EFFECT OF KHAT (*catha edulis*) ON BRONCHIAL ASTHMA IN JIMMA UNIVERSITY SPECIALIZED HOSPITAL, ADULT CHEST CLINIC,JIMMA ,ETHIOPIA

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ABSTRACT

Introduction-*asthma is a chronic inflammatory disorder of the airways. About 300 million people worldwide were affected by asthma leading to approximately 250,000 deaths per year. Khat having amphetamine like effect induces the release of catecholamine.. This study deals with the remedial effect of khat on bronchial asthma and shed light in providing new therapeutic option for the treatment of asthma.*

Objective-*to investigate the remedial effect of khat on bronchial asthma*

Methods - *comparative cross sectional study was conducted in JUSH Adult Chest Clinic on170 asthmatic patients with a 1.4 to 1 ratio of non-chewer to chewer between November 2010 and January 2010.Interviewer administered questionnaire, patient history and pulmonary function test using Spirometer was used to collect the data.*

Result and discussion –*of 170 asthmatic patients 72 were chewers and 98 were non chewers Forty nine (68.1%) of chewer and 51(56.1%) non chewer asthmatic patients had experience of asthma symptoms in less than one time per week. Thirty seven (51.4%) chewers and 38(38%) of non chewers had frequency of night time awake in less than two times per month. Forty two (58.3%) chewers and 53(54.1 %) non chewers had frequency of* β_2 *agonist use in less than two days per week. The mean* FEV_1*% of chewers and non chewers was 62% and 46% respectively while their PEFR% was 40% and 26%.The above differences encountered between chewer and non chewer asthmatic patients apparently because khat has amphetamine like effect and an increase in dopamine release plus inhibition of Ach.*

Conclusion-*in conclusion, chewer asthmatic patients had improved* FEV_1 *and PEFR than non chewers with a less frequent asthma attack and less frequent use of* β_2 *agonist.*

Recommendations-*as asthma is heterogeneous disease patient's close supervision in the disease management is compulsory. khat should be considered as partly medicinal plant as it has effect on air way modulation.*

ACKNOWLEDGMENT

Words alone cannot express the thanks I owe to my advisors, Dr. Andualem and Dr. Alemeshet, and also to Ato Teshome whose encouragement, guidance and support enabled me to build an understanding of the subject matter and for their unreserved effort in helping me develop this thesis paper.

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ABBREVIATIONS

AOR-adjusted odd ratio

CI-confidence interval

COPD-Chronic obstructive pulmonary disease

FVC-Forced vital capacity

FEV_1-Forced expiratory volume in one second

JUSH- Jimma University Specialized hospital

PEFR-Peak expiratory flow rate

SPSS- statistical package for social sciences

DEFINITION OF TERMS

Spirometer-the apparatus commonly used to measure the volume of air exchanged during breathing and the respiratory rate.

Spirometry-is the procedure of measuring ventlatory parameters

Expiratory reserve volume- volume of air that can be forcefully expired after a normal or resting expiration (about 1.0 L).

Forced vital capacity (FVC) - the maximum volume of air in lung after a forceful exhalation following forceful inhalation

Forced expiratory volume (FEV_1)-the volume of air expired forcefully in one second

Peak expiratory flow rate (PEFR) - a maximum expiratory air flow beyond which the flow cannot be increased any more even with greatly increased additional force

β_2 agonist-family of drugs that induces bronchodilation.

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CHAPTER1. INTRODUCTION

1.1. Background

The National Heart, Lung, and Blood Institute (NHLBI) defines asthma as a chronic inflammatory disorder of the airways, in which bronchial hyper-reactivity causes recurrent episodes of wheezing, breathlessness, chest tightness and cough associated with airflow obstruction that is reversible.[1] Asthma typically can range from a disease of very mild and intermittent symptoms to one of debilitating and life-threatening disease. [2]It is likely that the factors controlling the severity of asthma are many and dependent on each other. Potential factors include inflammatory, structural, hereditary/congenital, environmental and psychological/emotional. Studies show treatment of asthma remains problematic although there are therapies. [2]

Asthma is a disease of predominantly reversible airway obstruction characterized by a triad of bronchial smooth muscle contraction, airway inflammation, and increased secretions; it is a major health problem for all age groups. For the majority, control of asthma symptoms is readily achieved; however, in a small minority, asthma may cause death.[3]

The mechanism of action of asthma attack starts by the formation of abnormal large number of antibody (IgE) which causes allergic reactions that react with their complementary antigen. Eosinophilic asthma is a distinct phenotype of asthma that is associated pathologically by thickening of the basement membrane zone and pharmacologically by corticosteroid responsiveness.[4]

Although from the perspective of patients and societies the cost of control of asthma seems high, the cost of not treating asthma correctly is even higher. Of major therapies corticosteroids have been taking upper hand and others include; 5-lipoxygenase inhibitors, anti-IgE, and immunomodulatory drugs are also likely to have a place in treatment.[5] Improving therapy in this disease will require a better understanding of the phenotypes involved

Researches show Cathinone is an alkaloid that has been discovered in the leaves of the khat bush. Countries of East Africa and southern Arabia are known by their khat cultivation. Cathinone, which is S (–)-α-aminopropiophenone, found to have pharmacological resemblances with that of amphetamine. It was demonstrated that cathinone operates through the same mechanism as amphetamine, i.e. it acts by releasing catecholamine from presynaptic storage sites .Studies were confirmed by a clinical experiment showing that cathinone in humans' produces amphetamine-like effects.[6]

Dopamine, a family of catecholamine, may have beneficial effects on the respiratory system by decreasing oedema formation and improving respiratory muscle function, but can also have deleterious effects, by inhibiting ventilation. Dopamine may be beneficial in lung oedema, but harmful in cases of difficult weaning from mechanical ventilation. However, critically ill patients with chronic obstructive pulmonary disease (COPD) do not show this negative effect of DA on ventilatory drive.[7]

It has been reported that dopamine has no acute effect on human air way in normal subject or on those with asthma background. However, inhaled or infused dopamine decrease histamine induced bronco constriction in both normal and asthmatic subjects. Thus dopamine possibly modulates bronchial diameter, which is confirmed by administering inhaled dopamine and the DA_2dopaminergic blocker metoclopramide to subjects with various degrees of bronchial tone.[8]

This study deals with the remedial effect of khat on asthmatic patients since the main psychoactive ingredient in khat is cathinon, which has amphetamine like effect and moreover it stimulates excessive production of dopamine.

1.2. STATEMENT OF THE PROBLEM

Respiratory diseases are one of the most common forms of ill-health, of these asthma has become more common over the last 30 years in different countries of the world. Literatures indicate that as of 2009, 300 million people worldwide were affected by asthma leading to approximately 250,000 deaths per year .Many studies show a low risk of asthma in sub Saharan countries. Intercountry prevalence data of asthma and allergies in childhood indicates that prevalence as Ethiopia is 9.1%, Kenya 15.8%, Nigeria 13.0%, South Africa 20.3%,Algeria 8.7%, Morocco 10.4%, and Tunisia 11.9%.[9]

A survey done by European Commission reported that 13% of people in UK have had asthma at some point in their lives. The UK figure was the highest in the survey of 16 European Union member states, with runners-up Finland (11%) and Ireland (10.5%). Lowest in the table was Germany, with less than 4% of the population saying they had asthma, and Spain, with a total of 4.4%. [10, 11]
Researches done in US countries show asthma and chronic obstructive pulmonary disease (COPD) are among the ten leading chronic respiratory conditions causing restricted activity. They are now the third most common cause of death. In these Countries, respiratory disease accounts for over 10% of all resident deaths. [12]

As described in the above statements, respiratory diseases are also a leading cause of hospitalization and death .In order to alleviate these problems there should be different therapeutic options at hand . Khat has been used in traditional medicine in Ethiopia and Arabia as a diuretic in the treatment of gonorrhoea-as a prophylactic against malaria, asthma, coughing and diseases of the chest, stomach trouble and even as a preventive against plague. [13]

Despite the existence of the use and consumption of khat by a large sized population of Ethiopia especially those countryside known by their khat cultivation, very little is known about its effects other than its content of

psychoactive ingredients. Users' knowledge is limited to only mildly narcotic effect of the plant. This knowledge gap works also for researchers due to the lack of classification of the plant as a drug by international and national institutions .As a result, the crop has received little attention from researchers. There has been doubt on its medicinal use and its use beyond traditional remedy for asthma, influenza, cough and other chest problems is still mystery.

1.3. SIGNIFICANCE OF THE STUDY

Although majority of asthmatic patients show positive response to corticosteroids and many other therapeutic options indicated for asthma, there has been clear evidence that some patients are irresponsive or less responsive to many of those drugs. Since khat contains cathinone which is believed to decreases parasympathetic outputs on to airways resulting in bronchodilation and reduction of secretions. Presumably when chewed or ingested, khat decrease asthmatic attack episodes experienced by patients in either transient or prolonged manner. As a result, this study is able to show how khat, when used as a traditional remedy, can alleviate respiratory disease symptoms. There by it can be entertained as one of the options in the development of therapeutic approaches for the treatment of pulmonary diseases related to airway diameter and mucus secretion.

This study, therefore, is intended to gather and provide base line data about the effect of khat on bronchial asthma And finally disseminate the information to relevant and responsible stakeholders.

CHAPTER2. LITERATURE REVIEW

2.1.Pathophysiology, prevalence and risk factors of asthma

Asthma is an inflammatory disease of the lung. Once the airway becomes swollen and inflamed it becomes narrower, allowing less air through to the lung tissue and causing symptoms such as wheezing, coughing, chest tightness, and trouble breathing. Symptoms vary from patient to patient and can vary in the same patient over time. Symptoms may occur spontaneously, or be precipitated or exacerbated by various triggers. Asthma is commonly worse in the early morning hours or at night corresponding to circadian variations in bronchomotor tone and bronchial reactivity.[14]

A study revealed that asthma is now the most common chronic disorder of childhood, and affects an estimated 6.2 million children under the age of 18. In the United States alone, 30.8 million people – 10.6 percent of adults and 12.2 percent of children – have been diagnosed with asthma **(NIHS).**Genetic factors play an important role in the development of the disease; however, environmental factors also contribute to the disease process. Asthma can be triggered by a wide range of substances called allergens. The bronchial narrowing is usually either totally or at least partially reversible with treatments.[15]

From 2006 to 2008 7.8 % of U.S. population reported that they currently have asthma(**NCHS**,2010).Reported asthma rates are highest in child and adolescents population .In adults ,an increase in asthma prevalence rates was evident 1997 to 2001,with some decrease after 2001 and subsequent increase after 2003.The asthma prevalence rate also consistently decrease in older population. In 2008, the age –specific rates were 135(18-44 years), 120(age 45-64), 120(age 65-74), and 110(age 75+years) cases per 1,000.[16]

The life time asthma diagnosis in adult was highest among American/Indian/Alaska natives, followed by black or African American then whites and Asians. A similar pattern is seen for current asthma and asthma attack prevalence .Hispanic had lower rates across all three asthma prevalence categories than non-Hispanic whites and non Hispanic blacks.[16]

Previous research done on asthma in U.S.A shows that more than 16 million adults and about 7 million children have asthma. Annually, it's responsible for roughly 11 million outpatient visits, 2 million ED visits, nearly 500,000 hospital admissions, and close to 4,000 deaths. It's a common reason for school absenteeism among children, and causes adults to lose more than 10 million workdays each year. Although asthma is more common in boys than girls, it's more common among women than men. Prevalence, hospitalization, and mortality rates have stabilized over the past decade or so but had been on the rise in both sexes and across all age and racial groups from 1977 through 1996. Among adult patients, hospitalization and mortality rates are generally highest for blacks and women.[17]

Previous Literature shows that the prevalence of physician-diagnosed asthma in Cairo was 9.4%, while the prevalence of rhinoconjunctivitis was 15.3%. There is a higher prevalence and increased severity of asthma symptoms in children of lower socioeconomic groups, as defined by state school attendance in Cairo. [18]

Earlier studies indicate the prevalence of asthma in adults and older children in the Jimma region of Ethiopia is low compared to European levels, but is higher in older people compared to younger people, and in the urban compared to the rural setting. Studies shows part of the urban/rural difference in prevalence of asthma in Jimma appears to be due to differences in parasite load, but other factors, such as allergen exposures and indoor pollution, may also have roles.[19]

Similar studies conducted in Jimma shows the absence of major industry contributing to air pollution, and the prevalence of asthma in the general population is relatively low.[20]

Severe asthma remains poorly understood and frustrating to care for, partly because it is a heterogeneous disease. Patients with severe asthma

disproportionately consume health care resources related to asthma. Severe asthma may develop over time, or shortly after onset of the disease. The genetic and environmental elements that may be most important in the development of severe disease are poorly understood.[21]

Despite asthma and chronic obstructive pulmonary disease being widely regarded as heterogeneous diseases, a consensus for an accurate system of classification has not been agreed. Recent studies have suggested that the recognition of subphenotypes of airway disease based on the pattern of airway inflammation may be particularly useful in increasing the understanding of the disease. [22]

Many previous studies on asthma put different figures of PEFR and FEV1.A study done on FEV1 performance among patients with acute asthma shows that mean initial FEV1 was 38% of predicted. With improved spirometry overtime by I h 90 % of patients with severe airway obstruction were found to have FEV1 <25% of predicted. [23]

A clinical and laboratory based study conducted in Addis Ababa on 40 patients show that 36 patients were more than 25 years of age and the rest 4 are between 15 and 25,Spirometry result shows 14 were found to have above 70% FEV1 ,9 had 30-50% of predicted and three had below 30%.[24]

The loss of lung elastic recoil in asthmatic patients was associated with increased age, duration of disease, and progressive expiratory airflow limitation. [25]

Cross sectional studies at different times show females are more likely to develop late onset and persistent wheeze. Related findings indicate the prevalence of wheeze and asthma, with high rate in women through the reproductive years. The influence of gender is also seen for hospital admission, with more boys admitted before puberty and gender reversal event post puberty. the sex difference in admission rate are of a magnitude that is easily and consistently demonstrable .[26] Another study on 137 patients about gender distribution of acute asthma explains as there is no statistical significant differnce between male and female FEV1,respiratory rate and hospital admission percentage but there was mean initial higher FEV1 in female compared to males. [27] Related study done on

asthma and rhinitis show females are prone to develop asthmatic symptoms moderate to severe than males.[28]

2.2. USE, SIDE effects and Pharmacology of Khat

Khat is a shrubby plant, where the leaves and tops serve as a mild narcotic when chewed. Khat can also be dried and used in tea. The latter form is often called Abyssinian Tea. Khat can cause mild to moderate psychic dependence. Long time use of khat may cause constant euphoria, lethargy, depressions, nightmares, tremor or constipation. There are those who defend the use of khat, claiming that there are important positive health effects. Khat is supposed to have a distinct

> easing effect on symptoms of diabetes, asthma and stomach and intestinal tract disorders. [28]

A Study showed fresh Khat leaves, which are typically chewed like tobacco, produce a mild cocaine or amphetamine-like euphoria that is much less potent than either substance with no reports of a rush sensation or paranoia indicated. Casual users claim Khat lifts spirits, sharpens thinking, and, when its effects wear off, generates mild lapses of depression similar to those observed among cocaine users. Since there appears to be an absence of physical tolerance, due in part to limitations in how much can be ingested by chewing; there are no reports of physical symptoms accompanying withdrawal.[29]

khat has traditionally been used as a remedy for venereal diseases asthma, lung diseases, cold fevers, cough, and headaches. It has been used to prevent epidemics of pest and malaria. [30] Processed leaves and roots are used to treat influenza, cough, gonorrhea, asthma and other chest problems. The root is also used for stomach ache and an infusion is taken orally to treat boils. Advocates of Khat use claim that it eases symptoms of diabetes, asthma, and stomach/intestinal tract disorders.[31] On the other hand, opponents claim that Khat damages health, suppresses appetite, prevents sleep, and drains the economy. There has been much

talk on this subject at various levels and times and many groups of "experts" have been commissioned to study Khat in order to recommend banning it or restricting the continued use of it. [32]

Different Studies suggest that cathinon has positive inotropic and chronotrpic effects on heart, a pressure effect on arteries, increases blood pressure, respiratory rate and metabolic rate transiently. Reduced birth weight and inhibition of lactation have been reported in khat chewing mothers, possibly resulting from increased dopamine production. In relation to this effect, regular Khat chewing is thought to be, a predisposing factor for gastritis and peptic ulcer disease, nerve illness, cardiac arrthemia, tooth decay and constipation. [33]

According to the study done in 2002 in Jimma it is suggested that cathinon, which is an active ingredient of khat increase heart rate, arterial blood pressure respiratory rate transiently. It also improves cerebral blood flow, mental alertness and increase energy…[34] …Besides its reinforcing effects, khat is said to be a folk remedy for asthma, bronchial disorder, flue, cough and lethargy. [35]

Different studies show that half life of amphetamine and metabolites of methamphetamine are different .Methamphetamine has plasma half life of 12-34 (2-3days) and amphetamine(metabolite of methamphetamine) has 7-34 hours.[36] These four salts are metabolized at different rates and possess diverse half lives, thereby resulting in a less dramatic onset and termination of therapeutic action, as compared to single-salt amphetamine preparations The average elimination half-life in adults for dextroamphetamine and levoamphetamine is 10 hours and 13 hours, respectively.[37] When khat is chewed, absorption of cathinone is slow, with maximal plasma concentrations occurring at approximately 2 hours. Norpseudoephedrine and norephedrine also originate directly from the leaves. Maximal plasma concentrations of norephedrine and nor pseudoephedrine are reached at about 3.3 and 3.1 hours, respectively. Cathinone was eliminated from the central compartment with a mean half-life of 1.5 +/- 0.8h.[38] The half-life of cathine was 5.2 ± 3.4 h. The concentration become lower and

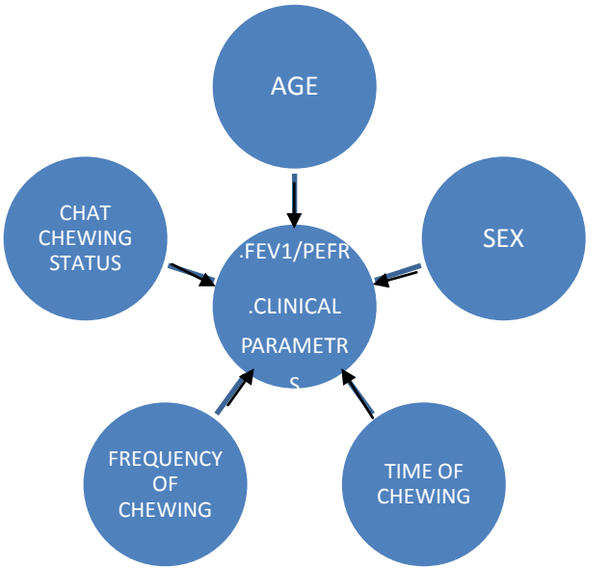
lower as time pass. After 30 hours there will not be in some case and cathinone appear in plasma till 50 hours. The highest concentration in plasma is recorded in 10 hours. [39] Little is known about the pharmacokinetics of cathinone. It is rapidly absorbed after oral administration and is metabolized in the liver with only a small fraction appearing in the urine. [33]

A study done by a group of authors on modulation of air way smooth muscle contraction found that cathinone presynaptically inhibits acetylcholine release from airway parasympathetic nerves through activation of both α_2 and 5-hydoxytryptamine 7 presynaptic receptors.They also conclude the dual mechanism of action of cathinone. This study may be particularly beneficial in airway diseases displaying a heightened cholinergic tone, such nocturnal asthma or chronic obstructive pulmonary disease .The study suggest the development of new anticholinergic molecules based on mechanisms of action other than antagonising muscarinic receptors [40]

While khat has been, and still is, used in traditional medicine, it cannot boast of any great potential for development as a drug for use in Western societies. In short, the incentives for detailed, serious investigation until recently have been lacking. Even so, there is a considerable, albeit scattered, body of literature which might help provide renewed insights in approaching what is seen by some as an increasingly serious khat problem. [41]

CHAPTER 3- CONCEPTUAL /THEORETICAL FRAMEWORK OF THE STUDY

3.1. CONCEPTUAL FRAMEWORK



As in many physiologic parameters, pulmonary function is affected by age: as age increase pulmonary function will decrease .This is the normal event that could happen to anyone. Depending on the individual's sex, pulmonary function will be varying, this is also true for many physiologic parameters. Therefore, if not very significant pulmonary function measures (FEV_1 & PEFR) are lower in female than male. Though it is hypothetical assumption, khat chewing could have effect on the ventlatory parameters which are the center of interest in this study. The assumption is, if a subject chew khat and ingests it he/she will have improved respiratory function within a limited period of time. The clinical parametrs also indicate the level of asthma and its control .

3.2. THEORETICAL FRAMEWORK /HYPOTHESIS

This study was designed to test the hypothesis that chewing khat and ingestion of its juice may improve the frequency of asthmatic signs and symptoms. The effect lasts for about 24-36 hours after chewing and this was proven by conducting measurements on ventilatory parameters like FEV_1 and PEFR. [36,37] Asthmatic patients who chewed khat in the past 24 hours before spirometry had better pulmonary function than asthmatic patients who didn't chew. The working hypothesis was formulated on the basis of its pharmacological effect through cathinon; active ingredient in fresh khat. Cathinone is regarded as an indirectly acting sympathomimetic alkaloid having catecholamine-releasing properties at both central dopaminergic and serotonergic synapses as well as at peripheral noradrenaline storage sites. The mechanism of action is the same as amphetamine which modulate respiratory air way muscles activities. [6, 7]

CHAPTER 4. OBJECTIVES

4.1. GENERAL OBJECTIVE

To investigate the effect of khat on bronchial asthma in chewers and non chewer patients in Jimma University specialized hospital adult chest clinic.

4.2. SPECIFIC OBJECTIVES

- To compare level of control and severity of asthma in chewer and non chewer asthmatic patients
- To measure and compare FEV_1 and PEFR of asthmatic chewers who chewed and did not chew before the test over the past 24 hours using digital spirometer

CHAPTER 5. METHODS AND MATERIAL

5.1. STUDY AREA AND PERIOD

The study was conducted in Jimma university specialized hospital adult chest clinic. The data collection period took two and half month that was beginning of November 2010 to January 2011.

5.2. STUDY DESIGN

Comparative cross sectional study was conducted in the adult chest clinic of Jimma specialized hospital on patients who were under follow-up. Data was collected by interviewing and by registering pulmonary function parameters (FEV_1 and PEFR) of asthmatic patients during the data collection period.

5.3. POPULATION

5.3.1. SOURCE POPULATION

All asthmatic and COPD patients who have been treated as new comer and under follow up in Jimma university specialized hospital adult chest clinic were source populations.

5.3.2. STUDY POPULATION

The study population include all asthmatic patients who were under follow up in Jimma University specialized hospital adult chest clinic during the stated period.
Participants have been treated every Thursday of the week and appointed one week to two months depending on the severity of the case.

5.3.4. SAMPLE SIZE AND SAMPLING TECHNIQUE

In this specific study , no probability sampling technique was done, rather all patients under follow-up in the Jimma University specialized hospital adult chest clinic were included. Averages of 25-30 asthmatic patients were visiting the clinic every week. Therefore, every Thursday with in the stated period data were collected in JUSH adult chest clinic from a total of 170 patients with 1.4 to 1 ratio of non chewer to chewer asthmatic patients. To get the possible larger sample size data collection period was extended to two and half months which basically include patients who were appointed for two months. Data was collected from patients based on the sequence of appearance to the clinic.

5.3.5. INCLUSION CRITERIA

All asthmatic patients who were diagnosed in JUSH and found to have bronchial asthma; patients who were under regular follow-up at Jimma University specialized hospital adult chest clinic, patients who were in a position to undergo spirometry test and patients who were willing to participate were included in the study

5.3.6. EXCLUSION CRITERIA

In this study subjects who had the following known problems and patients who were unable to undergo spirometry or unwilling to provide informed consent; were excluded

- Unstable cardiac function.
- Haemoptysis of unknown cause (e.g. TB).
- Pneumothorax.
- Chest and abdominal pain

5.4. STUDY VARIABLES

5.4.1. INDEPENDENT VARIABLES

- Age
- Sex
- Onset of illness
- Chewing status
    - Chewer
    - Non-chewer
- Frequency of khat chewing
- Time of chewing

5.4.2. DEPENDENT VARIABLES

- FEV_1/PEFR measure
- Control and severity indicator parameters (clinical parameters)
    - Night time awakening
    - Frequency of symptom
    - Use of short acting β_2 agonist

5.5. MEASUREMENTS

5.5.1. DATA COLLECTION INSTRUMENT

QUESTIONNAIRE

Data were collected using semi- structured questionnaire consisting of age, sex, height, weight of a patient, the health effect of khat on asthmatic patients and quality of life, information on attitude and use of khat, assessment on the their asthmatic episode .

PATIENT HISTORY

The patient's history was read from their cards and the information obtained was about their illness other than asthma, the drug they were using at the time of test and the type of drug prescribed by their physician for the treatment of asthma. The main purpose of that information obtained was to exclude patients from the study.

PULMONARY FUNCTION TEST

Pulmonary function test was performed using Datospir digital spirometer**.** Measurements or calculations were made on forced expiratory volume in one second (FEV_1) and peak expiratory flow rate (PEFR).Spirometry test on each patient was made five times and the highest out of the five readings was considered to be personal best of the patient. Adjustments were made on all patients' FEV_1 and PEFR since there was a potential leak while performing the test which the machine can not consider.

5.5.2. DATA COLLECTION TECHNIQUE

The data were collected by one nurse, one pharmacist and the principal investigator. During assessment of patient's health status a clinician was there as an assistant on follow up days during the study period. Prior to data collection, each material used as source of data for the study was arranged in sequence to avoid confusion and repetition during the data collection.

5.5.3. OPERATIONAL DEFINITION

1. CONTROL -is the degree to which symptoms, impairments, and risks are minimized by treatment. Control is the parameter assessed in patients receiving treatment. Good control is the goal of asthma management. Control is classified as

- Good control
- Poor control

Table1- clinical classification of asthma level of control

	Good control	Poor control
Symptoms	All ages except children 5–11 yr: ≤2 days/wk	All ages except children 5–11 yr: > 2 days/wk
Night time awakening	≤ 2 /mo	1–3/wk
Use of short-acting β_2-agonist for symptom control	≤2days/wk	> 2 days/wk
FEV_1or peak flow	>60%predicted/personal Best	≤60 predicted/personal best

2. CLASSIFICATION OF STUDY PARTICIPANTS

I . PATIENT STATUS

- New case-patients who came to the clinic for the first time
- Follow up-patients who were under regular follow up

II. CHEWING STATUS

Classification was based on the hypothesis that transient effect of khat on respiratory rate can remain for an about 24-36 hours after chewing and ingestion of the khat juice. This definition only works only while dealing with FEV_1 and PEFR measurements

CHEWING STATUS	FREQUENCY OF CHEWING
Heavy chewers	≥2 times per day for the last two days before the test
Light chewers	once per day for the last two days before the taste
Non chewers	who didn't chew for two or more days before the test

5.6. DATA PROCESSING AND ANALYSIS

On each data collection day, the investigator was on place to check the completeness and consistency of data collected by each personnel. Then the data was compiled and analyzed using calculator and SPSS version 16 computer program executing different statistical analysis. The principal analysis was descriptive statistical analysis but chi square, ANOVA, regression analysis, comparing means and non parametric two independent sample t tests were also used. A P value ≤ 0.05 was considered to be statistically significant. The result was summarized and presented using tables and bar graphs.

5.7. VALIDITY AND RELIABILITY

The Validity and reliability of data collection tools, questionnaire and spirometer were assured by undergoing pre-test on few patients who were willing to participate and the spirometer was calibrated as per the need and conditions before the actual study.

5.8. ETHICAL CONSIDERATION

Ethical clearance paper was obtained from ethical review board of the university. The consent of patients was assured before asking and taking tests. And the information obtained from the participant has been kept confidential and this was verified to participants verbally and in a written sheet. Special care was given to elders and no patient was found to be pregnant.

5.9. LIMITATIONS

The most prominent limitation was many potentially eligible individuals did not agree to undergo the test as desired. This leads in obtaining suspicious results and even exclusion of many patients from the study. A few patients were in doubt about their diagnostic method in the first place, either because they had not previously undergone an extensive diagnosis, or because their asthma medications were not working to relieve their symptoms. And other patients were not honest about their chewing habit as they were aware of its prohibition to use. The other major problem was the difficulty to accurately classify patients according to the guidelines due to poorly organized asthma management in the clinic that results in the study to misclassify patients.

CHAPTER 6. RESULTS

The study was done on 170 asthmatic patients who were under follow up in Jimma University adult chest clinic. Table 2 shows the characteristics of asthmatic patients who were under regular follow up in JUSH, adult chest clinic. Of the total 111(65.3%) were females and 59 (34.7%) were males. .47(48.0%) were chewer asthmatic patients aged between 35-54.of non chewer patients 57(33.5%) were in age range between 55-82.Of total chewer patients, 58(63.0%) were patients whose asthmatic onset was for more than ten years.29 (17.1%) were non chewer patients whose onset of asthma was for more than five years but less than ten years.

Table 2-Characterstics of asthmatic patients in JUSH adult chest clinic, 2010/2011

		Chewer	Non chewer	Total
Sex	Male	37 (62.7%)	22 (37.3%)	59(34.7%)
	Female	35 (31.5%)	76 (68.5%)	111(65.3%)
Age range	15-34	21(29.2 %)	17(17.3 %)	38(22.4 %)
	35-54	28(38.9%)	47(48.0%)	75(44.1%)
	55-82	23(31.9 %)	34(34.7%)	57(33.5 %)
Onset of illness	≥10yrs	34 (37.0%0	58 (63.0%)	92(54.1%)
	≥5yrs	13 (44.8%)	16 (55.2%)	29 (17.1%)
	5-2 yrs	13 (44.8%)	16 (55.2%)	24 (14.1%)
	≤2 yrs	16 (66.7%)	8 (33.3%)	25 (14.7%)

Table 3 shows frequency and association between clinical parameters and age. The statistical association between frequency of symptom and age was found significant.Frequency of night time attack and age were also found to have statistical significant association. Frequency of use of β_2 agonist was also seen to have statistical association with age.

Table 3-Effect of age on clinical parameters among asthmatic patients in JUSH, 2010/2011

Age category	**Frequency of symptoms**		**Frequency of night time attack**		**Frequency of β, agonist usage**	
	>1x/wk	≤1x/wk	>1x/wk	≤2x/month	>2 days/wk	≤2 days/wk
15-34	8(21.1%)	30(78.9%)	15(39.5%)	23(60.5%)	17(44.7%)	21(55.3%)
35-54	27(36.0%)	48(64.0%)	42(56.0%)	33(44.0%)	26(34.7%)	49(65.3%)
55-82	31(54.4%)	26(45.6%)	38(66.7%)	19(33.3%)	32(56.1%)	25(43.9%)
Total	66(38.8%)	104(61.2%)	95(55.9%)	75(44.1%)	75(44.1%)	95(55.9%)
χ^2	**11.117**		**6.839**		**6.065**	
p-value	**0.004**		**0.003**		**0.048**	

The association between all clinical parameters and age was statistically significant. The model was adjusted for good control (≤1x/wk for frequency of symptom, ≤2x/month for frequency of night time attack and ≤2 days/wk for frequency of β_2 agonist use).The likelihood of facing ≤1x/wk frequency of symptom for patients whose age ranges between 35-54 was two times than that of patients whose age range between 55-82.And also for patients whose age range between 15-24 the occurrence of ≤1x/wk frequency of symptom was also twice as much as its occurrence on patients age range between 35-85 . The incidence of experiencing ≤2x/month frequency of night time attack for patients whose age range between 35-54 was two times than patients whose age was in a range between 15-24.The probability of using β_2 agonist for ≤2 days/wk by patients age range between 15-34 was 1.45 times than patients whose age was 35-54.Table 4 shows clinical parameters correlates with age among asthmatic patients.

Table 4.Clinical parameter correlates with age among asthmatic patients in JUSH adult chest clinic 2020/2011.

	B	S.E.	AOD	95.0% C.I.
Frequency of symptom/age				
55-82	0.00		1.00	
35-54	.781	.390	*2.184	(1.016,4.694)
15-24	1.375	.506	*3.955	(1.466,10.667)
Frequency of night time awake /age				
55-82	0.00		1.00	
35-54	1.210	.479	*3.353	(1.312,8.571)
15-24	.718	.406	2.049	(0.924,4.544)
Frequency of β, agonist usage /age				
55-82	0.00		1.00	
35-54	.472	.457	1.603	(.655,3.922)
15-24	.850	.390	*2.339	(1.090,5.023)

***** indicate significant association

The linear regression analysis for the association of age with FEV_1 and PEFR was expressed in the following way:

FEV_1 =62.125-0.285 (age); p=0.010

PEFR =41.579-0.155(age); p=0.124

The increase in age by one year reduced FEV_1 by 0.0285 and also an age increase by one year reduced PEFR by 0.155.

Spirometric mean personal best of FEV1% predicted among men was 52%, while it was 38% for female asthmatic patients. And mean personal best of PEFR% predicted among men was 48%, while it was 32% for female asthmatic patients.

Table -5 indicates the association between sex and onset of illness and clinical parameters. Of male patients 26(39%) were having frequency of symptom for >1x/wk(χ^2=**1.046, p =0.306).**Among 111 female asthmatic patients 48(64.0%) experience frequent night time awakening in ≤2x/month(**χ^2=0.99,p=0.753)**. 50 (66.7%) of female patients experienced β_2 agonist usage for >2 days/wk times(χ^2=**0.112, p =0.738).**.There was no any statistical significant relationship between sex and frequency of asthmatic attack, frequency of night time attack and frequency of β_2 agonist usage. Table- 5 shows the association between clinical parameters and sex.

Thirty two (30.8%) were patients whose onset of asthmatic illness was in less than five years who have had frequency of asthmatic symptoms for ≤1x/wk(χ^2=**0.494, p =0.482).**.Twenty seven (36%) were patients who suffer from asthma since before five years and who had night time attack for ≤2x/month(χ^2=**3.369, p =0.066).**.Twenty nine (34.0%) asthmatic patients whose onset of illness was in less than 5 years had usage of β_2 agonist for ≤2 days/wk(χ^2=**3.369, p =0.066).**. The association between each clinical parameters and onset of illness was statistically not significant.

Table 5-Effect of sex and onset of ilness on clinical parameters among asthmatic patients in JUSH, 2010/2011

		Frequency of symptoms		Frequency of night time attack		Frequency of β_2 agonist usage	
		>1x/wk	≤1x/wk	>1x/wk	≤2x/month	>2 days/wk	≤2 days/wk
sex	Male	26(39.4%)	33(31.7%)	32(33.7%)	27(36.0%)	25(33.3%)	34(35.8%)
	Female	40(60.6%)	71(68.3%)	63(66.3%)	48(64.0%)	50(66.7%)	61(64.2%)
Onset of illness	≥10Yrs	37(56.1%)	55(52.9%)	59(62.1%)	33(44.0%)	38(50.7%)	54(56.8%)
	>5yrs	12(18.2%)	17(16.3%)	14(14.7%)	15(20.0%)	14(14.7%)	19(20.0%)
	5-2yrs	10(15.2%)	14(13.5%)	12(12.6%)	12(16.0%)	15(20.0%)	9(9.5%)
	≤2yrs	7(10.6%)	18(17.3%)	10(10.5%)	15(20.0%	12(16.0%)	13(13.7%)

Table 6 shows the percentage of respondents for clinical parameters. Of patients who had experience of asthma symptom in ≤1x/wk chewers account 49(68.1%) and 55(56.1%) were non chewers .The association between frequency of symptom and chewing status was statistically not significant.

37(51.4%) were asthmatic chewers and 38(38.8%) non chewer who had night time awake for ≤2x/month. The association between frequency of symptom and chewing status was statistically significant.

Out of 72 asthmatic chewer patients 42(58.3) were found to use short acting β_2 agonis for ≤2 days/wk where as 53(54.1%) were non chewers of their group. The association between frequency of symptom and chewing status was statistically not significant.

Table 6-Effect of Khat on clinical parameters among khat chewer asthmatic patients JUSH 2010/2011

Khat chewing status		**Frequency of symptoms (coughing, sneezing, dysnea…)**		**Frequency night time awakening**		**Frequency of short acting β_2 agonist use**	
		>1x/wk	≤1x/wk	>1x/wk	≤2x/month	>2 days/wk	≤2 days /wk
	Chewer	23(31.9%)	49(68.1%)	35(48.6%)	37(51.4%)	30(41.7%)	42(58.3%)
	Non chewer	43(43.9%)	55(56.1%)	60(61.2%)	38(38.8%)	45(45.9%)	53(54.1%)
Total		66(38.8%)	104(61.2%)	95(55.9%)	75(44.1%0	75(44.1%)	95(55.9%)
χ^2		**2.488**		**2.678**		**0.304**	
p-value		**0.115**		**0.012**		**0.581**	

Table 7 shows logistic regression model which was adjusted for good control (frequency of attack in ≤2x/month).The probability of experiencing night time attack in ≤2x/month for chewer patients was 0.633 times than that of non chewer patients.

Table 7.Clinical parameter correlates with khat chewing status among asthmatic patients in JUSH 2010/2011

				95.0% C.I.
	B	**S.E.**	**AOD**	
Frequency of night time awake / Chewing status				
No	0.00		1.00	
Yes	-.358	.356	*0.633	(1.778,3.059)

***** indicate significant association

The data obtained about the status of hospital admission show 27(37.5%) had hospital admission experience out of total chewer patients. (χ^2=0.01, P=0.973)

Fourteen (51.9%) were chewer asthmatic patients who had experience of hospital admission for >1 x/ yr .And these result show the association was statistically not significant. (χ^2=0.680, P=0.145).Below is a table showing the effect of khat on experience and rate of hospital admission among asthmatic patients.

Table 8-Effect of khat on experience and rate of hospital admission on asthmatic patients in JUSH adult chest clinic, 2010/11

		Experience of hospital admission		Rate of hospital admission	
		yes	no	>1 x/ yr	≤1 x/ yr
khat chewing status	chewer	27(37.5%)	45(62.5%)	14(51.9%)	13(48.1%)
	Non chewer	37(37.8%)	14(62.2%)	23(62.2%)	14(37.8%)
Total		64(37.64%)	59(34.7%)	37(57.8%)	27(42.2%)

spirometric test show the mean FEV_1% predicted of chewer and non chewer was 62.1% and 40% .The test statistics showed the association between FEV_1% predicted and chewing status was not significant(t=7.463,p=0.999).45.9% and 26.4% was PEFR % predicted mean personal best of chewer and non chewer asthmatic patients respectively. The test statistics showed the association between PEFR% predicted and chewing status was significant (t=7.311, p=0.000)

Among twice a day chewers 5(71.4%) had frequency of symptom in ≤1x/wk. 39(69.6%) of every day chewers had frequency of night attack for ≤1x/wk. 4(44.4%) patient had frequency of night time attack for >1x/wk among chewers who chewed khat for ≥1x/wk. This result show the association was statistically significant (χ^2=0.748, p=0.688).Below is a bar graph that shows frequency of symptoms of asthma among chewers.

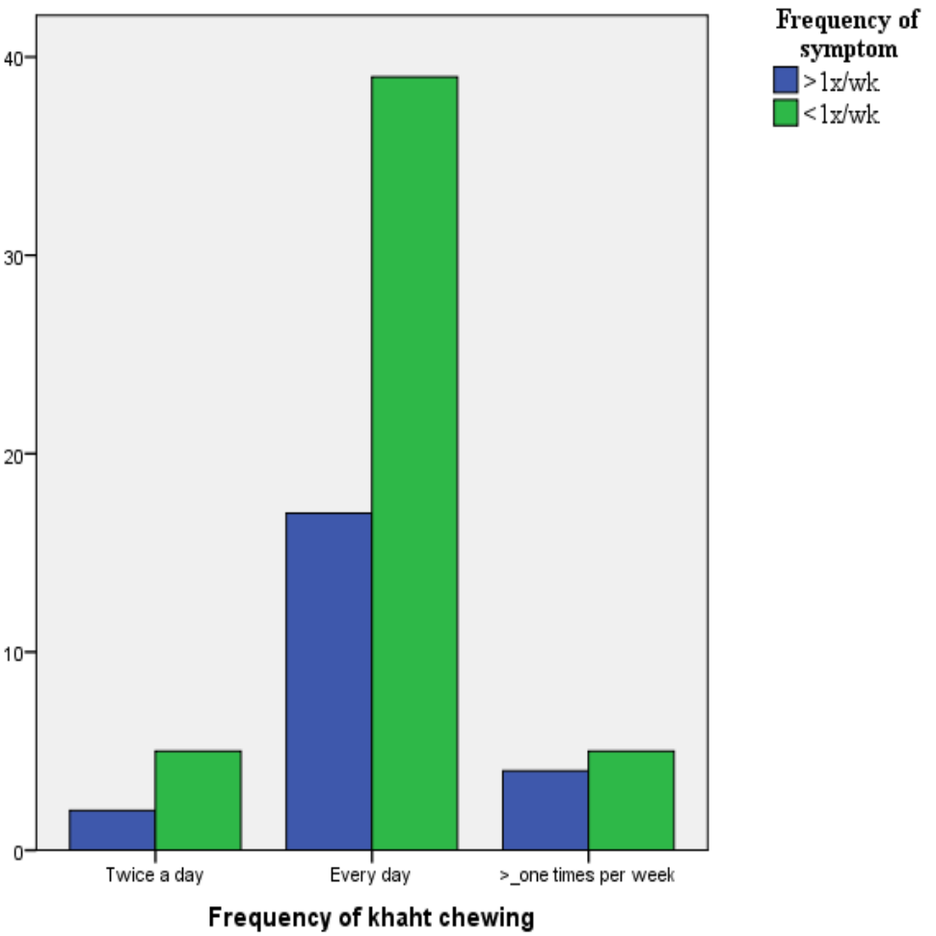


Figure 1- Frequency of asthmatic symptoms among khat chewers in JUSH adult chest clinic, 2010/2011

Among twice a day chewers 4(57.1%) had frequency of night time attack in ≤2x/month. 33(58.9%) of every day chewers had frequency of night attack for >1x/wk. Only one person had frequency of night time attack for ≤ 2x/month among chewers who chewed khat for more than one times per week. This result show the association was statistically significant (χ^2=7.323, p=0.026)

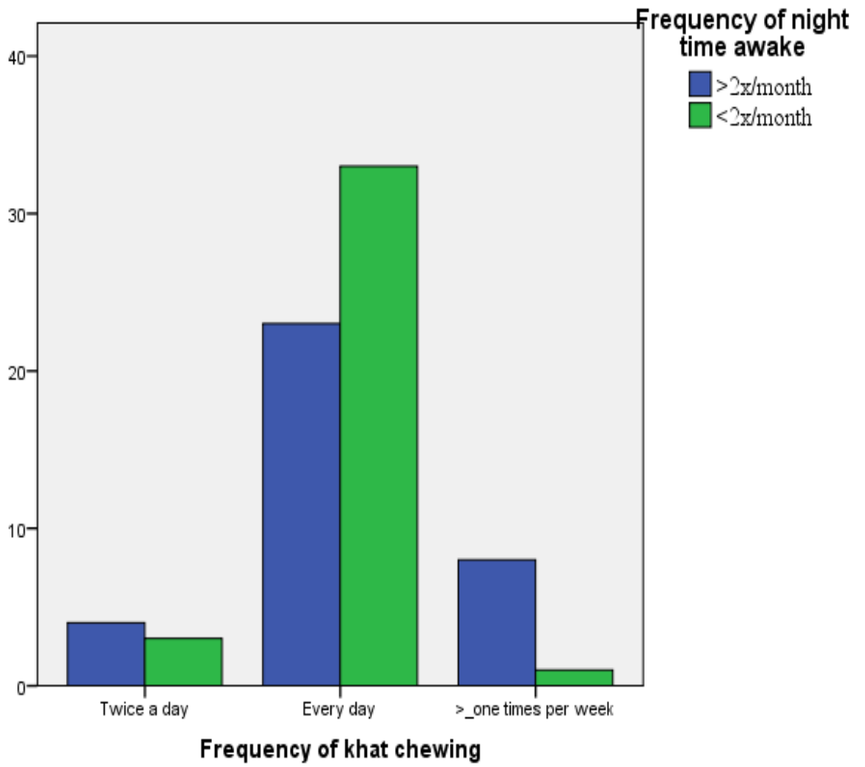


Figure 2-Frequency of night time awake among khat chewers in JUSH adult chest clinic, 2010/2011

Below is a bar graph that shows frequency of β_2 agonist usage among khat chewers. Three 3(42.5%) of patients who chew khat twice a day, frequency of use β_2 agonist was for more than two days per week.35(62.5%)chewer patients who chew khat every day was found to use β_2 agonist for more than two days per week . Of chewer patients who chew khat for more than one time per week 3(33.3%) patients were found to use f β_2 agonist for $\leq$ 2x/wk. This result was statistically not significant (χ^2= 2.718,p=0.257).

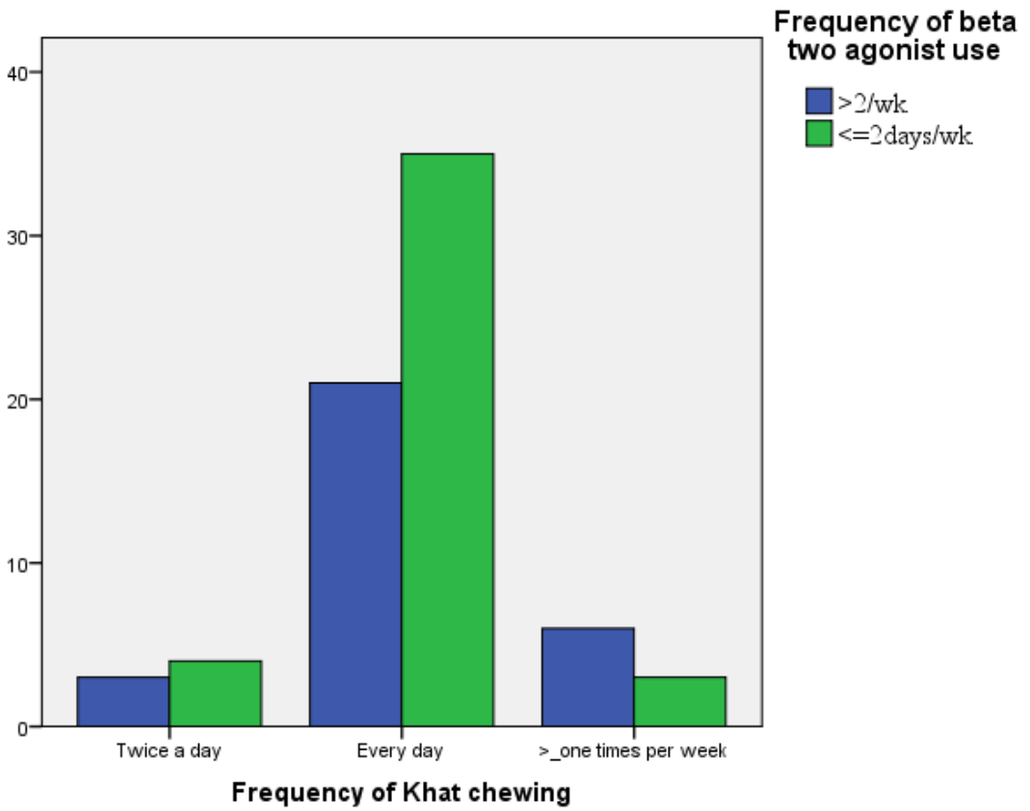


Figure 3-Fequency of khat chewing against frequency of β_2 agonist use in JUSH chest clinic, 2010/2011

Of chewer patients who chew khat twice a day the hospital admission was encountered in only one patient. Among every day chewers 23(41.1%) had experience of hospital admission. Of every day chewers 33(58.9%) had experience of hospital admission due to asthma case.6 (66.7%) chewers who chewed khat for more than one time per week experienced admission of hospital. The association between hospital admission history and frequency of khat chewing was found statistically not significant (χ^2=1.981, p=0.371).Below is a bar graph that shows experience of hospital admission among khat chewers.

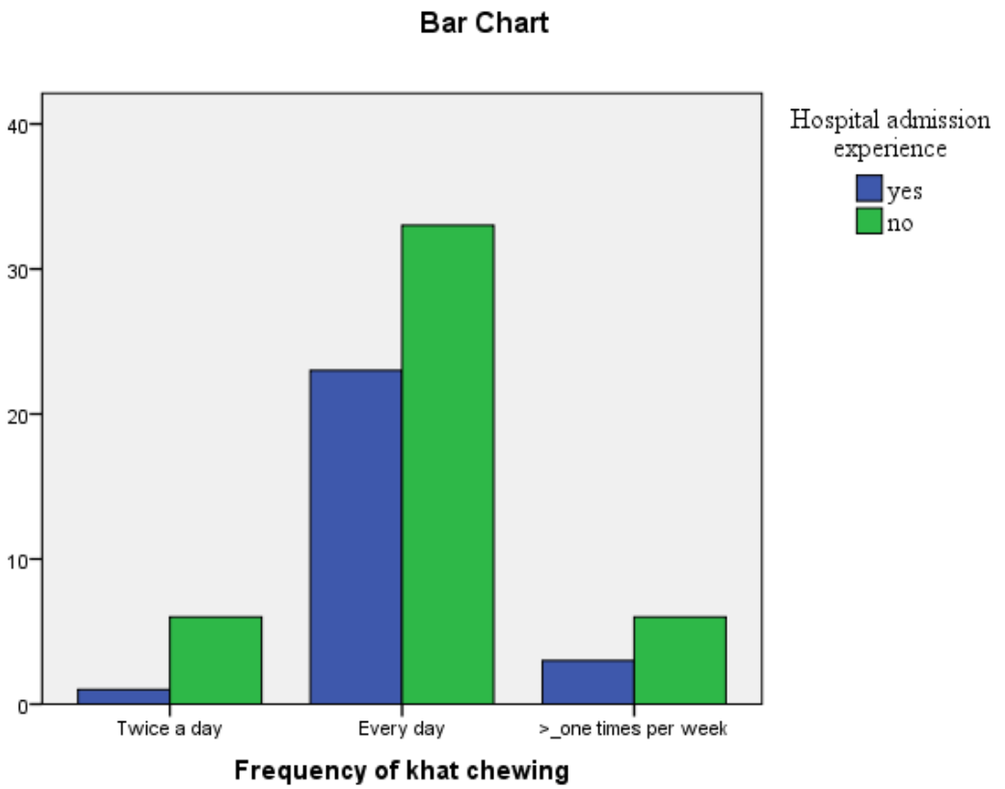


Figure 4-Frequency of hospital admission experience among khat chewer asthmatic patients in JUSH adult chest clinic, 2010/2011

Only one patient was found to have had hospital admission experience for more than once a year among chewers who have been chewing khat for twice a day. Of every day chewers 12(50%) patients were found to have had hospital admission experience for more than once per year (χ^2=0.064, p=0.617).

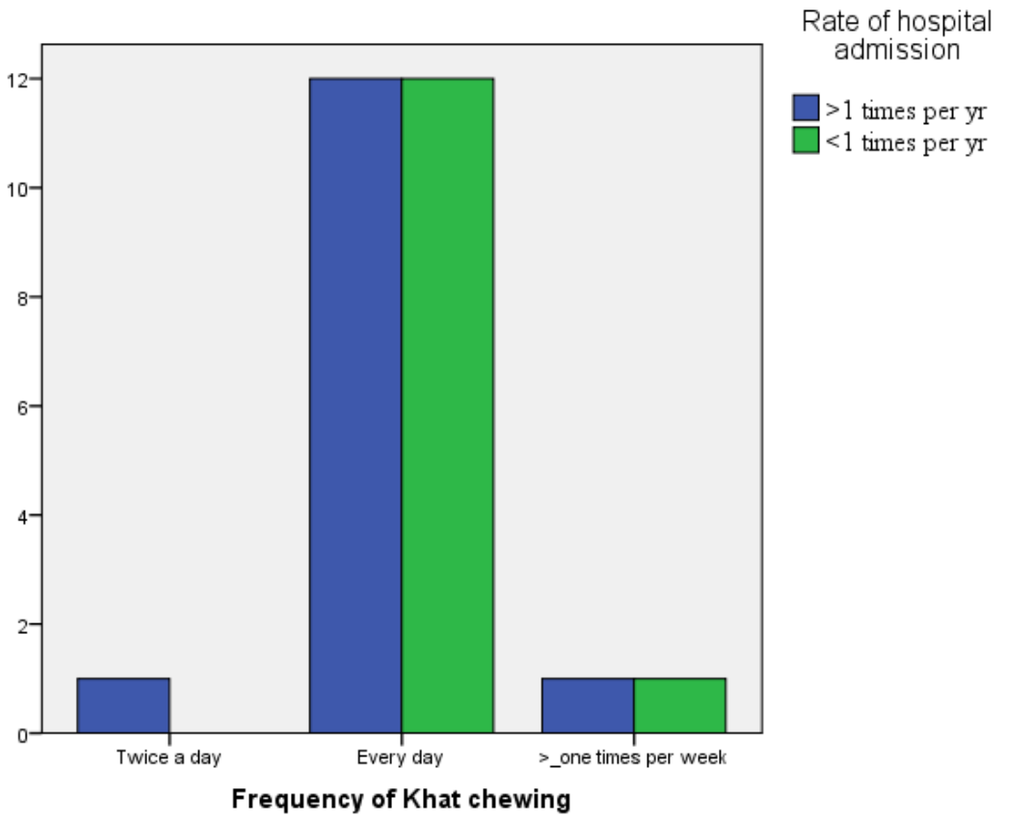


Figure 5-Frequency of hospital admission among khat chewer asthmatic patients in JUSH adult chest clinic, 2010/2011

Spirometric mean of FEV_1%predicted of chewer's who prefers to chew in the morning was 50.33%± 6.1 and among night chewers 62.06% ±18.55 (p=0.047). Spirometric mean of PEFR %predicted among morning chewer's was 30.67% ±7.09 (p=0.041).Table 9 shows FEV_1 and PEFR %predicted among khat chewers who prefer to chew in different times of the day. Spirometric mean of FEV_1%predicted among chewers who chewed khat within 12 hours before the test was 62.66% ±19.47 and among chewers who chew khat within 36 hours 62.7% ±8. And the test statistic was found strongly significant at 95% CI (p=0.001). Spirometric mean of PEFR %predicted among chewers who chewed khat within 12 hours before the test was 46.4% ±20.8 and among chewers who chew khat within 36 hours 51% ±7.8. And the test statistic was found significant at 95% CI (p=0.008).Table 10 shows FEV_1 and PEFR %predicted among khat chewer asthmatic patients within a specified period of time before spirometry.

Table9. FEV_1 and PEFR among khat chewer asthmatic patients who prefer to chew in different times of the day in JUSH 2010/2011

Preferable time of cheweing	FEV_1%predicted	PEFR %predicted
Morning	50.33% ±6.1	30.67% ±7.09
Afternoon	60.19% ±19.51	44.6%±20.26
Night	62.06%±18.55	45.90%±19.68

Table10. FEV_1 and PEFR among khat chewer asthmatic patients within a specified period of time before spirometry in JUSH 2010/2011

Specified time of chewing	FEV_1%predicted	PEFR %predicted
within 12 hours	62.66%±19.47	46.4%±20.8
with in 24 hour	61.4% ±18.86	44.6%±19.7
within 36 hours	62%±8	51%±7.8

Table 11 shows clinical parameters among chewer asthmatic patients who prefer to chew when they feel sick .12(48%) patient was found to have frequency of attack ≤1x/wk among chewer asthmatic patients who have had experience of chewing whenever they feel sick. Habit of khat chewing whenever a patient was experiencing asthma symptom and frequency of asthmatic symptom episode had association (χ^2=7.086, p=0.008)

Eleven (44.0%) of chewers had frequency of night attack in ≤2 /month having experience of chewing khat when they feel sick .The association between khat chewing habit when feel sick and frequency of night time awake was significant (χ^2=0.837p=0.041).

Frequency of short acting β_2 agonist usage in ≤2 days / wk was seen on 12(48.0%) patients who had experience of chewing khat whenever they feel sick. Association between the frequency of short acting β_2 agonist usage and habit of khat chewing while feeling sick was found statistically not significant. (χ^2=1.682,p=0.195)

Table 11.Clinical parameters among chewer asthmatic patients who prefer to chew when they feel sick in JUSH 2010/2011

		Frequency of symptom		**Frequency of night time awake**		**Frequency of β_2 agonist usage**	
		>1x/wk	≤1x/wk	>1x/wk	≤2x/ month	>2 days / wk	≤2 days/wk
Habit of chewing khat while feeling sick	yes	13(52.0%)	12(48.0%)	14(56.0%)	11(44.0%)	13(52.0%)	12(48.0%)
	no	10(21.3%)	37(78.7%)	21(44.7%)	26(55.3%)	17(36.2%)	30 (63.8%)
Total		23(13.5%)	49(68.3%)	35(48.6%)	37(51.4%)	30(41.7%)	42(58.3%)

According to national heart, lung and blood institution experts panel 3 guideline for diagnosis and management of asthma severity ,below is a table that shows patient distribution based on the severity of their asthma attack .35 (48.6%) of patients were chewers who had intermittent asthma and 14(19 %) were patients who chew khat and had severe persistent asthmatic episodes. On the other hand 34(34.7%) of non chewer patients who had intermittent asthma attack and 24(24.4%) were non chewer with severely persistent asthmatic episodes. And this result indicate there was statistical significance at the level of CI 95% (P=0.006)

Table 12- Effect of khat on level of severity on asthmatic patients in JUSH adult chest clinic, 2010 /2011

	Level of severity			
Khat chewing status	Intermittent	Mild	Moderately persistent	Sever
Chewer	35(48.6%)	10(13.9%)	13(18.1%)	14(19.4%)
Non chewer	34(34.7%)	12(12.2%)	28(28.6%)	24(24.5%)
Total	69(40.5%)	22(12.9%)	41(24.1%)	38(23.4%)

Below is a bar graph that show the level of control among asthmatic patients who were khat chewers and non chewers .43(59.7%) and 29(40.3%) were asthmatic chewers whose asthma was good controlled, poorly controlled respectively. And 23(23.5%) and 75(76.5%) were non chewer asthmatic patients who had good and poorly controlled asthma. The result was statistically not significant (χ^2=22.976, p=0.000)

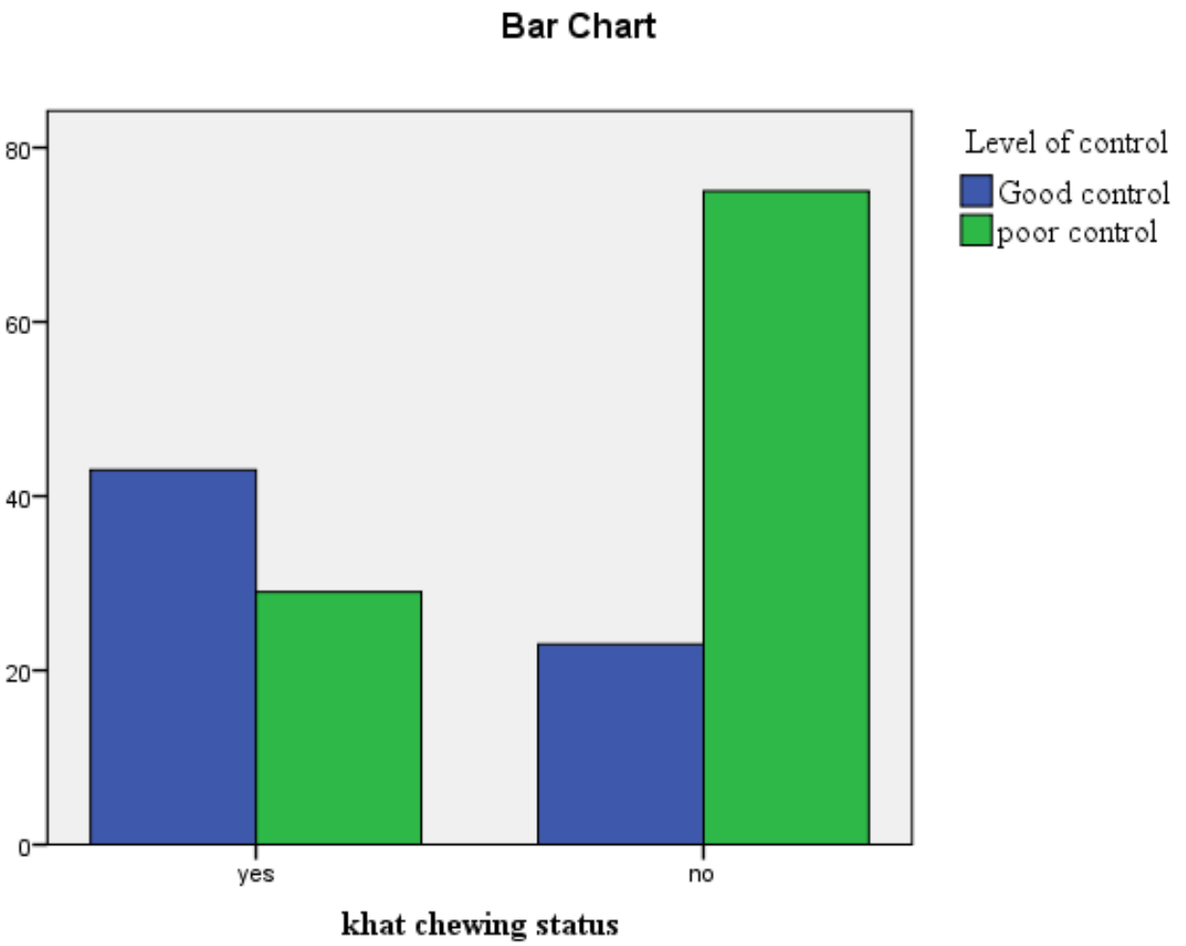


Figure 6- Asthma management among chewer and non chewer asthmatic patients in JUSH adult chest clinic, 2010/2011

CHAPTE 7. DISCUSSION

The possible risk factors for the asthmatic illness and frequency of asthma signs and symptoms in this study were age, sex, onset of illness and type of medication patients have been using. These factors are potential confounders in assessing the effect of khat on bronchial asthma.

Non chewer patients were larger in number than chewer patients. The number of chewer male asthmatic patients was larger than non chewers. Large number of non chewer patients was encountered in age range between 35-54.The number of chewer and non chewer patients with age range between 54-82 was close to each other.

According to the result of this study, the increase in age increased the frequency of asthma symptom. This was observed in the resent study as aged asthmatic patients had frequent asthmatic symptom for more than once per week. In the same way night time awakening due to asthma attack was also seen frequently in elderly patients. Frequent β_2 agonist use also seen in patients whose age ranges between 55-82.But the use of β_2 agonist was less frequent for larger number of asthmatic patients whose age range was 15-34.In addition, both ventilatory parameters FEV1 and PEFR were significantly decreased as age increased. The possible explanation for this could be as any other physiologic parameters normal pulmonary functions and responsiveness to certain medication becomes reduced and reduced as age increase. The result was in agreement with research done before indicating the loss of elastic recoil of the lung in asthmatic patients was associated with age.[23]

In this study, the numbers of female asthmatic patients are by far larger than male asthmatic patients .The result obtained was in line with previous studies that reveals asthma is more common in boys than girls before puberty but more common in females than males after puberty. [25]Sex did not show significant effect on patient's frequency of symptom, night time awake and β_2 agonist usage. Opposite to this finding, a study done on asthma and rhinitis show females are prone to develop asthmatic symptoms moderate to severe than males.[27]But significant variation was recorded regarding FEV_1 and PEFR between male and

females. Mean of both measurements were higher in males than in females. This is true as pulmonary volumes are lower in females than in males. But a study on the contrary put mean FEV1 of female asthmatic patients was higher than in males.[26]

Another study also exposed that females are more likely to develop late onset and persistent wheeze.[25]

Regarding onset of illness, frequent asthmatic attack was seen among patients whose onset of asthma was for more than ten years. Few of asthmatic patients whose onset of asthma in less than two years had frequency of symptom for more than once per week. This result was not statistically significant. Frequent night time awake was seen on patients whose onset of asthma was for more than ten years. But for the same patients, use of β_2 agonist was less frequent than the rest of patients. The result was close to the fact that regardless of the duration of illness patients could suffer from the disease equally. A study also shows that severe asthma may develop over time or shortly after the onset of the disease.[21]

According to history of patients obtained from their cards, short acting β_2 agonist (salbutamol) was the major drug. Patients have been using it regardless of the cause and the severity level of their attack. Taking in charge of individual differences in the responsiveness to a certain drug, it is very obvious to implement drug specificity for the effective treatment of the case. On top of that as the disease is heterogeneous there is a need for pre-screening on the severity and control level before treatment.[22]

Clinical parameters are the key guidelines for the assessment of asthma. Although the association between experience of symptoms (coughing, sneezing, dyspnea…) and chewing status was found statistically not significant ($p>0.05$), majority of chewers were the one who experienced symptoms in less than two times per month (68%) where in a similar category 56.1% of non chewers were there.Speaking of which relatively smaller number of chewer patients experienced symptoms in at least once per day. Concerning night time awake, chewing status and frequency of night time awake were found to be closely associated .The high statistical significance association could be due to majority of chewers prefer to

chew khat at night .The association between chewing status and the use of β_2 agonist was found statistically not significant ,but the percentage of chewer patients who used β_2 agonist in less or equal to two days per week was in relative term higher than non chewers to the same parameter .On the same pattern large number of non chewer patients were encountered to use β_2 agonist several times per day.

There was still percentage variability of experience and frequency of hospital admission between chewers and non chewers. Both chewers and non chewer asthmatic patients had equal experience .But what makes the two different was that higher proportion of patients who chew khat did not have hospital admission experience for more than once per year than non chewers.

FEV_1 and PEFR are the best ventilatory parameters which have been used for the assessment of obstructive and restrictive air way diseases. According to British Thoracic Society classification, 1997; FEV_1 of 60-79% is a sign for mild attack, FEV1 = 40-59% for moderate attack and FEV_1 < 40% for severe attack. The means FEV_1 and PEFR of asthmatic chewers and non chewers found to be different. The mean FEV_1 of asthmatic chewers and non chewers was 62% and 40% respectively. Accordingly chewer patients were attacked mildly while non chewers attacked moderately or severely. PEFR of chewer and non chewer were 46% and 26% respectively. This result showed that there was physiologic difference in air way diameters among chewers and non chewers. The statistical significante association between PEFR of chewer and non chewers could be potentially due to the effect of ingredients in khat having similar effect with that of amphetamine and effect on the release of dopamine which in turn has bronchodialating outcome by modulating airway smooth muscle contraction.[7]

According to the present study, of all chewer patient's majority of them were heavy chewers and the rest were light chewers. For obvious reasons the type of khat chewed and frequency of chewing affect the effect and extent of the effect of khat ingredients in the body. Regardless of the type of khat chewed, the frequency of asthmatic symptom among chewer asthmatic patients who chewed khat twice and once per day found almost equal. The reason could be patients were not

totally open to tell their habit of khat chewing in front of their physician and another possible reason could be the number of chewers who chewed khat twice per day were much smaller than every day chewers. The same justification could work for the frequency of hospital admission. Large number of everyday chewer patients used salbutamol (β_2 agonist) in less than two days per week .The reason might be as they used to chew khat every day; it has been a replacement or an option for their attack over a short acting β_2 agonist.

Regarding the preferable time of chewing and measurements of FEV_1/PEFR, there was a clear difference among morning and night time chewers.Night chewers had higher mean personal best of both measurements. On the other hand the mean personal best of PEFR and FEV_1 for patients who had chewing habit within a given period of time was found almost similar. The possible explanation for this could be there were a large number of patients who had chewing practice within 12 hours before the test than the rest of the given choices. Conversely the standard deviation for chewers who did chew within 36 hours was only 7.8, which was very narrow thus resulting in illogical to compare the group mean to the rest of the other options. The relative high mean of both PEFR and FEV_1 for chewers who practice khat chewing in 12 hours before the test was presumably because of the half life of khat ingredients (cathine and cathinone).Speaking of which the shorter the time gap between chewing and spirometric test the better will be the measurement outcomes. Literatures show amphetamine and metabolites of amphetamine have plasma half life ranging 10-13 hours where as cathinone and cathine average 8.6 hours [37,38].Therefore regardless of the amount and the type of khat chewed the presence of those active ingredient in the plasma brings about many physiologic changes ,among which air way dilation can be counted as one.

The above explanation can also be the reason for why asthmatic patients who run through khat chewing whenever they feel sick had an improved asthmatic attack, a less experience of β_2 agonist usage and also a less frequent night time awake. Concerning the effect of khat, all chewer patients who chewed khat whenever they experience asthmatic attack agree as it gives them relief apart from mental alertness. And their personal belief is that removes evil spirit and curses out off

their throat. This result was also observed in previous studies. [30] According to previous study regarding the use and consumption of khat, casual users claim khat lifts spirits and sharpen thinking. [29]

According to asthmatic severity and control guideline a large number of chewer patients had intermittent asthmatic episodes where as majority of non chewers had moderately persistent asthmatic attack. In the same way, majority of chewer asthmatic patients were found to be in well controlled situation. The rationale for why chewers had relatively well managed asthma and intermittent asthmatic episodes could be the effect of khat through its constituents upon activation of α_2 and $5HT_7$ receptors and also inhibition of Ach there by modulating air way smooth muscle contraction.[39]

All the above differences with statistical and some personal sound judgements support the formulated hypothesis that was designed to test the effect of khat on bronchial asthma.

CHAPTER 7. CONCLUSIONS AND RECOMMENDATIONS

7.1. Conclusion

In conclusion, apart from psychostimulating prosperities, khat has moderate potential benefit for the improvement of episodes of asthma attack. This study showed that chewer asthmatic patients had improved PEFR and FEV_1 and also relatively lesser recurrent asthma symptoms with a less frequent night time awake. Although the association was statistically not significant, the effect of khat was also seen on chewer patients while dealing with use of short acting β_2 agonist as relatively greater number of them used it in a less frequent manner than non chewer patients. In addition chewer patients experienced hospital admission in a lesser rate than non chewers. Generally speaking in a relative term chewer patients were found in a better asthma management with moderate asthma severity situation than non chewer patients. Considering the cost and the effectiveness of current asthma medication at individual level, this particular study can propose khat as one of the options in the therapy of asthma and related obstructive respiratory problems.

7.2. RECOMMENDATIONS

- As a prior sense of duty asthma management should include investigation of the real cause for the attack, identifying the relation between acute and chronic inflammation as well as airway hyperresponsiveness. These can be achieved through close supervision of patients by the physicians all the way through objective testing using spirometry and bronchial challenge testing (methacholine challenge test or histamine challenge test). The availability of such tools will encourage more precise management of anti-inflammatory therapy.

- Further progress in asthma care requires better understanding of the molecular and genetic basis for the clinical heterogeneity which has been seen in this disorder. Advanced pharmacogenetic studies potentially identify subsets of patients who preferentially respond to specific class of anti-inflammatory agents as opposed to others, thereby eliminating some of the trial and errors that have been often seen in asthma management. Therefore, providing treatment Options in pharmacotherapeutic approaches block exclusive pathways for asthma care.

- Another possible recommendation can be drawn is that khat, should be classified as medicinal plant as it has moderate bronchodilating effect.

- Further study at molecular level and experimental trials on animal model is required to decipher the genuine effect of khat on respiratory airways.

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ANNEX I

Informed consent for adult respondent's participation in the study entitled 'Remedial E*ffect of Khat on Asthma in Jimma University Specialized Hospital Chest Clinic'*

Principal investigator: **Eden Yitna**

Read and give a copy of the full informed consent to the participant

Statement: Dear sir/madam ,my name is **Eden Yitna** and I am working in Jimma university as instructor of medical physiology and currently I am attending post graduate program in medical physiology .Thus for my thesis I am working on a research that analyse effect of khat on bronchial asthma, this study is conducted in Jimma university specialized hospital chest clinic .Therefore asthmatic patients are the subject of the study .As a result, you ,since you are under follow up here in chest clinic is going to be part of participant. For this purpose your willingness in participating in the study as a study subject makes the investigation worthwhile .And the information you provide will help the stakeholders to put their hand in designing strategies for a new treatment option for asthma signs and symptoms.

Procedure: the procedure that the data collectors follow to collect the desired information will be interviewing and measuring your pulmonary functions .For the measurement of pulmonary function parameter we will use digital Spiromer which is the safest instrument to measure ventilatory parameters and the tubes that you are going to blow through will be evacuated after use. Your single breath with in second has sensible for the study to be valid. The information that we obtained will be exclusively confidential and it is kept not to be mentioned to anyone other than the investigators and your physician. If you are not willing to respond you have unreserved right to refuse.

Incentives: the study is very important internationally and in a national level and presumably everyone who are suffering from asthma and other obstructive diseases will take advantage from the outcome so your participation has great meaning .Therefore though there will not be any material or payment that we give for you but you will be mentally satisfied and we heartily thankful for your participation.

Certificate of consent for participant: I have been requested to give information and to undergo spirometry as well as height measurement to be incorporated in the study. I endorse willingly to participate in this study and appreciate the right to withdraw from participation and also realize the benefit of the study.

Name of the subject, date and signature/thumb impression of subject

_____,___/___/___(dd/mm/yy)

ANNEX II

Questionnaire

Dear sir/madam you are requested to give kind responses to this questionnaire based on the real situation practices up on act and Perception. It is your real cooperation that makes this research worthwhile**.**

1. Age _____

2. Sex _____

3. Height_____

4. Do you have health problem other than asthma?

a) Yes

b) No

5. If yes, specify _____

6. Are you taking drugs for your problem?

a) Yes

b) No

7. If yes, specify_____

8. since when you suffer from asthma? (in month/years)

Specify_____

9. How often symptoms are experienced?(coughing, sneezing, dysnea…)

a) Less than one times per week

b) More than one times per week

10. How often you are awakens at night?

a) ≤2/ month

b) >1/ week

11. Have you ever been admitted to hospital because of your asthma problem? Yes/no

12. If yes how often?

_____

13. How often you use a short-acting β_2-agonist (rescue) for symptom relief?

a) ≤ 2 days/wk

b) 2 days/wk

14 .which drugs are you currently use for your asthma problem

a) Quick Relief Asthma Medications

b) Inhaled Corticosteroids

c) Long Acting Beta-Agonists

d) Leukotriene Modifiers

15. Do you chew khat?

a) Yes

b) No

16. If yes, how often do you chew?

a) Twice a day

b) Every day

c) ≥one times per week

17. Did you chew khat before you come here?

b) Yes

c) No

18. If yes, when?

a) Within12 hours

b) Within 24 hours

c) Within 36 hours

d) Other

19. Your preferable time for chewing

a) Morning

b) Afternoon

c) Night

20. Do you have a habit of chewing khat when you feel sick?

a) Yes

b) No

21. If yes, what is your exact feeling after chewing?

_____

_____

_____

22. Do you believe khat gives you relief from your asthmatic episode?

a) Certainly I believe

b) I think so

c) I doubt

d) I do not believe

23. Patient pulmonary function

PATIENT CARD No	HEIGHT	FEV_1	PEFR	REMARK

THANK YOU!

ANNEX III

Procedure for the assessment of lung function with spirometry

10 June, 2003

VOL: 99, ISSUE: 23, PAGE NO: 57

Spirometry records breath movements, inhalation and exhalation, and is integral to the management of lung disease, alongside good history taking and careful documentation. Tests can indicate a patient's optimal response to treatment or triggers, and the rate of decline in lung function. It is useful to detect the presence of lung disease, those susceptible to developing lung disease and to classify patients into severity classifications to optimise management.

Measurements used in spirometry

Forced expiratory volume (FEV) gives a measurement of the volume of air exhaled in a given time - often 0.5, 1, 2, 3, 4 or even 6 seconds. At 1s, this is referred to as FEV1. On average, a healthy person can exhale more than 80 per cent of the air in the first second. Readings of FEV1 can be used to classify lung disease when compared with predicted values for age, sex, height and ethnic origin (British Thoracic Society, 1997):

- Mild: FEV1 = 60-79 per cent;

- Moderate: FEV1 = 40-59 per cent;

- Severe: FEV1 < 40 per cent.

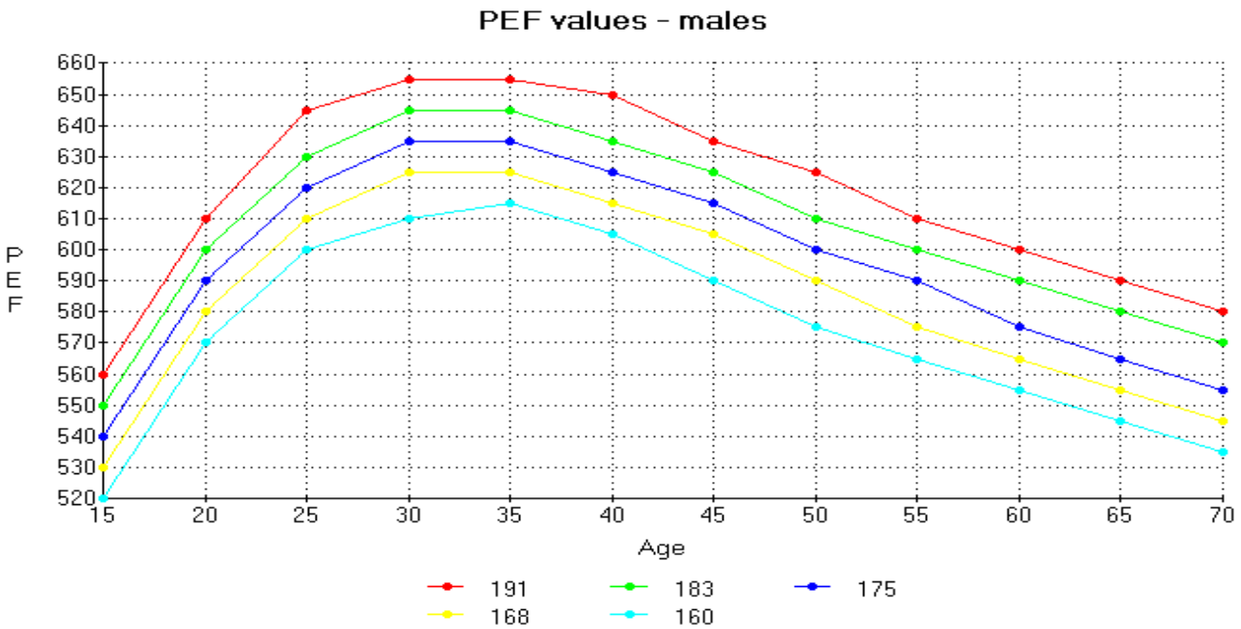
A restrictive pattern affects lung expansion and is characterized by a low FEV1, a low FVC and a high FEV1/FVC ratio. An obstructive pattern is one which affects

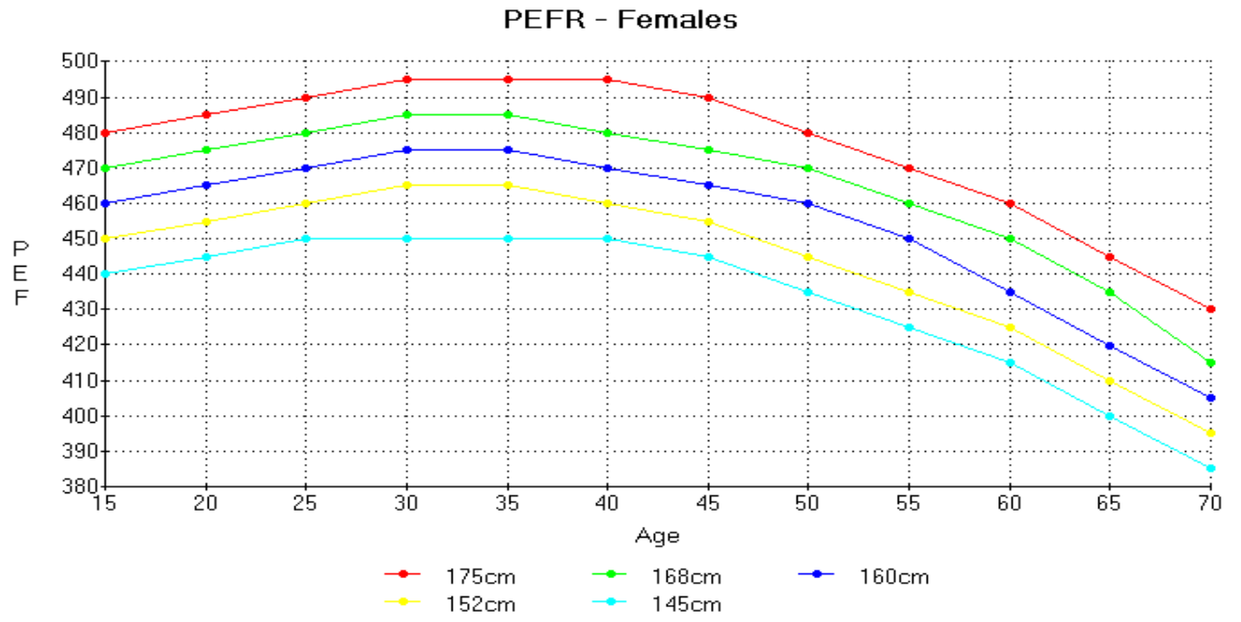
the rate at which air can be expelled from the lungs and is characterized by a reduced FEV1, normal FVC and a low FEV1/FVC ratio.

Major steps for spirometry

- Breathe in fully (the lungs must be absolutely full).
- Seal the lips around the mouthpiece and immediately….
- Blast the air out as fast and as far as possible until the lungs are completely empty.
- Repeat the test until three acceptable and reproducible results are obtained (up to a maximum of 8 efforts)
- The highest FEV_1 and FVC should be reported, even if they come from separate blows.

ANNEX IV


PEF values - males
660
650
640
630
620
610
600
590
580
570
560
550
540
530
520
P
E
F
15
20
25
30
35
40
45
50
55
60
65
70
Age
191
183
175
168
160


PEFR - Females
500
490
480
470
460
450
440
430
420
410
400
390
380
P
E
F
15
20
25
30
35
40
45
50
55
60
65
70
Age
175cm
168cm
160cm
152cm
145cm

ANNEX IV

CLINICAL CLASSIFICATION OF ASTHMA SEVERITY LEVEL

Severity	Symptom frequency	Nighttime symptoms	%PEFR/FEV_1 of predicted	FEV_1 Variability
Intermittent	<1/ week	≤2/ month	≥80%	<20%
Mild persistent	>1/week but <1/ day	>2/ month	≥80%	20–30%
Moderate persistent	Daily	>1/ week	60–80%	>30%
Severe persistent	Daily	Frequent	<60%	>30%

Adapted from National Heart, Lung, and Blood Institute: Expert Panel Report 3: Guidelines for the diagnosis and management of asthma