

## Evaluation of Prescription Pattern of Anticholinergics and Antihistamines for Outpatients: A Cross-sectional Health Survey Conducted in a Primary Care Hospital in Bangladesh

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**ABSTRACT:** Rational drug therapy is crucial for improving the health and economy of individuals and society. The aim of this study was to evaluate and assess the prescription pattern of anticholinergics and antihistamines in a primary healthcare facility in Bangladesh. A descriptive cross-sectional survey was carried out in order to determine current prescribing trends at Kushtia, Bangladesh. A total of 1000 prescriptions were collected and analyzed using Microsoft Excel. In the case of anticholinergics- Atropine Sulfate, Hyoscine Butyl Bromide, Tiemonium Methyl Sulfate, and Mebeverine Hydrochloride were noticed on prescriptions and Tiemonium Methyl Sulfate was most prevalent 95.83%. Each of the remaining three drugs was prescribed by 1.39%. Among all antihistamines, SGA was prescribed by 61.2% followed by FGA 36%. Among FGA, Ketotifen was most prevalent 62.2% followed by Chlorpheniramine Maleate, Diphenhydramine HCl, and Hydroxyzine HCl in between 11.2% to 14.3%. Pizotifen was the least (1%) in this category. Among SGA, Fexofenadine HCl, and Rupatadine, each was prescribed by 28.7% followed by Levocetirizine HCl (12.6%). Cetirizine HCl, Desloratadine, and Ebastine were ranging from approximately 7% to 10%. Bilastine (1.8%) and Mizolastine (0.6%) were the least in this category. In terms of the pregnancy category, most of the drugs (75.1%) were in the not classified group whereas category B and category C were prescribed by 5.8% and 19.1% respectively. Care should be taken while prescribing anticholinergics and antihistamines to pregnant women as most of the drugs fall under the not classified group of FDA.

**Keywords:** Drug prescription; Prescription Pattern; Anticholinergics; Antihistamines

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## 1. INTRODUCTION

Primary health care hospitals play an important role in improving the health status of the patients living in remote areas by reducing the health-related financial threat, and by enhancing the health professionals' response to the emergency patient's needs [1]. A vast number of people have to rely on community clinics, Upazila health complex of different bed capacities, and other health care facilities to get appropriate treatment for acute health-related problems [2]. Rational use of drugs in these facilities is a major concern for the reductions of morbidity and mortality rate with getting the benefit of medical, social, and economic growth of a country [3]. Due to the prompt of services at affordable cost, people of the rural areas seek primary treatment from these health care facilities for various diseases and among them, allergic conditions are often frequent. Allergy, a foreign substance-mediated immune response is a very common disease in Bangladesh as well as throughout the world. Around 10%-30% of individuals in developed countries [4] and 20%-25% of the population in Bangladesh [5] is suffering from different types of allergic disorder. The invasion of a foreign substance is encountered by a biologically active and first-line defensive chemical mediator, histamine, that work on histamine receptor in the brain and spinal cord along with other types of receptors [6,7]. The secreted histamine plays a role in the inflammatory response, gastric acid secretion, coughing, sneezing, itching, and so on. These symptoms can be best managed by first-generation and second-generation antihistaminic drugs [8]. The US Food and Drug Administration (FDA) approved the first-generation antihistamines to market in 1930 and the second-generation antihistamines in 1980 [9]. A major side effect, drowsiness by the first-generation antihistamines is due to crossing the drug into the blood-brain barrier, whereas the second-generation antihistamines cannot cross the blood-brain barrier and are hence considered free form inducing drowsiness [10]. Additionally, second-generation antihistamines are less likely to undergo interaction with other drugs and that's why they are considered safer [11]. Along with antihistaminic characteristics, these drugs also possess anticholinergic effects after therapeutic doses that can be used for pupillary dilatation, urinary retention, gastrointestinal motility, constipation, erectile dysfunction, peripheral vasodilatation, etc. [10, 12]. The antihistaminic and anticholinergic drugs are frequently administered by pregnant women and the FDA have classified all drugs on the basis of the safety of the fetus in 1979. According to FDA, category A drugs are those where there is no risk to the fetus in the first trimester as well as in later trimesters of

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pregnancy on adequate and well-controlled studies. Category B drugs have no risk on animal reproduction studies to the fetus but adequate and well-controlled studies are absent in pregnant women. Drugs showing adverse effects on the fetus on animal reproduction studies and adequate and well-controlled studies are absent in humans fall under category C. The most unsafe category D drugs show human fetal risk on investigational drugs or already marketed products in humans [13]. The objective of the present study is to evaluate and assess the prescription pattern of antihistaminic and anticholinergics in the selected primary care hospital using the WHO drug-use indicators. The study also analyzes the prescribed drugs in terms of availability in different doses, dosage forms, therapeutic indications, and pregnancy categories.

## **2. METHODS AND MATERIALS**

### **2.1. Study Design**

This cross-sectional, community-based health survey was conducted in Kushtia, a district of the western part of Bangladesh. Considering the prevalence of allergies and associated complexity throughout the country, the topic had been selected to monitor the prescription pattern from the collector's familiar and readily accessible district. Prescriptions were collected mostly from Bheramara Upazila Health Complex, Kushtia and some are from private clinics of the mentioned district between November 2020 to January 2021 after providing adequate training and instructions to the collector.

### **2.2 Study population**

A total number of prescriptions of 1000 patients was collected where the patients came to take medical services. The data was collected from the patients where at least one anticholinergic or one antihistaminic or both were prescribed during the study period. The follow-up patients, patients already recovered from diseases but having prescriptions with anticholinergics and antihistamines for the study period were also included in this study. The data collectors were tried to convince the patients to collect the prescription data and to take a short and soft interview with them.

### **2.2. Ethical considerations**

This study does not violate the WMA (*World Medical Association*) declaration of Helsinki (section 12). In this study, neither usage of hazardous material nor collection of any biologic sample from human subject was conducted. Any further approval from the institutional ethics committee was not applicable to conduct this research as only the

prescription collection and soft interview from the participants was carried out in this survey-based research.

### 2.3. Statistical analysis

The information of the collected prescription data was inputted into Microsoft excel and analyzed following descriptive statistics. Results were expressed graphically in frequency and percentage. The prescription data were doubled checked for accuracy.

## 3. RESULT

In this study, a total number of prescriptions of 1000 patients from a selected regions of Bangladesh were analyzed.

### 3.1. Demographic Characteristics of Patients

In our study, most of the patients in prescription data were female 50% (n=500) and 32.3% (n=323) were male. The gender of patients not identified in the prescription by 17.7% (n=177). The most prevalent age for taking antihistaminic and anticholinergic drugs is 21 years to 30 years accounting 22.31% followed by 17.69% among more than 50 years old patients and 16.15% among 31 years to 50 years old. The demographic characteristics of patients are given in Table 1.

**Table 1:** Demographic Characteristics of Patients.

	<b>Variables</b>	<b>Frequency (n=1000)</b>	<b>Percentage (%)</b>
<b>Gender distribution</b>	Male	323	32.30
	Female	500	50.00
	Unidentified Gender	177	17.70
<b>Age distribution</b>	Unidentified Age	92	9.23
	Less than 1 year	8	0.77
	1-10 year	92	9.23
	11-20 year	85	8.46
	21-30 year	223	22.31
	31-40 year	162	16.15
	41-50 year	162	16.15
	>50 years	177	17.69

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### **3.2. WHO prescribing indicators**

A total number of 4166 individual medicine were prescribed in 1000 prescriptions. The number of medicines prescribed ranges from 1 to 6 per prescription and the mean of medicines per prescription was 4.17. Total 72 anticholinergic drugs and total 273 antihistaminic drugs were identified in all the prescriptions. In this study, WHO prescribing indicators were assessed and summarized in table 2. After analysis, this study revealed that no drugs were prescribed by generic name and 58.2% of the total prescribed medicines are antibiotic.

**Table 2:** WHO prescribing indicators.

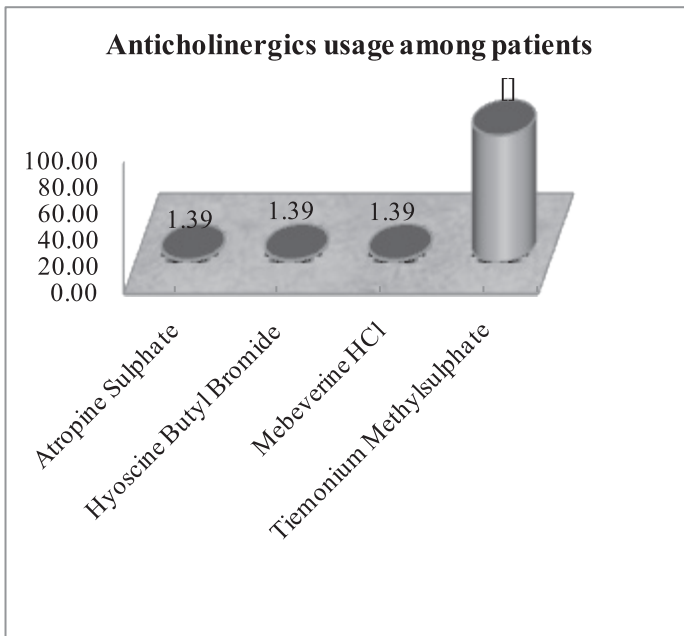
<b>Characteristics</b>	<b>Value</b>
Total number of prescriptions	1000
Total number of drugs prescribed	4166
Average number of drugs per prescription	4.17
Percentage of drugs prescribed by generic name	00
Percentage of patient encounters with an antibiotic prescribed	582
Percentage of patient encounters with an injection prescribed	31

### **3.3. Anticholinergics usage among patients**

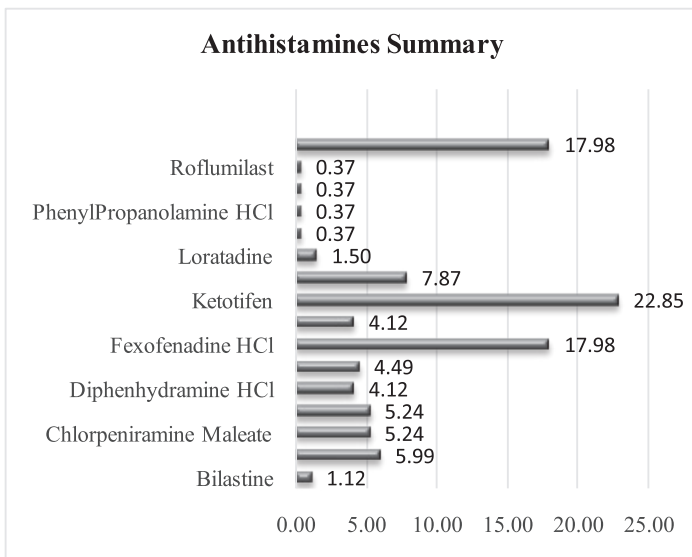
Total Four (4) types of anticholinergics have been prescribed. Among these, Tiemonium Methyl Sulfate has been found as the most prevalent 95.83% (n=69). The remaining 3 anticholinergics (Atropine Sulfate, Hyoscine Butyl Bromide, and Mebeverine HCl) have been found in 3 separate prescriptions among total of 72 anticholinergic drugs encompassing 1.39% (n=1) of each of the stated anticholinergic drugs.

### **3.4. Antihistamines usage among patients**

A total of 16 types of antihistamines have been prescribed. Based on the frequency of prescription, the most prevalent antihistamines are Ketotifen, Fexofenadine HCl and Rupatadine accounting 22.85% (n=61), 17.98% (n=48) and 17.98% (n=48) respectively. The next category antihistaminics which are prescribed as intermediate frequency includes Levocetirizine HCl, Cetirizine HCl, Chlorpheniramine Maleate, and Desloratadine, whose percentage of frequency ranges from approximately 5% to 8%. The lowest prescribed antihistamines i.e. Diphenhydramine HCl, hydroxyzine HCl, Ebastine, Loratadine, Phenylpropylamine HCl, Mizolastine, Bilastine, Pizotifen, and Roflumilast were observed in between ranges from 0.37% to less than 5%.



**Figure 1:** Anticholinergics usage among patients.

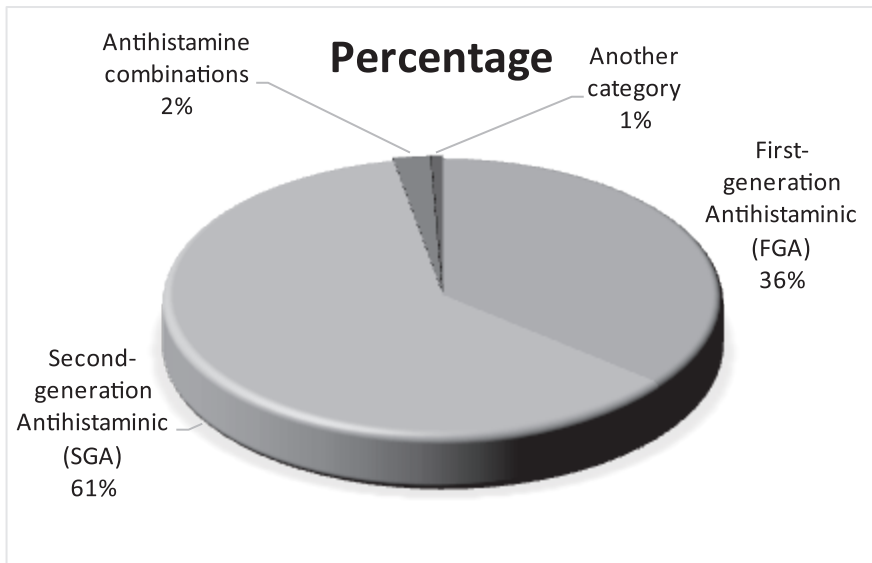


**Figure 2:** Antihistamines usage among patients.

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**3.4.1. Antihistaminic category**

The most frequent prescription antihistaminic are second-generation with a prevalence of 61.2% (n=167) followed by first-generation which encompasses 35.9% (n=98) among a total of 273 prescriptions. The antihistaminic combination was prescribed by 2.2% (n=6) while only 0.7% (n=2) of decongestant and phosphodiesterase-4 inhibitor were prescribed as antihistaminic drugs.



**Figure 3:** Antihistaminic category.

**3.4.2. First-generation Antihistamines (FGA)**

Figure 4 shows the percentage of first-generation antihistamines in prescription. Ketotifen, a first-generation sedating antihistamine is most frequently prescribed among all FGA accounting for 62.2% (n=61). Chlorpheniramine Maleate, Diphenhydramine HCl, and Hydroxyzine HCl were noticed to be prescribed between 11.2% to 14.3% (n=11 to 14). Pizotifen was suggested in the case of only one patient among all other FGA.

**3.4.3. Second-generation Antihistamines (SGA)**

Among SGA, Fexofenadine HCl and Rupatadine were most prevalent in our study, both of each was prescribed by 28.7% (n=48) followed by

Levocetirizine HCl encompassing 12.6% (n=21). Cetirizine HCl, Desloratadine, and Ebastine were in ranging from approximately 7% to 10% (n=12 to 16). Bilastine and Mizolastine were the least prescribed antihistamines among all SGA accounting for 1.8% (n=3) and 0.6% (n=1) respectively

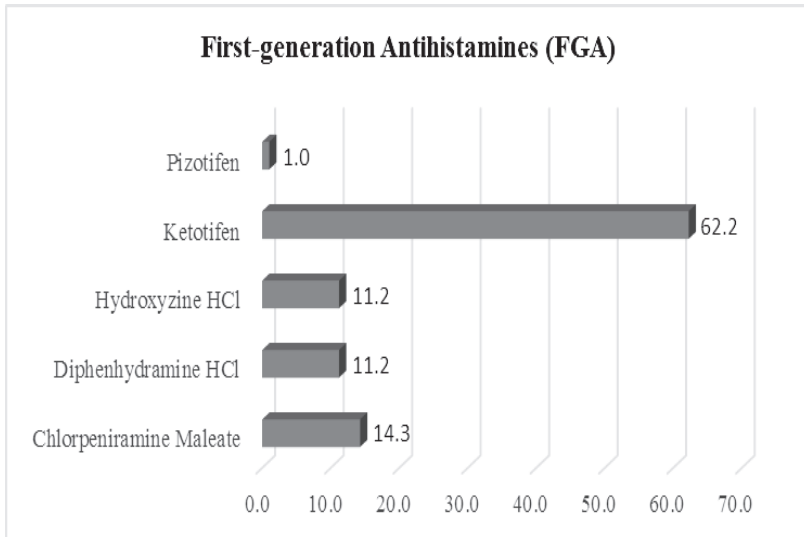


Figure 4: First-generation Antihistamines (FGA).

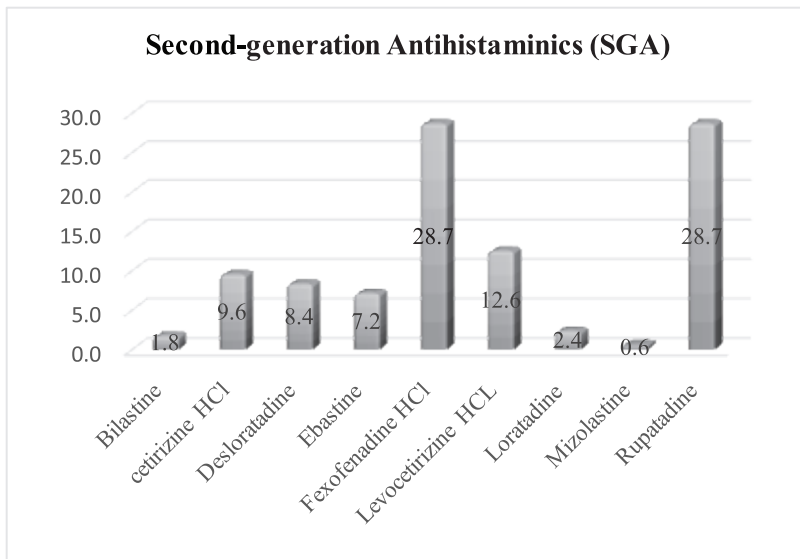


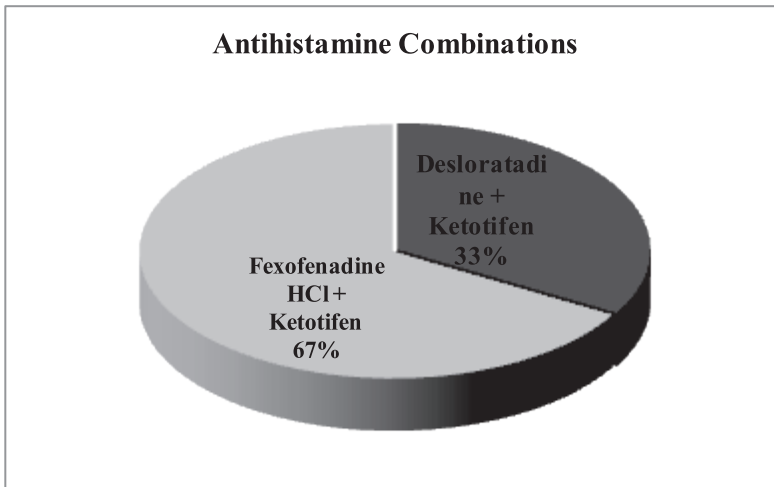
Figure 5: Second-generation Histamine H1 antagonists (SGA).



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**3.4.4. Antihistamine combinations**

Only two types of antihistaminic drugs were noticed in combination therapy. In this case, one second-generation non-sedating antihistamines (SGA) was combined with one first-generation sedative antihistamine and mast cell stabilizer (FGA). Fexofenadine HCl, an SGA, and Ketotifen, an FGA combination was observed in prescription in comparatively higher frequency than Desloratadine (SGA) and Ketotifen (FGA) combination.



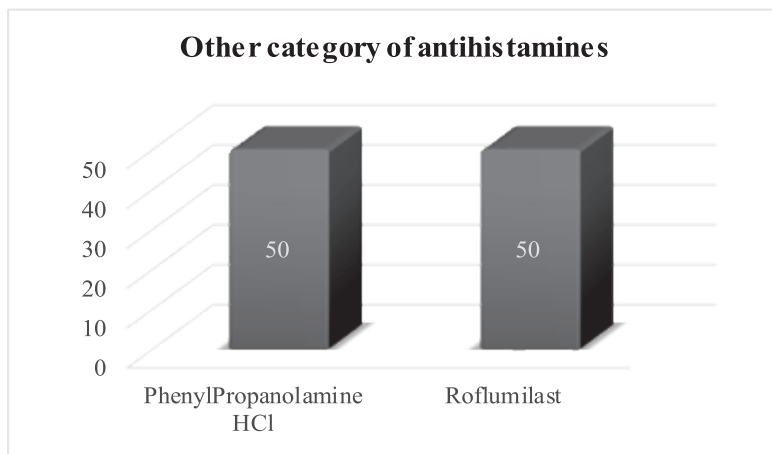
**Figure 6:** Antihistamine combinations.

**3.4.5. Other category of antihistamines**

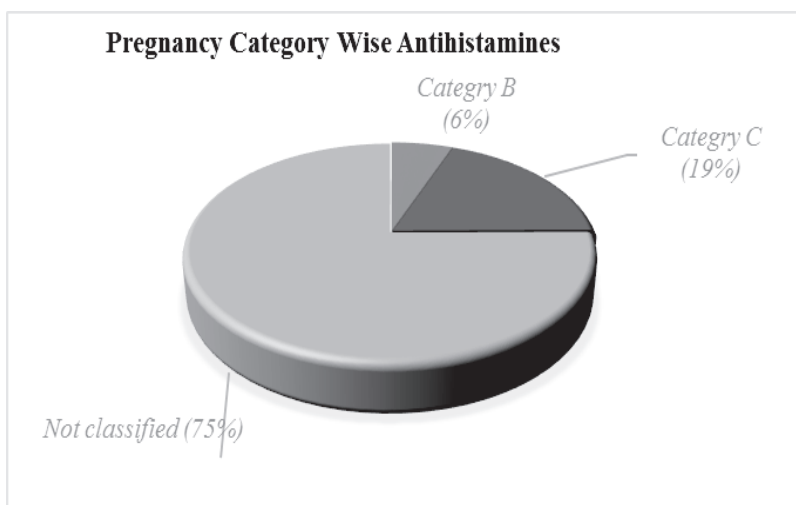
In one case, decongestant, and phosphodiesterase-4 (PDE-4) inhibitor has been noticed for the management of allergic conditions. Phenylpropanolamine HCl, a decongestant was observed in only one prescription, and Roflumilast, a phosphodiesterase-4 (PDE-4) inhibitor was found in another.

**3.4.6. Pregnancy category wise antihistamines**

In our study, we analyzed the pregnancy category of all prescribed antihistaminic drugs. Among them, 75.1% (n=208) have not been classified by FDA. Only 5.8% (n=16) of drugs fall under category B and the rest of the 19.1% (n=53) drugs fall under category C.



**Figure 7:** Other category of antihistamines.



**Figure 8:** Pregnancy category wise antihistamines.

**Table 3:** Summary of Anticholinergic usage among patients.

Anticholinergics	Frequency	Percentage
Atropine Sulphate	1	1.39
Hyoscine Butyl Bromide	1	1.39
Mebeverine HCl	1	1.39
Tiemonium Methyl sulphate	69	95.83

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**Table 4 :** Summary of Antihistaminic usage among patients.

<b>Antihistamines</b>	<b>Frequency</b>	<b>Percentage</b>
<b>First-generation Antihistamine (FGA)</b>		
Chlorpheniramine Maleate	14	14.3
Diphenhydramine HCl	11	11.2
Hydroxyzine HCl	11	11.2
Ketotifen	61	62.2
Pizotifen	01	01.0
Total	98	
<b>Second-generation Antihistamine (SGA)</b>		
Bilastine	03	01.8
Cetirizine HCl	16	09.6
Desloratadine	14	08.4
Ebastine	12	07.2
Fexofenadine HCl	48	28.7
Levocetirizine HCl	21	12.6
Loratadine	04	02.4
Mizolastine	01	00.6
Rupatadine	48	28.7
Total	167	
<b>Other category of antihistamines</b>		
Phenylpropanolamine HCl	01	50.0
Roflumilast	01	50.0
Total	02	
<b>Antihistamine combinations</b>		
Desloratadine + Ketotifen	02	33.3
Fexofenadine HCl + Ketotifen	04	66.7
Total	06	

#### 4. DISCUSSION

The prescribed anticholinergics are Atropine Sulfate, Hyoscine Butyl Bromide, Mebeverine HCl, and Tiemonium Methyl Sulfate. Atropine Sulfate act as an antimuscarinic, anti-spasmodic, mydriatics, and cycloplegic agent. The three (3) anticholinergic drugs (Hyoscine Butyl Bromide, Mebeverine HCl, and Tiemonium Methyl Sulfate) are available in solid unit dosage form (tablet and capsule) except Atropine Sulfate which is available only as parenteral dosage form (both IV and IM) with dose 0.6mg/ml. Hyoscine Butyl Bromide, in tablet dosage form, is available in the market with the strength of both 10mg, and 20mg, and in the parenteral dosage form (IV and IM), it is available as 20mg/ml. The maximum recommended dose of this drug is 100mg daily. Mebeverine HCl is available as both IR tablet and SR tablet and SR capsule form.

The IR product is dispensed with a dose of 135mg, and the SR tablet and capsule are dispensed as 200mg. The most frequently prescribed anticholinergic i.e. Tiemonium Methyl Sulfate is available as a tablet, syrup, and parenteral dosage form with the dose of 50mg, 10mg/5ml, and 5mg/2ml respectively. Anticholinergics are prescribed for a wide range of diseases. Atropine Sulfate is indicated for bradycardia, organophosphorus poisoning, and as an anesthesia adjunct. Hyoscine Butyl Bromide is indicated for various types of spasms like gastrointestinal spasms, genitourinary spasms, and abdominal pain. Irritable bowel syndrome and gastrointestinal spasms are mainly treated by Mebeverine HCl.

The mostly prescribed Tiemonium Methyl Sulfate is indicated for dysentery, diarrhoea, gastroenteritis, biliary colic, enterocolitis, cholecystitis, colonopathy, mild cystitis, spasmodic dysmenorrhea, and visceral muscle spasm. Among 4 anticholinergics Atropine Sulfate, Mebeverine HCl, and Tiemonium Methyl Sulfate are not classified as pregnancy category. On the other hand, Hyoscine Butyl Bromide falls on category C. A total of 16 types of antihistaminic drugs have been prescribed which include- Ketotifen, Fexofenadine HCl, Rupatadine, Levocetirizine HCl, Chlorpheniramine Maleate, Desloratadine, Diphenhydramine HCl, Phenylpropanolamine HCl, Mizolastine, Hydroxyzine HCl, Ebastine, Loratadine, Cetirizine dihydrochloride, Bilastine, Pizotifen, and Roflumilast.

All these prescribed drugs were categorized into 4 categories i.e. First-generation Antihistamines (FGA) (35.9%), Second-generation Antihistamines (SGA) (61.2%), Antihistamine combinations (2.2%), and another category (0.7%). Among all 273 antihistamines, the most prescribed drug is Ketotifen (62.2%) which is a first-generation antihistamine (FGA) followed by Fexofenadine HCl (28.7%) and Rupatadine (28.7%) both of which are second-generation antihistamines (SGA). The least prescribed FGA is Pizotifen (1%), and the least prescribed SGA is Mizolastine (0.6%). Our study reveals that the current trend of prescriptions for treating various allergic disorders is SGA to engulf the benefit of fewer drowsiness characteristics of these drugs. Additionally, most of the drugs fall under the not classified group of pregnancy category in our investigation. Among FGA, only Diphenhydramine HCl and Pizotifen fall on category B and among SGA, Loratadine and Fexofenadine HCl fall on the category of B and C respectively. All other antihistamines of both groups are under not classified group.

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## **5. CONCLUSION**

We revealed the prescription pattern and trend of anticholinergics and antihistamines usage in Kushtia, Bangladesh. Our study reveals that the current trend of prescriptions for treating various allergic disorders is SGA to engulf the benefit of fewer drowsiness characteristics of these drugs. This study strongly recommends being careful about prescribing as well as administering antihistamines and anticholinergics while pregnancy.

## **6. RECOMMENDATIONS**

Different geographical area with larger sample size is recommended for the continuation of the present work.

## **7. ACKNOWLEDGEMENT**

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*Conflict of Interest:* The authors declare no conflict of interest.

### *Abbreviations:*

FGA: First Generation Antihistamines; SGA: Second Generation Antihistamines; FDA: Food and Drug Administration; IV: Intravenous; IM: Intramuscular; IR: Immediate Release; SR: Sustained Release

## **REFERENCES**

- [1] Shakeel Ahmed Ibne Mahmood (2012), Health Systems in Bangladesh, Health Research Policy and Systems, January 2012, iMedPub Journals, Vol.1, No. 1:1, doi: 10.3823/1100, www.hsprj.com
- [2] Health Bulletin (2012), Secondary and Tertiary Healthcare, Chapter-5, Pages 53-60,  
[https://dghs.gov.bd/bn/licts\\_file/images/Health\\_Bulletin/HB2012\\_CH/HB2012\\_CH5\\_Senondary-tertiary-HCare.pdf](https://dghs.gov.bd/bn/licts_file/images/Health_Bulletin/HB2012_CH/HB2012_CH5_Senondary-tertiary-HCare.pdf)
- [3] David E. Bloom, Michael Kuhn, Klaus Prettnner (2018), Health and Economic Growth, November 2018, IZA-Institute of Labor Economics, Schaumburg-Lippe-Straße 5–9 53113 Bonn, Germany, IZA DP No. 11939, www.iza.org
- [4] Allison Ramsey, MD, Syed Shahzad Mustafa, MD (2021) Allergy: Symptoms and Treatment MedicineNet, allergies health center/allergies a-z list/allergy center /allergy article, [https://www.medicinenet.com/allergy/article.htm#allergy\\_facts](https://www.medicinenet.com/allergy/article.htm#allergy_facts).

- [5] M. Alamgir Chowdhury, ARM Lutful Kabir, Md. Monjurul Alam (2008), Allergic rhinitis, asthma and atopic diseases: Bangladesh perspective, Bangladesh J of Otorhinolaryngology, 14(2), Pages 66-70
- [6] F. Estelle R. Simons, MD, FRCPC and Keith J. Simons, PhD (2011), Histamine and H1-antihistamines: Celebrating a century of progress, Clinical reviews in allergy and immunology, J ALLERGY CLIN IMMUNOL, Volume 128, Number 6, December 2011 Pages 1139-1150. doi:10.1016/j.jaci.2011.09.005
- [7] Jean-Michel Arrang, Monique Garbarg & Jean-Charles Schwartz (1983), Auto-inhibition of brain histamine release mediated by a novel class (H3) of histamine receptor, Nature Publishing Group, Vol. 302, April 1983, Pages 832-837
- [8] Antiallergics and Medicines Used in Anaphylaxis, Histamine-1 receptor antagonists – A critical evaluation to update Section 3, Developed by Harinder Chahal For WHO, Developed by Harinder Chahal, For WHO Secretariat.  
[https://www.who.int/selection\\_medicines/committees/expert/19/applications/Histamine\\_3\\_AC\\_R.pdf?ua=1](https://www.who.int/selection_medicines/committees/expert/19/applications/Histamine_3_AC_R.pdf?ua=1)
- [9] Antihistamines, Cleveland Clinic, Health Library/ Drugs, Devices & Supplementary, last reviewed by a Cleveland Clinic medical professional on 07/13/2020.  
<https://my.clevelandclinic.org/health/drugs/21223-antihistamines>
- [10] Philipp S. Muether and Jack M. Gwaltney, Jr. (2001) Variant Effect of First- and Second Generation Antihistamines as Clues to Their Mechanism of Action on the Sneeze Reflex in the Common Cold, Antihistamines in Colds • CID 2001:33 (1 November 2001) Clinical Infectious Diseases 2001; 33:1483–8, the Infectious Diseases Society of America. Pages 1483 – 1488
- [11] F. Estelle R. Simons and Keith J. Simons (2008), H1 Antihistamines Current Status and Future Directions, World Allergy Organization Journal, September 2008, Pages 145 – 155
- [12] Kat Gál (2018) Anticholinergic drugs: What to know, Medical News Today, October, 2018.  
<https://www.medicalnewstoday.com/articles/323514>
- [13] Lisa A Boothby, Paul L Doering (2001), FDA Labeling System for Drugs in Pregnancy, Annals of Pharmacotherapy, December 2001, Volume-35, Pages 1485-1489. [www.theannals.com](http://www.theannals.com)