC and Suissa et al which has found the rise in 34% of diabetes incidence in patients using inhaled corticosteroids in a large group of COPD and asthma patients which can be linked to corticosteroid-induced hyperglycemia and immune system alterations (18, 19).Inhaled Corticosteroids dosage and frequency were critical factors influencing adverse drug reaction occurrence. Patients using 200 mcg dosages had significantly more adverse drug reaction compared to other doses. Moreover, those on a twice-daily regimen experienced more adverse drug reactions compared to those on a once-daily regimen, indicating a possible dose-dependent relationship between ICS use and adverse effects. This finding aligns with previous studies suggesting that higher cumulative exposure to ICS increases the risk of local and systemic side effects (5).

In terms of ADR severity and onset, 16% of patients experienced daily ADR episodes, 56.8% at least once a week, and 27.2% at least once a month. Notably, 68% of the patients developed ADRs after a month of ICS use, while 32% experienced ADRs within the first week. A similar study (81.5%) reported at least one adverse effect, and 131 (65.5%) had a daily perception of at least one symptom. Likewise 28.5% had vocal symptoms and 77% had pharyngeal symptoms respectively. The most commonly reported adverse effects were dry throat, throat clearing, sensation of thirst, and hoarseness which suggest that prolonged ICS exposure may increase the risk of ADRs, necessitating regular patient monitoring (20). In our study the most common local adverse drug reaction was tooth decay(35.80%) followed by throat irritation (20.99%)tongue abrasion(19.75%),oral candidiasis (17.28%) and others taste disturbances, dry mouth, hoarseness of voice which could be due to reduced salivary flow leading to increased risk of dental caries, local deposition of inhaled corticosteroids in the Oro-pharyngeal mucosa and improper use of inhaler (20.21).A similar study had shown rise of incidence of oral candidiasis from 3.3% to 16.3% after the initiation of use of inhaled corticosteroids (5).

Management strategies for ADRs varied among patients. The most common methods included salt and water gargle (30.9%), which is similar to the study done by Kajiwara et al in which gargling with water after use of ICs was effective in reducing local adverse effects (22).Similarly,was the use of antifungal cream for oral candidiasis, mouthwash and regular tooth brushing, Betadine gargle and other methods such as oral ointments. These strategies highlight the importance of patient education in minimizing ICS-related ADRs and maintaining medication adherence. Similar studies suggest that digital measurement of use of medicaments inhaler along with spacers are effective in reducing local adverse effects (23).The study was conducted in a single setting tertiary care hospital with limited number of patients but still it can help to know the prevalence of adverse effects and methods like proper use of inhalers with appropriate doses and duration of therapy which will be effective in preventing adverse drug reactions and it can help to manage the adverse effects through various methods like use of salt and water gargling, using mouthwashes and proper maintenance of oral hygiene in respiratory disease patients.

Conclusion

Inhaled corticosteroids are essential for managing asthma and COPD which are the most common respiratory diseases but they are associated with significant local adverse effects, which can impact patient adherence and treatment outcomes. This study concluded that ICS-related local adverse reactions, such as tooth decay, throat irritation, and tongue abrasion, were prevalent, particularly among females and illiterate patients. Higher ICS doses and frequent usage increased the risk of adverse drug reaction. Preventive measures, including proper inhaler techniques, salt and water gargling, and mouthwash use, can help mitigate these effects. Educating patients on ICS side effects and management strategies is crucial in improving adherence and ensuring prevention of long term complications of respiratory disease.

Author Contribution

Concept design: BR,SK,SP,SG; Literature search: BR,SK,SP,SG; Data collection: BR,SK,SP; Data analysis: BR, SG, SK; Draft manuscript: BR,SP,SK,SG; Final manuscript and accountability: BR,SK,SP,SG

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Conflict of interest
None

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