Aberrant Use of H_1 Blockers, A Clinical Study In Hyderabad, Pakistan.

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ABSTRACT

Allergy is a type of hypersensitivity disorder comes under the category of immune system. A numeral conditions caused by hypersensitivity of the immune system to something in the environment typically causes no or little problem in maximum population. These diseases include food allergies, hay fever, allergic asthma, dermatitis, and anaphylaxis. Symptoms may include itchy rashes, red eyes, runny nose, shortness of breath and swelling. Among 4 (four) types of histamine receptors in human body H_1 receptor is found in Peripheral nervous system which includes smooth muscles, epithelium layer & also in Central Nervous System. Its function, in central nervous system is to maintain body temperature, sleep and wake cycle, appetite, endocrine homeostasis, mood, memory and learning. In peripheral nervous system it is responsible to cause Bronchoconstriction, Vasodilatation, Responsible of Hives because of insect stings it causes pain, itching, which is also responsible to cause Motion sickness and Rhinitis. Oral medications like H_1 Blockers and decongestants are used to reduce symptoms. People taking H_1 receptor antagonist as a self-medication can central for more severity of his/her cases. Taking as a self-medication, they do not take any recommended dose, so dose can fluctuate as over dose or under dose. As by taking Loratadine for a long term may lead to drug resistance and also they are addicted to these drugs. A descriptive cross sectional study is publicized by collecting the patient data on predesigned questionnaire.

Methodology: Total number of 300 patients was enrolled via purposive sampling from different hospitals, pharmacies and clinics of Hyderabad, Pakistan. The study was observational & then the dose of total sample size was compared with the standard British National Formulary 71 edition and the data was analyzed by using SPSS software version 22, Microsoft Excel & other statistical tools.

Results: Patients having flu were more in number of 28%; 22.66% of common cold; 21.33% of skin rash; 18.33% of cough and 9.66% patients were of others which includes Urticaria and Red Flare. 23% patients used Loratadine which is 2nd generation H_1 receptor antagonist (anti-histamine) 22% patients were taking Chlorpheniramine which was the only 1st Generation H_1 blocker used among the patients. 45% patients were taking BD dose, 27% of OD & 25% patients were taking TDS and only 3% patients were taking SOS. Through the survey & pre-designed questionnaire, it was found that most of the patients were taking anti-histamine without the prescription of doctor (174 / 300 patients) as all anti-histamines are easily available in all pharmacies and the patients were experiencing side effects because of no dose adjustment by Doctor or a Pharmacist. Among all 59.3% patients were experiencing Dry nose, 57.6% head ache, 56% of dry mouth, 58.6% patients were experiencing drowsiness, 52.3% were feeling sickness and 34.6% patients were having problem in driving due to hang over effects.

Conclusion: It is concluded that patients were using H_1 Receptor antagonists because of easy availability of drugs in our pharmacies and because of unavailability of Pharmacist in pharmacies, so frequent use of anti-histamine with no dose adjustment can lead severe side effects with drug dependence.

Key Words: Aberrant use; H_1 Blockers; Anti-allergic; Allergic Patients.

1. INTRODUCTION

"A protein molecule that is responsible for receiving the chemical signals from external environment particularly outside the cell" is known as Receptors. (Shah. S et al., 2016). Moreover, these receptors (molecules) may also recognize the endogenous receptors for example the acetylcholine receptors recognize the acetylcholine and response according to their function. Depending upon the mechanism of action, receptors are of 03 type's i.e. Channel linked or ligand gated receptors, Enzyme linked receptors and G-Protein coupled receptors. The histamine receptors belongs to the G-Protein coupled receptors and of 4 various types (H_1 to H_4) (Shah. S

et al., 2016). The example of H_1 receptors antagonists includes Loratidine, Cetrizine, Fexofenadine, Clemastine etc, H_2 receptors antagonists includes Ranidine, Cimetidine, Famotidine, H_3 receptors includes Ciproxifan and H4 includes Thioperamide (Holgate,1998) Each receptor has their distinguished functions as H_1 receptors has itching particularly on skin, contraction of ileum, asthma induced due to allergy and vasoconstriction. Allergy may also define as if the immune system interacts with those things which are present in environment may leads to hypersensitivity reactions (Dykewicz. and Fineman, 1998). These reactions sometimes caused problems with the number of allergic diseases such as asthma due to allergy, dermatitis, hay fever and food allergy. Different types of sign and symptoms such as red eyes, skin rashes, runny nose, swelling and emphysema are most common. (Pise and Padwal, 2015). There are various types of allergens present in the environment but the most common are of pollens and food. In advance countries, 20% of population has allergic rhinitis & 6% were suffering from food allergy & in various countries the asthma were ranged from 1 to 18% allergy is one of the most facing common problem (Joel et al.,2010). Successful therapeutic management is the key for rational use of medicines. According to WHO rational use of medicine may define as "the receiving of medicines according to the clinical needs with appropriate dose, frequency & cost effective". Major objective of clinical pharmacy is rational use of drugs. Irrational or aberrant use of drugs is utilization of medicines which is opposite to the rational use. Following are the types of inappropriate use of medicines: two or more medicines of same generics are used, self-medications of various drugs particularly antibiotics, frequent use of injectable as compared to oral formulations, prescription of medicines not following the guidelines. People taking 2nd generation H_1 antagonist as a self-medication can central for more severity. Dose can fluctuate as over or under as individual is taking self-medication. For a long term, these drugs can cause resistance and also addiction. Safety and effectiveness in the children have not been confirmed yet; so these medications without prescription should never be used in the patient earlier than 6 years. This study will help to ensure the safe use of antihistamine in allergic patients and it will also help to ensure rational therapy by monitoring and evaluating outcomes. This study will also help our health organizations as it will provide the assessment on antihistamine and will highlight the importance of role of Pharmacist and other health care provider in health care system. The objectives of the study are to: To quantify the number of allergic patients utilizing Second Generation H_1 Receptor Antagonist, To assess the proper dose of H_1 Blockers in Allergic

patients, To check any serious effects produced due to intake of 2nd Generation H_1 Anti-histamine.

2. METHODOLOGY

A descriptive cross sectional study was conducted on questionnaire which was pre-designed and the patient's data was conducted. A total 300 patients were registered through purposive sampling from clinics, pharmacies and out-door patients tertiary care hospitals of Hyderabad, Pakistan. Duration of study was 1 year and it was observational. All the results were compared with the standard (BNF) British National Formulary 69 edition and Microsoft Excel 2010 was used to analyze data. Before inclusion, an informed consent was signed from each patient.

2.1 Inclusion criteria: Outdoor patients from age 18 – 60 years.

2.2 Exclusion criteria: Indoor patients; Hepatitis B & C; HIV AIDS patients; cancer and Pulmonary & Extra-pulmonary tuberculosis patients.

3. RESULTS AND DISCUSSION

A total 300 patients were enrolled from different clinical settings (Private clinics, Tertiary care hospital and Retail pharmacies) the data was collected on a predesigned questioner. All data was interpreted and following results were obtained.

OPD patients

|	Hospital	Retail Pharmacies	Clinics
■ OPD patients	36.33%	35.33%	28.33%
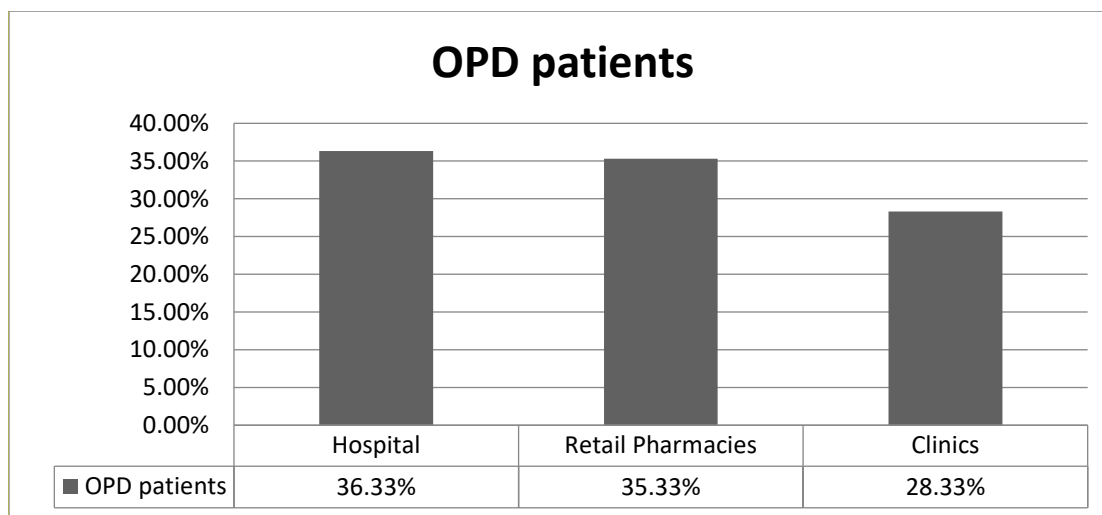
Figure 1 Types Of Clinical Settings

Fig 1 shows the 36.3% (109) patients were from tertiary care hospital; 35.5% (106) patients were from retail pharmacies & 28.3% (85) patients were from different clinics of consultants of Hyderabad, Pakistan.
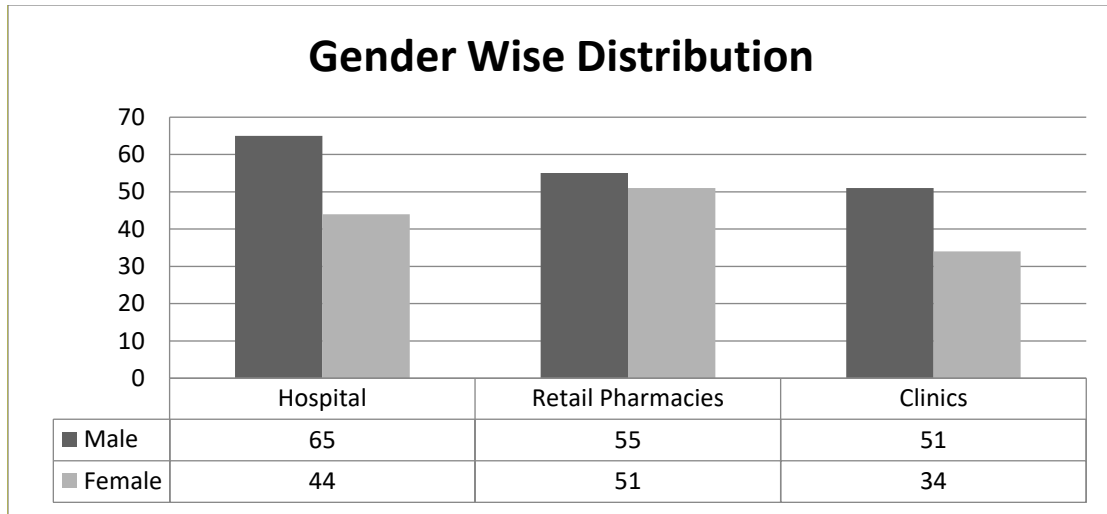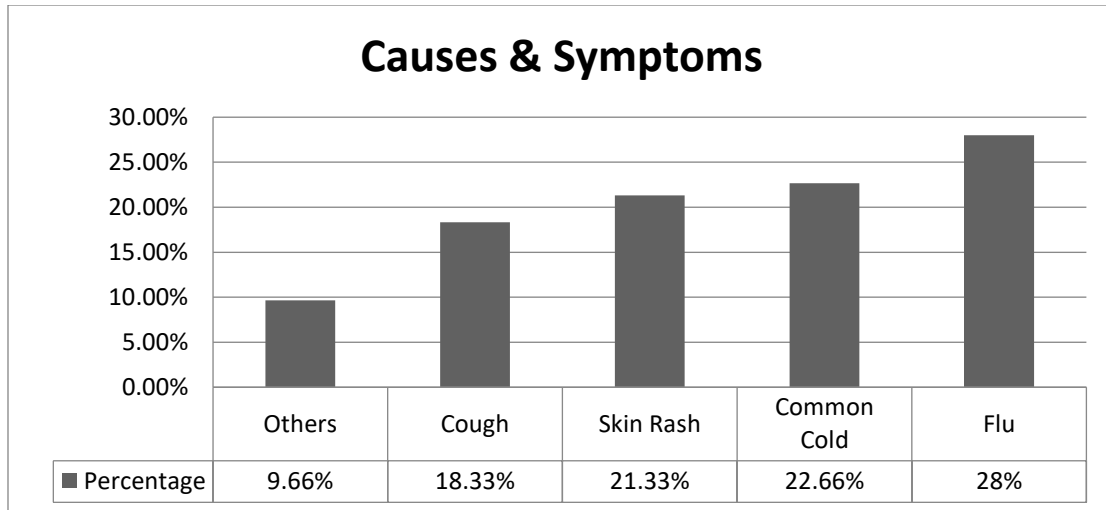
Figure 2 Gender Wise Distributions of Patients in Clinical Settings

Graphical representation of clinical setting of gender is shown in fig 2; 65 male and 44 female patient were from tertiary care hospital, 55 male and 51 were females from retail pharmacies & from consultant clinics 51 male and 34 females were enrolled.
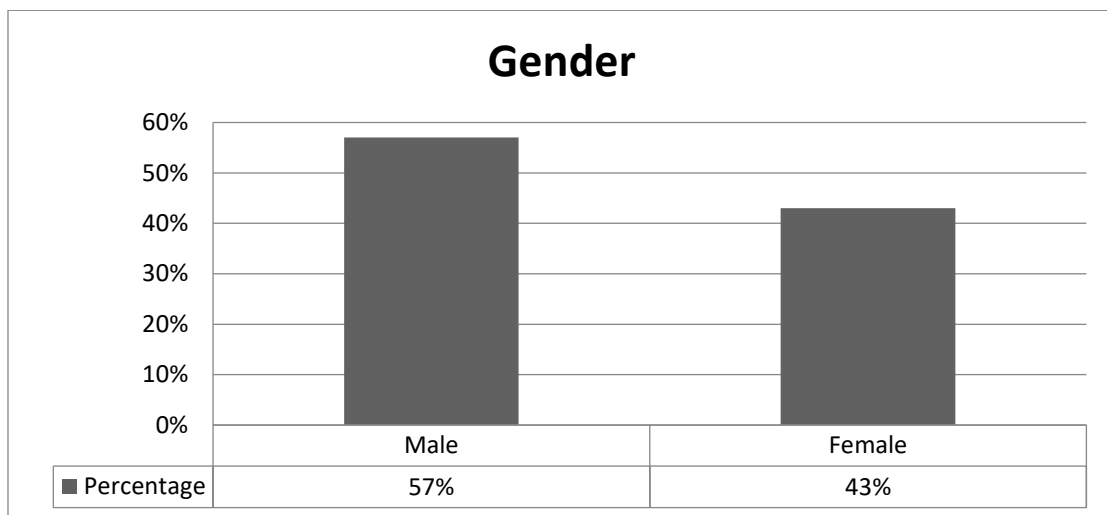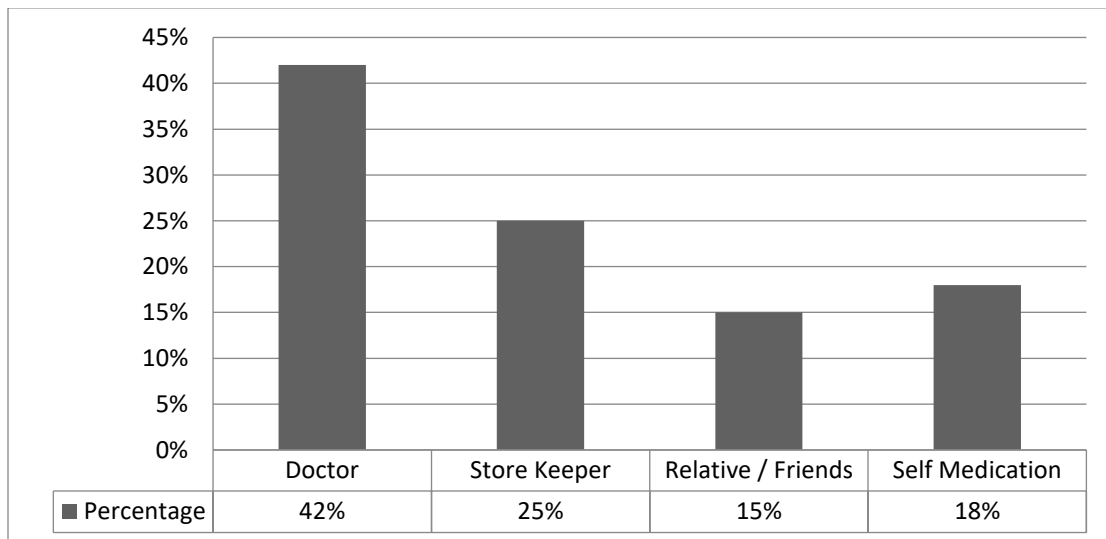

Figure 3 Sample Size Based On Gender

Fig 3 shows the major contribution of male patients which were 171 from 300 patients and rests of 129 were females.

Causes & Symptoms

| Percentage	Others	Cough	Skin Rash	Common Cold	Flu
Percentage	9.66%	18.33%	21.33%	22.66%	28%

Figure 4 Causes & Symptoms

As shown in Fig 4; the causes and symptoms of patients that why they were using H_1 Blockers? Mostly patients were taking because of Flu which is 28% (84) which were maximum as compared to others; Common Cold patients were 22.7% (68), 21.3% (64) were of Skin Rash, 18.3% (55) patients having Cough and out of 300, 9.7% (29) patients were of Urticaria and Red Flare.

Percentage	Doctor	Store Keeper	Relative / Friends	Self Medication
Percentage	42%	25%	15%	18%

**Figure 5** Who Suggest To Take H_1 Blocker?

Fig 5 shows who suggest the patients to take H_1 Blockers. During the study, maximum number of patients were taking medicines by the prescription of Doctors/Pharmacist 42% (126); 25% (76) patients were suggested by Medical Store keepers; 15% (45) patients were taking medicines

by their Relatives / Friends and Family suggestions; 17.7% (53) patients took anti-allergic as a Self-Medication.
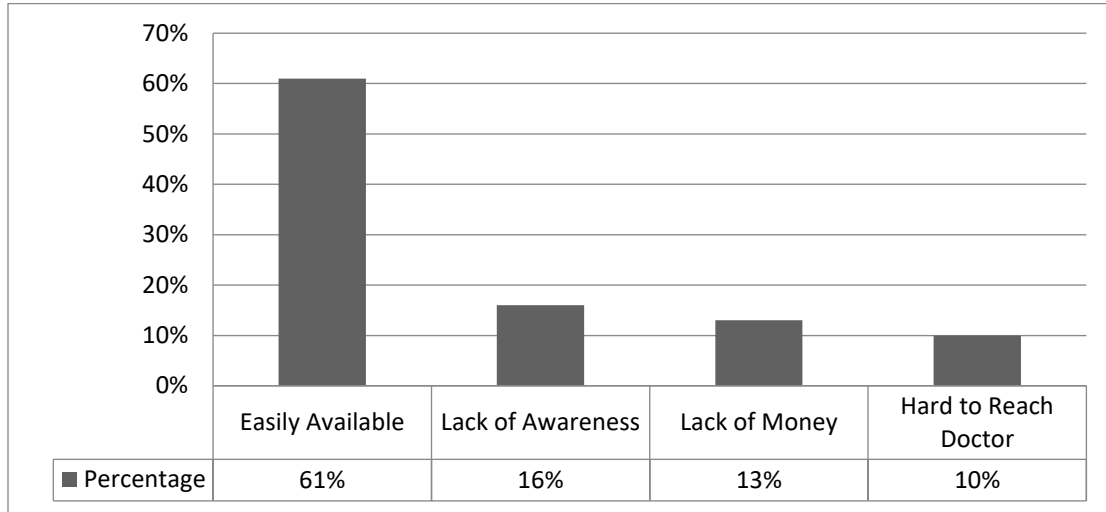

Figure 6 Reason to Refrain Doctor?

A question was asked from patients 174 patients those who were taking as a self medication and suggested by others, that what was the reason not to visit a medical practitioner? Fig 6 shows, 61% patients said that antihistamines are easily available in pharmacies, 27 patients 16% were lack of awareness as they were from urban areas of sindh, 13% cannot afford doctor's high charges and 10% patients replied that they are living in site areas of Hyderabad to its hard to reach doctor.
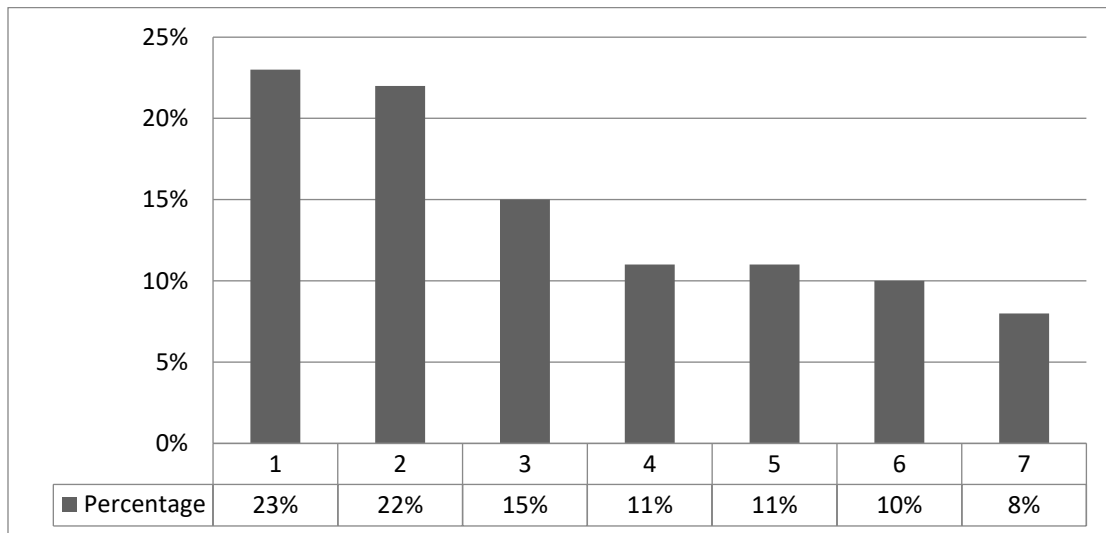
Figure 7 Name of H_1 Blockers Used.

1. Loratadine; 2. Chlorpheniramine; 3. Cetirizine; 4. Fexofenadine; 5. Ebestine; 6. Levocetrizine; 7. Desloratadine.

Fig 7 shows that during the study only one drug was used from 1st generation that is chlorpheniramine 22% rest all 2nd generation was used by patients; among all loratadine was used 23%.

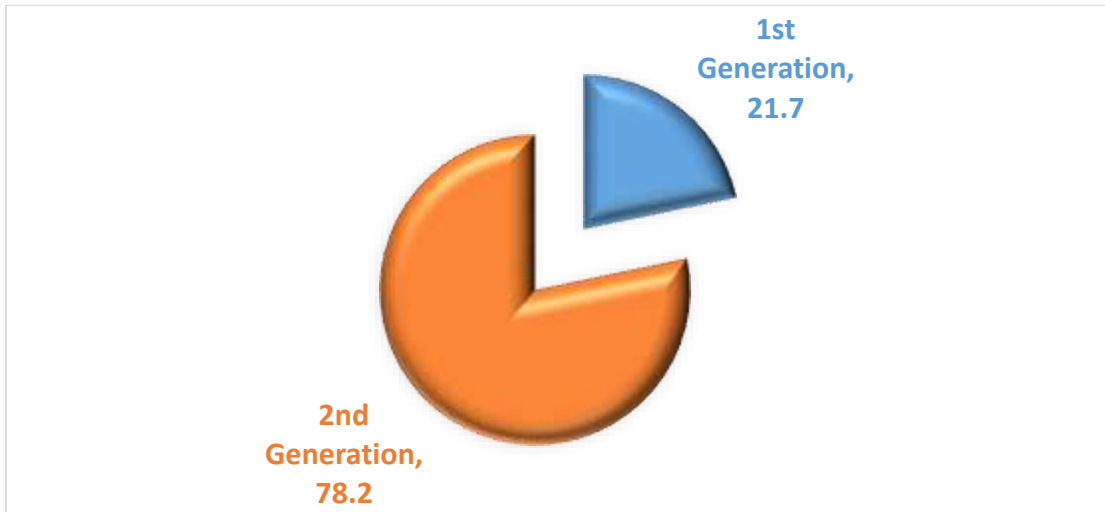|	1	2	3	4	5	6	7
Male	39	35	25	18	17	20	17
Female	30	30	20	16	15	10	8
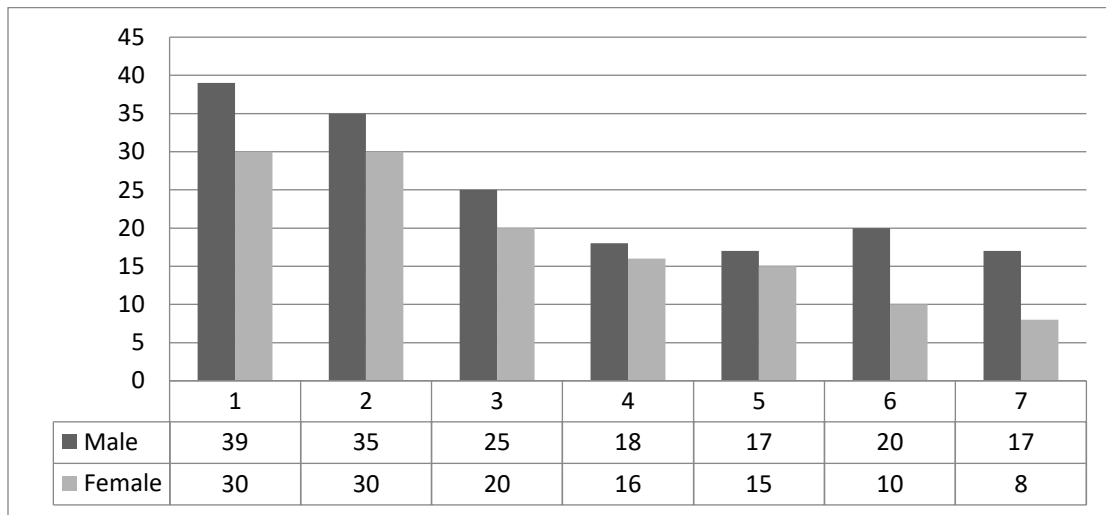
Figure 8 Use Of Antihistamine Gender Wise

1. Loratadine; 2. Chlorpheniramine, 3. Cetrizine; 4. Fexofenadine; 5. Ebestine; 6. Levocetrizine; 7. Desloratadine

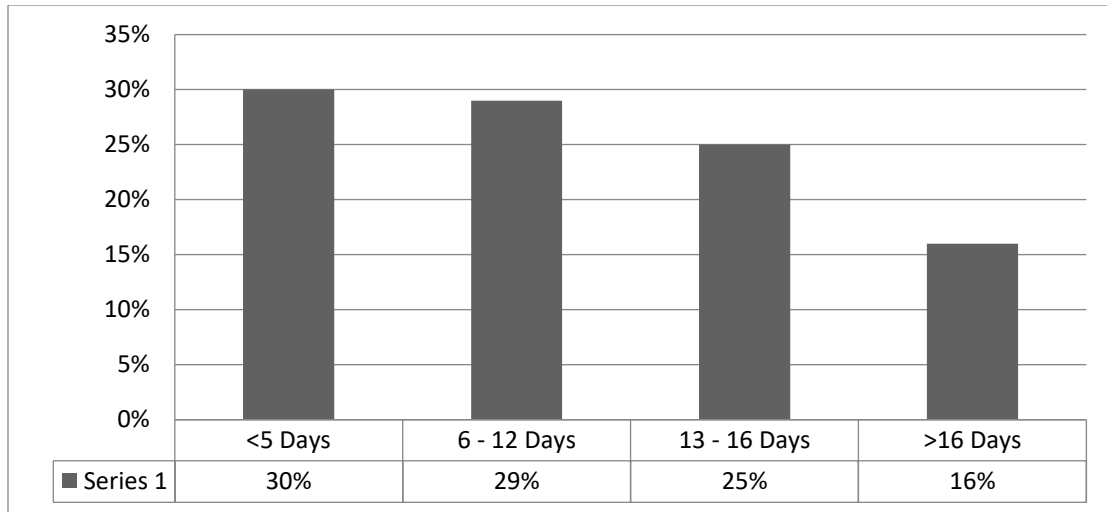A simple graphical presentation is shown in Fig 8 which shows the use of anti-allergic medicine gender wise.

Figure 9 Generation of H1 Blocker

	Others	t.i.d	OD	b.d
■ Series 1	3%	25%	27%	45%
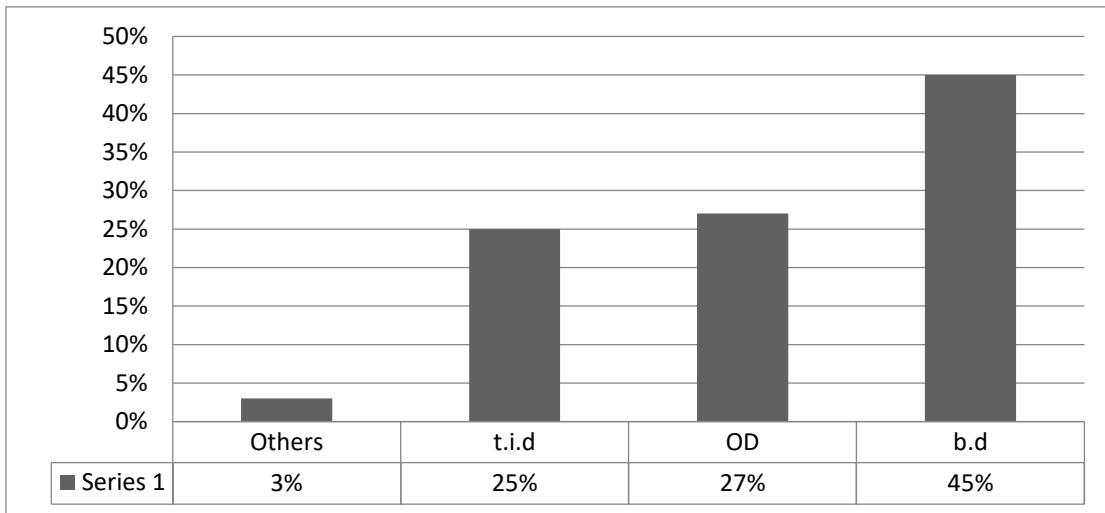
Figure 10 Frequency of Doses

Fig 10 shows 45% (136) patients were using H_1 blocker as twice a day which was highest as compare to other frequencies.

Figure 11 Duration Of H_1 Blocker Used

Fig 11 shows 91 patients were using anti-histamine for less than 5 days. Whereas, 88 patients were using for 6 – 12 days, 73 for 13 – 16 days and rest of other were using for more than 16 days.
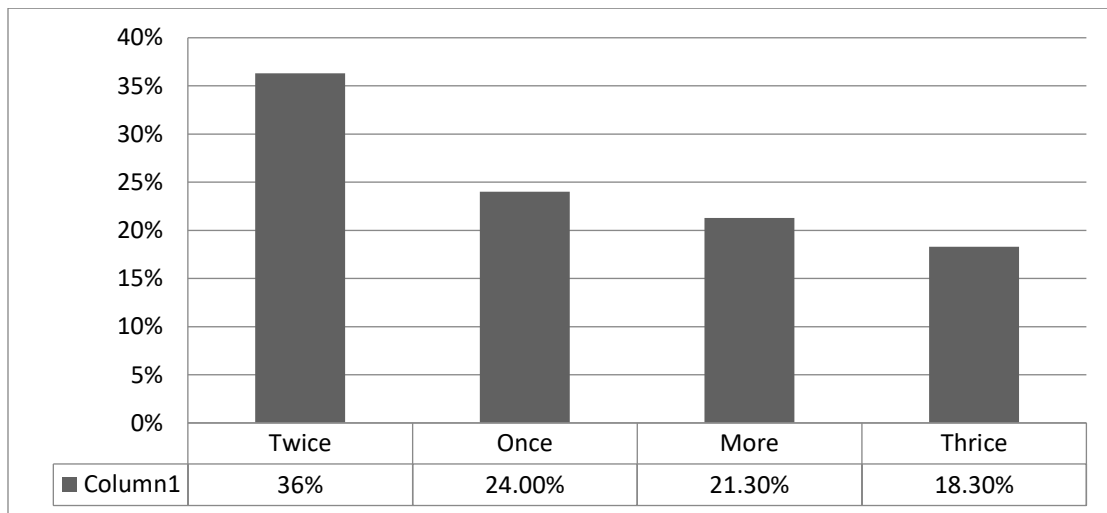
Figure 12 How Many Times Used In The Period Of Last 3 Months

Question was asked that how many times they have taken anti-histamine in last 3 months? Fig 12 shows 109 patients were taken twice in last 3 months which were maximum as compare to others.
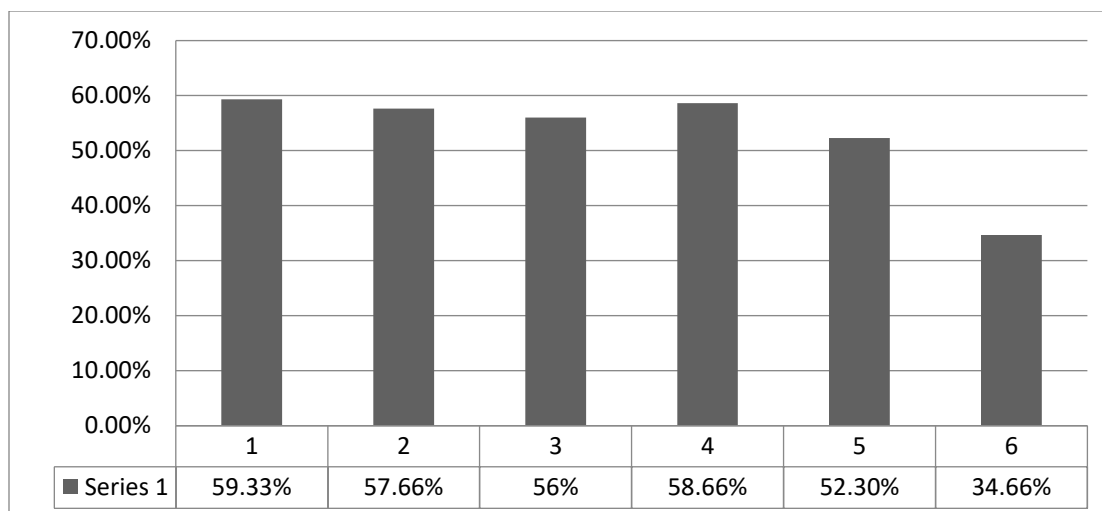
**Figure 13** Side Effects Of H_1 Receptor Blocker
1. Dry nose; 2. Head ache; 3. Dry mouth; 4. Drowsiness; 5. Feeling sickness; 6. Problem during driving.

Numbers of side effects were observed by the patients. Each side effect were observed personally and individually in all 300 patients. Fig 13 shows 178 patients were having Dry nose, while 173, 168, 161, 157 and 104 / 300 were experiencing Head ache, Dry mouth, Drowsiness, feeling sickness, hang over effect and have a problem in driving respectively.

Table 1 Frequency Used & Recommended Doses

S.No	H1 Blocker	OD	bid	tid	Others	Recommended dose
1.	Chlorpheniramine	9	20	34	2	4 mg after every 4 to 6 hours with the max: 24 mg per day.
2.	Loratadine	16	30	20	3	10mg once Daily
3.	Cetirizine	10	23	10	2	10 mg Once Daily
4.	Fexofenadine	13	19	2	0	Seasonal Allergic Rhinitis: 60 mg BD / 120 mg OD Urticaria: 180 mg OD
5.	Ebestine	7	20	5	0	20 mg Once Daily
6.	Levocetirizine	14	14	0	2	5 mg Once Daily
7.	Desloratadine	12	10	3	0	5 mg One Daily

Recommended doses for all H1 blockers which were used by patients were compared from BNF 71 edition as shown in Table 1.
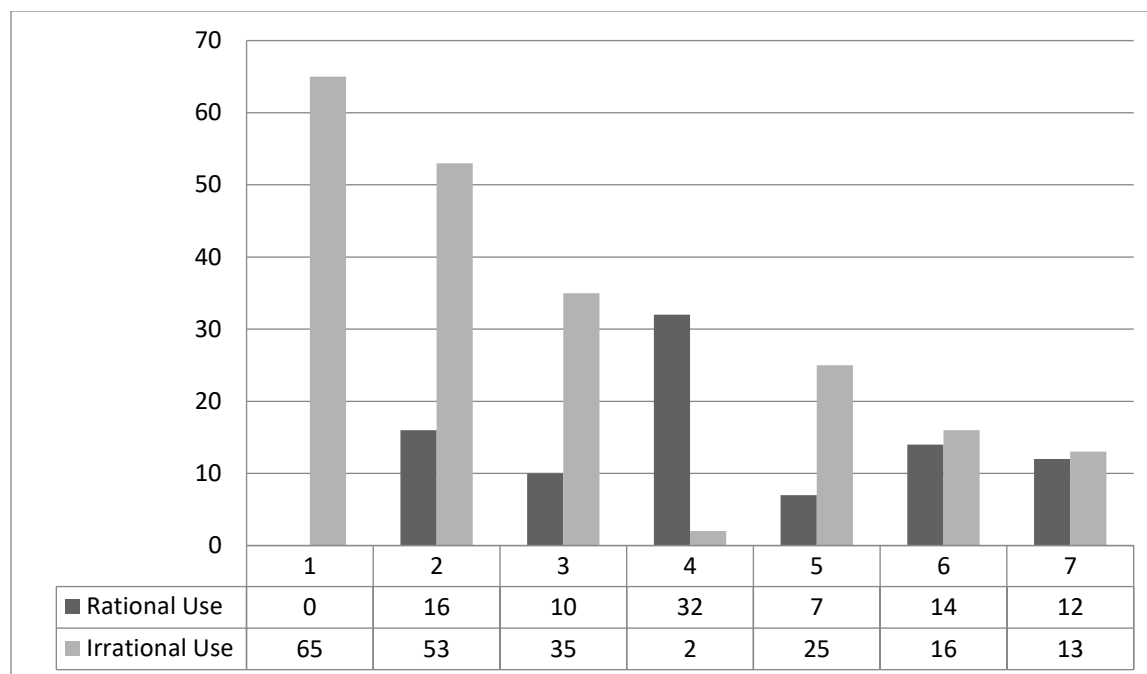
Figure 14 Rational and Irrational Use of H1 Blockers

1. Chlorpheniramine; 2. Loratadine; 3. Cetirizine; 4. Fexofenadine; 5. Ebestine; 6. Levocetrizine; 7. Desloratadine

H_1 antagonist medications are commonly used in various skin problems mainly pruritus and if not treated than it may damage the patients comfort (Criado, et al., 2013) (Tivoli, 2009) Moreover; the current study shows that 22% of H_1 Blockers was prescribed while another study showed that 40% of H1 blockers were prescribed. Further studies showed more usage of H_1 antagonist as compared to afzal khan Ak study which is 63.63%. In current study, majority of patients were between the age of 16-30 years while in afzal khan Ak study 52% of patients were more than 51 years (Khan et al., 2013) According to another study The most common conditions are common cough and cold in which antihistamine were mostly prescribed while current study were also somewhat same results (Chan 1987) Another study reveals that Chlorpheniramine were most commonly prescribed while current study described that Loratidine was the most commonly prescribed drug (Anil and Beenta, 2009).

4. CONCLUSION

It is concluded that the patients who are taking H_1 blockers without prescription are experiencing side effects more as compare to the one who are taking by the recommendation of Doctor /

Pharmacist. Study analysis also shows that patient taking anti-histamine for longer period of time due to lack of knowledge. Frequently usage of anti-histamine can cause drug dependence and hang over effects. No any severe adverse effects were seen during the study period of one year. Health care professions Doctor/Pharmacists should play their vital role in rational use of drugs.

References:

- Anil K., and P. Beenta, (2009) prescription Writing Trends of Antihistamines at the University Health Centre Indian J Pharm Sci.; 71(3): 307–310.

- Bhuvana K. B, R.T. Patil, (2010) Drug prescribing pattern of topical corticosteroids in dermatology unit of a tertiary-care hospital. Int J Med Sci Public Health. 2015;4(12):1702-7.

- Chan K,. (1987) A study of prescribed H1- antihistamine preparations over a period of 12 months in community pharmacy J Clin Pharm Ther. 12(1):1-9.

- Criado, P. R., R.F.J. Criado, C. W. Maruta, C.A. Machado (2013) Filho. An Bras Dermatol., 85(2):195-210.

- Dykewicz M.S. and S. Fineman, (1998) Executive Summary of Joint Task Force Practice Parameterson Diagnosis and Management of Rhinitis. Ann Allergy AsthmaImmunol,, 81:463 -468.

- Holgate, S.T. (1998) "Asthma and allergy—disorders of civilization?", QJM, , 91(3): 171–84

- Joel J. J, N. Jose, C. S. Shastry (2010) Patterns of skin disease and prescribing trends in rural India. Schol Acad J Pharm. 2013;2(4):304-9

- Khan A., A. K, Mirshad, P. V. M. Muneersha (2013) Evaluation of H1- Antihistamine usage among dermatology inpatients at a teaching hospital in Southern India Der Pharmacia Lettre, , 5 (6):115-118.

- Pise H. N, S. L Padwal, (2015) Drug prescribing and dispensing pattern in pediatrics outpatient clinic of a rural tertiary-care teaching hospital. Natl J Physiol Pharm Pharmacol.;5(4):313-7.

- SHAH, S., GHOTO, M., MEMON, N., DAYO, A., MEMON, A., ARAIN, M., ... & MANGI, R. (2016). Irrational Use of H1 Receptor Antagonist In Various Allergic Patients, A Clinical Study in Hyderabad, Sindh. *Sindh University Research Journal-SURJ (Science Series)*, *48*(4).

- Tivoli, Y. A., R. M Rubenstein. (2009) Clin Aesthetic Dermatol , 2(7):30–36.

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