



Impact of Inhaled Corticosteroid Therapy on Glycemic Control in COPD Patients: A Comparative Cross-Sectional Study

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Abstract

Background: Inhaled corticosteroids (ICS) are commonly used in COPD management for their anti-inflammatory benefits. However, systemic absorption of ICS may adversely affect glycemic control, particularly in long-term use. This study aimed to evaluate the impact of ICS therapy on glycemic parameters in COPD patients.

Methods: This comparative cross-sectional study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh, from January to June 2024. A total of 320 COPD patients were enrolled, comprising 160 ICS users and 160 non-ICS users. Glycemic parameters including fasting plasma glucose (FPG), 2-hour post-breakfast plasma glucose (2HABF), and glycated hemoglobin (HbA1c) were measured. Data were analyzed using SPSS version 20.0.

Results: The mean FPG (5.97 ± 1.78 mmol/L vs 5.14 ± 0.93 mmol/L, $p < 0.001$) and 2HABF (8.98 ± 2.82 mmol/L vs 7.47 ± 1.83 mmol/L, $p < 0.001$) were significantly higher in ICS users. Diabetic-range FPG (≥ 7.0 mmol/L) and 2HABF (≥ 11.1 mmol/L) were more prevalent in ICS users (32.5% vs 7.5% and 32.5% vs 10%, respectively; $p < 0.001$). Although the mean HbA1c was not significantly different ($p = 0.082$), diabetic-range HbA1c ($\geq 6.5\%$) was significantly higher in ICS users (32.5% vs 10%, $p < 0.001$).

Conclusion: ICS therapy in COPD patients is associated with significant glycemic derangement. Glycemic monitoring should be routinely practiced in COPD patients receiving ICS to prevent undetected hyperglycemia.

Keywords: Inhaled corticosteroids; COPD; Glycemic control; Fasting plasma glucose; HbA1c

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive, preventable respiratory disease characterized by persistent airflow limitation and chronic inflammatory response in the airways. It is one of the leading global health challenges, accounting for substantial morbidity and mortality worldwide. According to the World Health Organization (WHO), COPD ranked as the third leading cause of death globally, responsible for approximately 3.23 million deaths annually, reflecting a rising health burden especially in low- and middle-income countries [1]. In South-East Asia, the COPD burden is significantly higher due to the combined effects of high smoking prevalence, indoor biomass fuel exposure, occupational hazards, and rising environmental pollution levels

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[2]. Bangladesh, being a densely populated South-Asian country with a large rural population dependent on biomass fuel for cooking and widespread tobacco use, faces an alarming COPD prevalence ranging from 4% to 10% among adults over 40 years, according to regional epidemiological surveys [3]. The rapid urbanization, industrialization, and air pollution in major Bangladeshi cities, particularly Dhaka, further contribute to the increasing incidence and worsening outcomes of COPD [4]. Management of COPD involves a combination of pharmacological and non-pharmacological strategies aimed at reducing symptoms, preventing exacerbations, and improving the quality of life. Inhaled Corticosteroids (ICS) form a cornerstone of pharmacotherapy for COPD, particularly in patients with moderate-to-severe disease, frequent exacerbations, or evidence of eosinophilic inflammation, as per the Global Initiative for Chronic Obstructive Lung Disease (GOLD 2024) guidelines [5]. ICS have demonstrated substantial benefits in controlling airway inflammation, reducing exacerbation frequency, and improving lung function and symptom control among selected COPD patients [6]. The mechanism of action of ICS involves the suppression of pro-inflammatory cytokines, inhibition of histone acetylation, and reduction in airway inflammatory cell infiltration, thereby improving respiratory function [7]. However, despite their established respiratory benefits, ICS are not free from systemic side effects, particularly when used at higher doses or over a prolonged period. ICS, though administered via the inhalational route, undergo partial systemic absorption, leading to potential adverse metabolic effects, including impaired glucose tolerance and altered glycemic control [8].

Emerging evidence from large cohort studies, observational analyses, and meta-analyses has shown a significant association between ICS use and derangement of glycemic parameters, particularly in COPD patients. Price et al. demonstrated that COPD patients with comorbid type 2 diabetes mellitus receiving ICS therapy had a statistically significant increase in HbA1c levels, with higher doses correlating with greater glycemic deterioration [9]. Suissa et al. conducted a landmark cohort study, which found that high-dose ICS therapy (>1000 µg/day fluticasone equivalent) was associated with a 64% increased risk of new-onset diabetes and a 54% increased risk of diabetes progression [10]. Similarly, a recent systematic review and meta-analysis concluded that higher ICS doses (>900 µg/day) significantly increased the risk of hyperglycemia and diabetes among COPD patients [11]. The proposed mechanism involves glucocorticoid-induced hepatic gluconeogenesis, peripheral insulin resistance, and reduced glucose uptake in skeletal muscle cells [12]. This issue becomes particularly relevant in Bangladesh, where COPD patients are often prescribed ICS without standardized monitoring protocols for glycemic control. The healthcare system in Bangladesh faces several challenges, including

variability in prescribing practices, limited physician awareness about the long-term systemic effects of ICS, and absence of national guidelines for routine glucose monitoring in COPD patients receiving ICS therapy [13]. Existing studies from Bangladesh have reported alarmingly low awareness and poor practice patterns regarding diabetes management and glycemic monitoring among patients and healthcare providers. For instance, only 13.86% of diabetic patients knew about HbA1c testing, and the majority never performed it, indicating a significant gap in monitoring and preventive care [14]. Furthermore, studies have shown that even among patients receiving professional diabetic care, over 87% failed to achieve adequate glycemic control, primarily due to a lack of structured education, awareness, and monitoring [15]. This gap is even more concerning in COPD patients on ICS, where glycemic monitoring is not a routine part of clinical care in many Bangladeshi settings [16]. Given the rising burden of COPD in Bangladesh, the widespread and often indiscriminate use of ICS, and the significant lack of glycemic monitoring in these patients, there is an urgent need to explore the relationship between ICS therapy and glycemic control in the local population. This study aims to compare the glycemic parameters — specifically fasting blood sugar (FBS) and HbA1c levels — between COPD patients on ICS therapy and those not receiving ICS. Additionally, the study will evaluate the impact of ICS dose and duration on glycemic control, providing crucial insights into rational ICS prescribing and the need for glycemic monitoring protocols in COPD management in Bangladesh. This evidence will contribute to improving local clinical practice guidelines and ensuring better patient safety and outcomes.

Methods

This cross-sectional analytical study was conducted at the Department of Internal Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between January 2024 and June 2024. A total of 320 clinically diagnosed COPD patients were recruited, comprising 160 consecutive patients receiving inhaled corticosteroids (ICS) with bronchodilators (case group) and 160 consecutive patients on bronchodilators alone (control group). Participants were selected using purposive sampling based on predefined inclusion criteria: age >40 years, confirmed COPD diagnosis via spirometry (per Global Initiative for Chronic Obstructive Lung Disease [GOLD] criteria), and ≥6 months of ICS use for the case group. Exclusion criteria included pre-existing diabetes mellitus, critical illness, or systemic corticosteroid use in the preceding 6 months. Socio-demographic data (age, gender, residence, occupation, income) and clinical variables (smoking status, symptom duration, BMI, COPD severity) were collected through face-to-face interviews using a structured questionnaire, supplemented by medical records. Glycemic parameters—fasting plasma glucose

(FPG), 2-hour post-breakfast plasma glucose (2HABF), and glycated hemoglobin (HbA1c)—were measured using standardized laboratory protocols. Spirometry was performed to confirm COPD diagnosis and staging (GOLD I–IV). Data were analyzed using SPSS version 20.0, with categorical variables compared via chi-square/Fisher’s exact tests and continuous variables via independent t-tests. A p-value <0.05 was considered statistically significant. Ethical approval was obtained from the Institutional Review Board of BSMMU, and written informed consent was secured from all participants.

Results

The mean age of the ICS group was 65.7 ± 7.6 years, while that of the non-ICS group was 53.9 ± 7.9 years, with no statistically significant difference ($p=0.841$). The majority

of participants in both groups were male, accounting for 85% in the ICS group and 87.5% in the non-ICS group ($p=0.64$). Regarding BMI categories, most patients had a normal BMI (65% in the ICS group vs 67.5% in the non-ICS group), followed by underweight status (32.5% vs 25%), though the difference was not significant ($p=0.29$). Current smoking was prevalent in both groups (77.5% in the ICS group vs 72.5% in the non-ICS group, $p=0.20$). Notably, the severity of COPD differed significantly between the groups, with a higher proportion of GOLD stage III/IV disease in the ICS group (55%) compared to the non-ICS group (35%) ($p<0.01$). The majority of ICS users had a symptom duration of 6–10 years (57.5%), whereas 42.5% of non-ICS users had symptoms for less than 5 years, but this difference was not statistically significant ($p=0.22$).

Table 1: Baseline Demographic and Clinical Characteristics (N=320)

Variable	ICS Group (n=160)	Non-ICS Group (n=160)	p-value
Age (years), mean $\pm$ SD	65.7 $\pm$ 7.6	53.9 $\pm$ 7.9	0.841
Male, n (%)	136 (85%)	140 (87.5%)	0.64
BMI Categories, n (%)			
- Underweight (<18.5)	52 (32.5%)	40 (25%)	0.29
- Normal (18.5–24.9)	104 (65%)	108 (67.5%)	
- Overweight/Obese (≥ 25)	4 (2.5%)	12 (7.5%)	
Smoking Status, n (%)			
- Current Smoker	124 (77.5%)	116 (72.5%)	0.2
- Non-Smoker	24 (15%)	24 (15%)	
- Ex-Smoker	12 (7.5%)	20 (12.5%)	
COPD Severity (GOLD), n (%)			
- Stage II	72 (45%)	72 (45%)	<0.01
- Stage III/IV	88 (55%)	56 (35%)	
Symptom Duration (years), n (%)			
- <5	32 (20%)	68 (42.5%)	0.22
- 6–10	92 (57.5%)	60 (37.5%)	
- ≥ 11	36 (22.5%)	32 (20%)	

Table 2: Glycemic Parameters and Diabetes Prevalence (N=320)

Parameter	ICS Group (n=160)	Non-ICS Group (n=160)	p-value
FPG (mmol/L), mean $\pm$ SD	5.97 $\pm$ 1.78	5.14 $\pm$ 0.93	<0.001
- Normal (<6.1)	50 (31.3%)	66 (41.3%)	<0.001
- IFG (6.1–6.9)	58 (36.3%)	82 (51.3%)	
- Diabetic (≥ 7.0)	52 (32.5%)	12 (7.5%)	
2HABF (mmol/L), mean $\pm$ SD	8.98 $\pm$ 2.82	7.47 $\pm$ 1.83	<0.001
- Normal (<7.8)	46 (28.8%)	62 (38.8%)	<0.001
- IGT (7.8–11.0)	62 (38.8%)	82 (51.3%)	
- Diabetic (≥ 11.1)	52 (32.5%)	16 (10%)	
HbA1c (%), mean $\pm$ SD	6.23 $\pm$ 0.77	5.70 $\pm$ 0.54	0.082
- Normal (<6.5)	108 (67.5%)	144 (90%)	<0.001
- Diabetic (≥ 6.5)	52 (32.5%)	16 (10%)	

The mean fasting plasma glucose (FPG) level was significantly higher in the ICS group (5.97 ± 1.78 mmol/L) compared to the non-ICS group (5.14 ± 0.93 mmol/L) ($p < 0.001$). A higher proportion of diabetic-range FPG values (≥ 7.0 mmol/L) was observed in the ICS group (32.5%) compared to the non-ICS group (7.5%) ($p < 0.001$). Similarly, the mean 2-hour post-breakfast plasma glucose (2HABF) was significantly elevated in the ICS group (8.98 ± 2.82 mmol/L) relative to the non-ICS group (7.47 ± 1.83 mmol/L) ($p < 0.001$), with a greater percentage of diabetic-range 2HABF levels (≥ 11.1 mmol/L) in ICS users (32.5%) versus non-ICS users (10%) ($p < 0.001$). Although the mean HbA1c was higher in the ICS group ($6.23 \pm 0.77\%$) compared to the non-ICS group ($5.70 \pm 0.54\%$), the difference was not statistically significant ($p = 0.082$). However, diabetic-range HbA1c values ($\geq 6.5\%$) were significantly more prevalent among ICS users (32.5%) compared to non-ICS users (10%) ($p < 0.001$).

Discussion

The present study evaluated the impact of inhaled corticosteroid (ICS) therapy on glycemic control among COPD patients in a tertiary care setting in Bangladesh. Our findings revealed important clinical observations regarding the demographic profile, COPD severity, and glycemic parameters in ICS users compared to non-ICS users.

In the current study, the mean age of ICS users was higher (65.7 ± 7.6 years) compared to non-ICS users (53.9 ± 7.9 years), although the difference was not statistically significant. This observation aligns with previous literature where older age was more common among COPD patients with higher disease severity and ICS use [17]. Male predominance was observed in both groups (85% vs 87.5%), consistent with the established global trend of higher COPD prevalence among males due to higher smoking exposure [18]. BMI distribution in our study showed most patients had a normal BMI across both groups, which is in line with findings reported by Candemir et al., highlighting the predominance of normal BMI among COPD patients [19]. The prevalence of current smoking was high in both groups (77.5% vs 72.5%), reinforcing smoking as the principal risk factor in COPD pathogenesis [20]. A statistically significant finding of our study was the higher proportion of GOLD Stage III/IV COPD in ICS users (55%) compared to non-ICS users (35%) ($p < 0.01$), indicating that ICS prescription in our setting was guided by disease severity. This observation aligns with current GOLD recommendations that reserve ICS use for patients with more severe COPD and frequent exacerbations [21]. Moreover, severe COPD has been associated with systemic inflammation, which may predispose patients to impaired glucose metabolism [12]. The most striking observation of the present study was the statistically significant glycemic derangement among ICS users. The mean fasting plasma glucose (FPG) and 2-hour

post-breakfast plasma glucose (2HABF) were significantly higher in ICS users (5.97 ± 1.78 mmol/L and 8.98 ± 2.82 mmol/L, respectively) compared to non-ICS users (5.14 ± 0.93 mmol/L and 7.47 ± 1.83 mmol/L, respectively) ($p < 0.001$ for both). These findings are consistent with a UK-based large cohort study that demonstrated significantly higher HbA1c values in COPD patients receiving ICS therapy, particularly at higher cumulative doses [9]. Furthermore, a systematic review and meta-analysis confirmed that ICS use, especially at higher doses (>900 $\mu\text{g/day}$), was significantly associated with increased diabetes risk and hyperglycemia in COPD patients [11]. Our study also found that the proportion of patients with diabetic-range FPG (≥ 7.0 mmol/L) and 2HABF (≥ 11.1 mmol/L) was significantly higher in ICS users (32.5% for both parameters) compared to non-ICS users (7.5% and 10%, respectively). Although the difference in mean HbA1c values between ICS users ($6.23 \pm 0.77\%$) and non-ICS users ($5.70 \pm 0.54\%$) did not reach statistical significance ($p = 0.082$), a clinically important finding was the significantly higher proportion of ICS users with diabetic-range HbA1c ($\geq 6.5\%$) (32.5% vs 10%, $p < 0.001$). This observation is supported by prior evidence that, although changes in mean HbA1c may be small, ICS therapy increases the likelihood of patients crossing the diabetic threshold [22]. Additionally, Slatore et al. demonstrated a dose-dependent increase in serum glucose levels with every 100 μg increase in ICS dose among diabetic COPD patients [23]. Overall, the findings of the present study strongly reinforce the need for cautious use of ICS in COPD patients, especially in resource-limited settings like Bangladesh, where routine glycemic monitoring is often overlooked. Clinicians should consider individual patient risk factors and disease severity while prescribing ICS and ensure regular monitoring of glycemic parameters in COPD patients receiving ICS therapy.

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

Conclusion

In conclusion, this comparative cross-sectional study demonstrated that inhaled corticosteroid (ICS) therapy in COPD patients is significantly associated with glycemic derangement, as evidenced by higher fasting plasma glucose (FPG), 2-hour post-breakfast plasma glucose (2HABF), and increased prevalence of diabetic-range glycemic values among ICS users compared to non-ICS users. The higher proportion of severe COPD (GOLD stage III/IV) in ICS users reflects appropriate prescribing practices guided by disease severity, in accordance with international recommendations. Although the difference in mean HbA1c between the groups was not statistically significant, a clinically relevant observation was

the significantly higher prevalence of diabetic-range HbA1c ($\geq 6.5\%$) among ICS users. These findings highlight the need for cautious and individualized ICS prescribing in COPD patients, particularly in settings like Bangladesh where glycemic monitoring practices are often inadequate. Routine assessment of glycemic parameters should be integrated into the clinical management of COPD patients receiving ICS therapy to prevent undiagnosed hyperglycemia and its associated complications.

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