

# FREQUENCY OF SELF REPORTED ALLERGIC REACTIONS TO THE DRUGS AMONG MEDICAL STUDENTS OF PESHAWAR

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## ABSTRACT

**Objective:** To determine the frequency of self reported drug induced allergic reactions among medical students of Peshawar.

**Materials and Methods:** A cross-sectional study was conducted on 300 students from various public and private sector medical colleges of Peshawar from Sept 2020 to June 2021. After a brief introduction and explaining the purpose of this study, a close-ended self-reported questionnaire was distributed among them. The questionnaire was comprised of demographic data, family history of atopic disease, source of drug allergy, signs and symptoms of allergy, and route of drug administration.

**Results:** Among 300 students, 23 participants indicated drug allergy with a self-reported frequency of 7.67%. The most frequently implicated drugs were antibiotics (52.17%), of which levofloxacin was the most common antibiotic followed by NSAIDs (17.39%). The most commonly reported allergic manifestations were cutaneous (34.8%), followed by gastrointestinal (17.4%) and respiratory (13.4%) symptoms. Of total allergic cases, 78% subjects had taken the drug in oral dosage form.

**Conclusion:** Self-reported allergic reactions to the drugs were highly prevalent with antibiotics as the most common source and cutaneous manifestations as the most common sign of drug allergy.

**KEYWORDS:** Drug allergy, Drug hypersensitivity, Self-reported, Prevalence

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## INTRODUCTION

According to World Health Organization, adverse drug reaction (ADR) is an unintended, unwanted, and noxious response to a drug at doses used therapeutically in humans.<sup>1</sup> They occur in a small portion of population but not rare; with the documented incidence of 10-25% in different clinical settings. One of the unpredictable and dose-independent types of ADR is drug allergy or drug hypersensitivity, comprising 15% of all adverse drug reactions, generally serious, and requires drug withdrawal.<sup>2</sup>

In 2003, World Allergy Organization (WAO) defined drug allergy as an immunologically mediated drug hypersensitivity reaction. The mechanism of drug allergy or

hypersensitivity could be either IgE or non-IgE mediated, with T-cell mediated reactions largely present in the later and producing stereotype symptoms that are unrelated to the pharmacodynamic profile of the drug.<sup>3</sup> They may occur even with much smaller doses and severity ranging from mild clinical manifestations like skin rashes to life-threatening conditions i.e. anaphylactic shock, serum sickness, Steven-Johnson syndrome and hemolytic anemia, etc. The target organs primarily affected by drug allergy are skin, airways, gastrointestinal tract, blood vessels, and blood.<sup>4</sup> This highlights the clinical significance of drug allergic reactions, which may prolong the duration of hospital stay, affect drug prescribing patterns of physicians and increase the socio-economic cost.

Several prospective studies evaluated the prevalence of ADRs but mostly they are type A reactions, so did not account for the drug allergy or hypersensitivity which is type B reaction.<sup>5-7</sup> There are few studies on the prevalence of drug hypersensitivity reactions in the general population where it is estimated that approximately 3-4% of children and more than 7% of the adult population experience a drug hypersensitivity reaction.<sup>8-10</sup> Moreover, surveys had been conducted in different parts of the world like Turkey,

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Portugal, UAE, and Brazil revealing some data on the epidemiology of drug-induced allergic reactions ranging from 5-25% of the population studied.<sup>11-15</sup> In our country, data related to ADRs is scarce and most of the available reports are limited to specific ADRs targeting only hospitalized patients. To the best of our knowledge, currently, there is no local data available regarding the frequency of allergic reactions to commonly used drugs in this region. This study was an attempt to explore it which will help us analyze the magnitude of the problem and identify common drugs causing hypersensitivity reactions in our local population. The target population was medical students considering their educational background that would help us deduce more reliable results.

## MATERIALS AND METHODS

A multi-centered cross-sectional study was conducted from Sept 2020 to June 2021 for which a sample size of 300 subjects was calculated by Raosoft's sample size calculator using a 5% margin of error and 95% confidence level. After taking ethical approval from the institutional research committee, undergraduate students from various public and private sector medical colleges of Peshawar were enrolled in the study (irrespective of age, gender, economic status, and ethnic background). Non-probability, convenient sampling technique was used for the selection of participants. Each participant was informed about the study aspects in detail followed by their verbal consent. A well-structured close-ended questionnaire was distributed among students comprising of data regarding demographics, family history about the allergy, and personal experience of drug allergy. Participants who answered "YES" to the question were further asked to complete the remaining questions in the questionnaire like the type of drug involved, its dosage form, signs and symptoms of drug allergy.

The collected data was analyzed and transformed into appropriate graphs and tables using an excel sheet and SPSS version 22. Numeric values were expressed as Mean  $\pm$  SD whereas the frequency of affirmative answers to each question was analyzed in percentages.

## RESULTS

In this cross-sectional study, a total of 300 students from various medical colleges were enrolled having a mean age of  $22.83 \pm 1.9$  years. 195 (65%) males and 105 (35%) females responded to the questionnaire. Among studied participants, 23 (7.67%) reported the incidence of drug allergy (Figure 1) of which 18 (78.2%) were male and 05 (21.7%) were female. 06 (26%) subjects revealed a positive history of drug allergy in the family.

As shown in Figure 2, 12/23 (52.17%) allergic participants indicated antibiotics as their source of allergy followed by NSAIDs/painkillers i.e. 4/23 (17.39%). A lower frequency of 1/23 (4.35%) was observed each with amitriptyline-

tyline, carbamazepine, and alprazolam. Few participants i.e. 4/23 (17.39%) indicated more than one drug as a source of allergy. Among antibiotics, the highest frequency of 4/12 (33.3%) was observed with levofloxacin followed by moxifloxacin 3/12 (25%) and co-amoxiclav. Table 1 shows the distribution of clinical manifestations of drug allergy in different categories where majority of the participants indicated cutaneous reactions followed by gastrointestinal, respiratory, cardiovascular, nasal, ocular, and other signs. Moreover, the allergic participants were also inquired about drug dosage form to which the majority (18/23) identified oral dosage form followed by injectable i.e. intravenous and intramuscular. Very few participants (2/23) reported the usage of multiple dosage forms as shown in Figure 3.

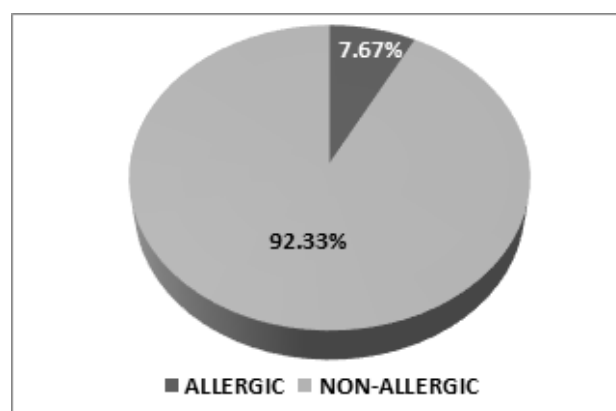


Fig 1: Frequency of self-reported drug(s) allergy

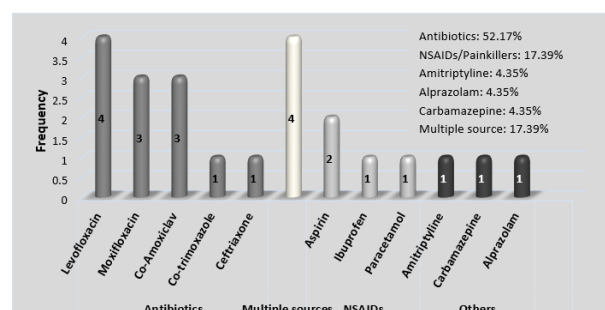


Fig 2: Distribution of sources of drug allergy

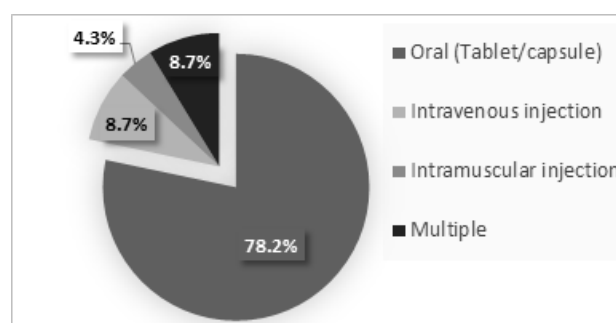


Fig 3: Distribution of dosage form

**Table 1: Distribution of clinical manifestations of drug allergy**

Clinical Manifestations	N (%)
<b>Cutaneous</b> Hives, Skin rashes, Urticaria, Pruritis, Angioedema	8 (34.8)
<b>Gastrointestinal</b> Nausea, Vomiting, Diarrhea, Abdominal pain	4 (17.4)
<b>Respiratory</b> Throat obstruction, Cough, Wheeze, Difficulty in breathing, speaking, or swallowing	3 (13.4)
<b>Cardiovascular</b> Palpitation, Tachycardia	1 (4.3)
<b>Eye</b> Itching, Redness & Secretion	1 (4.3)
<b>Nasal</b> Sneezing, Itching, Secretion, Congestion	1 (4.3)
Fever, Hypotension, Fainting	1 (4.3)
Other	4 (17.4)
Total	23 (100)

## DISCUSSION

Worldwide studies indicate that allergic reactions to the drug(s) are responsible for significant morbidity and mortality. It is estimated that 3-7% of the population experience adverse drug reactions but data regarding drug hypersensitivity in the general population remains largely unknown. The current study was an attempt to determine the magnitude of drug allergic reactions in our community. We included medical students (due to their medical knowledge) of Peshawar as appropriate representative of the general adult population because reports are suggesting the prevalence of these reactions similar in university students and the general population.<sup>14, 16</sup>

Our study indicated the frequency of self-reported drug allergy as 7.67% resembling the results of studies done in an adult population of Portugal with the frequency of 7.8%<sup>14</sup> and the United Arab Emirates with the frequency of 7%.<sup>12</sup> However, there are reported frequencies of drug allergies much higher in the surveys conducted in Brazil (12.1%), Turkey (13.4%), and Maputo state of Africa (25%).<sup>13, 15, 17</sup> On the other side, a Turkish study on medical students reported a drug hypersensitivity prevalence of 4.7%, relatively less than the frequency revealed in our study.<sup>15</sup> Hence, a huge disparity has been observed in the results of studies done previously regarding the subject matter. This could be due to variation in the target population like the general population, hospitalized patients, and medical students. Other possible explanations for the observed discrepancies may include the differences in sample size, data collection technique, prescribing patterns, and self-medication habits. In this study, 78.2% males were found to be drug allergic as compared to 21% females. This is not in concordance with the study done in the Portuguese population where females

were significantly more likely to claim a drug allergy than men.<sup>14</sup> There has no significant association been observed or reported between the incidence of drug allergic reactions and gender.

In our study, majority of the participants indicated antibiotics as their source of drug allergy followed by NSAIDs/painkillers resembling the results of many studies done globally.<sup>11, 14, 17-20</sup> However, there are reports where NSAIDs were identified as the most frequently associated drugs with allergic reactions.<sup>13, 21, 22</sup> The reason of this high frequency of antibiotic-induced allergy could be lack of regulation in the sale of antibiotics in our country, causing over-exposure of the general population to self-medication. Among antibiotics, surprisingly the highest frequency of allergy was observed with levofloxacin, unlike other studies where beta-lactams were reported as commonly involved antibiotics.<sup>11, 13, 21</sup> This discrepancy may be attributed to physician/patient preferences for levofloxacin over beta-lactams. Clinical manifestations of drug allergy were classified as cutaneous, ocular, respiratory, cardiovascular, and digestive signs. Our findings regarding cutaneous reaction as a common sign of allergy comply with many other studies done in the past.<sup>11, 13, 23, 24</sup>

In this study, the most important limitation lies in the precise differentiation of immune-mediated and non-immune mediated ADRs. A person giving a history of drug allergic reaction may not be allergic to it for several reasons i.e. reaction may have been due to a disease, a combination of drugs, presence of other factors like recall bias, etc. As our study population was medical students, some of them may have self-diagnosed themselves. Moreover, the generalizability of our findings to the whole community is not yet possible due to the small sample size and non-probability sampling technique adopted for this study. Despite these limitations, it was the very first attempt to provide epidemiological data regarding self-reported drug allergic reactions in the region.

## CONCLUSION

Self-reported allergic reactions to the drugs were highly prevalent in the study population. Antibiotics were the most common source of drug allergies followed by NSAIDs with cutaneous manifestations as the most common sign of drug allergy. The high prevalence necessitate education of patients about the management of drug allergies while prescribing drugs.

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#### AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

- Faisal MS:** Concept, study design and manuscript write up
- Amin RU:** Data collection
- Ahmad MS:** Data collection
- Jamal A:** Data analysis and interpretation
- Hayat W:** Statistical analysis, Bibliography
- Haq KU:** Execution of study and critical review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.