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# Glycaemic Status of Patients with Chronic Obstructive Pulmonary Disease on Inhaled Corticosteroid

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**Abstract:** *Background*: Although the hyperglycaemic effects of systemic glucocorticoid therapy are well known, the effect of inhaled corticosteroids (ICS) on carbohydrate metabolism is still a subject of debate. The systemic bioavailability of ICS is claimed to be minimal and the side effects are negligible. *Objectives*: The aim of the study was to assess to the effect of inhaled corticosteroid on glycaemic status in patients with COPD. *Methods*: This Cross-sectional analytical study of COPD patients attending at Internal Medicine department of BSMMU, Dhaka, Bangladesh, between May 2016 to April 2017. After approval of the protocol by IRB and ethical committee, cross-sectional analytical study was done in the department of Internal Medicine, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Total 80 COPD patients were recruited consecutively upon fulfilling the inclusion criteria. Socio-demographic data and disease related data were collected by face to face interview using a semi-structured case record form. The COPD patients were categorized according to global initiative for obstructive lung diseases (GOLD) criteria. The collected data then edited, analyzed and be presented as graphs, tables & charts. *Results*: There was no statistical difference in the mean age of both group which was 53.85±7.9 and 56±7.6 in control and case respectively. 77.5% of the case and 72.5% of control population are indulging in smoking while only 15% from each group are non-smoker. Large number of cases are service holder and businessman 35% and 20%, which is true for control group also 20% and 47.5%. Most of the cases are from higher socioeconomic background (45%), whereas in control group it is 37.5%. In 20% cases symptoms duration was less than 5 years, where as in control group it was 42.5%. 32% of cases and 7.5% of control group were diagnosed as diabetic when fasting plasma glucose taken into account, while in case of 2- hours plasma glucose the number were 32.5% and 10% respectively and in case of HbA1c the number were 23.5% and 10% respectively. *Conclusion*: Pre-diabetes and diabetes are highly prevalent among people with COPD which remain undiagnosed & untreated. So, the study findings will help in early intervention of glycaemic control among COPD patients.

**Keywords:** Glycaemic, Chronic Obstructive, Pulmonary Disease, Inhaled Corticosteroid, Plasma Glucose, Glycaemic Status

# 1. Introduction

Chronic obstructive pulmonary disease (COPD) is a group of chronic inflammatory pulmonary disorders that encompasses emphysema, chronic bronchitis and small airway obstruction and is characterized by largely irreversible airflow obstruction affecting around 10% of the population over the age of 40 yrs. [1] Its main feature is poorly reversible obstruction of airflow that is progressive and is associated with a systemic inflammatory response. Consequently, the widespread use of inhaled corticosteroids at higher doses in patients with COPD, along with the elevated incidence of diabetes in this age group and their uncertain effectiveness, can have an impact on the risk-benefit profile of inhaled corticosteroids in COPD. [2] Type 2 diabetes mellitus, chronic obstructive pulmonary disease (COPD), and asthma are increasing in prevalence worldwide. Many patients have an indication to use inhaled corticosteroids (ICS) for coexisting asthma or COPD. ICS have been shown to have systemic effects, but their effect on glucose metabolism in patients has not been well defined. Although considered a safe therapy, there are concerns about the systemic effects of ICS, including bone formation in children and cataract development in adults. Additionally, several studies suggest ICS can suppress the function of the hypothalamic pituitary adrenal axis. While such adverse effects have been detected in research studies, they are thought not to be clinically important. A significant increase (1.0%) in glycosylated hemoglobin (%HbA1c) and persistent glucosuria has been reported previously in a patient with asthma who used inhaled fluticasone propionate (FP) at a high dose (2 mg/day) [3] It is unclear whether lower doses of ICS might disturb glucose metabolism. Worthy of additional consideration is the increasing evidence, independent of glucocorticoid use, that COPD is associated with a higher risk of developing type 2 diabetes mellitus. [4] Analysis of the Nurses' Health Study Cohort showed an association between COPD and onset of diabetes mellitus, which did not occur with asthma despite similar uses of corticosteroids. [5] The American Diabetes Association recommends glucose monitoring be initiated in any patient not known to be diabetic who receives therapy associated with high risk for hyperglycaemia, including high-dose glucocorticoid therapy. [6] Non-critically ill hospitalised patients are advised to have a random BGL of <10 mmol/L (unless tighter control was used previously or insulin therapy is used). It is clear that prudent glycaemic observation and management should occur in respiratory wards. Prednisolone is an oral corticosteroid with a plasma half-life of 2–4 h. However, the duration of action has been reported to be 12–36 h. [7] A recent study explored the relationship between prednisolone dosing and BGL pattern in a population of patients admitted to hospital with COPD. Despite the continued prevalence of COPD and DM, the high morbidity and mortality rates, there has been little research on the impact of inhaled corticosteroid on patients' glycaemic control.

# 2. Objectives

a) General objective:

To determine the effect of inhaled corticosteroid on glycaemic status in patients with COPD.

b) Specific Objectives:

1) To determine HbA1C of COPD patients on ICS.
2) To determine the fasting plasma glucose (mmol/L) & 2 hrs after breakfast plasma glucose (mmol/L) of COPD patients on ICS.

# 3. Methodology and Materials

This was a cross-sectional analytical study. This study was conducted at the department of Internal Medicine in Bangobandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, during May, 2016-April, 2017. The protocol of this study was approved by IRB and ethical committee. A total of 80 patients with COPD were included in this study, of them clinically diagnosed 40 consecutive COPD patients who were receiving both bronchodilator & inhaled corticosteroids were recruited as case group and clinically diagnosed 40 consecutive COPD patients receiving only bronchodilator without inhaled corticosteroid/systemic steroid were recruited as control, group. Spirometry was done for confirmation and staging of COPD according to GOLD at indoor and OPD patients of Department of Internal Medicine, BSMMU. Sample size was calculated by using the following formula: (Patients per group (n)=$f$ (α, β) × 2 × $\frac{(SD)^2}{d^2}$, (when comparing two independent group means) where, n=sample size in each group, $f$ (α; β)=10.5 for 90% $d^2$ power with 5% (0.05) significance, d=3 (we wish to detect difference between two means), SD=4 (Pooled standard deviation of each group) Using the above formula the expected sample size was calculated as 76. But due to time constrains sample size was finally fixed as 40 in each group. Samples were selected using purposive sampling technique through inclusion and exclusion criteria of this study. A predesigned questionnaire for socio-demographic and other variables and a check list for collection of disease information and measurement were used for data collection. Face to face interview was conducted by the Researcher himself. In case of illiterate patient data was collected from the patient's attendant. The collected data were analyzed and performed by statistical package for social science (SPSS), version-20. All collected data were checked and verified thoroughly to reduce inconsistency and for omission and improbabilities. Categorical variables were compared by chi-square test. In case group, association of glycaemic status with different

doses of ICS was seen by Pearson's correlation coefficient. The level of significance was set at 5% and p-value of < 0.05 was considered as significant.

1. Inclusion Criteria
   1) Case:
      a) Age more than 40 years
      b) Gender (male & female)
      c) Patients on inhaled bronchodilator & corticosteroid therapy for > 6 months
   2) Control:
      a) Age more than 40 years
      b) Gender (male & female)
      c) Patients who were not taking inhaled corticosteroid/systemic steroid during his /her illness
2. Exclusion Criteria
   1) Patients with prior diagnosis of pre- diabetes & diabetes mellitus with COPD
   2) Critically ill patients

# 4. Results

A total of 80 patients with COPD were included in this study, of them clinically diagnosed 40 consecutive COPD patients who were receiving both bronchodilator & inhaled corticosteroids were recruited as case group and clinically diagnosed 40 consecutive COPD patients receiving only bronchodilator without inhaled corticosteroid/systemic steroid were recruited as control, group. Table 1 shows the age distribution of the control group. The mean age of case group was 65.65±7.63 years, on the other hand, the mean age of control group was 53.85±7.9 years (p=0.841). Table 4 shows the gender distribution of both the case and control groups having corticosteroids. Among the total studied patients, male was 69 (86.30%), and female were 11 (13.70%). Total underweight (<18.5) were 23 (28.80%), normal weight was 53 (66.30%), over weight (25.0-29.9, were 03 (3. 80%), obese was 01 (2,5%) in both the groups. Total rural residences were 46 (57.5%), urban residences were 34 (42.5%) in both the cases (Table 6). Total illiterate was 31 (38.80%), primary level was 12 (15%), secondary level was 11 (13.80%), higher secondary level was 17 (21.30%), bachelor or above was 09 (11.30%) in both the cases (Table 7). Total service was 22 (27.5%), business was 29 (36.30%) in both the cases, retired were 15 (18.80%), unemployed were 14 (17.5%) in both the groups (Table 8). Total monthly income, (< 10000 BDT) were 17 (21.30%), monthly income (10000 -30000BDT) were 30 (37.5%) in both the groups, monthly income (>30000BDT) were 33 (41.30%) in both the groups (Table 9). Total smokers were 60 (75%), non-smokers were 12 (15%), ex-smokers were 08 (10%) in both the groups (Table 10). Total duration of symptom (<5years) were 25 (31.30%), duration of symptom, (6-10years) were 40 (50%), duration of symptom, (11-15years) were 15 (18.80%) in both the groups (Table 11). In case group, stage (i) was 00 (00%), and in control group, stage (i) was 07 (17.55). The total stage (i) was 07 (8.80%) in both the groups. In case group, stage (ii) was18 (45%), and in control group followed the same18 (45%). The total of stage (ii) was 36 (45%) in both the cases. In case group, stage (iii) was 20 (50%), and in control group, stage (iii) was 14 (35%). The total stage (iii) was 34 (42.5%). In case group, stage (iv) was 02 (05%), and in control group stage (iv) was 01 (2.5%). The total stage (iv) was 03 (3.80%) in both the groups. (Table 13) shows the distribution of FPG (mmol/L) value between case and control groups. In case group, DM (>7) was 13 (32.5), and in control group, DM (>7) was 03 (7.5%). The total DM (>7) was 16 (20%) in both the groups. In case group, IFG (6.1-6.9 was 02 (5%), and in control IFG (6.1-6.9 was 04 (10%) which was double than case group. The total IFG (6.1-6.9 was 06 (7.5%) in both the cases. In case group, Normal (< 6.1) was 25 (62.5%), and in control group, Normal (< 6.1) was 33 (82.5 %). The total Normal (< 6.1) was 58 (72.5) in both the groups. (Table 14) shows the comparison of mean FPG value between case and control groups. In case group, the mean FPG-value was 5.97±1.78 On the other hand, in control group, the mean FPG-value was 5.14±0.93 (p=0.01). (Table 15) shows the distribution of 2HABF value (2-hrs plasma glucose (mmol/L) between case and control groups. In case group, DM (> 11.1) was 13 (32.5%), and in control group, DM (> 11.1) was 04 (10%)/. The total DM (> 11.1) was counted 17 (21.3%) in both the cases. In case group, IGT (7.8 - 11.1) was counted 04 (10%), and in control group, IGT (7.8 - 11.1) was counted 05 (12.5%). The total IGT (7.8 - 11.1) was counted 17 (21.3%) in both the cases. In case group, Normal (< 7.8) was counted 23 (57.5%, and in control group, Normal (< 7.8) was counted 31 (67.5%). The total Normal (< 7.8) 2hrs plasma (mmol/L) was counted 54 (67.5%) in both the cases. (Table 16) shows the comparison of mean 2HABF value between case and control groups. In case group, the mean 2HABF value was 8.98±2.82 and in control group, the mean 2HABF value was 7.47±1.83 (p=0.01). (Table 17) shows the distribution of HbA1C (mmol/L) value of case and control groups. In case group, DM (> 6.5) was counted 13 (32.5%), and in control group, DM (> 6.5) was counted 04 (10%). The total DM (> 6.5) was counted 17 (21.3%) in both the cases. In case group, Normal (< 6.5) was counted 27 (67.5%), and in control group, Normal (< 6.5) was counted 36 (90%). The total Normal (< 6.5) HbA1C (mmol/L) value was counted 63 (78.8%) in both the cases. (Table 18) shows the comparison of mean HbA1C value between case and control groups. In case group, the mean HbA1C value was 6.235±0.77146, and in control group, the mean HbA1C value was 5.765±0.54092 (p=0.082).

***Table 1.*** *Age distribution of the studied patients (control group) (n=40).*

| Age group | Frequency | % |
|---|---|---|
| 40-49 | 15 | 37.5 |
| 50-59 | 15 | 37.5 |
| 60 or above | 10 | 25 |
| Total | 40 | 100 |

***Table 2.*** *Age distribution of the studied patients (case Group) (n=40).*

| Age group | Frequency | % |
|---|---|---|
| 40-49 | 09 | 22.4 |
| 50-59 | 16 | 40.00 |
| 60 or above | 15 | 37.5 |
| Total | 40 | 100 |

***Table 3.*** *Comparison of mean age between case and control groups (n=80).*

| Group | N | Mean | SD | p-value |
|---|---|---|---|---|
| Case | 40 | 65.65 | 7.63 | 0.841 |
| Control | 40 | 53.85 | 7.9 | |

***Table 4.*** *Gender Distribution of the studied patients (n=80).*

| Gender | | Patients having corticosteroids | | Total |
|---|---|---|---|---|
| | | Case | Control | |
| Male | Count | 34 | 35 | 69 |
| | Percentage | 85.00% | 87.50% | 86.30% |
| Female | Count | 6 | 5 | 11 |
| | Percentage | 15.00% | 12.50% | 13.70% |
| Total | Count | 40 | 40 | 80 |
| | Percentage | 100.00% | 100.00% | 100.00% |

***Table 5.*** *Distribution of BMI of the studied patients having corticosteroid or not (n=80).*

| BMI | | Case | Control | Total |
|---|---|---|---|---|
| Under weight (<18.5) | Count | 13 | 10 | 23 |
| | Percentage | 32.50% | 25.00% | 28.80% |
| Normal (18.5-24.9) | Count | 26 | 27 | 53 |
| | Percentage | 65.00% | 67.50% | 66.30% |
| Over Weight (25.0-29.9) | Count | 0 | 3 | 3 |
| | Percentage | 0% | 7.50% | 3.80% |
| Obese (30-39.9) | Count | 1 | 0 | 1 |
| | Percentage | 2.50% | 0.00% | 2.50% |
| Total | Count | 40 | 40 | 80 |
| | Percentage | 100.00% | 100.00% | 100.00% |

***Table 6.*** *Residential status of the studied patients (n=80).*

| Residence | | Case | Control | Total |
|---|---|---|---|---|
| Rural | Count | 20 | 26 | 46 |
| | Percentage | 50.00% | 65.00% | 57.50% |
| Urban | Count | 20 | 14 | 34 |
| | Percentage | 50.00% | 35.00% | 42.50% |
| Total | Count | 40 | 40 | 80 |
| | Percentage | 100.00% | 100.00% | 100.00% |

***Table 7.*** *Educational status of the studied patients (n=80).*

| Educational status | | Case | Control | Total |
|---|---|---|---|---|
| Illiterate | Count | 13 | 18 | 31 |
| | Percentage | 32.50% | 45.00% | 38.80% |
| Primary level | Count | 7 | 5 | 12 |
| | Percentage | 17.50% | 12.50% | 15.00% |
| Secondary level | Count | 8 | 3 | 11 |
| | Percentage | 20.00% | 7.50% | 13.80% |
| Higher secondary level | Count | 8 | 9 | 17 |
| | Percentage | 20.00% | 22.50% | 21.30% |
| Bachelor and above | Count | 4 | 5 | 9 |
| | Percentage | 10.00% | 12.50% | 11.30% |
| Count | | 40 | 40 | 80 |
| Percentage | | 100.00% | 100.00% | 100.00% |

***Table 8.*** *Occupation of the studied patients (n=80).*

| Occupation | | Case | Control | Total |
|---|---|---|---|---|
| Service | Count | 14 | 8 | 22 |
| | Percentage | 35.00% | 20.00% | 27.50% |
| Business | Count | 10 | 19 | 29 |
| | Percentage | 25.00% | 47.50% | 36.30% |
| Retired | Count | 9 | 6 | 15 |
| | Percentage | 22.50% | 15.00% | 18.80% |
| Unemployed | Count | 7 | 7 | 14 |
| | Percentage | 17.50% | 17.50% | 17.50% |
| Count | | 40 | 40 | 80 |
| Percentage | | 100.00% | 100.00% | 100.00% |

***Table 9.*** *Monthly income of the studied patients (n=80)*

| Monthly income (BDT) | | Case | Control | Total |
|---|---|---|---|---|
| < 10000 | Count | 7 | 10 | 17 |
| | Percentage | 17.50% | 25.00% | 21.30% |
| 10000 -30000 | Count | 15 | 15 | 30 |
| | Percentage | 37.50% | 37.50% | 37.50% |
| > 30000 | Count | 18 | 15 | 33 |
| | Percentage | 45.00% | 37.50% | 41.30% |
| Total count | | 40 | 40 | 80 |
| Total percentage | | 100.00% | 100.00% | 100.00% |

***Table 10.*** *Smoking status of the studied patients (n=80).*

| Participants' smoking status | | Case | Control | Total |
|---|---|---|---|---|
| Smoker | Count | 31 | 29 | 60 |
| | Percentage | 77.50% | 72.50% | 75.00% |
| Non- smoker | Count | 6 | 6 | 12 |
| | Percentage | 15.00% | 15.00% | 15.00% |
| Ex-smoker | Count | 3 | 5 | 8 |
| | Percentage | 7.50% | 12.50% | 10.00% |
| Count | | 40 | 40 | 80 |
| Percentage | | 100.00% | 100.00% | 100.00% |

***Table 11.*** *Duration of symptoms between case and control groups (n=80).*

| Duration | | Case | Control | Total |
|---|---|---|---|---|
| <5years | Count | 8 | 17 | 25 |
| | Percentage | 20.00% | 42.50% | 31.30% |
| 6-10years | Count | 23 | 17 | 40 |
| | Percentage | 57.50% | 42.50% | 50.00% |
| 11-15years | Count | 9 | 6 | 15 |
| | Percentage | 22.50% | 15.00% | 18.80% |
| Count | | 40 | 40 | 80 |
| Percentage | | 100.00% | 100.00% | 100.00% |

***Table 12.*** *Stages of COPD between case and control groups (n=80).*

| Stages | | Case | Control | Total |
|---|---|---|---|---|
| i | Count | 0 | 7 | 7 |
| | Percentage | 0.00% | 17.50% | 8.80% |
| ii | Count | 18 | 18 | 36 |
| | Percentage | 45.00% | 45.00% | 45.00% |
| iii | Count | 20 | 14 | 34 |
| | Percentage | 50.00% | 35.00% | 42.50% |
| iv | Count | 2 | 1 | 3 |
| | Percentage | 5.00% | 2.50% | 3.80% |
| Count | | 40 | 40 | 80 |
| Percentage | | 100.00% | 100.00% | 100.00% |

***Table 13.*** *Distribution of FPG value between case and control groups (n=80).*

| FPG (mmol/L) | | Case | Control | |
|---|---|---|---|---|
| DM (>7) | Count | 13 | 3 | 16 |
| | Percentage | 32.50% | 7.50% | 20.00% |
| IFG (6.1-6.9) | Count | 2 | 4 | 6 |
| | Percentage | 5.00% | 10.00% | 7.50% |
| Normal (< 6.1) | Count | 25 | 33 | 58 |
| | Percentage | 62.50% | 82.50% | 72.50% |
| Total | Count | 40 | 40 | 80 |
| | Percentage | 100.00% | 100.00% | 100.00% |

***Table 14.*** *Comparison of mean FPG value between case and control groups (n=80).*

| | | N | Mean | Std. Deviation | P Value |
|---|---|---|---|---|---|
| FPG-value | Case | 40 | 5.97 | 1.78 | <0.01 |
| | Control | 40 | 5.14 | 0.93 | |

***Table 15.*** *Distribution of 2HABF value between case and control groups (n=80).*

| | 2-hrs plasma glucose (mmol/L) | | Case | Control | Total |
|---|---|---|---|---|---|
| 2-hrs plasma glucose (mmol/L) | DM (> 11.1) | Count | 13 | 4 | 17 |
| | | Percentage | 32.50% | 10.00% | 21.30% |
| | IGT (7.8 - 11.1) | Count | 4 | 5 | 9 |
| | | Percentage | 10.00% | 12.50% | 11.30% |
| | Normal (< 7.8) | Count | 23 | 31 | 54 |
| | | Percentage | 57.50% | 77.50% | 67.50% |
| Total | | Count | 40 | 40 | 80 |
| | | Percentage | 100.00% | 100.00% | 100.00% |

***Table 16.*** *Comparison of mean 2HABF value between case and control groups (n=80).*

| | | N | Mean | Std. Deviation | P value |
|---|---|---|---|---|---|
| 2HABF | Case | 40 | 8.98 | 2.82 | <0.01 |
| | Control | 40 | 7.47 | 1.83 | |

***Table 17.*** *Distribution of HbA1C value of case and control groups (n=80).*

| HbA1C (mmol/L) | | Case | Control | Total |
|---|---|---|---|---|
| DM (> 6.5) | Count | 13 | 4 | 17 |
| | Percentage | 32.50% | 10.00% | 21.30% |
| Normal (< 6.5) | Count | 27 | 36 | 63 |
| | Percentage | 67.50% | 90.00% | 78.80% |
| Total | Count | 40 | 40 | 80 |
| | Percentage | 100.00% | 100.00% | 100.00% |

***Table 18.*** *Comparison of mean HbA1C value between case and control groups (n=80).*

| | | N | Mean | Std. Deviation | p-value |
|---|---|---|---|---|---|
| HbA1C value | Case | 40 | 6.235 | 0.77146 | 0.082 |
| | Control | 40 | 5.765 | 0.54092 | |

# 5. Discussion

Although the dysglycemic effects of systemic glucocorticoid therapy are well known, the effect of inhaled corticosteroids (ICS) on carbohydrate metabolism is still a subject of debate. The systemic bioavailability of ICS is claimed to be minimal and the side effects negligible. However, some large retrospective cohort studies showed a definite association between ICS use and incident diabetes or worsening glycemic control in pre-existing diabetes. There are no professional-body recommended guidelines on the diagnosis and management of steroid-induced diabetes for the general population. This review aims to evaluate the systemic dysglycemic effect of ICS treatment and to propose a management algorithm. Systemic glucocorticoid therapy can lead to various metabolic complications in glucose homeostasis including insulin resistance, hyperglycemia and increased risk of diabetes. [8] As with oral corticosteroids, ICS have been associated with an increased risk of developing diabetes and also worsening of glycemic control in patients with known diabetes. In this cross-sectional analytical study, total of 80 subjects was included for the study on the basis of inclusion and exclusion criteria, 40 of them were taken as case and 40 as age matched control. There was no defaulter or drop out cases, so finally 80 subjects were enrolled in this study, clinically diagnosed 40 consecutive COPD patients (50%) who were receiving both bronchodilator & inhaled corticosteroids were recruited as case. Clinically diagnosed 40 consecutive COPD patients (50%) receiving only bronchodilator without inhaled corticosteroid/systemic steroid were recruited as control. Both groups were well matched for age and other socio-demographic variables. There was no statistical difference in the mean age of both group which was 53.85±7.9

and 56±7.6 in control and case respectively. This findings were somewhat different from some previous other study done by Faul et al. [9] and Slatore et al [10], where mean age was somewhat more than our study group, that is 64 and 65.4 respectively. Spirometry was done for confirmation and staging of COPD according to GOLD at indoor and OPD patients of Department of Internal Medicine, BSMMU. ICS are considered an integral part of anti-inflammatory treatment in patients with asthma, although their effectiveness in COPD remains controversial. [11]. In patients with COPD, the use of ICS is primarily recommended for severe disease and in those with frequent episodes of exacerbations. [12] Nevertheless, they are increasingly being used even in patients with less severe disease. [13] In our study it is also found that significant number of GOLD stage 1 and 2 are using inhaled steroids which are not justified. Similar trend has found in most of the previous studies. Using a population-based study on COPD patients, we found that the use of inhaled corticosteroids is associated with a significant increase in the risk of incident of diabetes. The observed treatment-related changes in % N HbA1c in this study are consistent with another report of hyperglycemia and glucosuria in an asthmatic patient who took very high doses of inhaled FP at a dose of 2 mg/day; however, the mean increase resulting from FP therapy, relative to the individual's own baseline, is substantially smaller than in that individual case. [14] Socio-demographic characteristics of the study showed that among the cases 85% were males and 15% were females while in control group it was 87.5% and 12.5% respectively. This is somewhat similar to most previous studies. A study done by Saltore et al [10] had found 97% of respondent were male. Most of the population belongs to male sex which is probably due to more smoking rate among male, these findings are somewhat similar to a previous study done by Faul et al. [9] and Mirrakhimov et al. [15] 77.5% of the case and 72.5% of control population are indulging in smoking while only 15% from each group are non- smoker, these picture is somewhat different in the study done by Christofer et al [16], where the number of smoker in case and control group are 27% and 22% respectively. These signify the high disease burden among smoker. Proper education, awareness creating program, symposium, anti-smoking movement and strong stand of policy maker, all can improve this picture and can help in reducing future prevalence of the disease burden. In respect of occupation it is found that there is a large number of cases are service holder and businessman (35% and 20%), which is true for control group also (20% and 47.5%). Most of the cases are from higher socioeconomic background (45%), whereas in control group it is 37.5%. This demographic variable also differe from study done by Christofer et al. [16]. They found that 89% of case population and 87% of control population are belongs to lower socio-economic group. But this figure is somewhat similar to study done by Kian et al [17], they had found that the number is 42.8% and 40.6% respectively. In 20% cases symptoms duration was less than 5 years, where as in control group it was 42.5%. And duration more than 11-15 years was 22.5% and 15% respectively. We had found that 32% of cases and 7.5% of control group were diagnosed as diabetic when fasting plasma glucose taken into account, while in case of 2 hours after breakfast plasma sugar the number were 32.5% and 10% respectively and in case of HbA1c the number were 23.5% and 10% respectively. The major strength of the present study was that it evaluated data from randomized controlled trials and analyzed based on intention-to-treat, which mitigated the risk of confounding. We found that the risk for onset of diabetes mellitus / hyperglycemia in inhaled corticosteroid treated patients with COPD increased with increasing age, increasing BMI and increasing COPD severity, as measured by decreasing baseline FEV1. The significant increases in risk observed in this part of the analysis for age and BMI have been well established. However, the increased risk for low baseline FEV1 is novel. This study was not designed to determine the mechanisms or a cause and effect relationship behind this association. Large intervention studies in patients have demonstrated that intensive glycemic control reduces the onset and delays the progression of diabetic complications, including retinopathy, nephropathy, and neuropathy. [18] Risk reductions in various outcomes ranged between 25% to 75%, and these reductions appeared to be related to the duration and severity of hyperglycemia. The United Kingdom Prospective Diabetes Study demonstrated a continuous relationship between glycemic control and various complications, such that for a reduction in % HbA1c of 1.0, there was a 35% reduction in the risk of complications, a 25% reduction in diabetes-related deaths, a 7% decrease in all-cause mortality and an 18% reduction in combined fatal and non-fatal myocardial infarction. Accordingly, modest deterioration in glucose control attributable to COPD therapy, even on the order of the differences observed in this study, could contribute to the development of diabetic in at-risk populations. The treatment that has shown to increase survival in COPD is smoking cessation. This is the only measure that slows the accelerated decline in lung function in these patients.

# 6. Limitations of the Study

There are some limitations in the present study that may have some potential impacts on the results. First, the baseline risk and number of cases was low and the confidence intervals were wide enough to have missed a clinically important effect of ICS on the risk of onset of diabetes. Second, we did not have biochemical validation of cases. Thus, case misclassification was possible, which would have diluted the results. Third, there was no follow-up. As ICS are recommended as maintenance therapy, future studies will be needed to evaluate the long term effects of ICS on these endpoints. The study only included patients on inhaled corticosteroids not the systemic one. Therefore, the study's results could not be generalized for all types of COPD patients. However, from the public health perspective, COPD patients on ICS are the most important group of COPD patients and these are the most common group of patients used to evaluate the onset of diabetes.

# 7. Conclusion and Recommendations

Although recent studies have suggested that high dose inhaled corticosteroid (ICS) therapy might contribute to the

development of type 2 diabetes mellitus in COPD patients, this concept remains controversial and requires further investigations. Nevertheless, there's reason to think about clinical implications associated with high dose ICS therapy in COPD patients. In Addition, ICS overuse presents a critical issue that has got to be addressed. As we learn more regarding the adverse effects related to ICS therapy, adequate patient selection and monitoring are going to be necessary to improve the safety and efficacy of those treatments. In this regard current evidence may suggest that care should be taken when administering high dose ICS within the development and progression of diabetes, As well as improved therapeutic regimens to reduce side effects (i.e. optimal dosing) can lead to improved management of COPD patients. Care providers and policy makers need to ensure not only the resource and health care system, but also they should acquire sufficient knowledge, attitude and skills in their profession, so that one is attracted and act on their for the care they have. A significant proportion of individuals are affected by COPD in our country. This study showed that onset of diabetes is more in patients on ICS than in patients of bronchodilators. To ameliorate their disease burden, community awareness about health care facilities and self-concern of COPD patients for their own health needs are to be emphasized. The primary referral units at grass root level, community clinics, union sub enters for health and family welfare, upazilla health complexes are required to be equipped infrastructural for improving and addressing health problems of COPD patients and to provide appropriate referral service. Built in service components' may improve self-reporting of new diabetic patients. Compliance to medication and ensuring proper lifestyle is a crucial issue for COPD patient for its future treatment reception, Care providers and policy makers need to ensure the resource of health care system along with sufficient knowledge, attitude and skills in their profession to improve the specified outcome.

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