Allergic Drug Reactions: How Do The Dermatologists Of Vadodara City Perceive And Contribute To Pharmacovigilance Program?

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Abstract: Background: The pharmacovigilance is imperative in defining safety profile of the drug. As cutaneous Adverse Drug Reactions (ADRs) are very common, dermatologists' contribution to pharmacovigilance program of India (PvPI) is important. This study was conducted to know dermatologists' perception about ADRs; their awareness and participation inPvPI. Material and Methods: A Prospective, cross-sectional survey was conducted amongst dermatologists, approaching via Whatsapp or during academic meetings. Pre-validated questionnaire including their demographic details, perception of risk of allergic reactions, awareness of PvPI and ADRs reporting was utilized. Data analysis was done with Microsoft Excel and Graph Pad prism software. Results: Out of 73 dermatologists, 44 responded the survey (Coverage rate 60%).Highest and lowest risk amongst antimicrobials for ADRs was perceived for sulphonamides and cephalosporins respectively. Amongst non-antimicrobials, it was Non-steroidal anti-inflammatory drugs (NSAIDs) and local anaesthetics respectively. Awareness about PvPI was seen in 94% and 38% of dermatologists working in an institute and in a private set up respectively. Amongst them, 78% and 18% had ever reported ADRs to PvPI. Conclusions: Sulphonamides and NSAIDs were perceived to have higher risk of ADRs. Limited number of dermatologists have contributed to national ADR database amongst the ones who are aware of PvPI. [Desai M Natl J Integr Res Med, 2021; 12(2):22-27]

Key Words: Adverse drug reactions, Awareness, Dermatologists, Perception, Reporting

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Introduction: Allergic drug reactions, which form one fourth of Adverse Drug Reactions (ADRs), are of major concern in clinical practice and drug development[1,2]. Anticipation of allergic reaction is an important component which can be possible with reporting of every single occurrence of it. Pharmacovigilance Program of India (PvPI) plays a vital role in ADRs reporting with support of Adverse Drug Monitoring Cells (AMCs).

Cutaneous ADRs contributes to 40-60% of spontaneously reported ADRs at AMCs of PvPI[3,4]. Dermatologists are the major source for strengthening PvPI registry and creating drug safety data[5,6]. There are various studies showing attitude and practice of various health professionals towards PvPI implementation and ADR reporting[7-10].

Majority of the studies were focused on teaching institutes or tertiary care centre except few of them[10]. Participation of dermatologists, especially working in private set up, in PvPI is not yet explored. This study was conducted to understand how allergic drug reactions are perceived by dermatologists, and, their awareness and participation in pharmacovigilance program through ADR reporting.

Material and Methods: This prospective, observational, cross-sectional study was conducted after the approval of Institutional Human Ethics Committee (IHEC). All collected information was kept confidential.

Collection of Details about the Participants: Initially, we approached chairman of a local association of dermatologist to collect the name, mobile number, E-mail address of the practicing dermatologists in the city. There were 55 practicing dermatologists and 18 resident doctors (pursuing residency in dermatology) in Vadodara city.

Survey Questionnaire: A pre-validated survey questionnaire was prepared to collect the information. Survey questionnaire included demographic information (age group, gender) and professional experience. A visual analogue scale (VAS) of 0 to 5 (5 cm), being 0 for the no risk and 5 for the maximum risk, was used to collect

the perception of risk of allergic reactions of 12 pharmacology groups. The pharmacology groups include: Sulfonamides, penicillins,cephalosporins, fluoroquinolones, antitubercular drugs, anti-retroviral drugs, anti-malarial drugs, antiepileptic drugs, nonsteroidal anti-inflammatory drugs (NSAIDs), neuromuscular blockers, drugs used during general anaesthesia and local anaesthetic agents. They were identified from the earlier systematic reviews of allergic reactions on Indian populations[11-13]. The inclusion of these pharmacology groups as a part of survey questionnaire was also validated with the help of senior dermatologist of our institute.

We also kept one open ended question to provide the opportunity for all the participants to write any other pharmacology group/drug which was not included in the list and they felt risk of allergic reaction in their practice with its risk score on VAS. The information about awareness of PvPI and ADR reporting were collected through open ended questions.

Data Collection: Two approaches were used to collect the data. In first approach, survey questionnaires were delivered to dermatologists through WhatsApp using the Survey Monkey online tool with its available basic free version on the net (Survey Monkey, 2012). Information about the purpose of the study and electronic consent form was also delivered to participants. Dermatologists were followed through WhatsApp messages at weekly interval for three times to ensure their response.

Second, dermatologists were approached during their two academic monthly meetings organized during the study period. The hard copy of case record form (CRF) and informed consent form were used to collect the data in such events.

Participants were briefed about the study objectives, procedures, consent, filling of CRF and earlier approach through WhatsApp. They were advised to refrain from filling the CRF in case of earlier electronic response.

Outcome Analysis and Statistical Analysis: Data were extracted in Microsoft Excel Sheet, 2007. Categorical data was presented in percentage. Age group and professional experience were presented in mean (standard deviation – SD). Data of perception of allergic reaction of pharmacology groups (0-5 scale) were presented in median (inter quartile range – IQR).

Their subgroup analysis was performed based on professional experience (resident doctors and practicing dermatologists) and their awareness about PvPI. They were compared using Kruskal-Wallis test followed by Mann-Whitney test. All statistical analysis was done through Graph Pad prism 7.04 demo version and $p<0.05$ was considered as statistically significant difference.

Results: General characteristics of participants (Table 1). Out of 18 resident doctors (≤3 years) and 55 practicing dermatologists (>3 years) in a city, 14 resident doctors and 30 practicing dermatologists participated in the survey (coverage rate-60%).

Online response was received from 32% of the participants amongst which 72% were from private practice set up and 28% were from institutional set up. Rest of the participants responded in hard copy of case record form during their monthly academic meeting.

Out of total 44 participants, there were 19 (43.2%) male participants and 25 (56.8%) female participants. The mean (SD) was 40.2 (10.8) and 12.9 (9.7) for age group of participants and professional experience respectively.

Table 1: Demographic Details of the Study Participants (N=44)

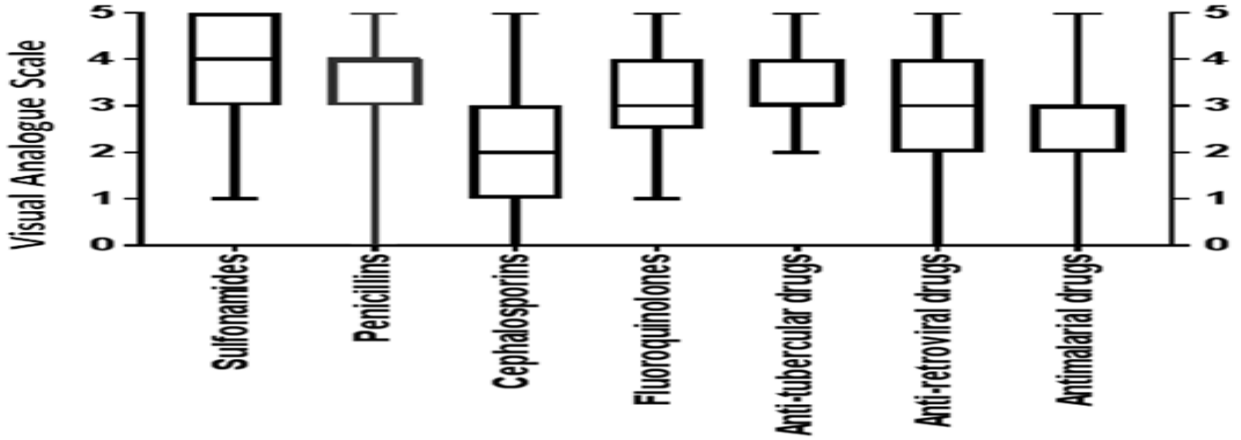
Demographic variables	n (%) or mean ± SD
Mode Of Response	
Online (WhatsApp)	14 (32)
Offline (Hard Copy)	30 (68)
Gender	
Male	19 (43)
Female	25 (57)
Age (Years)	40.2± 10.8
Experience (Years)	12.9 ± 9.7
Work Profile	
Private Practice	26
Institutional Practice	18

Perception of risk of allergic drug reactions of various pharmacology groups among dermatologists.

Highest and lowest perceptions of risk of allergic drug reactions were perceived for sulphonamides [4(3,5)] and cephalosporins [2(1,3)], respectively.

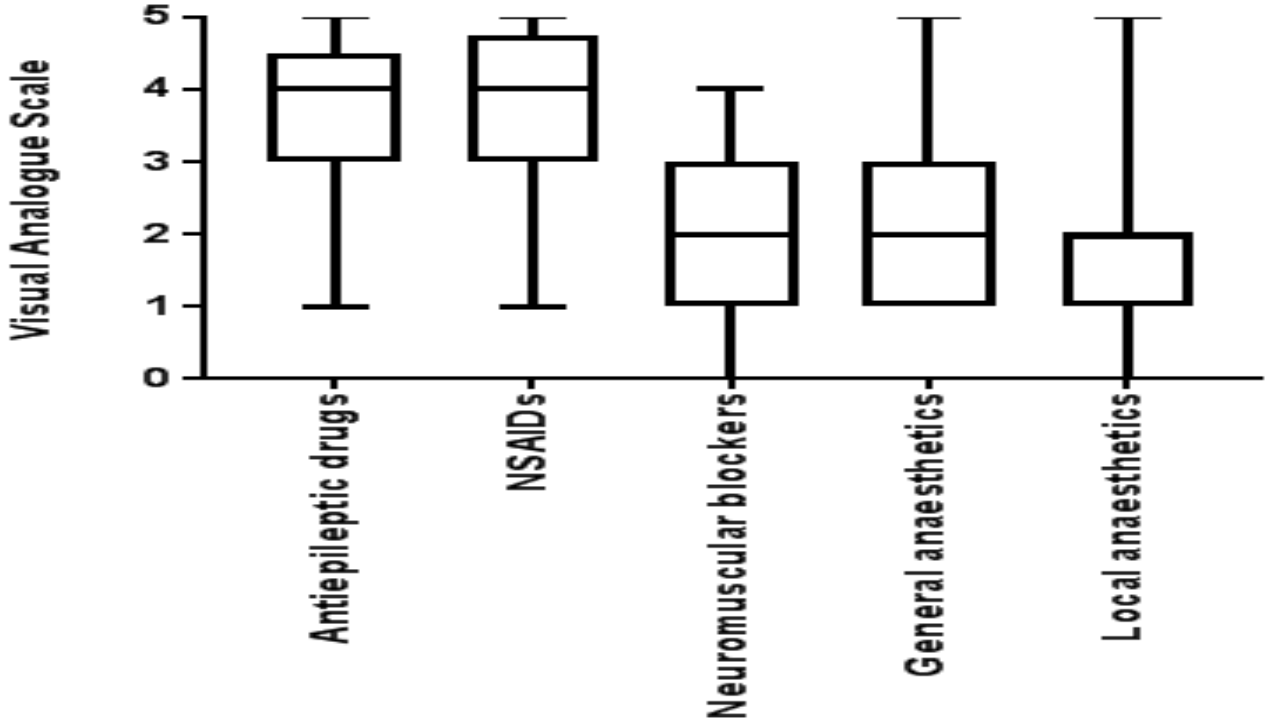
The perception of risk of allergic drug reactions was significantly higher for sulfonamides, penicillins, fluoroquinolones, anti-tubercular drugs, anti-retroviral drugs as compared to cephalosporins (P<0.05). The perceived risk of allergic reactions for sulfonamides was also significantly higher than anti-malarial drugs (P<0.05)(Figure 1).

Figure 1: Perception of Risk Of Allergic Drug Reactions of Antimicrobials among Dermatologists



Highest and lowest perceptions of risk of allergic drug reactions were perceived for NSAIDs [4(3,4.75)] and local anaesthetics [2(1,2)], respectively. The perception of risk of allergic reactions was relatively higher for anti-epileptic drugs and NSAIDs compare to neuromuscular blockers, general anaesthetics and local anaesthetics. (P<0.05)(Figure 2)

Figure 2: Perception of Risk Of Allergic Drug Reactions of Non-Antimicrobial Drugs among Dermatologists



*NSAIDs – Non steroidal anti-inflammatory drugs.

Through open ended question, 5 participants, who were aware about PvPI, suggested 10 pharmacology groups-topical antibiotics, angiotensin converting enzyme inhibitors(ACE inhibitors), erythromycin, fluconazole, cyclophosphamides, methotrexate, topical steroids, systemic steroids and immune modulators which were not included in questionnaire but they felt risk of allergic reactions in their practice. Highest risk score was assigned to ACE inhibitors. Out of these 5 participants, 3 had ever reported ADR to PvPI.Through open ended question, five participants, who were not aware about PvPI, suggested seven pharmacology groups-framycetincream, neomycincream, nimesulide, tetracycline, fluconazole,itraconazole and anti-diarrheal drugs which were not included in

questionnaire but they felt risk of allergic reactionsin their practice. Out of these 5 participants, nonehad ever reported ADR to PvPI.

Subgroup analysis of perception of allergic reactions between resident doctors (≤3 years) and practicing dermatologists (>3 years).Resident doctors and practicing dermatologists did not show significant difference in perception score ofrisk of allergic reactions for all pharmacology groups (P>0.05). Subgroup analysis of perception of allergic reactions as per awareness about PvPI. All participants were categorised based on their awareness about PvPI into two groups (aware or not aware) to comparethe perception of risk of allergic reactions for each pharmacologic group. Participants who were aware about PvPI showed lower perception risk score for neuromuscular blockers than those who are not aware about it [2(1,3) vs. 3(2,4);p<0.05]. Participants did not differ in perception risk score of allergic reaction for other pharmacology groups based on their awareness about pharmacovigilance program (P>0.05).

Awareness and reporting of ADRs to PvPI(Table 2). Out of 44 participants, 27 (61.4%) and 23 (52.3%) were aware about PvPI and nearest ADR monitoring centres, respectively. A total of 19 (43.2%) had ever reported ADRs to PvPI.

Amongst 18 institutional practitioners, included 14 resident doctors and four consultants working in a tertiary care centre, 94% and 83% were aware of PvPI and AMCs respectively. ADRs were reported to AMCs by 78% of them.

Out of 26 private practitioners, ten (38%) and eight (31%) were aware of PvPI and AMCs respectively. ADR reporting was done by 19% of them.

Table 2: Awareness and Reporting of ADRs To PvPI (N=44)

Awareness/ Reporting	Institutional Practitioners N=18 (%)	Private Practitioners N=26 (%)	Total N=44 (%)
Pharmacovigilance Program	17 (94)	10 (38)	27 (61)
ADR Monitoring Cell	15 (83)	08 (31)	23 (52)
Reporting of ADR	14 (78)	05 (18)	19 (43)
Total	18	26	44

Discussion: This survey-based study was conducted among the dermatologists of the city of Western India to assess the perception of allergic reactions to various pharmacology drugs and their awareness and participation to pharmacovigilance program of India (PvPI).

Among the antimicrobial agents, sulphonamides were perceived to have highest risk of allergic drug reactions by dermatologists. This is in line with the earlier Indian systematic review of CADR suggesting sulphonamides are responsible for one-tenth of reported cutaneous ADR in Indian population[11].Penicillins,fluoroquinolones, anti-tubercular drugs and anti-retroviral drugs were also perceived to have higher risk of allergic reactions. Among antimicrobials, earlier Indian studies observed sulphonamides/cotrimoxazole[14-18], penicillins[18-20], fluoroquinolones group[21,22] and anti-tubercular drugs[23].Fluoroquinolones, sulpha drugs, penicillins and anti- tubercular drugs were also frequently implicated in serious cutaneous ADRs in Indian population[12]. Cephalosporins were perceived to have lower risk of CADRs by participating dermatologists. However, they have implicated for most common causative antimicrobials in earlier North Indian study[24]. This difference could be due to variation in drug use pattern of antimicrobials across various parts of India.

NSAIDs and anti-epileptic drugs were perceived to higher risk of allergic reactions among non-antimicrobials. Earlier Indian systematic review of cutaneous ADR observed that NSAIDs and anti-epileptic drugs are responsible for one-third of cutaneous ADRs and one-half of serious CADRs[11,12]. The reported frequency of cutaneous ADRs with NSAIDs and antiepileptics were ranged from 15.50 to 39.1and 3.75 to 32.88 percentage, respectively[14-17,20-22,24].

Neuromuscular blocking agents and anaesthetic agents have been implicated for anaphylactic reactions in an earlier Indian systematic review[13]. The relatively low perception of allergic reactions for these drugs could be due to rarity of event of

anaphylaxis.Though perception of risk of allergic reactions for antimicrobials, NSAIDs and antiepileptic drugs did not differ among dermatologists irrespective of their awareness of PvPI program and ADR reporting habit, they have highlighted seventeen pharmacology drugs/groups having risk of allergic reactions in their practice.

Our findings suggest the more than half of the dermatologists are not aware about pharmacovigilance program and ADR monitoring centres. This is in accordance with the earlier Indian studies assessing knowledge and awareness of Indian health care professionals about pharmacovigilance program[25,26]. A recent systematic review observed the gap in knowledge and ADR reporting practice in India[27]. Lack of knowledge and awareness is the common factor responsible for underreporting of ADRs[26].

In today's scenario, identification and reporting of ADR are neglected by the health care professionals in clinical practice. It was identified that high proportion of the participants was not aware about how to fill ADR form. Few felt that form is very clumsy. There is need to educate dermatologists, especially of private set up (which forms almost double the strength of institutional practitioners in present study population) about pharmacovigilance program to improve their participation and strengthen the national database.

PvPI has made lot efforts in the form of running adverse drug reaction monitoring centres in many medical colleges, launching android mobile to report ADRs by health care professionals and collaborating with various national programs[28,29].

PvPI has also encouraged consumers to report ADRs through toll free numbers and e-mail. It has designed vernacular language ADR forms in various regional Indian languages. It should make more efforts to publicise various ways to report ADRs through sensitization and training program to ensure participation of private practitioners to strengthen the ADR database of India. WhatsApp notification to nearest AMC can be promoted.

Conclusion: Sulphonamides, NSAIDs and antiepileptic drugs were perceived to have higher risk of allergic reactions among participating dermatologists of this study. The significant numbers of dermatologists are not aware about pharmacovigilance program and have not contributed to national ADR database.

Dermatologists are one of the important stakeholders in identifying and reporting ADRs. They, especially private practitioners, must be sensitized adequately for pharmacovigilance program and facilitated to report reactions.

Limitations: Though this study identifies higher perception for ADRs and awareness of PvPI amongst dermatologists working in private set up, it is lacking in labelling probable reasons for under reporting of ADRs.

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Conflict of interest: None

Funding: None

Cite this Article as: Desai M, Thakkar S, Patel T.Allergic Drug Reactions: How Do The Dermatologists Of Vadodara City Perceive And Contribute To pharmacovigilance Program? Natl J Integr Res Med 2021; Vol.12(2): 22-27