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## Original Research Article

# Evaluation of impact of adherence to inhaled therapy and critical mistakes in inhalation technique on clinical outcomes in patients with obstructive airway diseases in India

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## ABSTRACT

**Introduction:** Adherence to inhaled therapy is more relevant in respiratory diseases because, to achieve therapeutic efficacy, it is necessary that the patient adhere to the recommended therapy as well as use their inhalers correctly with appropriate inhalation technique.

**Materials and Methods:** This was a prospective, observational study that included 126 patients >18 years of age of all genders, diagnosed with an obstructive airway disease, and prescribed inhaler medication. Adherence was assessed using the Test of Adherence to Inhalers (TAI) questionnaire, and inhaler device technique was assessed every 3 months. At the end of one year, outcome data like the number of exacerbations, the number of admissions, including critical-care admissions, the number of days of hospitalization, adverse events, and their associations were analyzed.

**Results:** Poor adherence to inhaled therapy was found in 40.48% of patients, with the majority of patients (69.05%) having an unwitting or ignorant pattern of non-adherence. Out of 75 patients using MDI (Metered Dose Inhaler), 34.67% had critical mistakes in technique, and out of 51 patients using Rotahaler, 23.53% had critical mistakes in technique. There was no significant relationship between level of adherence and critical mistakes with gender, BMI category, or past history of smoking. Patients with poor adherence and those with critical mistakes in inhalation technique had poor health outcomes.

**Conclusion:** This study highlights the role of adherence and identifies barriers responsible for non-adherence to inhaled therapy. Identifying the behaviors responsible for non-adherence and counseling the patients on the correct inhalation technique can improve the health outcomes of chronic respiratory diseases.

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## 1. Introduction

Obstructive airway disease is a large spectrum of chronic inflammatory disorders characterized by the obstruction of airways and includes asthma, chronic obstructive pulmonary disease (COPD), chronic bronchitis, bronchiectasis, and asthma-COPD overlap syndromes.<sup>1</sup>

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Globally, there is a high burden of these chronic respiratory diseases, out of which 69% are due to asthma and 29% due to COPD.<sup>2</sup> A systematic review and modeling study in 2019 estimated that the global prevalence of COPD was 10.3%, accounting for 391.9 million cases, and highlighted that four in every five cases of COPD are found in low and middle-income countries (LMIC).<sup>3</sup> According to the recent Global Burden of Disease (GBD) study, there are 34.3 million

people with asthma in India, and asthma causes 27.9% of disability-adjusted life years (DALYs). In comparison to the global proportion of asthma burden, India has three times higher mortality and almost two times higher DALYs. India contributes to 75.6% and 20% of DALYs due to COPD and asthma, respectively, which is an alarming rate of health loss, cause of which needs to be studied in detail.<sup>4</sup>

Inhaled therapy is the cornerstone therapy in the management of these obstructive airway diseases, as recommended by the major guidelines.<sup>5,6</sup> There are various types of inhalers used to deliver the aerosolized medications into the lungs such as metered-dose inhalers (MDIs), dry powder inhalers (DPIs), such as Rotahaler, soft mist inhalers, and nebulizers. The recent Global Initiative for Asthma 2022 update suggests that the treatment for such diseases is not “one size fits all”, as even after explaining the treatment plan to the patient, there needs to be emphasis on adherence to inhaled therapy and its correct inhalation technique.<sup>5</sup>

The terms adherence and compliance are different, yet they are still used interchangeably on many occasions. Compliance is defined as “the extent to which the patient’s behavior matches the prescriber’s recommendations”, in which the patient is expected to unquestioningly comply with the doctor’s prescribed regimen.<sup>7</sup> However, the term “compliance” has evolved into “adherence” as it takes into account the patients’ perspectives on medication-taking, so that non-adherence to medications is not solely attributed as the patient’s responsibility.<sup>8</sup> Thus, adherence has been defined as “the extent to which a person’s behavior, taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider”.<sup>9</sup>

There have been various methods to assess adherence to inhalers, such as subjective (physician assessment or various self-reported questionnaires), objective tools (analysis of prescriptions, weighing inhaler canisters, electronic monitoring devices), or biochemical methods (drug level monitoring).<sup>10,11</sup> Each method has its own advantages and disadvantages, but some methods tend to be resource-dependent, costly, and difficult to implement in clinical practice. The Test of Adherence to Inhalers (TAI) questionnaire was developed by Spanish researchers in 2016 which not only addresses non-adherence to inhaler therapy but also identifies the patterns or behaviors contributing to non-adherence to inhaler therapy.<sup>12</sup> Non-adherence to inhaled therapy can be due to intentional or unintentional behaviors.<sup>13</sup> Non-adherence can be attributed to patient behaviors defined as erratic, deliberate, or unwitting/ignorant behavior. Erratic behavior refers to sporadic causes such as forgetfulness or busy schedule whereas deliberate behavior refers to when patients intentionally do not adhere to medications due to fear of side effects, fear of complications, financial burden, etc.

Unwitting or ignorant behavior is when the patient is not aware of facts such as knowledge and understanding of inhaler dosage or inhalation technique.<sup>12</sup> Additionally, poor adherence to the inhaled therapy has also revealed high rates of hospitalizations due to exacerbations as well as higher mortality.<sup>14</sup> Hence, it becomes pertinent that we assess the role of adherence and inhalation technique and correlate it with the health outcomes of patients with obstructive airway diseases.

Several studies addressing this problem have been published, but they are mainly from the western population.<sup>12,14–18</sup> Adherence to inhaler medications using the TAI questionnaire, along with critical mistakes in inhaler technique have not been studied widely in Indian settings, except in a few limited papers in which solely adherence to asthma was assessed.<sup>19–21</sup> Hence, we conducted this prospective observational study not only to assess the adherence to inhaler therapy but also to identify the factors contributing to the non-adherence, identify the critical mistakes in inhalation technique, and study its impact on health outcomes in patients with obstructive airway diseases such as asthma as well as COPD and bronchiectasis.

## 2. Methods and Materials

This prospective, observational, single centre study was conducted at the outpatient department of pulmonary medicine in Bhaktivedanta Hospital and Research Institute over a period of 12 months, from May 2021 to May 2022, after obtaining approval from the Institutional Ethics Committee of the hospital. A total of 126 patients with obstructive airway disease were enrolled in the study, which included participants of all genders and >18 years of age who had been diagnosed with an obstructive airway disease on pulmonary function test (PFT) and were prescribed preventive and maintenance inhaled medication for the past six months. Patients who were unable to perform a pulmonary function test, patients with neuromotor incoordination, patients with restrictive lung diseases like idiopathic pulmonary fibrosis (IPF), nonspecific interstitial pneumonia (NSIP), bronchiolitis obliterans organizing pneumonia (BOOP), and usual interstitial pneumonia (UIP) were excluded.

Post written consent, sociodemographic data and relevant histories of the patients were obtained, and TAI questionnaire was administered. This questionnaire includes 12 items (first 10 items are related to the patient domain, and last 2 items are related to the health care professional domain). The first 10 items are scored from 1 to 5 (worst to the best possible score), and the last two items are scored as 1 or 2 (where 1 is bad and 2 is good). For the 10-item TAI questionnaire, the total score range is between 10 and 50. Scores <45 suggest poor adherence, 46–49 suggest intermediate adherence, and a score of 50

suggest good adherence. In the 12-item TAI questionnaire, items 1 to 5 are designed to identify erratic non-adherence behavior (score<25), items from 6 to 10 identify deliberate or intentional non-adherence behavior (score<25), and the last two items are designed to identify unwitting non-adherent behavior (score<4). Patients were followed up for the duration of 1 year at intervals of three months, where they were evaluated for inhaler device technique at each clinic visit. At the end of the study duration of 1 year, outcome data like number of exacerbations, number of admissions including critical care admissions, number of days of hospitalisation, and adverse events were noted.

The numeric data were summarized by descriptive statistics like n, mean  $\pm$  SD, median, minimum, and maximum. Before applying any statistical test, a normality test was performed. The categorical data were summarized by frequency count, and percentage and significance were analyzed using the chi-square test. All statistical data was analyzed by IBM SPSS software v.28.0. A p-value less than 0.05 was considered statistically significant.

### 3. Results

In our study, out of a total of 126 patients, 46.83% (n=59) patients were male while 53.17% (n=67) patients were females. The mean age of patients in our study was 61.79  $\pm$  13.07 years, and majority of the patients were >65 years of age (53.20%). The mean BMI of the patients was 23.35  $\pm$  2.98 kg/m<sup>2</sup>, where the majority of patients, 67.5% (n=85) had a normal BMI, and 4% (n=5) were obese. The mean duration of the obstructive disease was 20.60  $\pm$  12.43 years, and the mean number of co-morbidities was 2.48  $\pm$  1.17. Amongst the 126 patients, 33.33% (n=42) suffered from bronchial asthma, while 62.70% (n=79) and 3.97% (n=5) of patients suffered from COPD and bronchiectasis, respectively. Based on the type of inhaler used, 59.52% (n=75) patients used MDI, while 40.48% (n=51) of patients used DPI such as a Rotahaler, with a mean frequency of inhaler dosing of 2.69  $\pm$  1.02 per day. When the outcomes were analyzed, it showed the mean number of exacerbations per year was 3.66  $\pm$  1.88, the mean number of hospital admissions was 3.41  $\pm$  2.35 per year, the mean number of critical care admissions was 1.88  $\pm$  1.52 per year, while mean number of days of hospitalisations was 18.32  $\pm$  14.53 days. (Table 1).

In our study, poor adherence was noted in 40.48% (n=51) of patients, while intermediate adherence and good adherence were noted in 16.66% (n=21) and 42.86% (n=54), respectively. An erratic pattern of non-adherence was noted in 51.59% (n=65), deliberate pattern was noted in 56.35% (n=71) and an unwitting or ignorant pattern was noted in 69.05% (n=87) (Table 2).

A total of 30.16% (n=38) of patients using inhaler devices had a critical mistake in their inhalation technique. Out of 75 patients using MDI, 34.67% (n=26) had

critical mistakes in technique, and out of 51 patients using Rotahaler, 23.53% (n=12) had critical mistakes in technique. The most common mistake by patients using MDI was not placing the mouthpiece of the inhaler between the teeth and closing their lips around it (30.67% of those using MDI), while the most common mistake by patients using Rotahaler was not loading the dose correctly (19.61% of those using Rotahaler) (Table 3).

There was a significant relationship between the level of adherence to inhaler therapy and age (P= 0.009). There was no significant relationship between level of adherence and gender (P= 0.46), BMI category (P= 5.769), or past history of smoking (P= 0.15). Patients with >3 co-morbidities had relatively poor adherence as compared to other groups (P value <0.05). Patients with disease duration <21 years had relatively better adherence, while those with disease duration >21 years of disease were found to have poor adherence (P=<0.05). Patients with poor adherence had a higher incidence of >4 exacerbations per year, >4 no. of admissions, >2 critical care admissions, >18 days duration of hospitalization and higher adverse events as compared to other groups (P=<0.05) (Table 4).

In our study, patients who were younger had a relatively lesser incidence of critical mistakes as compared to older patients (p value =0.05). There was no significant relationship between gender (P=0.10), BMI (P=0.8), past history of smoking (P=0.15), number of co-morbidities (P=0.09) and critical mistakes in inhalation technique. Patients whose duration of disease was <21 years had a lower incidence of critical mistakes as compared to those whose duration of disease was >21 years (p value<0.05). Patients who had a critical mistake in inhaler technique had a higher incidence of >4 exacerbations, >4 admissions, >2 critical care admissions, >18 days of hospitalization and higher adverse events as compared to those with no critical mistake (p value<0.05) (Table 5).

### 4. Discussion

As with all other chronic disorders, adherence to the prescribed inhaler therapy is a significant factor in determining control over the disease.<sup>14</sup> Literature on adherence to inhaled therapy using the TAI questionnaire is scarce in India, except for an isolated study from Kerala in India.<sup>19</sup> To the best of our knowledge, this is the first Indian paper addressing three factors, such as adherence to inhaled therapy, critical mistakes in inhalation technique, and their association with sociodemographic determinants and patient outcomes.

Our study showed that out of the total 126 patients, 40.48% had poor adherence to inhaler therapy, which is synonymous with the study in Kerala showing 44% of poor adherence.<sup>19</sup> However, another study from our neighboring country, Bangladesh, shows a significantly higher percentage of 86% poor adherence, whereas studies

**Table 1:** Sociodemographic and health status of the patient population.

|  | Number (n)  | Percentage (%) |
|--|-------------|----------------|
| <b>Gender</b>  |             |                |
| Male   | 59          | 46.83%         |
| Female   | 67          | 53.17%         |
| <b>Age (years)</b>                                       |             |                |
| <25  | 04          | 03.20%         |
| 26-45  | 13          | 10.30%         |
| 46-65  | 42          | 33.30%         |
| >65  | 67          | 53.20%         |
| <b>Body Mass Index (BMI) (kg/m<sup>2</sup>)</b>          |             |                |
| 18.5 -24.9 (Normal)                                      | 85          | 67.50%         |
| 25-29.9 (pre-obese)                                      | 36          | 28.60%         |
| >30 (Obese)  | 05          | 04.00%         |
| <b>Comorbidities</b>                                     |             |                |
| Cardiac disease  | 37          | 29.36%         |
| Renal disease  | 14          | 11.11%         |
| Neurologic disease                                       | 14          | 11.11%         |
| Pulmonary tuberculosis                                   | 9           | 07.14%         |
| Malignancy   | 7           | 05.56%         |
| Diabetes mellitus  | 46          | 36.51%         |
| Hypertension   | 61          | 48.41%         |
| Other  | 38          | 30.15%         |
| <b>Type of Obstructive Airway Disease</b>                |             |                |
| Bronchial asthma   | 42          | 33.33%         |
| COPD   | 79          | 62.70%         |
| Bronchiectasis   | 05          | 03.97%         |
| <b>Type of inhaler used</b>                              |             |                |
| MDI  | 75          | 59.52%         |
| Rotahaler  | 51          | 40.48%         |
| <b>Characteristics and Health Status of the patients</b> |             |                |
|  | <b>Mean</b> | <b>SD</b>      |
| Age(years)   | 61.79       | ±13.07         |
| BMI (kg/m <sup>2</sup> )                                 | 23.35       | ±2.98          |
| Duration of disease (years)                              | 20.60       | ±12.43         |
| Frequency of inhaler dosage (doses/day)                  | 2.69        | ±1.02          |
| No. of co-morbidities                                    | 2.48        | ±1.17          |
| No. of exacerbations per year                            | 3.66        | ±1.88          |
| No. of admissions in hospital                            | 3.41        | ±2.35          |
| No. of critical care admissions                          | 1.88        | ±1.52          |
| No. of days of hospitalisation                           | 18.32       | ±14.53         |

**Table 2:** Level of adherence and pattern of non-adherence.

| Test of Adherence to Inhaler (TAI) interpretation | Number of patients (n)          | Percentage of patients (%) |
|---|---------------------------------|----------------------------|
| 10-item   | Poor adherence (<45)            | 51<br>40.48%               |
|   | Intermediate adherence (46-49)  | 21<br>16.66%               |
|   | Good adherence (=50)            | 54<br>42.86%               |
| Item 1-5  | Erratic pattern (<25)           | 65<br>51.59%               |
|   | Non-erratic (=25)               | 61<br>48.41%               |
| Item 6-10 score                                   | Deliberate pattern (<25)        | 71<br>56.35%               |
|   | Non-deliberate (=25)            | 55<br>43.65%               |
| Item 11-12 score                                  | Ignorant/unwitting pattern (<4) | 87<br>69.05%               |
|   | Non-ignorant (=4)               | 39<br>30.95%               |

**Table 3:** Frequency of critical mistakes in the inhalation technique according to the type of inhaler.

| S.No.   | Critical step  | No. of critical mistake | Percentage |
|---|--|-------------------------|------------|
| <b>Total no. patients with critical mistakes while using MDI (n=26, 34.67%)</b>       |  |                         |            |
| 1   | Did not remove the cover   | 7                       | 9.33%      |
| 2   | Did not shake the inhaler well   | 1                       | 1.33%      |
| 3   | Did not hold the inhaler upright   | 0                       | 0%         |
| 4   | Did not exhale gently out away from the  | 0                       | 0%         |
| 5   | Did not place mouthpiece of the inhaler between the teeth and close lips around it | 23                      | 30.67%     |
| 6   | Did not actuate canister once at the beginning of inhalation                       | 12                      | 16%        |
| 7   | Did not inhale slowly and deeply   | 12                      | 16%        |
| 8   | Did not hold breath for at least 10 seconds  | 18                      | 24%        |
| 9   | Did not rinse the mouth  | 0                       | 0%         |
| <b>Total no. patients with critical mistakes while using Rotahaler (n=12, 23.53%)</b> |  |                         |            |
| 1   | Did not remove the cover   | 1                       | 1.96%      |
| 2   | Did not load the dose correctly  | 10                      | 19.61%     |
| 3   | Did not hold the inhaler upright   | 0                       | 0%         |
| 4   | Did not exhale gently out away from the  | 0                       | 0%         |
| 5   | Did not place mouthpiece of the inhaler between the teeth and close lips around it | 4                       | 7.84%      |
| 6   | Did not inhale slowly and deeply   | 2                       | 3.92%      |
| 7   | Did not hold breath for at least 10 seconds  | 3                       | 5.88%      |
| 8   | Did not rinse the mouth  | 5                       | 9.80%      |

from Vietnam and Greece showed 50% and 74% of poor adherence, respectively.<sup>15–17</sup> Even though TAI sometimes overestimates the non-adherence to inhaled therapy,<sup>22</sup> our finding of 40.48% of poor adherence to inhaled therapy in India should not be ignored, as it has also been proven in our paper to be associated with higher rates of exacerbations, hospitalizations, and adverse events in the future.

The most common pattern for poor adherence in our study was found to be the ignorant pattern (69.05%), followed by the deliberate pattern (56.35%) and the erratic pattern (51.59%) respectively. Ngo et al. also reported a higher prevalence of the ignorant pattern (77.1%),<sup>16</sup> whereas another study reported higher a prevalence of the erratic pattern (79.9%).<sup>17</sup> Notably, a single patient may exhibit multiple forms of non-adherence. Plaza et al.<sup>23</sup> further compared the differences in adherence patterns in asthma vs. COPD patients, showing that the pattern of non-adherence in asthmatics was more frequently erratic and deliberate than in COPD patients, who showed unwitting non-adherence. Hence, it is important to not just evaluate the non-adherence but also the pattern or behavior responsible for the medication non-adherence. The recently developed 12-item TAI questionnaire is a reliable, validated questionnaire that can be used to identify such barriers to medication non-adherence.<sup>12</sup> It can be used in clinical practice due to its quick and cost-effective nature, as well as to design educational strategies to prevent medication non-adherence in the future.

Ignorant patterns are mainly due to a lack of knowledge and understanding of inhaler dosage or

inhalation technique.<sup>12</sup> Such critical errors in the inhalation technique can lead to suboptimal drug delivery to the lungs, leading to poor outcomes. A recent meta-analysis on inhaler technique errors in asthma and COPD proved that critical error rates are as high as 14%–92% across all inhaler devices.<sup>24</sup> In our cohort, out of 75 patients using MDI, 34.67% had a critical mistake in technique, and the most common mistake in MDI usage was not placing the mouthpiece of the inhaler between the teeth and closing the lips around it. Among the 51 patients using DPI such as Rotahaler, 23.53% had a critical mistake in technique, where the most common mistake was not loading the dose correctly. These findings could have contributed to the higher percentage of unwitting behavior in our study.

Ngo et al.<sup>16</sup> proved that MDI users had more errors compared to DPI users, where full exhalation was the leading error in all patients, regardless of the type of inhaler. Similarly, a systemic review and meta-analysis conducted in USA in 2019 stated that 8 out of 10 patients using MDI made at least 1 inhalation technique error.<sup>25</sup> MDI usage can be demanding as compared to other types of inhalation devices, as MDIs require more hand-breath coordination, better cognition, and an adequate ability to hold breath. This enumerates the need for patient education on the correct inhalation technique using either leaflets, video education, or face-to-face education.<sup>26</sup> Klijn et al.<sup>27</sup> also proved that the effect of these educational interventions seems to wane over time, thus highlighting the need for periodical check-ups to demonstrate the correct inhalation technique to the patients at each clinic visit.

**Table 4:** Association of Level of adherence with sociodemographic variables and outcomes.

|                                       | Poor adherence<br>TAI score < 45 | Intermediate adherence<br>TAI score 46-49 | Good adherence<br>TAI score = 50 | Total | Chi-square value | df | P value       |
|---------------------------------------|----------------------------------|---|----------------------------------|-------|------------------|----|---------------|
| <b>Gender</b>                         |                                  |   |                                  |       |                  |    |               |
| Male                                  | 27(45.7%)                        | 8(13.6%)                                  | 24(40.7%)                        | 59    | 1.532            | 2  | 0.46          |
| Female                                | 24(35.8%)                        | 13(19.4%)                                 | 30(44.8%)                        | 67    |                  |    |               |
| <b>Age group</b>                      |                                  |   |                                  |       |                  |    |               |
| <25                                   | 1(25%)                           | 0(0%)                                     | 3(75%)                           | 04    |                  |    |               |
| 26-45                                 | 1(8%)                            | 4(31%)                                    | 8(61%)                           | 13    | 17.15            | 6  | <b>0.009*</b> |
| 46-65                                 | 12(29%)                          | 7(17%)                                    | 23(54%)                          | 42    |                  |    |               |
| >65                                   | 37(55.2%)                        | 10(15%)                                   | 20(29.8%)                        | 67    |                  |    |               |
| <b>Body Mass Index</b>                |                                  |   |                                  |       |                  |    |               |
| 18.5-24.9 (normal)                    | 34(40%)                          | 17(20%)                                   | 34(40%)                          | 85    | 5.769            | 4  | 5.769         |
| 25-29.9 (pre-obese)                   | 13(36.1%)                        | 4(11.1%)                                  | 19(52.8%)                        | 36    |                  |    |               |
| >30 (obese)                           | 4(80%)                           | 0(0%)                                     | 1(20%)                           | 5     |                  |    |               |
| <b>History of smoking</b>             |                                  |   |                                  |       |                  |    |               |
| Yes                                   | 11(61.1%)                        | 2(11.1%)                                  | 5(27.8%)                         | 18    | 3.712            | 2  | 0.15          |
| No                                    | 40(37.0%)                        | 19(17.6%)                                 | 49(45.4%)                        | 108   |                  |    |               |
| <b>Number of comorbidities</b>        |                                  |   |                                  |       |                  |    |               |
| < 3                                   | 33(32.7%)                        | 19(18.8%)                                 | 49(48.5%)                        | 101   | 12.865           | 2  | <b>0.002*</b> |
| >3                                    | 18(72%)                          | 2(8%)                                     | 5(20%)                           | 25    |                  |    |               |
| <b>Duration of disease</b>            |                                  |   |                                  |       |                  |    |               |
| <21 years                             | 21(26.2%)                        | 20(25%)                                   | 39(48.8%)                        | 80    | 21.86            | 2  | <b>0.00*</b>  |
| >21 years                             | 30(65.2%)                        | 1(2.2%)                                   | 15(32.6%)                        | 46    |                  |    |               |
| <b>Exacerbations per year</b>         |                                  |   |                                  |       |                  |    |               |
| ≤ 4                                   | 17(19.3%)                        | 18(20.5%)                                 | 53(60.2%)                        | 88    | 63.166           | 2  | <b>0.00*</b>  |
| >4                                    | 34(89.5%)                        | 3(7.9%)                                   | 1(2.6%)                          | 38    |                  |    |               |
| <b>No. of admissions</b>              |                                  |   |                                  |       |                  |    |               |
| <4                                    | 9(12.5%)                         | 12(16.6%)                                 | 51(70.9%)                        | 72    |                  |    |               |
| >4                                    | 42(77.7%)                        | 9(16.6%)                                  | 3(5.7%)                          | 54    |                  |    |               |
| <b>No. of Critical care admission</b> |                                  |   |                                  |       |                  |    |               |
| <2                                    | 16(18.4%)                        | 17(19.5%)                                 | 54(62.1%)                        | 87    | 59.47            | 2  | <b>0.00*</b>  |
| >2                                    | 35(89.7%)                        | 4(10.3%)                                  | 0(0%)                            | 39    |                  |    |               |
| <b>Duration of Hospitalization</b>    |                                  |   |                                  |       |                  |    |               |
| <18 days                              | 12(16%)                          | 13(17.3%)                                 | 50(66.7%)                        | 75    | 51.984           | 2  | <b>0.00*</b>  |
| >18 days                              | 39(76.5%)                        | 8(15.7%)                                  | 4(7.8%)                          | 51    |                  |    |               |
| <b>Adverse events</b>                 |                                  |   |                                  |       |                  |    |               |
| Yes                                   | 10(91%)                          | 1(9%)                                     | 0(0%)                            | 11    | 13.154           | 2  | <b>0.000*</b> |
| No                                    | 41(35.6%)                        | 20(17.4%)                                 | 54(47%)                          | 115   |                  |    |               |

On further analysis, we found that patients who were younger had significantly better adherence as compared to patients who were older, irrespective of their gender, which was similar to the findings of Rafi et al.<sup>15</sup> We found no significant relationship between level of adherence and gender, BMI, or past history of smoking. A systematic review and meta-analysis of 47 studies showed that good adherence to inhaled therapy was seen in older patients, whereas females had poor adherence in asthma, and smoking habits were associated with increased adherence in European countries.<sup>18</sup> The study in Kerala also found that employment status and area of residence may be predictors

of non-adherence, which were not studied in our research.<sup>19</sup>

Patients with >3 comorbidities had relatively poor adherence as compared to other groups, which is consistent with the findings of Rafi et al. and Ierodiakonou et al.<sup>15,17</sup> This can be explained as patients with multiple comorbidities can find it difficult to adhere due to the increased burden of medications and financial restraints. Additionally, it was found that there was a significant association between age and critical mistakes in inhalation technique. Younger patients had a relatively lesser incidence of critical mistakes as compared to older patients. There was no significant relationship between critical mistakes and

**Table 5:** Association of critical mistake in inhalation technique with sociodemographic variables and outcomes.

|                                       | Critical mistake in technique absent | Critical mistake in technique present | Total | Chi-square value | df | P value       |
|---------------------------------------|--------------------------------------|---------------------------------------|-------|------------------|----|---------------|
| <b>Gender</b>                         |                                      |                                       |       |                  |    |               |
| Male                                  | 37(62.71%)                           | 22(37.28%)                            | 59    | 2.677            | 1  | 0.10          |
| Female                                | 51(76.11%)                           | 16(23.88%)                            | 67    |                  |    |               |
| <b>Age group</b>                      |                                      |                                       |       |                  |    |               |
| <25                                   | 4(100%)                              | 0(0%)                                 | 4     |                  |    |               |
| 26-45                                 | 12(92.3%)                            | 1(7.7%)                               | 13    | 7.53             | 3  | <b>0.05*</b>  |
| 46-65                                 | 31(73.8%)                            | 11(26.2%)                             | 42    |                  |    |               |
| >65                                   | 41(61.2%)                            | 26(38.8%)                             | 67    |                  |    |               |
| <b>Body Mass Index</b>                |                                      |                                       |       |                  |    |               |
| 18.5-24.9 (normal)                    | 59(69.4%)                            | 26(30.6%)                             | 85    | 0.33             | 2  | 0.8           |
| 25-29.9 (pre-obese)                   | 26(72.2%)                            | 10(27.8%)                             | 36    |                  |    |               |
| >30 (obese)                           | 3(60.0%)                             | 2(40.0%)                              | 5     |                  |    |               |
| <b>History of smoking</b>             |                                      |                                       |       |                  |    |               |
| Yes                                   | 10(55.6)                             | 8(44.4)                               | 18    | 2.03             | 1  | 0.15          |
| No                                    | 78(72.2%)                            | 30(27.8%)                             | 108   |                  |    |               |
| <b>Number of comorbidities</b>        |                                      |                                       |       |                  |    |               |
| < 3                                   | 74(73.2%)                            | 27(26.8%)                             | 101   | 2.83             | 1  | 0.09          |
| >3                                    | 14(56%)                              | 11(44%)                               | 25    |                  |    |               |
| <b>Duration of disease</b>            |                                      |                                       |       |                  |    |               |
| <21 years                             | 65(81.2%)                            | 15(18.8%)                             | 80    | 13.451           | 1  | <b>0.00*</b>  |
| >21 years                             | 23(50%)                              | 23(50%)                               | 46    |                  |    |               |
| <b>Exacerbations per year</b>         |                                      |                                       |       |                  |    |               |
| ≤ 4                                   | 78(88.6%)                            | 10(11.4%)                             | 88    | 48.937           | 1  | <b>0.000*</b> |
| >4                                    | 10(26%)                              | 28(74%)                               | 38    |                  |    |               |
| <b>No. of admissions</b>              |                                      |                                       |       |                  |    |               |
| <4                                    | 66(91.6%)                            | 6(8.4%)                               | 72    | 37.99            | 1  | <b>0.00*</b>  |
| >4                                    | 22(41%)                              | 32(59%)                               | 54    |                  |    |               |
| <b>No. of Critical care admission</b> |                                      |                                       |       |                  |    |               |
| <2                                    | 78(89.6%)                            | 9(10.4%)                              | 87    | 52.38            | 1  | <b>0.00*</b>  |
| >2                                    | 10(26%)                              | 29(74%)                               | 39    |                  |    |               |
| <b>Duration of Hospitalization</b>    |                                      |                                       |       | 33.424           | 1  | <b>0.00*</b>  |
| <18 days                              | 67(89.3%)                            | 8(10.7%)                              | 75    |                  |    |               |
| >18 days                              | 21(41.1%)                            | 30(58.9%)                             | 51    |                  |    |               |
| <b>Adverse events</b>                 |                                      |                                       |       | 15.27            | 1  | <b>0.00*</b>  |
| Yes                                   | 2(18%)                               | 9(82%)                                | 11    |                  |    |               |
| No                                    | 86(74.7%)                            | 29(25.3%)                             | 115   |                  |    |               |

gender, BMI, past history of smoking, or the number of comorbidities. Previous studies have shown that older age and female gender are associated with a higher device error rate.<sup>28</sup>

Our study also highlights that patients with poor inhaler adherence and critical mistakes in inhalation technique were associated with >4 exacerbations per year, >4 no. of admissions, >2 critical care admissions, >18 days duration of hospitalization, and higher adverse events as compared to other groups, respectively. These findings are consistent with previous studies showing that poor adherence and critical mistakes in inhalation technique can lead to poor health outcomes.<sup>16,29</sup> Finally, patients can benefit from identifying barriers to adherence and correcting their critical

mistakes in inhalation technique, which can improve their health status. Future long-term research studies can aid medical professionals in creating therapeutic strategies and instructional materials that will most effectively treat chronic respiratory conditions.

## 5. Conclusion

Study results evidenced that poor adherence and critical mistakes in inhaler technique were associated with a higher number of exacerbations, a higher number of admissions, a higher number of critical care admissions, and a longer duration of hospital stay for treatment, thereby increasing morbidity in patients with obstructive airway disease. Corrections in inhalation technique and education on

responsible behavior for necessary adherence will improve health outcomes.

## 6. Limitations

1. This study was a single center study performed in a tertiary care centre. Hence, the study population might not be representative of the general population. Long-term studies are required to provide better information on the role of adherence and inhalation technique in the long-term management of obstructive airway disease.
2. The socioeconomic status of the patients was not taken into account in this study, which could be a barrier to non-adherence to inhaled therapy.

## 7. Conflict of Interest

None.

## 8. Source of Funding


None.


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