

St. Paul's Hospital Millennium Medical College Graduate Study Program



Magnitude and associated factors of appropriate inhaler use among patients with Chronic Obstructive Pulmonary Disease at chest clinic in St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia: Institutional-based cross-sectional study.

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A thesis to be submitted to the department of Internal Medicine, St. Paul's Hospital Millennium Medical College in partial fulfillment of the requirement for specialty certificate in Internal Medicine

February 2024, ADDIS ABABA, ETHIOPIA.

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List of Abbreviations and Acronym:

BAI: breath-actuated pressurized metered-dose inhaler

COPD: Chronic Obstructive Pulmonary Disease

DPI: Dry Powder Inhaler

FEV1: Forced Expiratory Volume in one second

FVC: Forced Vital Capacity

GOLD: Global Initiative for Chronic Obstructive Lung Disease

LASSYC: The Latin American Study of 24-hour Symptoms in Chronic Obstructive Pulmonary Disease

OPD: Outpatient Department

PCCM: Pulmonology and Critical Care Medicine

pMDI: Pressurized Metered Dose Inhaler

SMI: Soft Mist Inhaler

SPHMMC: Saint Paul Hospital Millennium Medical College

TAI: Test of the Adherence to Inhaler

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ABSTRACT

Introduction: Inhalation therapy is the backbone of Chronic Obstructive Pulmonary Disease control. Appropriate inhaler technique is crucial for the effective management of Chronic Obstructive Pulmonary Disease. Device mishandling is a big problem in clinical practice bringing a significant challenge to the optimal disease management of patients with Chronic Obstructive Pulmonary Disease.

Objectives: This study aims to assess the magnitude of appropriate inhaler utilization and to identify factors influencing patient adherence to inhalers and relationships between specific inhaler errors.

Methods: An institutional-based cross-sectional, using a semi-structured questionnaire and a validated tool, Test of the Adherence to Inhalers(TAI), was conducted on a sample of 257 COPD patients, who fulfilled the inclusion criteria at St. Paul's Hospital, Millennium Medical College. Data entry was done using EPI data and analyzed using SPSS software version 26. A multivariate logistic regression analysis was used to determine variables that will be independently associated with poor inhaler technique at a p-value ≤ 0.05 .

Results: About 253 participants were included. About 61% of the participants demonstrated inappropriate inhaler use. The most commonly mis-performed critical error was failure to breathe out gently (as far as is comfortable) and failure to hold breath for 5 to 10 seconds. Being male was associated with 2.1 folds increment of appropriate inhaler use compared to female (AOR=2.1, 95%CI=1.16, 3.69) and study participant whose education level of collage and above had 2.9 folds increment of appropriate inhaler use compared to those of haven't formal education (AOR=2.9, 95%CI=1.23, 6.83). Study participant who was not taking training were 60% less likely to have appropriate inhaler use compared to trained ones (AOR=0.4, 0.17, 0.90) and study participant whose duration of inhaler 10-15 years had 5.1 folds increment of appropriate inhaler use compared to whose duration of inhaler use was <1 years (AOR=5.1, 95%CI=1.32, 79.64).

Conclusion: COPD patients with no training about the correct use of inhaler were 60% less likely to use the inhaler correctly compared with those patients who had the training. It is recommended that care providers could direct their focus of demonstration towards common errors, including failure to breathe out gently and to hold breathe for 5 to 10 sec. in order to increase correct inhaler use.

Key words: inhaler, chronic obstructive pulmonary disease, appropriate inhaler use

1. Introduction

1.1 Background

According to Global initiative for Obstructive Lung Disease(GOLD) 2023, Chronic Obstructive Pulmonary Disease(COPD) is a heterogeneous condition of chronic respiratory symptoms ranging from chronic and progressive dyspnea, cough, sputum production, and exacerbations attributed to persistent, likely progressive airflow obstructions resulting from abnormalities of the airways and/or alveoli. It is a lifestyle-related disease caused by exposure to cigarette smoking and other environmental noxious exposures including indoor and outdoor pollutions. It results from lifetime interactions of genetics and environment. A diagnosis of COPD is considered in a patient who has dyspnea, chronic cough or sputum production, with or without exposure to risk factors for the disease. Spirometry is important to confirm diagnosis of COPD. The presence of non-fully reversible airflow limitation expressed in terms of the ratio of forced expiratory volume in the first one second to the forced vital capacity($FEV_1/FVC < 0.7$ post-bronchodilator) measured by spirometry confirms the diagnosis of COPD(1).

Management of COPD includes non-pharmacologic and pharmacologic interventions. Inhaled medications are the mainstay of COPD treatment. They provide rapid delivery of medications to the lungs to maintain high local concentration at target areas to prevent adverse effects from systemic exposure. They also provide high-dose of local drug administration to decrease systemic toxicity. Inhaled therapies for COPD include bronchodilators and corticosteroids which can be administered via different types of devices including pressurized metered dose inhalers (pMDIs), dry powder inhalers (DPI), soft mist inhalers (SMI) and breath-actuated pressurized metered-dose inhalers (BAI) (2–4).

There are about four classes of inhaler devices used to deliver a variety of inhaled medications including bronchodilators like beta-agonists and anticholinergic as well as glucocorticoids: the pressurized metered dose inhaler (pMDI), the dry powder inhaler (DPI), the soft mist inhaler (SMI) and breath-actuated pressurized metered-dose inhalers (BAI) giving over 200 drug-inhaler device combinations. Among these devices, pMDIs and DPI are most commonly used worldwide, pMDIs are being prescribed most despite the limitation that patients need to inhale correctly and coordinate breathing and actuation to ensure effective drug delivery(5,6).

Approaches to appropriate inhalation varies with class of devices and, in turn, devices within classes could have slight differences in specific handling and inhalation technique to optimize delivery and administrations. Pressurized metered dose inhaler (pMDI) are used to deliver a standardized dose upon pressing of the canister and require the patients to coordinate the timing of the canister depression and their inhalation. Apart from breath-actuation, breath control is vital to the appropriate inhalation of pMDIs. Combination of fast inhalation and energy of the pressurized dose delivery can result in oropharyngeal deposition of the medication unless appropriate breath- actuation is established.

Unlike pMDIs, BAIs reduces actuation-breath coordination errors via the power of the patient's breath to trigger the actuation. In contrast to pMDIs and BAIs, DPIs are inspiratory flow driven working with the patient's inspiratory effort as both the trigger and the actuation energy for the dispensed dose avoiding the coordination requirement. DPIs need a minimum inspiratory flow, which can be a barrier for patient with compromised lung function as in elderly and in exacerbation, to achieve targeted dispensing of the prescribed therapeutic dose. Appropriateness of inhaled therapy needs delivery of targeted dose to lower lung areas. It is achieved when the dispensed dose leaving the device and breath control are matched appropriately(5,6).

1.2 Statement of the Problem-

Chronic Obstructive Pulmonary Disease (COPD) is a common treatable and preventable chronic condition affecting about 10.3% of the population globally. It has its own effective pharmacotherapies requiring long-term adherence in order to bring positive outcomes(1). Prevalence of COPD in Ethiopia is largely unknown. It is under-reported due to under diagnosis, and under recognition. From a community based cross sectional study which was conducted in Abeshge district of Gurage Zone, the prevalence of COPD was 17.8%(7).

Inappropriate inhaler use and non-adherence to inhalers is a global challenge to patients in particular and society in general. Worldwide, magnitude of adherence to COPD therapy is alarmingly low. It is as low as 22% in south Korea, 23.4% in United States, 23.9% in Belgium, 25% in Canada, 29.2% in China, 32.4% in Spain, 27.4% in Nigeria(8). In most countries, except Brazil and Italy, adherence rate in asthmatic patients is nearly as low as that of COPD: 22.2% in United States, 24.9% in France, 18% in Ethiopia(8,9).

Surprisingly, the level of adherence in COPD patients is very low, lower than that recorded for other chronic diseases, nearly 33%(10). JM Sánchez-Nieto et al., in a prospective non randomized single group study in Madrid using TAI showed that 72.8% had inappropriate inhaler use and 67.5% had Low adherence, the most common (65.8%) error being erratic (forgetting to use inhaler), followed by unwitting and deliberate in 57.5 and 43.5% respectively(11). According to Lignot S, et al. under 40% of patients are capable of doing perfect inhalation according to the package instructions leaflet regardless of device type(12). According to a study done on asthmatic patients in university of Gondar teaching and referral hospital in 2016, 50.6% of patients had inappropriate inhaler use, prevalence of non-adherence(10 item TAI score less than 45) being 18.3% (13).

Despite the progressive nature of COPD, the negative effects of poor adherence to prescribed treatment are well known(14). Level of appropriate inhaler use is very low and this has a negative influence on outcomes. Handling errors of inhaler devices are underestimated in clinical practice and are contributing factors for increased rate of mortality, poor disease control, poor quality of life and severe COPD exacerbation according to Duarte-de-Araújo A, et al., a study done in Hospital de Guimarães, Portugal(15).

The presence of huge inappropriate inhaler use and non-adherence to COPD management brings a significant clinical and socio-economic consequence. Errors in inhaler technique and non-adherence brings poor control of COPD, resulting in increased risk of hospitalization,

emergency visits, systemic glucocorticoid use, avoidable escalation of therapy and reduced quality of life(16,17). Inappropriate inhaler use results in suboptimal drug delivery to target sites thus reducing the effective medication dose. Inhaler errors are also associated with increasing economic burden; according to Lewis et al poor inhalation technique costs about ¾ billion euros in direct and indirect costs only for two DPI inhalers used about 1 year(18,19). According to a study in Mexico, 28–68% of patients failed to use their inhalers appropriately. In this similar study, there was an estimated 7-15.7 billion United States Dollar direct loss(20).

Locally, a number of studies regarding appropriate use of inhalers are done on asthma patients. To my best knowledge, less is studied in COPD patients. Treatment of COPD is so complex than asthma, with patients needing to make behavioral and lifestyle changes such as smoking cessation and adherence to exercise therapy along with optimal medication adherence.

1.3 Significance of the Study-

According to existing local data, less is recognized about adherence in COPD. There are only few published studies conducted to address non-adherence even in asthmatic patients in Ethiopia. Apart from this scarcity of data, most studies lacks the methodology specific to inhalational therapy.

This study tried to find the level of non-adherence and to identify factors associated with non-adherence. The results of this study will help to fill local data gap, and help to understand factors that promote adherence to medication, and increase effective management of COPD. The aim of this institutional based study is to provide local data regarding magnitude of inhaler misuse and factors associated with appropriate inhaler use. It will serve as baseline towards subsequent studies to look for outcomes of inappropriate inhaler use.

2. LITERATURE REVIEW:

2.1 Magnitude of Non-Adherence and Inappropriate Inhaler Use

Adherence is the level to which a patient correctly accepts a health plan issued and agreed to by the patient and a clinician in health care decision-making. It includes the initiation, implementation, and persistence of a treatment plan. It is fundamental in optimal disease management. Administration of inhaled medication requires knowledge and understanding of the appropriate inhaler technique. Non-adherence encompasses poor initiation, implementation (including poor inhalation technique) and non-persistence. Improper use of inhalers can interfere with effective drug delivery to the airways, leading to poor disease control(5,8).

The magnitude of incorrect inhaler use has been well documented; in several studies, more than one-half of the patients used their inhaler inappropriately(12,15,21,22). A prospective cross-sectional study done in South Korea showed that at least one critical error was observed in 42.9% of participants. Most errors were found in pMDIs accounting about 57% followed by SMI (nearly 43%)(23).

According to a study done in France, Critical errors were made in majority (60 %) of the patients mainly with non-breath-actuated devices including pMDI and Respimat®), where poor hand–lung incoordination was the main attributing factor. Most common errors were failure to hold breath a few second after inhalation (27%), unable to exhale before actuation (23%) and inhalation through nose. These errors were found in 50-57% and were device independent (12).

2.2 Factors Associated With Inappropriate Inhaler Use:

Several factors predispose to inappropriate inhaler use. Among these factors patients' perception of their disease, lack of education about the proper use of inhalational medications, poly pharmacy, age, disease severity, co-morbidities, choice of training methods, checking patient inhaler technique at subsequent visits, smoking, choice of medicines, limited patient-clinician interaction, cost of medicines and device selection are important factors affecting the level of non-adherence. type of treatment or medication, the quality of patient provider communication, the social support are important contributors of inhaler non- adherence(24,25)

Training is critical to appropriate inhaler use and subsequent disease control. According to a study done in Barcelona, Spain, a significant proportion of patients did not get training on proper use of inhaler device; about 39%–67% of clinicians do not train their patients on the correct use of their inhalers. Appropriate inhaler technique training and close inhaler technique checks are vital(26,27). Reassessing of inhaler technique during regular visit is an important time to address appropriate inhaler use. Based on real survey, 29% of patients never checked regarding their device handling to see if they were using their inhaler correctly. Patients who were checked were significantly more adherent than unchecked patients were. Demonstration of inhaler use was the

most common method of training followed by video, instructions for use, and leaflet in 83%, 58%, 51% and 34% respectively (3). In a cross-sectional study among asthmatic patients on inhalers conducted in university of Gondar teaching and referral hospital, patients who were untrained about appropriate technique were 8 times more likely to be non-adherent compared to trained one(13).

Patients with good understanding of their illness and medications tend to have greater adherence(28,29)

No association was demonstrated between GOLD stage of COPD and adherence level; 81%, 80% and 77% of patients with moderate, severe and very severe COPD, respectively were having good adherence(30).

Changing inhaler device type is another factor leading to inhalation error. Device switching parallels worsening of disease control, increased exacerbations, low quality of life(20).

According to David Price et al., younger age is related to lower adherence(3). This might be due to mild to moderate degree of severity of COPD in this group of age.

There is a great variation of inhaler devices with various technical requirements. Selecting suitable inhaler tend to promote adherence to inhaler therapy(31). According to David Price et al., there was no measurable difference in adherence between genders, disease severity and duration of disease(3).

Comorbidities are nearly integral part of COPD. Nearly 86% to 98% of COPD patients have at least one comorbidity(32). Both comorbidities and poor adherence to inhalers are prevalent in COPD. About 77% of COPD patients have more than 2 comorbidities, among these obesity accounts nearly 82% followed by hypertension (73%), diabetes mellitus (58%)(33).

Assessing adherence to COPD management is complex. There are many proposed methods including clinician estimates, patient self-reporting, pharmacy records, and electronic monitoring. Patient's self-report methods accompanied with inhaler technique assessment are considered the most suitable for measuring adherence to medication in clinical practice, even though patients tend to over-estimate adherence. Among self-reporting tools to determine adherence, TAI questionnaire help to identify non-adherence and barriers related to the use of inhalers in patients with COPD and asthma(34). TAI is a reliable and homogeneous questionnaire designed to identify non-adherence and to classify from a clinical perspective the barriers related to the use of inhalers in asthma and COPD. The 12-items TAI instrument allowed the classification of three non-adherence patterns into erratic, deliberate and unwitting behaviors. The 10-items TAI scores for identifying the groups of adherent, intermediate adherent and non-adherent patients(35).

There are only few studies investigating the appropriate use of inhalers among COPD patients in Ethiopia. This study was conducted to find the level of non-adherence and to identify factors associated with non-adherence. The results of this study will help to fill local data gap, and help to understand factors that promote adherence to medication, to increase effective management of COPD.

2.3. Conceptual Framework

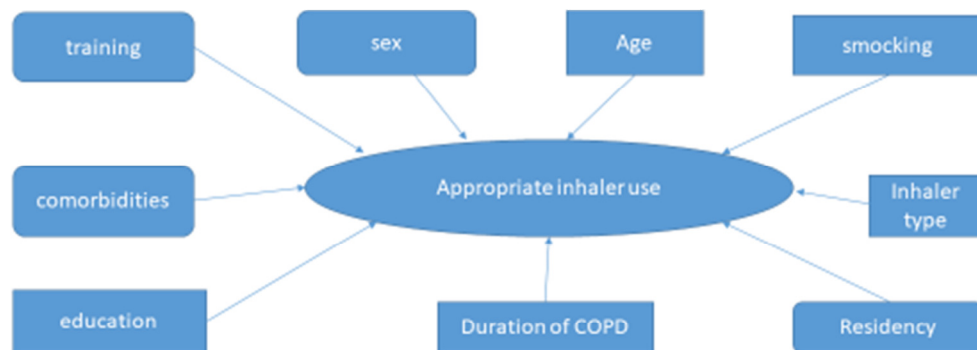


Figure 1: conceptual framework showing the possible factors affecting appropriate inhaler use, Feb 2024

3. Objectives

3.1 General Objective

To assess the magnitude of appropriate inhaler utilization and its associated factors among patients with physician-diagnosed COPD, SPHMMC, Ethiopia, 2023

3.2 Specific Objectives

1. To assess the magnitude of appropriate inhaler use.
2. To assess factors associated with appropriate utilization of inhalers.

4. Methods and Materials

4.1 Study Design and Study Setting:

The study was a cross sectional study in stable COPD patients. It was conducted in SPHMMC medical outpatient department (OPD) chest clinic among COPD patients from August 2023 to January 2024. St Paul Hospital Millennium Medical College is one of a few university referral hospitals in the country, located in the capital city, Addis Ababa, of Ethiopia. The hospital gives outpatient and inpatient services for referred cases from across the country. Chest clinic is one of the outpatient services in the hospital. In the chest clinic where care is given for clients with COPD and other pulmonary disorders, there are two pulmonologists, monthly rotating year II internal medicine residents actively giving different services including teaching inhaler technique.

4.2 Population:

4.2.1 Source population

Source population was all adult COPD patients on follow up at chest OPD in SPHMMC

4.2.2 Study population

Study population was all adults with stable COPD at chest OPD in SPHMMC that fulfil the inclusion criteria.

4.3 Eligibility Criteria:

4.3.1 Inclusion criteria

Male and female outpatients, Age ≥ 18 years,

Patients able to give informed consent,

Stable disease (without exacerbation treatment and changes in current treatment in the previous 1 month),

Patients already on prescribed inhaler

4.3.2 Exclusion criteria

Patients not on inhaler medications at the time of data collection,

Patients with acute exacerbation,

4.4 Sample Size and Sampling Technique and Procedure:

4.4.1 Sample size determination

The Sample size for the first objective was calculated based on proportion of correct use of all inhaler devices using a single population proportion formula. Bao et al. conducted a similar study at the Department of Respiratory, University Medical Center Ho Chi Minh City, Vietnam from September 2020 to May 2021 and reported a correct inhaler use rate of 18.7%(36). Using this proportion and with the assumption of confidence level of 95%, margin of error of 5% and 10% non-response rate, the sample size was calculated as follows:

$$n = (Z\alpha/2)^2 p(1-p) / d^2$$

Where n=sample size

Z= 95% confidence interval (1.96)

P= prevalence = 18.7%

d = margin of error = 0.05

$$n = (Z_{\alpha/2})^2 p (1-p) / d^2$$

$n = (1.96 \times 1.96) \times 0.187 \times 0.8130 / (0.05 \times 0.05) = 233$ considering 10% non-response rate the final calculated sample will be 257.

4.4.2 Sampling Technique and Procedure

Information from registration logbook and patients' medical records was used to identify patients. A monthly average of 48 (from March 2023 to July 2023) COPD patients were registered, making yearly COPD visits approximately 576. Survey sampling was used to incorporate study participants. Participants who meet eligibility criteria and those providing consent were enrolled in the study.

About 348 participants were screened in the study period from August 2023 up to January 2024; ninety-one participants were excluded from participation in the study. Among these, 51 were not with their inhaler, 28 did not provide consent and 12 had respiratory distress at OPD visit.

Data collectors made a scheduled study visit, explain the patient the purpose of the research, and invite to participate. At study visit, selected patients were asked to provide data on disease-related symptomatology, adherence to inhalers, and inhalation technique was assessed according to inhaler specific checklists.

4.5 Study Variables:

4.5.1 Dependent variables

Appropriate inhaler use (yes or no)

4.5.2 Independent variables

- Age,
- Sex,
- Education level,
- Residency area,
- Smoking history,
- Duration of COPD,
- Training,
- Inhaler type,
- Number of inhaler type ,
- Comorbidities.

4.6 Operational Definitions:

A physician considers COPD diagnosis when a patient is presented with chronic respiratory symptoms including, chronic cough with or without sputum production, and progressive dyspnea, in the absence of other confirmed chronic respiratory diseases like interstitial lung disease, obstructive sleep apnea, and pulmonary hypertension.

Inappropriate inhaler use: In this study, inappropriate inhaler use was defined as 10 item TAI score less than 50(35).

Adherence: Adherence is considered *good* if patient is taking full daily inhaler requirement in terms of frequency and dose (The 10-item TAI scores with 50), intermediate adherent for scores 46 to 49 for, and non-adherence(poor) if scores ≤ 45 (35).

An erratic and deliberate non- adherent behavioral pattern are defined in the presence of scores ≤ 24 for items #1 to #5 and items #6 to #10, respectively(35).

The unwitting pattern is defined in the presence of a score 1 in at least one of the #11 or #12 items of the questionnaire(35).

Critical errors: critical errors are defined variously in different literatures. Generally, errors resulting in insignificant or no deposition of drug in to lungs are considered critical error. These incorporates unable to open the device correctly, failure to form tight seal around the mousepiece, difficulty of deep enough inhalation(23). Device specific critical errors are provided along with the checklists including:

A, Turbuhaler: Failure to grasp upright while priming, unable to prime (rotating grip anticlockwise and then back until the click sound is heard)(23).

B, pMDIs: Failure to shake well, failure to hold inhaler upright, failure to synchronize between actuation and inhalation, failure to breathe deeply(23)

Urban residency: The one who live in city or town

Rural residency: The one who live outside of city or town

Smocking: cigarette use including second hand

Education level was defined as follows:

low-level: pre-primary, primary,

middle-level: secondary and preparatory;

high-level: tertiary and above

4.7 Data Collection Tool And Procedures:

Primary data was collected from the study subjects using structured and pretested questionnaire including 12-item TAI and checklists.

The 12-item TAI help to assess intentional non-adherent behavioral patterns as well as non-adherence patterns observed by the health care professional.

The 12-item TAI questionnaire was developed in Spain to assess the non-adherence level. It has two main domains, including the patient and the health professional domains, developed to assess the adherence to inhaled medication. The patient domain is a 10-item TAI (items #1 to #10) each item scored from 1 to 5

(where 1 being the worst possible score and 5 being the best possible score, with a range from 10 to 50. The 10-item TAI help to classify adherence levels. The health professional domain is a two- item TAI (items#11 and #12) each item scored 1 or 2 where 1 is bad and 2 being good(35).

Inhalation technique was evaluated using prepared checklists of correct steps and critical errors created for each inhaler, and inhalers' misuse was defined when one or more errors that are critical were made, whatever the number or types of inhalers in use.

The questionnaire was prepared in English. Finally, the questionnaire was pre- tested on 5% of patients before the actual data collection.

Trained three medical students, and pulmonology and critical care medicine rotating residents collected data. Medical record of the study subjects, which was recorded by treating doctors, was used to confirm the clinical related variables.

4.8. Data Processing And Analysis:

Data was collected from the patients and the medical record charts of patients diagnosed with COPD using structured data collection format. After the completeness of all the information on the questioners was checked, cleaned, coded, and entered using EPI DATA and analyzed using SPSS software version 26. Data was summarized descriptively using frequencies and percentages.

Each variables were evaluated independently in a bi-variable analysis to see their relationship with the dependent variable and those with a p-value of 0.2 or less were considered a candidate variable for multivariable logistic regression analysis. In multivariable analysis, variables with a p-value of less than 0.05 were considered as significantly associated with the dependent variable and association was expressed with AOR(adjusted odds ratio) at 95% CI (confidence interval). Tables and charts were used for data presentation.

4.9. Ethical Considerations:

Ethical clearance was obtained from Institutional Review Board of SPHMMC. Data collection was commenced after obtaining the permission. Written Informed consent was obtained from each respondent after explaining the purpose of the study. Participants were informed that participation is voluntary and they could withdraw from the study at any stage if they desire. Participant's confidentiality was guaranteed by not recording their personal identifiers on the questionnaire. All information that was obtained from the individual will be treated confidential and will be used only for the study purpose.

4.10. Plan for Dissemination of Results:

The results of this study will first be presented to the staffs of Internal medicine and public health departments during the research defense presentation. It will also be submitted to the hospital's pulmonology unit. Further efforts will be made to publish the information in peer-reviewed journals and make presentations in scientific conferences.

5. Result

5.1 Sociodemographic Characteristics of the Study Participants

In this study, 253 study participants were involved making a response raspssste of 98.4%. Fifty-nine percent of the study participants were female and 35.2% of the study participants were in the age group of 36-50 years with mean and SD of 53.2 ± 14.5 respectively. Three-fourth of the study participants were urban in residency and 32.8% had an education level of primary level.

Table 1. The sociodemographic characteristics of the study participants, August 2023 to Feb 2024

Variables	frequency	Percent
Sex of the study participants		
Male	104	41.1
Female	149	58.9
Age in years		
18-35	29	11.5
36-50	89	35.2
51-65	83	32.8
>65	52	20.6
Residence		
Urban	194	76.7
Rural	59	23.3
Education level		
Illiterate	69	27.3
Primary	83	32.8
Secondary	51	20.2
Higher	50	19.8

5.2 Disease-related Characteristics of the Study Participants

Most of (84.2%) of the study participants were taking training about techniques of inhaling and among trained participants, 51.9% received from demonstration. Nearly 36% of the study participants had a duration of disease 1-5 years with a mean duration of 12.77 years and 71.1% of the participants use inhalation within 1-5 years duration. Most of (80.6%) the participants

were never smoker and 49.8% of the study participants had comorbid disease. Forty-seven percent of the study participants used to take ploy-pharmacy.

Table 2. Disease related characteristics of the study participants, August 2023 to Feb 2024

Variable	Frequency	Percent
Prior training about inhaler		
Yes	213	84.2
No	40	15.8
Methods of training (n=213)		
Demonstration	111	51.9
Video	3	1.4
Doctors	64	29.9
Pharmacy	36	16.8
Duration of disease in years		
<1	14	5.5
1-5	92	36.4
6-10	51	20.2
11-15	19	7.5
>15	77	30.4
Duration of inhaler use in years		
<1	19	7.5
1-5	180	71.1
6-10	31	12.3
11-15	12	4.7
>15	11	4.3
Smoking history		
Current smoker	1	0.4
Ex-smoker	48	19
Never smoker	204	80.6
Comorbidity		
Yes	126	49.8
No	127	50.2
Poly pharmacy		
Yes	119	47
No	134	53

5.3 The types of Comorbid Disease

Among participants having comorbid disease, 69.1% of the study participants had hypertensive disorder followed by diabetes mellitus (23.8%), heart failure (15.9%) and nerve as shown the figure below.

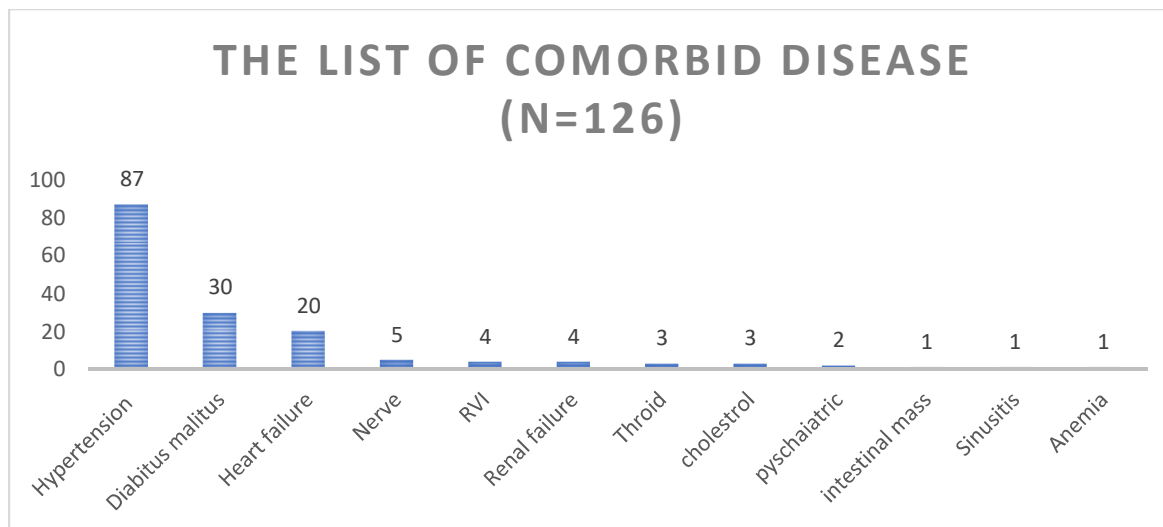


Figure 2: the list of comorbid diseases of the study participants, February 2024

5.4 The characteristics of Inhalers practice

5.4.1 The magnitude of appropriate inhaler use

The finding of the study showed that 39% of the study participants had appropriate adherence of inhaler as shown in the figure below

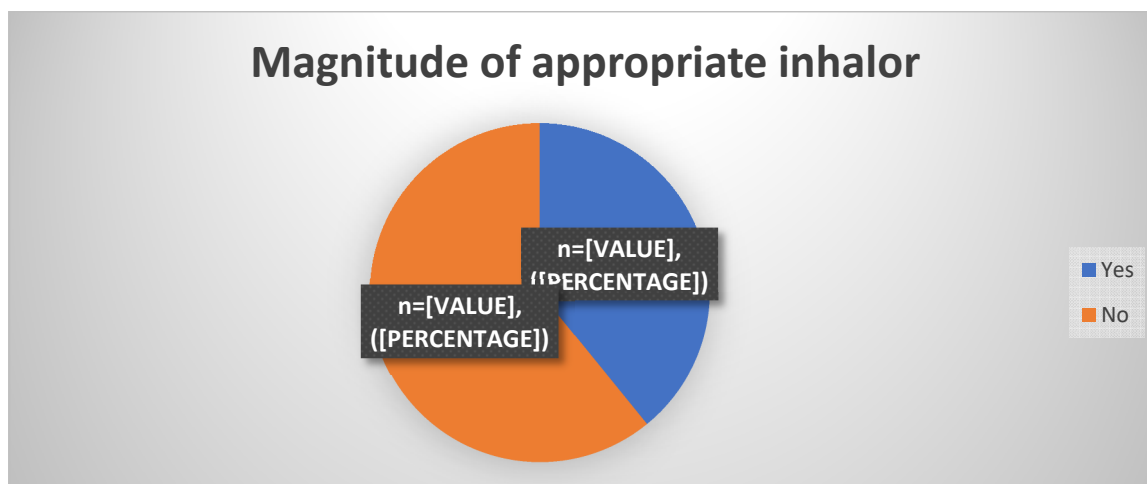


Figure 3: The magnitude of appropriate inhaler use, February 2024

5.4.2 The study participants level of adherence

The finding of the study also showed that, 39% of the participants had good adherence, 36% had intermediate adherence and 25% had poor adherence to inhaler use.

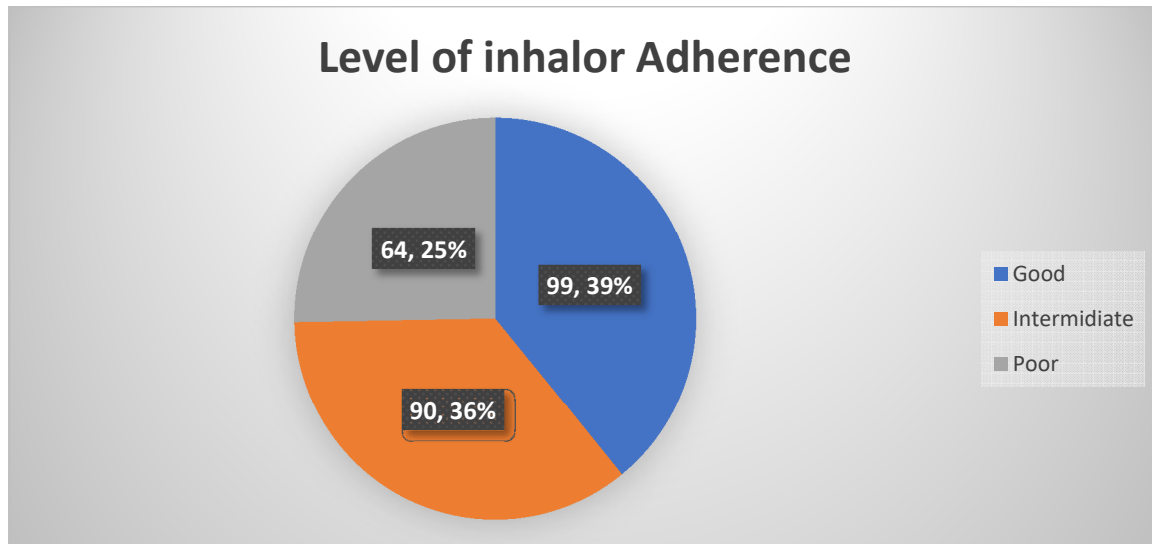


Figure 4: Level of inhaler adherence, Feb 2024

5.4.3 The erratic and deliberate non-adherence behavioral pattern

Thirty-eight percent and 49.4% of the study participants had erratic and deliberate non-adherence behavioral pattern respectively as shown in the figure below.

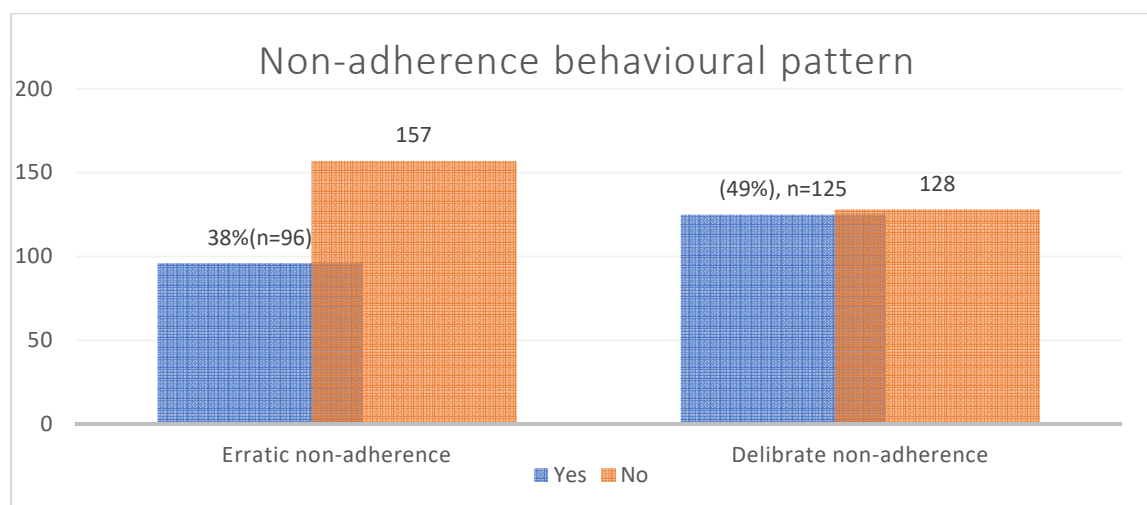


Figure 5: The erratic and deliberate non-adherence behavioral pattern, February 2024

Concerning to the specific characteristics of the inhaler measurement, 4.3% of the study participants always forget to take the usual inhaler prior to seven days of data collection and 18.6% of the study participants used to forget to take the inhalers approximately half the time. Almost seventy-eight percent of the study participants were not used to stop taking inhalers when feeling good of their illness and 92.9% of the participants were not used to stop taking inhalers when they were nervous or sad and 93.3% were not stop inhaler by fearing side effect as shown the table below.

Table 3. The characteristics of study participants Inhalers practice, August 2023 to Feb 2024

Patient Domain(10-item): questions, responses	All	More than half	Approximately half	Less than half	none
1. During the last 7 days, how many times did you forget to take your usual inhalers?	11(4.3)	9(3.6)	17(6.7)	30(11.9)	186(73.5)
2. Do you forget to take inhalers?	Always(1)	Mostly(2)	Sometimes(3)	Rarely(4)	Never(5)
		11(4.3)	47(18.6)	12(4.7)	183(72.3)
3. When you feel good about your illness, do you stop taking your inhalers?	4(1.6)	17(6.7)	24(9.5)	11(4.3)	197(77.9)
4. When you are on vacation or weekend, do you stop taking your inhalers?		6(2.4)	6(2.4)	9(3.6)	232(91.7)

5. When you are nervous or sad, do you stop taking your inhalers?		5(2)	7(2.8)	6(2.4)	235(92.9)
6. Do you stop taking your inhalers because of fear of side effects?		5(2)	6(2.4)	2.4)	236(93.3)
7. Do you stop taking your inhalers because of considering they are useless to treat your condition?		7(2.8)	4(1.6)	8(3.2)	234(92.5)
8. Do you take fewer inhalations than those prescribed by your doctor?		10(4)	15(5.9)	8(3.2)	220(87)
9. Do you stop taking your inhalers because you believe they interfere with your everyday or working life?		5(2)	4(1.6)	8(3.2)	236(93.3)
10. Do you stop taking your inhalers because you have difficulties to pay them?	9(3.6)	27(10.7)	56(22.1)	21(8.3)	140(55.3)

5.5 Health professional domain characteristics of inhaler

In this study, 96.4% of the study participants were able to remember the dose and frequency of the prescribed regimen and 70% of the study participants were used to make critical errors.

Table 4. Health professional domain characteristics of inhaler use, *August 2023 to Feb 2024*

Variable	Response	Frequency
Does the patient remember the prescribed regimen (dose and frequency)		
Yes	244	96.4
No	9	3.6
The technique of using the evaluated inhaler device by the patient		
With critical mistake	180	71.1
Without critical mistake	73	28.9

Table 5: utilization characteristics of DPI-Symbicort Turbohaler, *Feb 2024*

Technique	Response (n=135)	
	Yes (%)	No (%)
Unscrew the cover and lift it off	134(99.3)	1(0.7)
Hold your Symbicort Turbohaler upright with the red grip at the bottom	125(92.6)	10(7.4)

Turn the red grip as far as it will go in one direction. Then turn it as far as it will go in the other direction (it does not matter which way you turn it first). You should hear a click sound	119(88.1)	16(11.9)
Breathe out gently (as far as is comfortable). Do not breathe out through your Turbohaler.	54(40)	81(60)
Place mouthpiece between teeth (without biting) and close lips to form a good seal. Breathe in as deeply and as hard as you can through your mouth (5-10 seconds)	121(89.6)	14(10.4)
Remove inhaler from mouth	113(83.7)	22(16.3)
Breathe out gently (away from inhaler)	125(92.6)	10(7.4)

Table 6: Utilization characterization of pMDI, August 2023 to Feb 2024

Technique	Response (n=118)	
	Yes (%)	No (%)
open the inhaler, remove the mouthpiece cover	118(100)	0
Hold the inhaler upright with your thumb on the base and your finger on the top of the canister	110(93.2)	8(6.8)
Shake the inhaler up and down 4 to 5 times	104(88.1)	14(11.9)
Breathe out as much as is comfortable	45(38.1)	73(61.9)
Put mouthpiece around your lips and make a seal around the mouthpiece	113(95.8)	5(4.2)
Start to breathe in slowly. As you begin to breathe in, push the top of the canister to release a dose. Continue breathing in slowly and gently until your lungs are full	110(93.2)	8(6.8)
Remove the device and hold breath for 5 to 10 seconds then exhale slowly	98(83.1)	20(16.9)
Breath normally	118(100)	0
Put the mouthpiece cover on and close	118(100)	0

Dry powder inhalers- (Symbicort Turbohaler) was used most often, nearly 53%. Among 135 participants on DPI- symbicort turbohaler, 96(71%) tend to practice critical errors. The same proportion of participants on pMDI, 71%, used to make critical errors.

Table 7: critical errors among study participants, August 2023 to Feb 2024

measurement	frequency	Percent
Turbuhaler		
Critical error	96	71.1
No critical error	39	28.9
PMDI		
Critical error	84	71.2
No critical error	34	28.8

5.6 Determinant Factors of Appropriate Inhaler Use

Logistic regression was used to measure the association of dependent and independent variable. Accordingly, sex, education level, training about inhaler were an association with appropriate inhaler by bivariate logistic regression. The multivariate logistic regression revealed that being male sex was associated with 2.1 folds increment of appropriate inhaler use compared to female (AOR=2.1, 95%CI=1.16, 3.69) and study participant whose education level of collage and above had 2.9 folds increment of appropriate inhaler compared to those of under college education (AOR=2.9, 95%CI=1.23, 6.83).

Study participant who was not taking training were 60% less likely to have appropriate inhaler use compared to trained ones (AOR=0.4, 0.17, 0.90) and study participant whose duration of inhaler 10-15 years had 5.1 folds increase its appropriate inhalers compared to whose duration of inhaler use was <1 years (AOR=5.1, 95%CI=1.32, 79.64).

Table 8. The bivariate and multivariate logistic regression of association between dependent and independent variable among COPD at chest clinic in SPHMMC, August 2023- February 2024.

Variable	Appropriate inhaler		p-value	COR with 95%CI	P-value	AOR with 95%CI
	Yes	No				
Sex of the study participants						
Male	54	50	0.001	2.5(1.48, 4.19)	0.014	2.1(1.16, 3.69)
Female	45	104	1		1	
Age in years						
18-35	14	15	1		1	
36-50	29	60	0.130	0.52(0.22, 1.22)	0.110	0.47(0.18, 1.19)
51-65	35	48	0.569	0.78(0.33, 1.83)	0.594	0.77(0.29, 2.00)
>65	21	31	0.492	0.73(0.29, 1.81)	0.333	0.59(0.20, 1.72)
Residence						
Urban	82	112	1		1	
Rural	17	42	0.066	0.55(0.29, 1.04)	0.711	0.87(0.42, 1.79)
Education level						
Illiterate	20	49	1		1	
Primary	20	53	0.350	1.4(0.69, 2.76)	0.702	1.2(0.55, 2.42)

Secondary	20	31	0.241	1.6(0.74, 3.40)	0.478	1.4(0.57, 3.28)
Collage and above	29	21	0.002	3.4(1.57, 7.27)	0.015	2.9(1.23, 6.83)
Training about inhaler						
Yes	91	122	1		1	
No	8	32	0.009	0.34(0.15, 0.76)	0.048	0.4(0.17, 0.90)
Duration of disease in years						
<1	5	9	1		1	
1-5	35	57	0.867	1.1(0.34, 3.57)	0.514	0.42(0.03, 5.69)
6-10	17	34	0.868	0.9(0.26, 3.11)	0.333	0.26(0.02, 3.99)
11-15	12	7	0.124	3.1(0.73, 12.98)	0.915	1.2(0.07, 20.17)
>15	30	47	0.818	1.1(0.35, 3.76)	0.493	0.39(0.03, 5.81)
Duration of inhaler						
<1	6	13	1		1	
1-5	69	111	0.565	1.3(0.49, 3.71)	0.300	3.5(0.33, 38.65)
6-10	13	18	0.465	1.6(0.47, 5.21)	0.318	3.6(0.29, 45.72)
11-15	7	5	0.147	3.0(0.68, 13.61)	0.049	5.1(1.32, 79.64)
>15	4	7	0.789	1.2(0.26, 5.91)	0.410	3.2(0.19, 52.32)

6. Discussion

Using an inhaler properly is crucial for effective management of chronic obstructive pulmonary disease. It is also a predictor of treatment compliance and adherence. In this cross sectional study, appropriateness of inhaler technique was assessed using validated tool, TAI.

The finding of this study revealed that 39% of the study participants had appropriate inhaler use. This finding was higher than Bao, L.K et al. (36) (18.7%), Chau et al. (37) (24.3%), Chaicharn et al.(38) (25.2%), Melzer et al. (39) (34.5%), and Johanna et al. (40) (34.0%). In developed countries, appropriate inhaler use ranges from 28-35% and it remains unchanged since 1975(41). The higher rate of appropriate inhaler use in this study might be due to limited number of device types studied.

In this study, 61% of the study participants used their inhalers inappropriately. This finding was supported by the study done Molimard M, et al, Duarte de et al.(60.4%)(12,15).

Among inhaler devices, pMDIs and DPI are most commonly used worldwide, pMDIs are being prescribed most despite the limitation that patients need to inhale correctly and coordinate breathing and actuation to ensure effective drug delivery(5,6). In this study, Dry powder inhalers-

(Symbicort Turbohaler) was used most often, nearly 53%. About 71% of participants tend to practice critical errors. Among these, 58 % (n=104) were female. The critical errors most commonly mis-performed were failure to breathe out gently (as far as is comfortable) (60%), and failure to prime (rotating grip anticlockwise and then back until the “click” sound is heard) in 12% when using Dry powder inhalers- Symbicort Turbohaler.

Two critical errors most commonly misperformed were failure to breathe out as much as is comfortable (62%) and failure to hold breathe about 5 to 10 seconds (17%) when pMDI is used.

The finding of the study also revealed that 71.1% of the study participants had critical mistake on technique of using the evaluated inhaler device, despite 84% got previous training about inhaler handling.

Sex may affect appropriate use of inhalers in COPD, though evidences are conflicting. In this study, being male was associated with 2.1 folds increase with regard to appropriate inhaler use compared to female (AOR=2.1, 95%CI=1.16, 3.69). This finding was supported by a meta-analysis done by : Calzetta, L et al. (41) and contradicted with the study done by David Price et al (3). The possible reasons might be due to disparities in healthcare access and quality that affect the education and support individuals receive in using inhalers. This can be influenced by socioeconomic factors, which may affect both males and females. Cultural expectations regarding health-related behaviors, including medication use, can play a role. Variations in access to health education and information might contribute to differences in inhaler use. According to some studies, males have better hand to eye coordination than females, leading to inadequate hand- breath coordination in females. This could affect proper use of MDIs. This needs further investigation(42).

Study participant whose education level of collage and above had 2.9 folds increase its appropriate inhaler compared to those of have not formal education (AOR=2.9, 95%CI=1.23, 6.83). This finding was supported by the study done by global initiative for chronic obstructive lung(26). Proper education might provide health literacy on how to use their inhalers correctly including understanding of the steps involved, proper coordination, and breath-holding techniques. Education helps individuals understand the importance of adhering to their prescribed inhaler regimens. When individuals have a clear understanding of their condition and

treatment plan, they are more likely to engage in self-care practices and make informed decisions about their health(28).

Study participants who were not taking training were 60% less likely to use inhalers appropriately compared to trained one (AOR=0.4, 0.17, 0.90). This finding was congruent with the study done by Restrepo RD et al and Mirahvittles et al (25,27). Proper training ensures that individuals are using their inhalers correctly, which is essential for the medication to reach the lungs and provide optimal relief of respiratory symptoms. Training helps individuals understand the correct inhalation technique, ensuring that the medication is delivered directly to the lungs. This improves the drug's efficacy and helps manage respiratory symptoms more effectively.

In this study it was found that the rate of training and education about inhaler use(84%) was lower compared with Ahn et al., 95.2% (23). Patients may not fully understand the correct steps involved in using their inhaler, leading to improper technique. Among the study participants who got inhaler technique training, nearly 84%, nearly 52% got training through demonstration. About 16% of participants reported they didn't get any training, this is a concerning gap when compared with a study done by S. C, akmaklı et al., where only 1.7% reported untrained on appropriate inhaler use technique (41). A study done by Miravittles et al. showed about 39-67% of clinicians fail to train their patients on the appropriate use of inhalers(27). According to Price et al., 30% of COPD patients never get training on inhaler use(3). Appropriate inhaler technique training and close inhaler technique checks are vital. Proper training helps users minimize the risk of side effects and maximize the benefits of the medication.

7. Strength and Limitations

This research has some limitations. Firstly, each participant was observed using their own inhaler by a single trained observer i.e. assessment by multiple observer was not done. Most patients did not have pulmonary function test, hence inclusion of asthmatic patients cannot be excluded. This study was not randomized, controlled, and was done in a single center, so selection bias cannot be excluded. The other limitation was only two types of inhaler devices were assessed during this study.

This study has several strengths including, first it is a primary data collected from direct observation of inhalation technique. A validated 12-item TAI was used.

8. Conclusion and Recommendation

In conclusion, inappropriate inhaler use is common. Nearly one fifth of COPD patients are untrained regarding proper inhaler use. COPD patients with no training about the correct use of inhaler were 60% less likely to use the inhaler correctly compared with those patients who had the training. This has a significant implication, since inappropriate inhaler use has been related to poor disease control and high medical costs(18,43).

It is recommended that care providers could take time to demonstrate appropriate inhaler technique. The most commonly mis-performed critical error was failure to breathe out gently (as far as is comfortable) and failure to hold breath for 5 to 10 seconds. It is recommended that care providers could direct their focus of demonstration towards these errors to increase correct inhaler use.

Females are more likely to perform inappropriate inhaler use compared to males. It is recommended to do further study to figure out the impact of sex on appropriate inhaler use. It could be better care providers give due attention training female patients on inhaler use.

Further research is needed to investigate the impact of inappropriate inhaler use on disease outcome.

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10. Annexes:

Annex 1: Information Sheet

Research Title: Magnitude and associated factors of appropriate inhaler use among patients with Chronic Obstructive Pulmonary Disease at chest

clinic in St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia: March 2023 to February 2024

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Sponsor: St. Paul's Hospital Millennium Medical College

Annex 2: Data Collection Tool:

Part i: Socio-Demographic and clinical Data

1). Sex: 1. Male 2. Female

2). Age: _____

3). Residential area: 1. urban 2.Rural

- 4). Educational level: 1.unable to read and/ or write 2.primary 3. Secondary and preparatory 4. Higher
- 5). Prior training about inhaler: 1.Yes 2.No
- 6). if yes, which method of training: 1. leaflet 2. Demonstration 3.video 4. Other
- 7). Duration of disease in years _____
- 8). Duration of inhaler use I years _____
- 9). Smoking history: 1. Current smoker () 2. Ex-smoker (), 3. Never smoker ()
- 10). Comorbidity: 1. Yes 2. No
- 11). If any mention please, 1. Hypertension 2. Diabetes 3. Heart failure 4. RVI
5. Chronic renal Failure 6. Obesity 7. Other _____
- 12). Poly-pharmacy: 1. Yes 2. No

Part ii: Test of the Adherence to Inhalers (TAI) Questionnaire

Table 1: Description of Test of the Adherence to Inhaler Questionnaire,		
Patient Domain: questions, responses		Scores(1-5)
1	During the last 7 days, how many times did you forget to take your usual inhalers? All (1) More than half (2) Approximately a half (3) Less than half (4) None (5)	
2	Do you forget to take inhalers? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	
3	When you feel good about your illness, do you stop taking your inhalers? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	
4	When you are on vacation or weekend, do you stop taking your inhalers? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	
5	When you are nervous or sad, do you stop taking your inhalers? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	
6	Do you stop taking your inhalers because of fear of side effects? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	
7	Do you stop taking your inhalers because of considering they are useless to treat your condition? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	
8	Do you take fewer inhalations than those prescribed by your doctor? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	

9	Do you stop taking your inhalers because you believe they interfere with your everyday or working life? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	
10	Do you stop taking your inhalers because you have difficulties to pay them? Always (1) Mostly (2) Sometimes (3) Rarely (4) Never (5)	
Health professional domain: questions, responses		
11	Does the patient remember the prescribed regimen (dose and frequency)? (checking the medical record) No (1) Yes (2)	
12	The technique of using the evaluated inhaler device by the patient is* (checking the inhalation technique) With critical mistakes (1) Without critical mistakes (2)	

Part iii: checklists for commonly used inhalers

Table 2: Dry powder inhalers(DPI)- Symbicort Turbohaler			
SN.	Technique	score,	
		Yes	No
1	Unscrew the cover and lift it off		
2	Hold your Symbicort Turbohaler upright with the red grip at the bottom		
3	Turn the red grip as far as it will go in one direction. Then turn it as far as it will go in the other direction (it does not matter which way you turn it first). You should hear a click sound		
4	Breathe out gently (as far as is comfortable). Do not breathe out through your Turbohaler.		
5	Place mouthpiece between teeth (without biting) and close lips to form a good seal. Breathe in as deeply and as hard as you can through your mouth (5-10 seconds)		
6	Remove inhaler from mouth		
7	Breathe out gently (away from inhaler)		

NB. Critical errors include:

- Failure to open the device correctly,
- Failure to hold the device upright while priming,
- Failure to prime (rotating grip anticlockwise and then back until the “click” sound is heard)
- Failure to seal the lips around the mouthpiece during inhalation,
- Not inhaling forcefully or deeply enough.

Table 3: Pressurized Metered Dose Inhalers(pMDI)			
Sn	Technique	score	
		yes	no
1	open the inhaler, remove the mouthpiece cover		
2	Hold the inhaler upright with your thumb on the base and your finger on the top of the canister		
3	Shake the inhaler up and down 4 to 5 times		
4	Breathe out as much as is comfortable		
5	Put mouthpiece around your lips and make a seal around the mouthpiece		
6	Start to breathe in slowly. As you begin to breathe in, push the top of the canister to release a dose. Continue breathing in slowly and gently until your lungs are full		
7	Remove the device and hold breath for 5 to 10 seconds then exhale slowly		
8	Breath normally		
9	Put the mouthpiece cover on and close		

NB: critical errors include:

- Failure to shake well,
- Failure to hold inhaler upright,
- Failure to synchronize between actuation and inhalation,
- Failure to breathe deeply

Annex 3: Declaration

I the undersigned resident declare that this thesis is my original work, in partial fulfillment of the requirement for certificate of specialty in internal medicine.

I also declare that it has never been presented in this institution and all the resources and materials used in the research work have duly acknowledged.

Name of the Resident: _____

Signature: _____

Date: _____

Annex 4: Advisors' approval sheet:

This is to certify that a thesis entitled “Magnitude and associated factors of appropriate inhaler use among patients with Chronic Obstructive Pulmonary Disease at chest clinic in St. Paul’s Hospital Millennium Medical College, Addis Ababa, Ethiopia February 2024” submitted in partial fulfillment of the requirement for a degree of specialty in internal medicine and proposed by Dr. Belay Tilahun under our supervision.

Thus, we approved that he has fulfilled the requirements and he can submit the thesis to SPHMMC internal medicine department and school of public health.

Investigator's name:	signature	Date
Dr. Belay Tilahun	_____	__/__/__

Name of the advisors:	signature	Date
1. Dr. Messay Assefa	_____	__/__/__
2. Mr. Getachew Tilahun	_____	__/__/__