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A Polyherbal Unani Formulation in
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(Bronchial Asthma)

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PREFACE

The Central Council for Research in Unani Medicine (CCRUM) is an autonomous organization under Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy (AYUSH), Ministry of Health & Family Welfare, Government of India. The CCRUM, ever since it started functioning in January 1979, has been developing scientific research into various fundamental and applied aspects of Unani Medicine. Over the years, the Council has made great strides in its research programmes covering clinical research, drug standardization, survey and cultivation of medicinal plants, and literary research. At present, 23 research centres are functioning under the Council in different parts of the country. A leading research organization of Unani Medicine, the Council is also engaged in developing collaborations with reputed scientific research institutions in the country and abroad.

Under its clinical research programme, the CCRUM is busy validating on scientific lines the efficacy of certain Unani formulations in different common and chronic diseases, such as Bars (Vitiligo), Daus Sadaf (Psoriasis), Waja-ul-Mafasil (Rheumatoid Arthritis) and Zeequn Nafas (Bronchial Asthma) at its various centres. The Council's Regional Research Institute of Unani Medicine (RRIUM), Srinagar, Jammu & Kashmir has conducted a study on the clinical evaluation of a coded Unani formulation, UNIM-352, in cases of Zeequn Nafas (Bronchial Asthma). The present report contains the outcome of the study based on clinical, chemical and toxicological testing of the coded drug. The study has revealed the efficacy and safety of the coded Unani formulation in Zeequn Nafas, which is a chronic inflammatory disorder of the airways characterized by recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or early in the morning. Interestingly, it was

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Buqrat (Hippocrates) (460 BC–377 BC) – the Father of Medicine – who first studied the effects of climate, water, clothes, drinks, eating habits, and other factors on the causation of Zeequn Nafas, and also thought that the disease could be hereditary. Later, other savants of Unani Medicine like Jalinoos (Galen) (c. 129 AD–c. 210 AD), Majusi (c. 925 AD–c. 994 AD), Rabban Tabari (838 AD–870 AD), Al-Razi (Rhazes) (865 AD–925 AD) and Ibn Sina (Avicenna) (980 AD–1037 AD) added their observations to the existing knowledge of the disease. Indian physicians like Hakim Muhammad Azam Khan (1815 AD–1902 AD) and Hakim Ajmal Khan (1868 AD–1927 AD) also threw important light on the problem.

It should not be out of place to mention here that the Kashmir Valley is prone to different types of chest diseases including Zeequn Nafas. The incidence of the disease in Kashmir is higher in the months of March, October and November. According to a study, five to nine percent of the population of India suffer from the disease, and that the occurrence of the disease is rising in the country. Despite intensive research being carried out worldwide on this disease, its satisfactory and safe treatment still defies the modern medical world. In view of this, the present study should be of interest for those suffering from the disease as well as the students and teachers of Unani Medicine and the scientists engaged in research on this problem.

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INTRODUCTION

The term 'Zeequn Nafas' is composed of two words 'Zeeq' and 'Nafas' meaning 'narrowing' and 'breathing', respectively. In other words, it means difficulty in breathing. Zeequn Nafas is mentioned by the ancient physicians and philosophers like Buqrat (Hippocrates - 460 – 377 BC) and Jalinus (Galen - 129–210 AD). Buqrat described this disease as breathlessness or panting. Majusi has also mentioned this disease in his book *Kamil al-Sana'ah* with reference to Buqrat and Jalinus. Unani scholars have mentioned this disease under different headings in their treatises, e.g. *Rabw*, *Buhar, Dama*, *Intasabun Nafas,* etc. (Tabari 1928; Razi 1957; Ibn Sina 1906; Majusi 2010; Khan 1289H; Khan 1978; Kabiruddin 1960). Zeequn Nafas is a condition in which there is difficulty in breathing due to narrowing in air passages caused by accumulation of Balgham Lazij (viscous phlegm) in Urooq Khashna (bronchioles).

It is also known as Intisabun-Nafas, which is also a combination of two words '*Intisab*' meaning 'to stand' and '*Nafas*' meaning 'breath'. In this condition, some time the patient is unable to breathe or feels uneasy in sitting or laying position. So he stands to take breath and feel comfortable (Kabiruddin 1960).

The basic cause of breathlessness in Zeequn Nafas is narrowing of *Urooq Khashna* that may be due to various reasons, such as:

- Accumulation of Balgham Lazij (viscous phlegm) in air passage
- Insibab-e-Mawaad-e-Nazla
- Warm (inflammation)
- Abnormal shape of chest
- Constipation
- Polluted environment

- Gaseous collection in the chest putting pressure and leading to bronchial constriction (Khan 1289H, Razi 1957; Majusi 2010; Tabari 1928; Ibn Sina 1906).

Sometimes bronchial asthma may be associated with other diseases like Zaatul Janb (Pleurisy), Humma-e-Diq (Pulmonary Tuberculosis), Zaatur Riya (Pneumonia), Nuqsuddam (Anaemia), Sual-e-Muzmin (Chronic Bronchitis), Warm-e-Gurda (Nephritis). Zeequn Nafas due to these conditions is called Zeequn Nafas Shirki (Razi 1957; Kabiruddin 1960).

Types of Zeequn Nafas

Rabban Tabari (838–923 AD) has described various types of Zeequn Nafas:

1. Zeequn Nafas Qasir (caused by weakness of the respiratory muscles)
2. Zeequn Nafas Mutatabae (caused by inflammation of the diaphragm or excessive heat)
3. Zeequn Nafas Mustaqeem (caused by weakness or atony of the respiratory muscles)
4. Zeequn Nafas Qawi (caused by Iltihab and Hararat)
5. Zeequn Nafas Zaeef (caused by Burudat)
6. Zeequn Nafas Aseer (caused by accumulation of viscid secretions in the bronchial tree or gaseous collection in the chest putting pressure on the bronchial tree externally).

Hakim Ajmal Khan (1868-1927) has described following two types of Zeequn Nafas:

1. Zeequn Nafas Yabis (Bronchial asthma without expectoration caused due to spasm in the bronchial tree and the respiratory muscles)

2. Zeequn-Nafas Martoob (Bronchial asthma with expectoration that is caused due to spasm alongwith accumulations of phlegm in the bronchial tree)

Eminent physician Hakim Azam Khan (1815-1902 AD) has described following eight types of the disease:

1. Rabw Nazli (Allergic Asthma)
2. Rabw Balghami (Catarrhal Asthma)
3. Rabw Dukhani (Asthma due to pulmonary insufficiency
4. Rabw Istarkhai (Asthma due to paresis of respiratory muscles
5. RabwYabus (Asthma due to fibrosis of lungs)
6. Rabw Barid (Asthma due to cold)
7. Rabw Warmi (Potter's Asthma)
8. Rabw Haar (Hot type Asthma)

Alaamaat (Symptoms and Signs)

Zeequn Nafas is characterized by paroxysm of breathlessness with or without cough, cold and fever. Symptoms may be mild, moderate and sometimes severe. The patient looks restless and weak; face becomes red, and pulse becomes Azeem (magnus), Saree (rapid) and Layyin (soft). Sometimes sweating, low body temperature and increased respiratory rate are observed. Bouts of breathlessness and cough may remain from two to three hours to 24 hours. (Jurjani 1878; Khan 1289H; Kabeeruddin 1960).

Usool-e-Ilaj (Principles of Treatment) (Razi 1957; Ibn Sina 1906; Khan 1978; Arzani 1988)

- The patient should be kept in clean, calm and airy room free from air pollution during attack of the disease.

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- Ta'deel-e-Mizaj (correction of temperament).
- Tanqia Mawad (cleansing of viscous humour), Mulattif, Munaffis Balgham and Mukhrij Balgham drugs are recommended.
- Sometimes Muqi (emetics) are recommended for evacuation of Balgham.
- *Mohallil-e-Auram* and *Daf-e-Tashannuj* are also recommended.
- Treat the underlying cause in case of Zeequn Nafas Shirki.
- Avoid exposure to excessive heat and cold.
- Avoid constipation.
- Avoid mental and physical stress.
- Avoid use of citrus fruits, oily food and red chilies.
- Avoid use of diuretics because it may increase the consistency of *Balgham*

Zeequn Nafas is known as bronchial asthma in modern medicine. Asthma is a Greek word meaning short drawn breath, panting or labored breathing. Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or early in the morning. These episodes are usually associated with wide spread, but variable, air flow obstruction within the lung that is often reversible either spontaneously or with treatment (Colledge, *et. al.* 2010; Kumar & Clark, 2004; Stein, 1998).

It has been identified as one of the five most pressing global lung problems (Barnes, *et. al.,* 1996). The prevalence of asthma is rising and 5-9% of general population in India is suffering from

bronchial asthma (Gupta, *et. al*., 1999). Different terms such as allergic or asthmatic bronchitis, wheezy bronchitis, intrinsic and extrinsic asthma are frequently employed in clinical practice.

The currently available important anti-asthma drugs can be classified as controllers (required for maintenance treatment) and relievers (required for quick relief, rescue drugs).

Controllers (Prophylactic, Preventive, Maintenance)

- Taken daily to keep asthma under control
- Steroids, Long-acting beta-2 agonists, Sustained-release
- Theophyllines, Leukotriene receptor antagonists, and Cromones

Relievers (Quick relief, Rescue)

- Rapid-acting drugs that relieve broncho-constriction
- Short-acting beta-2 agonists, anticholinergics, theophyllines, short-course oral steroids (Colledge, *et. al.* 2010; Kumar & Clark, 2004; Stein, 1998)

Need of the Study

Varying climatic conditions in Kashmir valley associated with other factors predisposes respiratory diseases. The living habits in rural as well as urban areas are quite different, which predisposes higher incidence of bronchial asthma.

Despite intensive ongoing research all over the world, satisfactory and safe treatment of Zeequn Nafas (bronchial asthma) still defies the modern medical world. Long-term use of corticosteroids and bronchodilators in the treatment of bronchial asthma leads to suppression of immune system and other disorders. The present

study was conducted in search of a safe, effective and economical Unani formulation for the treatment of Zeequn Nafas.

Rationale of the Study

The Unani system of medicine is based on the teachings of Hippocrates who advocated that the chief function of a physician is to aid the Quwwat-e-Mudabbira-e-Badan (natural forces of the body) in combating diseases. The Central Council for Research in Unani Medicine (CCRUM) has been engaged in developing safe and effective Unani treatment for chronic and stubborn diseases like vitiligo, bronchial asthma, psoriasis, etc. Studies to test efficacy of the coded Unani formulation UNIM-352 in cases of bronchial asthma were conducted at the Council's Regional Research Institute of Unani Medicine (RRIUM), Srinagar. Most of the ingredients of UNIM-352 are Munaffis-e-Balghum, Mukhrij-e-Balgham, Daf-e-Sual, Daf-e-Humma, Muhallil-e-Auram. The drugs having above properties are effective in the management of Zeequn Nafas (Ghani 1998; Nabi 1932; Lubhaya 1977; Hakim 1922).

Objective of the Study

- To evaluate the toxicity of the coded Unani drug UNIM-352 in experimental animals.
- To evaluate the clinical efficacy of UNIM-352 in patients of bronchial asthma.
- To evaluate the clincial safety of UNIM-352 in patients of bronchial asthma.

MATERIAL AND METHOD

Centre of the Study

The study was carried out at Regional Research Institute of Unani

Medicine, Srinagar. Total numbers of 2,844 patients were enrolled from the general out-patient department (GOPD) of the institute.

Inclusion Criteria

Diagnosed cases of bronchial asthma, with breathlessness, cough, with or without expectoration, wheezing, tightness of chest, impaired lung function test of either sex and between 10 and 70 years of age were included in the study.

Subject Selection

Patients having breathlessness along with one or more of the following complaints were selected for the study:

- Wheezing
- Tightness of chest
- Cough
- Cough with expectoration
- Impaired lung function test

Exclusion Criteria

Patients having chronic bronchitis, bronchiectasis, diabetes mellitus, pregnancy, lactation, impaired renal function and impaired liver function were excluded from the study.

Investigations

The following investigations were conducted for the inclusion, exclusion, grading of the patients and for assessment of efficacy of the test drug.

- Chest X-ray

- Lung function test
- Hematological and biochemical test
- Sputum test for AFB
- Blood sugar
- Liver function test (LFT)
- Kidney function test (KFT)
- Stool (routine & microscopic)
- Urine (routine & microscopic)
- E.C.G.

Grading Criteria

Grade	State of dyspnoea
Minimal (Grade I)	Patient feels breathlessness on strenuous exercise only
Mild (Grade II)	Patient feels breathlessness on walking up a straight hill
Moderate (Grade III)	Patient is forced to walk slower than normal and stops to breathe after 500 meters or so.
Severe (Grade IV)	Patient feels breathlessness on walking slowly for 100 meters, and the pulse rate increases to 120 per minute or more.

Diet Instructions

Patients were advised to follow the under mentioned recommended and restricted diets.

Recommended Diet

Ghiza-e-Lateef (easily digestible), Musakhkhin (heat producing) were recommended to the patients, such as Maa-ush-Shaeer (barley water), Maa-ul-Asl (honey water), Chuqandar (Beet root) chicken soup; almond oil, spinach, Kaddu (pumpkin), Saib (apple), Behi (quince), Hareera, mutton soup, etc.

Restricted Diet

The patients were advised to avoid cold and phlegm producing flatulent food items, such as lemon, chilled water, grapes, orange, oily foods and red chili.

Study Drug

The study drug UNIM-352 is a coded polyherbal Unani formulation in the form of Majoon (Semi-solid preparation) containing Seer (*Allium Sativa* Linn.); Karanjwa (*Caesalpinia bonducella* Flem.); Hulba (*Trigonella foenum-graecum* Linn.); Katan (*Linum usitatissimum* Linn.); Chillbeenj (*Strychnos potatorum*); Karanj (*Pongamia pinnata* (Linn.) Pierre; and honey. The drug was prepared and supplied by the pharmacy of Central Research Institute of Unani Medicine (CRIUM), Hyderabad. Most of the ingredients used in UNIM-352 are Munaffis-e-Balgham (Expectorant) and Mukhrij-e-Balgham (Phlegmagogue) (Ghani 1998; Nabi 1932; Lubhaya 1977; Hakim 1922). Before carrying out the clinical trial, standardization and toxicity studies of UNIM-352 were conducted on animals. The details are as follows:

Physico-chemical Standardization of UNIM-352 and its Ingredients

Physico-chemical standardization of the coded Unani formulation UNIM-352 was carried out on the following parameters:

Physico-chemical studies

1.	Appearance	:	Semi solid
2.	Colour	:	Black
3.	Smell	:	Pungent and repulsive
4.	Taste	:	Sweet followed by bitterness
5.	Alcohol soluble matter	:	55% (w.r.d.)
6.	Water soluble matter	:	86% (w.r.d.)

7. Successive extractives :

    a. Pet. ether (60-80) : 0.62%

    b. Alcohol : 49.5%

    c. Water : 13.3%

8. Total ash : 1.003% (w.r.d.)

    Acid insoluble ash : 18.6% (w.r.ash.)

9. Qualitative tests

    a. Alkaloids : Present

    b. Steroids : Present

    c. Carbohydrates : Present

    d. Flavonoids : Present

    e. Glycosides : Absent

    f. Resins : Present

10. (a) Total reducing sugars : 0.40 gm/gm drug

    (b) Non-reducing sugar : 0.22 gm/gm drug

11. Total alkaloids : 16%

12. Volatile oil : 0.8-1.0% v/w drug

13. T.L.C. of extracts:

S. No.	Extract	Solvent system	No. of spots	R.F. value	Spraying reagent
1.	Pet. ether	100% chloroform	5	0.03 0.07 0.15 0.48 0.88	 Iodine vapors
2.	Pet. ether	Benzene: ethyl Acetate: (95:5)	6	0.10 0.17 0.22 0.52 0.80 0.86	 Iodine vapors
3.	Chloroform	Chloroform: Diethyl ether (1:1)	6	0.13 0.20 0.46 0.57 0.71 0.96	 Iodine vapors
4.	Chloroform	Chloroform: Methanol (95:5)	5	0.08 0.35 0.43 0.58 0.87	 Iodine vapors
5.	Alcohol	Chloroform: Methanol (95:5)	6	0.16 0.29 0.39 0.52 0.69	Iodine vapors Iodine vapors
6.	Water	Butanol: Ethanol: Water (4:1.1:0.9)	3	0.09 0.28 0.40 0.41	 Cerric Ammonium Sulphate

Absorbent: - Silica Gel G

Some of the Ingredients of UNIM-352

Seer (*Allium Sativum* Linn.)

Karanjawa seeds
(*Caesalpinia bonducella* Flem.)

Methi seeds
(*Trigonella foenum-graecum* Linn.)

Katan seeds
(*Linum usitatissimum* Linn.)

Nirmali/Chilbeenj seeds
(Strychnos potatorum, Linn)

Karanj seeds
(*Pongamia pinnata* (Linn.) Pierre)

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Toxicological Study of UNIM-352

Study to assess the toxic effects of the coded Unani formulation UNIM-352 was conducted at RRIUM, Srinagar. The coded formulation was administered in rats in a dose of 2000mg/kg/day orally for a period of 90 days. Young adult, healthy albino wistar rats of either sex weighing between 150 g and 200 g were used in the study. The animals were divided into four groups (two control and two test groups of either sex) of ten animals each caged separately, maintained at an ambient temperature of 20-26°C with 12-hourly light/dark schedule. They had access to pelleted diet and water *ad libitum.* Group I & II (male & female) were served as control and received equal volume of distilled water orally whereas Group III and Group IV (male & female) were served as test groups and received the study drug 2000mg/kg/day orally for a period of 90 days.

Animals were observed for their general appearance, behaviour, feed/water consumptions, and their body weights were recorded during the study. At the end, they were sacrificed by exsanguination and biochemical and haematological parameters were estimated in the laboratory by standard methods to assess their organ functions. The biochemical parameters included blood urea, total serum protein, SGOT, SGPT, serum alkaline phosphatase, and serum acid phosphatase to monitor the functional status of different organs. The hematological parameters included Hb, TLC, DLC as general screening markers for haematology, or any kind of acute or chronic tissue damage.

There was no mortality in the test and control groups of animals during the course of the study. The test group animals remained healthy, and gained body weight in comparison to the controls. The biochemical and haematological parameters of test group animals were also found to be within the normal limits in comparison to the control group.

It may be concluded that UNIM-352 was found safe and free from any adverse effect.

Dosage

The coded Unani formulation UNIM-352 in the form of Majoon (Semi-solid preparation) was given in the dose of 10 gm twice daily with lukewarm water.

Duration of protocol therapy

Twelve weeks.

Sample size

Two thousand eight hundred and forty-four (2844) cases of Zeequn Nafas were studied.

Safety assessment parameters

A   Clinical

- Adverse event if any

B   Laboratory

- Biochemical/ pathological parameters (Haemogram, LFT, KFT, etc.)

Efficacy assessment parameters

A   Clinical

- Improvement in the clinical signs and symptoms

B   Laboratory

- Improvement in the lung function test
- Improvement in the radiological examination (if any)
- Improvement in biochemical and pathological parameters (if any)

Methodology

On the first visit, the patients were clinically examined, provisionally diagnosed and enrolled for the study. Then they were subjected to thorough laboratory investigations. Two thousand, eight hundred and forty-four (2844) cases of Zeequn Nafas were registered for the study in the Out Patient Department (OPD) of Regional Research Institute of Unani Medicine, Srinagar. Grading of the patients were done, and they were classified according to age, sex and duration of the disease. The severity of bronchial asthma was evaluated by Spirometry.

The drug UNIM-352 was given to the patients in prescribed dose. Follow-up of the patients was done on four, eight and 12 weeks of the treatment. After completion of the treatment, the patients were assessed at 1-2 weeks intervals up to next four weeks.

Observation and Discussion

The following observations were recorded during the study.

Month-wise Incidence

Month-wise registration record in relation to the disease.
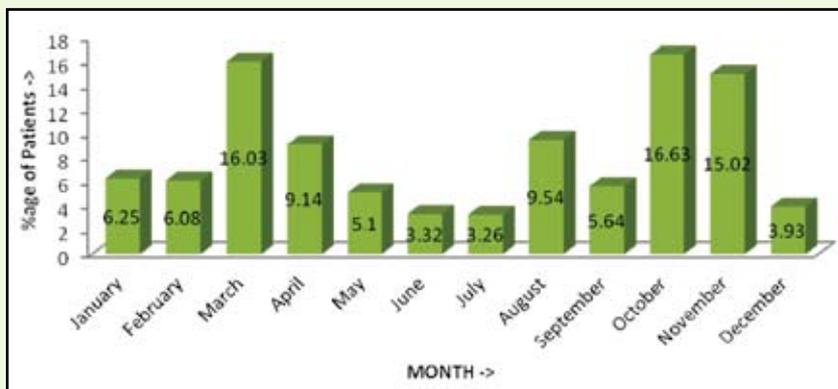
Graph 1

Age and Sex distribution
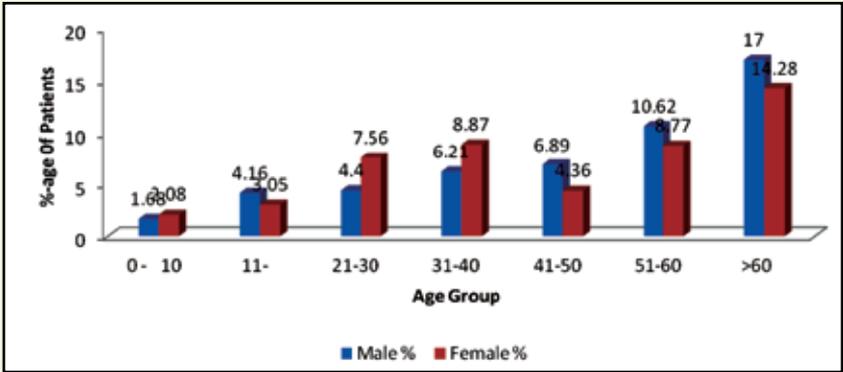
Graph 2
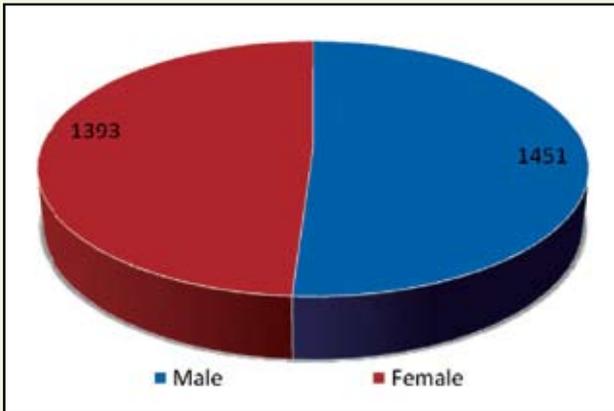
Graph 3

Out of the 2844 patients registered, 50.99% were male and 49.01% female, indicating that the occurrence of the disease is slightly higher among males. This supports the study of Harward, *et. al.* 1985. The bargraph 2 shows the incidence of Zeequn Nafas increasing gradually as the age advances (Agarwal, *et. al.* 2006). The highest incidence has been recorded in the age group above

60 years. From this it can be concluded that the elderly suffer from the disease more than the youngsters.

Duration of onset of disease
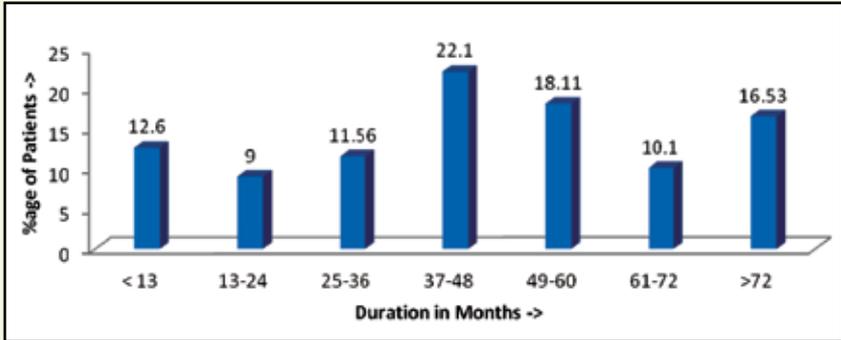
Graph 4

As evident from the graph above, almost all the cases were chronically affected by Zeequn Nafas. Of the 2844 cases, 22.1% cases were suffering from this disease for 37 to 48 months followed by 18.11% for 49-60 months followed by 16.53% for 73 months and above.

Distribution of patients according to Tobacco use
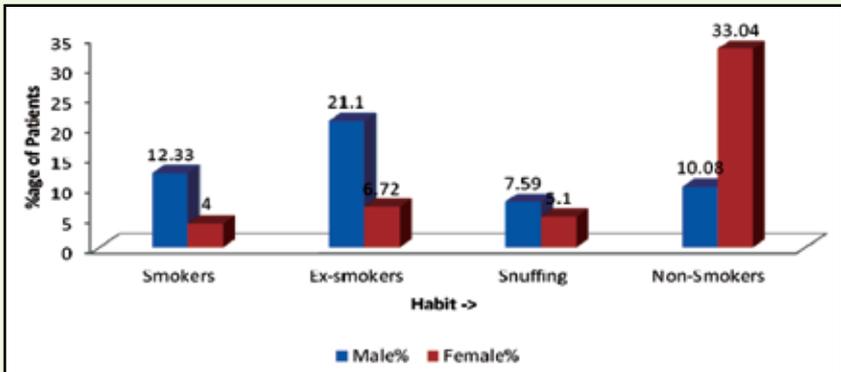
Graph 5a
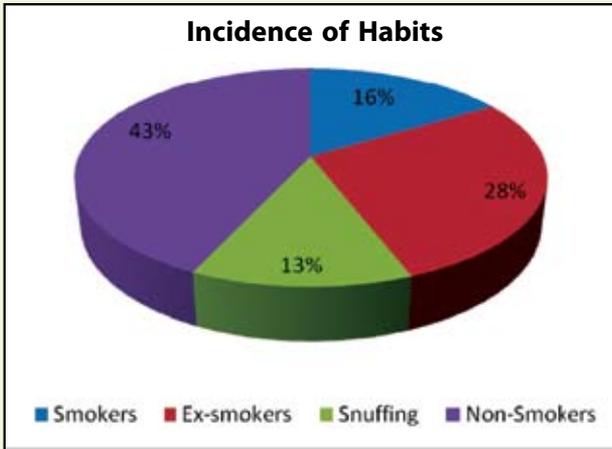
Graph 5b

In this study non-smokers (43%) have been found to have a high incidence of Zeequn Nafas. Our data are also supported by the study published in *Journal of Allergy and Clinical Immunology* (Vesterinen, et. al. 1988, Siroux, et. al. 2000, Jindal and Gupta 2004, Thomson, *et. al.* 2013.)

Occupation
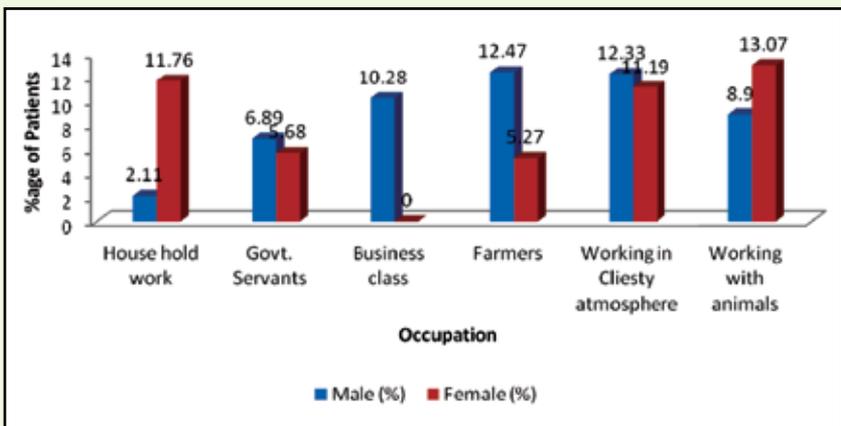
Graph 6a

The study also revealed that females working with animals and in household jobs are more prone to the disease in comparison to males, whereas among male farmers and businessmen working in luxurious atmosphere, and those working in government sector are more prone to the disease than the females.

Socio-economic status
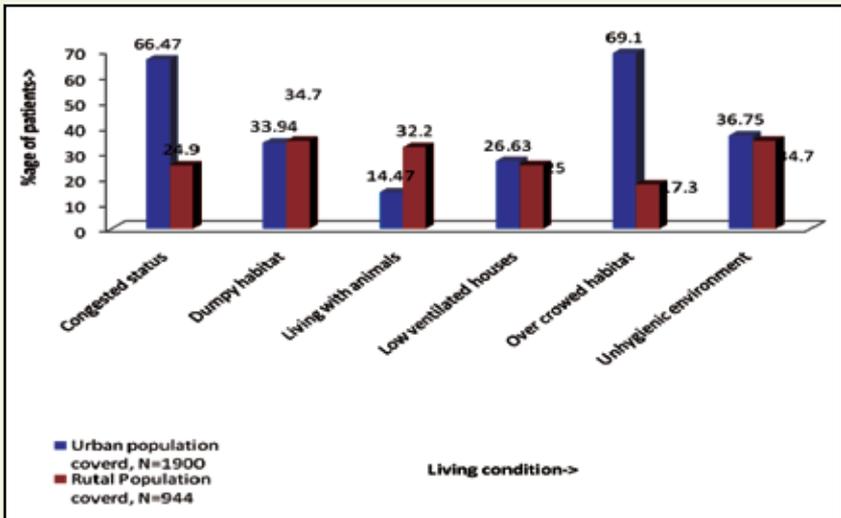
Graph 6b

The study showed that the people living in congested and crowded urban areas are more affected, whereas in rural areas people living in dumpy habitat and unhygienic environment (34.7%) were more prone to Zeequn Nafas. (Graph 6- a, b). Socio-economic status also plays an important role in the incidence of the disease. People living in congested and crowded urban areas were more affected (Wright and Fisher 2003, O'Neill, *et al.* 2003; Weiss and Wagener 1990).

## Safety evaluation of the coded Unani formulation UNIM-352 in Zeequn Nafas patients

Investigation	Parameter	Before	After
Haemoglobin	Gm%	Mean = 10.19 S.D = 1.32	Mean = 10.7 S.D = 1.12
E.S.R	mm/1hr	Mean = 18.1 S.D = 3.7	Mean = 16.4 S.D = 2.9
Total Leucocytes Count	Mg/dl	Range=6500 – 9100	Range=6100 - 10200
Differential Leucocytes Count %	Neutrophils	Range = 47 - 64	Range = 51 - 65
	Lymphocytes	Range = 15 - 25	Range = 15 - 26
	Monocytes	Range = 2 - 5	Range = 2 - 5
	Eosinophils	Range = 1 - 3	Range = 0.5 – 3.4
	Basophills	Range = < 1	Range = < 1
Vital Capacity		Range = 500 - 2800	Range = 2500 - 3500
FEV1		Range = 800 - 1450	Range =850 - 2300
LFT	S. Bilirubin	Range = 0.7 – 1.5	Range = 0.7 – 1.2
	SGOT	Range = 20 - 35	Range = 18 – 33
	SGPT	Range = 38 – 72	Range = 37 - 63
KFT	Blood Urea	Range = 17 – 29	Range = 18 - 28
	S. Creatinine	Range = 0.5 – 1.3	Range = 0.5 – 1.3
	S. Uric Acid	Range = 2.8 - 6	Range = 3 – 4.9

The above table shows that there was no change in pathological and biochemical markers at the level significance $p < .05$ before and after the intervention of UNIM-352.

Effect of UNIM-352 on Signs and Symptoms
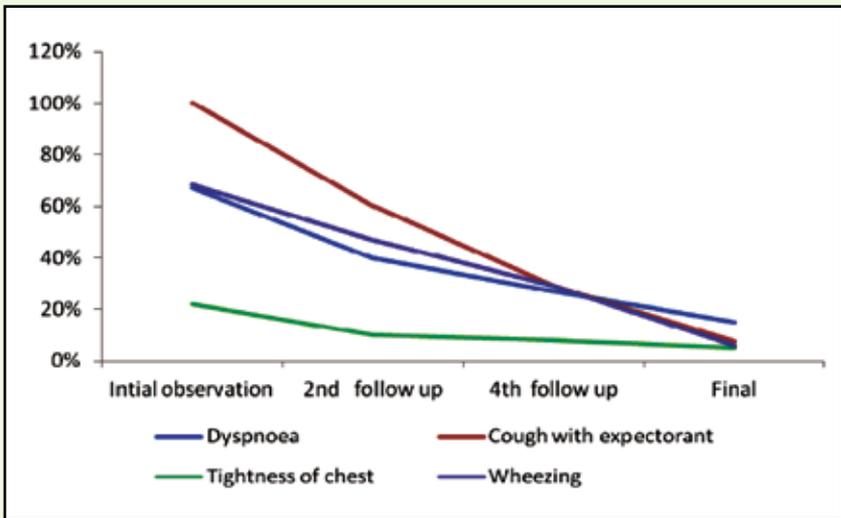

Graph 7a
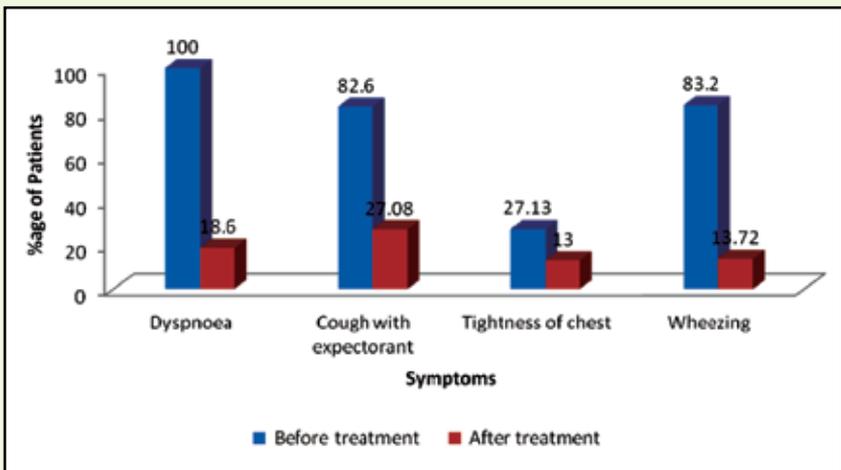
Graph 7b

Dyspnoea was seen among all patients registered for the study followed by wheezing and cough with expectoration. Thightness of chest was seen in severly ill patients. The above representation (graph 7 a, b) shows effect of UNIM-352 on different sysmptoms (mentioned in graph7 a, b) taken as parameters at different stages during the therapy. All the symptoms were analysed separetly to measure effectiveness of the therapy. The therapy showed significant relief (P< 0.05) of all the four parameters taken into consideration.

Grade-wise Effect of UNIM-352 on Respiratory Rate after 12 Weeks.
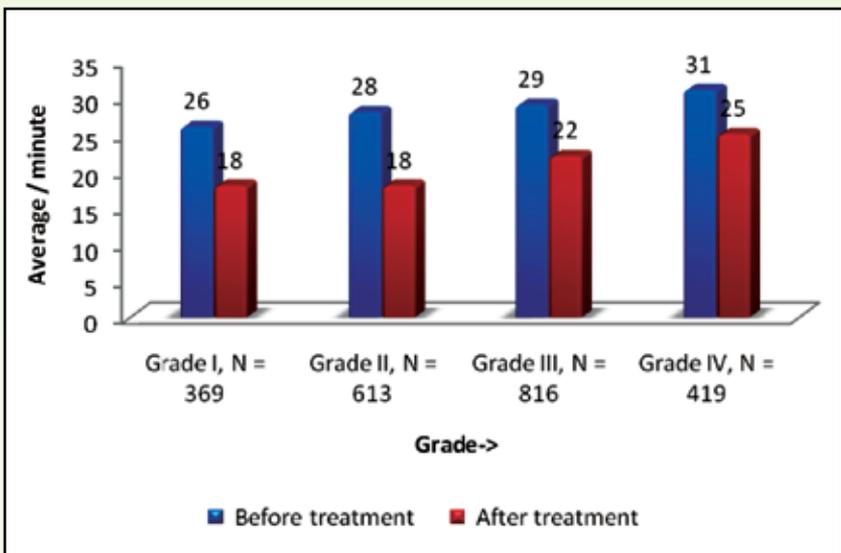

Graph 8a

## Grade-wise Effect of UNIM-352 on Pulse Rate after 12 Weeks.
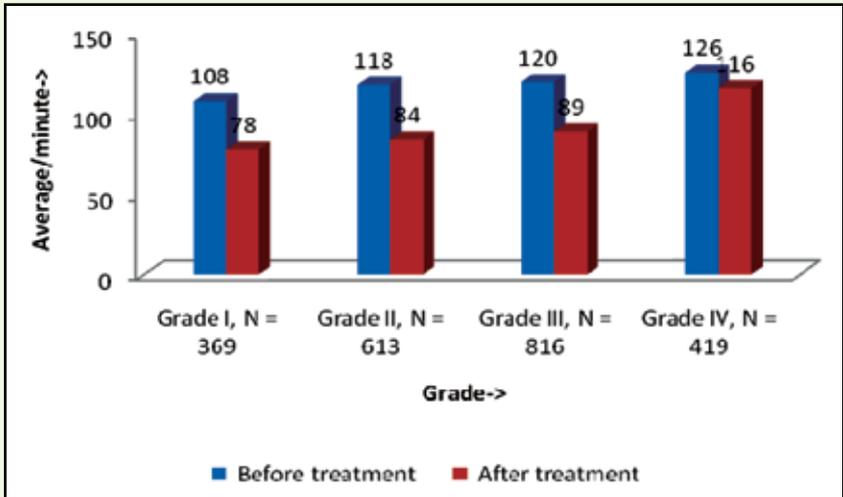
Graph 8b

Grade-wise Effect of UNIM-352 on Peak Expiratory Volume after 12 Weeks.
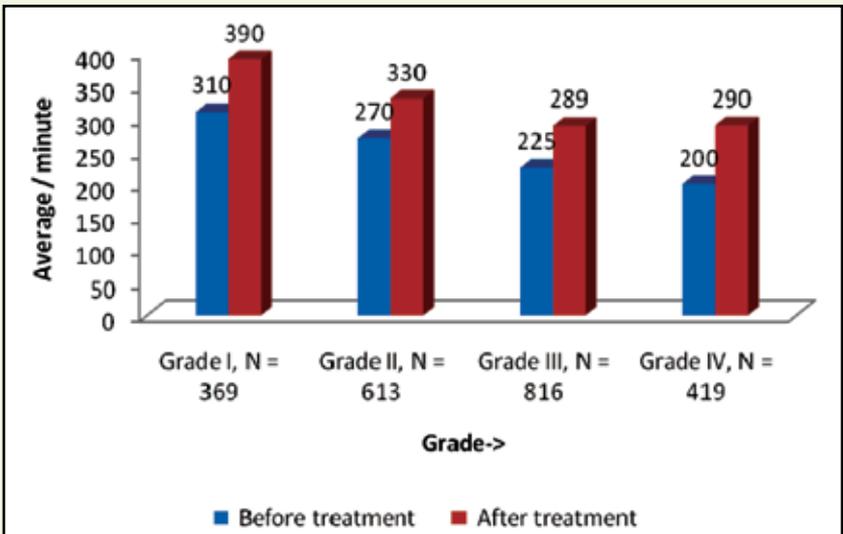

Graph 8c

## Grade-wise Effect of UNIM-352 on Vital Capacity after 12 Weeks.
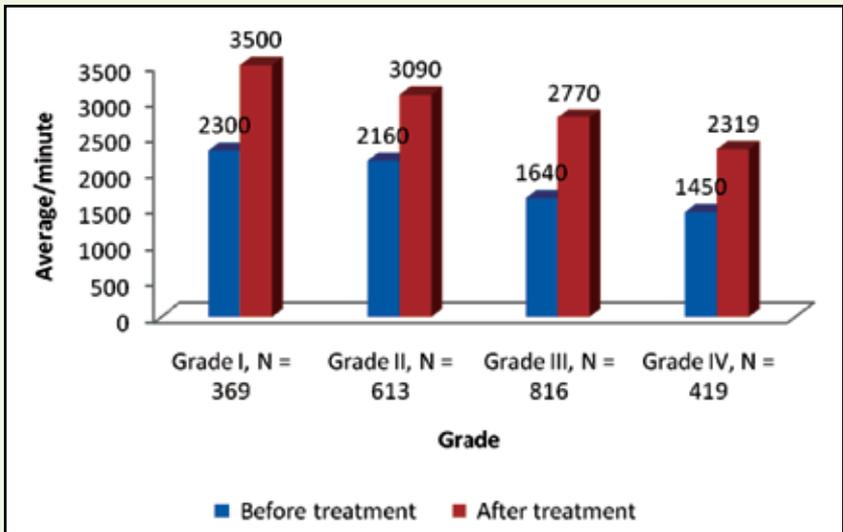
Graph 8d

Lung function test was done before and after the treatment in all the patients. The above data shows a significant improvement in the lung function tests after completion of therapy (UNIM-352) in all the groups.

## State of withdrawal of Broncho-dilators and Cortisones
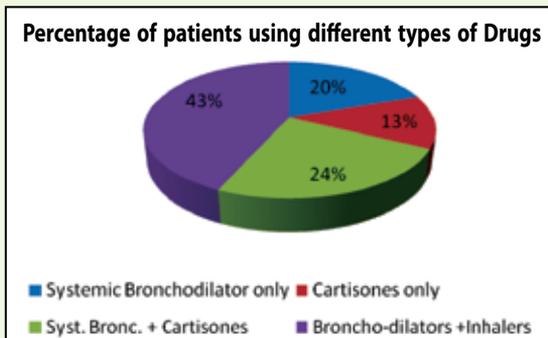
Graph 9a
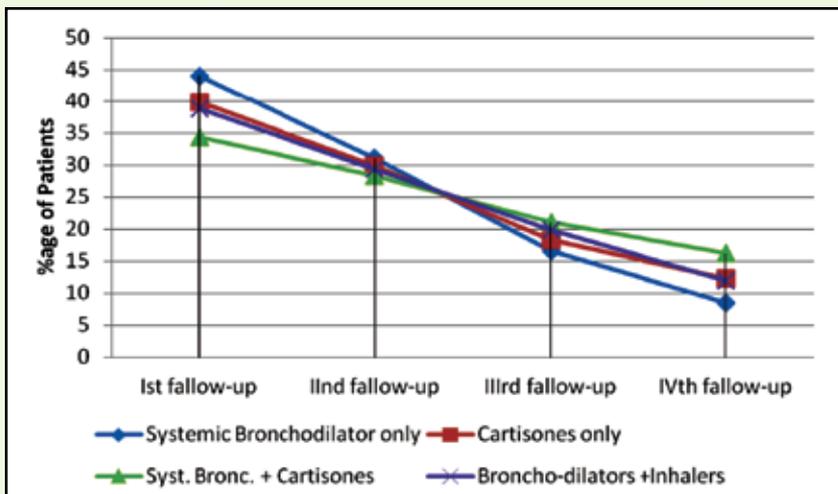
Graph 9b

Of the 2217 patients, 1643 (74%) patients used broncho-dilators and Cortisones or both at base level. After completion of protocol therapy it was found that 87.64% patients had withdrawn the use of bronchodilator and cortisones.

Effect of UNIM-352 in different age groups
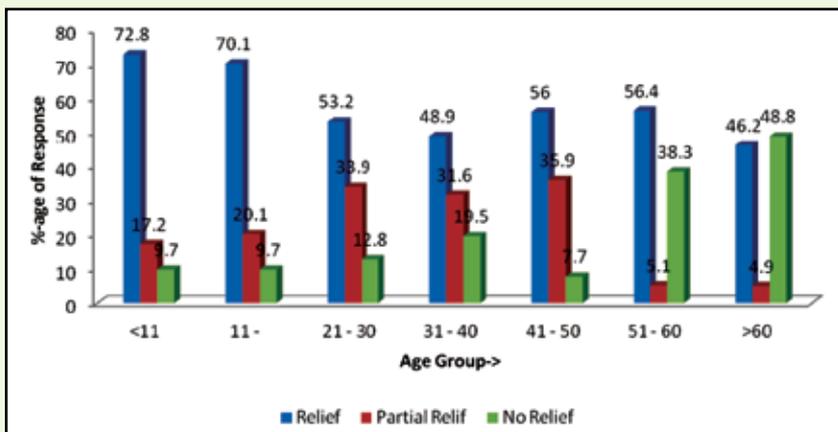
Graph 10

The study showed significant relation between the age and therapy $(r) = -0.37$ as the therapy showed significant response in the age at <20 years and has same relation of onset of disease (95% confidence interval: -0.7672 to 0.2226). The therapy successfully reduced the symptoms (p=.0071) significantly.

Sex-wise response of UNIM-352 in Zeequn Nafas patients
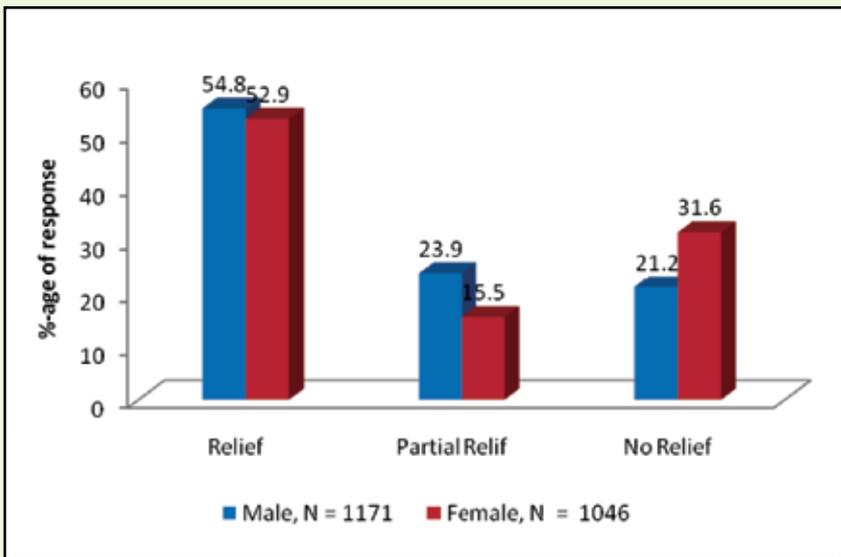
Graph 11

Out of the 2217 patients who completed the protocol therapy, 54.8 % males and 52.9% females got relief, 23.9% males and 15.5% females got partial relief in their signs and symptoms, while 21.2% males and 31.6% females did not get significant relief in their signs and symptoms.

**Effect of UNIM-352 in relation to duration of onset of the disease**
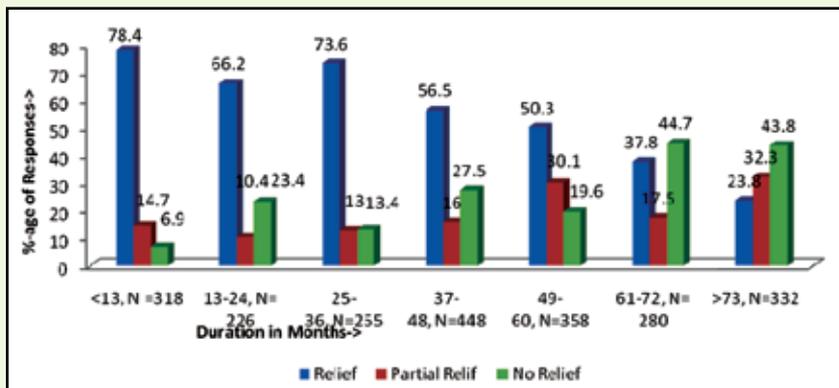
Graph 12

It was observed that UNIM-352 showed a good response (78.45%) in patients who had signs and symptoms of Zeequn Nafas for less than 13 months. The lowest response (23.8%) was observed in patients having this disease for more than 72 months

Overall response of UNIM-352 in Zeequn Nafas patients
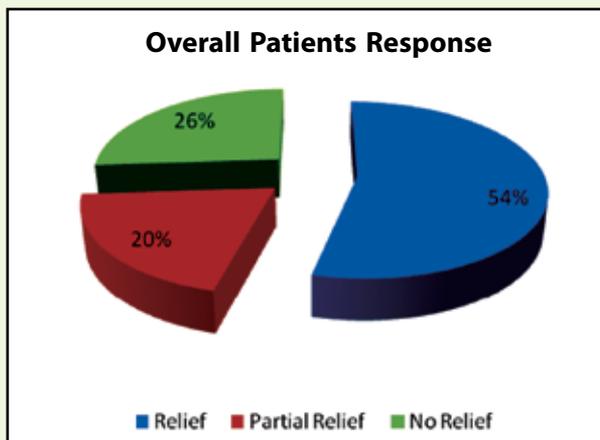
Graph 13

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The study showed that 54% patients got relief, 20% patients got partial relief in their signs and symptoms, while 26% patients did not respond to the therapy.

The criteria used for the assessment of relief were as follows:

1. Relief   =   100-70% regression in symptoms
2. Partial Relief =   71-40% regression in symptoms
3. No Relief   =   < 40% regression in symptoms

Summary and Conclusion

- The aim of the present study was to investigate the efficacy and safety of UNIM-352 in patients of Zeequn Nafas. Analysis of the data showed wide differences in subjects and their variables. Therefore it is observed that future study on a larger sample size of heterogeneous age groups with restricted selection criteria will be beneficial.

- The disease advances as the age increases.

- The non-smokers have high incidence of Zeequn Nafas in comparison to the smokers.

- The females working with animals and in household jobs are more prone to the disease in comparison to males, whereas male farmers, business class, working in luxurious atmosphere and government sector are more prone to the disease than the females.

- The Unani formulation UNIM-352 is safe and effective for clinical use.

- UNIM-352 significantly improved the lung functions and significantly reduced the use of bronchodilator and cortisones.

- The study supports the classical reported action of ingredients of UNIM-352 such as Seer (*Allium Sativum* Linn.), Karanjawa

seeds (*Caesalpinia bonducella* Flem.), Methi seeds (*Trigonella foenum-graecum* Linn.), Katan seeds (*Linum usitatissimum* Linn.), Nirmali/Chilbeenj seed*s (Strychnos potatorum, Linn)*, Karanj seeds (*Pongamia pinnata* (Linn.) Pierre) which are effective for treatment of Zeequn Nafas.

- The coded Unani formulation UNIM-352 also improves general wellbeing of patients by improving Quwwat-e-Mudabbira-e-Badan and thus supports the theory and philosophy of Unani Tib.

- The coded Unani formulation UNIM-352 successfully reduced the symptoms and signs of the disease and it acts as Munaffis-e-Balgham (expectorant) possibly Mufatteh Urooq-e-Khashna (Broncho-dilator) and Antihistaminic.

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