Contents lists available at ScienceDirect



Saudi Pharmaceutical Journal



journal homepage: www.sciencedirect.com

Healthcare Providers' knowledge, attitudes and practice in relation to drug hypersensitivity reactions at King Abdulaziz Medical City in Riyadh

Mohammed Alrashed ^{a,b,c,*}, Ahmed A. Alanazi^d, Khalid Bin Saleh ^{a,b,c}, Faisal Alanazi^e, Ahmed S. Alanazi^f, Sumayyah Mashraqi^g, Madhawi Mahdali^a, Abdullah Alshammari^g, Mohammed A Alnuhait^g, Mohammed Alzahrani^{a,b,c}, Tariq Alqahtani^{a,b,c}

^a Department of Pharmacy Practice, College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

^b King Abdullah International Medical Research Center, Riyadh, Saudi Arabia

^c Department of Pharmaceutical Care Services, King Abdulaziz Medical City, Riyadh, Saudi Arabia

^d Department of Pharmacy Practice, College of Pharmacy, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia

^e Janssen Pharmaceutical Companies of Johnson & Johnson, Saudi Arabia

^f Clinical Pharmacy Department, Pharmaceutical Service, King Fahad Medical City, Riyadh, Saudi Arabia

⁸ Pharmaceutical Practices Department, College of Pharmacy, Umm Al Qura University, Makkah, Saudi Arabia

ARTICLE INFO

Keywords: Hypersensitivity reactions Emergency department Health care providers

ABSTRACT

Background: Drug hypersensitivity reactions (DHRs) are immune-mediated responses triggered by exposure to a drug. DHRs are responsible for serious adverse drug reactions (ADRs) and are considered the fifth leading cause of death. This study aims to assess and evaluate the knowledge, practice, and attitudes of healthcare providers (HCPs) towards DHRs.

Methods: A cross-sectional survey was conducted at King Abdulaziz Medical City (KAMC) in Riyadh, Saudi Arabia. Healthcare providers, including pharmacists, physicians, and nurses, were recruited using a convenience sampling method to complete the survey. The survey comprised three domains: knowledge (14 items), attitudes (5 items), and practices (6 items), utilizing a standardized self-administered questionnaire.

Results: The survey was completed by 373 healthcare providers. The respondents were predominantly female (72.1 %) with a mean age of 33.8 ± 7.8 years. Of the respondents, 64 % were nurses, 25 % pharmacists, and 11.3 % physicians. Educational levels varied, with 53 % holding a bachelor's degree, 22 % an associate degree, and 25 % a master's degree or higher. The median knowledge score was 48. Female healthcare providers, those with advanced levels of education, and physicians had higher knowledge scores compared to male and nurse participants (p < 0.05). One-third of the respondents (33 %) were satisfied with their knowledge of DHRs, and 42 % believed HCPs should receive more advanced training in DHR management. Less than a quarter of HCPs reported inquiring about patients' histories of hypersensitivity reactions.

Conclusions: The study revealed that healthcare workers had a relatively low level of knowledge about drug hypersensitivity reactions and lacked a consensus on DHR management. While displaying a positive attitude towards DHRs, they often did not translate this attitude into consistent clinical practice.

1. Introduction

Drug hypersensitivity reactions (DHRs) are a group of immunemediated responses that occur after exposure to a drug. DHRs are responsible for approximately 6 % of all adverse drug reactions (ADRs) and are the fourth to sixth leading cause of death (Lazarou et al., 1998; Wilkerson, 2021). The Geel and Coombs classification system categorizes hypersensitivity reactions into four types based on their immunological mechanisms. Type I hypersensitivity, also known as immediate hypersensitivity, is mediated by IgE antibodies and typically occurs rapidly upon exposure to an allergen. Type II hypersensitivity involves cytotoxic reactions where IgG or IgM antibodies target cell surface antigens, leading to cellular damage. Type III hypersensitivity is characterized by the formation of immune complexes that deposit in tissues, triggering inflammation. Lastly, Type IV hypersensitivity, or delayed-type hypersensitivity, is a cell-mediated response primarily

* Corresponding author at: College of Pharmacy, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. *E-mail addresses:* alrashidm@ksau-hs.edu.sa, rxedmo@gmail.com (M. Alrashed).

https://doi.org/10.1016/j.jsps.2024.102042

Received 2 May 2023; Accepted 17 March 2024

Available online 19 March 2024

1319-0164/© 2024 The Authors. Published by Elsevier B.V. on behalf of King Saud University. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

involving T cells, manifesting 48–72 h after allergen exposure (Demoly and Hillaire-Buys, 2004; Schnyder et al., 2008; Pichler, 2003). The severity of these reactions ranges from mild to life-threatening and can drastically affect the patient's quality of life, leading to prolonged hospitalization and potentially permanent damage (Gastaminza et al., 2019). Despite the availability of various diagnostic methods for DHRs, their practical use for clinicians in evaluating patients with suspected drug allergies is often limited. One significant issue is the unclear immunochemistry of most drugs, with Penicillin being the primary exception (Weiss and Adkinson, 1998). Healthcare providers continue to face significant challenges in providing accurate diagnoses and managing DHRs. Recent guidelines and international consensus documents on drug allergy have aided clinicians in decision-making (Mertes et al., 2011; Mirakian et al., 2009). However, the application of these protocols in actual clinical settings is inconsistent. A systematic review by Gaudin et al. (2023) highlights the difficulties general practitioners (GPs) encounter in differentiating DHRs from other drug side effects, a task complicated by a lack of comprehensive data from primary care. Similarly, a study by Kalikyan et al. (2022) in Armenia showed a clear need for creating a national registry for patients with severe DHRs and developing a straightforward algorithm for patient management. Both studies underscore the necessity for targeted educational programs and improved clinical decision-making tools in primary care. Consequently, there is an urgent need for additional research to assess and evaluate the knowledge, practice, and attitude (KAP) of healthcare providers toward DHRs. This cross-sectional study utilized a convenience sample of physicians, nurses, and pharmacists to evaluate their KAP regarding DHRs. The aim was to support the planning, implementation, and evaluation of educational initiatives concerning DHRs, as KAP studies are increasingly recognized for their role in improving disease control activities (Schultz et al., 1994).

2. Methods

2.1. Study area/setting

A cross-sectional survey was conducted at King Abdulaziz Medical City (KAMC) in Riyadh, Saudi Arabia, involving a diverse group of healthcare providers including physicians, pharmacists, dentists, respiratory therapists, and nurses. Participants provided demographic information such as their level of education, years of experience, departmental affiliation, and current job title. Data were collected using a systematically structured questionnaire, which was validated through a pilot study involving a subset of healthcare professionals to ensure its relevance and reliability (Wang et al., 2016). The questionnaire included in the supplementary consists of 25 close-ended questions across three domains: knowledge (14 items), attitudes (5 items), and practices (6 items). The knowledge domain features multiple-choice questions covering the categories, mechanisms, diagnostic methods, and management of DHRs, with each question offering four possible answers. For the attitudes domain, five statements were rated on a 5point Likert scale, from strongly disagree to strongly agree, to gauge respondents' views on the necessity of educational sessions on DHRs, the impact of DHRs on patient quality of life, and the accessibility of diagnostic methods. The practice domain's six items also used a 5-point Likert scale, assessing frequency of actions from never to always, including questions about pre-drug administration practices, inquiring about the patient's allergy history, and the timely management of DHRs. In the analysis, missing data and incomplete responses were handled using established imputation techniques to preserve the study's statistical validity. This study has received approval from the King Abdullah International Medical Research Center (KAIMRC). Ethical considerations were strictly adhered to throughout the study. Prior to participation, informed consent was obtained from all participants.

Table 1

Demographic characteristics of study participants.

Factor	
Gender n (%)	
Female	269 (72 %)
Male	104 (28 %)
Age (years) mean \pm SD	$\textbf{33.8} \pm \textbf{7.8}$
median (IQR)	32 (28–40)
Level of Education n (%)	
Associate degree	83 (22 %)
Bachelor's degree	198 (53 %)
Master's or above	92 (25 %)
Current designation n (%)	
Physician	42 (11 %)
Nurse	238 (64 %)
Pharmacist	93 (25 %)
Hospital department n (%)	
Critical Care	63 (17 %)
Surgery	45 (12 %)
Internal Medicine	78 (21 %)
Pediatrics	35 (9 %)
Oncology	21 (6 %)
Pharmacy	86 (23 %)
Cardiology	38 (10 %)
Other	7 (2 %)
Years at institution mean \pm SD	$\textbf{4.9} \pm \textbf{4.8}$
median (IQR)	3 (1–7)

2.2. Data collection

Subjects were randomly selected to participate until the desired sample size was achieved. Data were collected using a standardized, self-administered questionnaire. We thoroughly explained the study's purpose to the respondents, and written informed consent was obtained prior to their participation. Participants were instructed to complete and return the survey within one hour. Each session took approximately 30–45 min. The primary outcome of the study was to evaluate and compare the knowledge, attitudes, and practice domains among healthcare professionals (HCPs). Secondary outcomes included an assessment of factors potentially associated with lower rates of knowledge, attitudes, and practices, such as gender, age, level of education, current job title, years of service at the institution, and hospital department affiliation.

2.3. Statistical analysis

Utilizing data from published quality improvement studies, we estimated that a total of 300 participants would be required to achieve 90 % power to detect significant differences in the three domains of the study. Data were entered into Microsoft Excel and subsequently imported into SPSS version 23.0 for analysis. Statistical analyses were conducted using Spearman's rank correlation, Mann-Whitney *U* test, or Kruskal-Wallis test, as appropriate. A p-value of less than 0.05 was considered statistically significant for all tests.

3. Results

3.1. Demographic characteristics of study participants

A total of 373 healthcare professionals (HCPs) completed the survey and were evaluated for statistical analysis. The demographic information of the respondents is summarized in Table 1. Female respondents comprised 72 %, while male respondents accounted for 28 %. The mean age of the respondents was 33.8 ± 7.8 years. Of the 373 respondents, 64 % were nurses, 25 % were pharmacists, and 11 % were physicians.

Knowledge of Respondents Regarding DHRs



Fig. 1a. Knowledge of participants regarding DHR.

Regarding educational attainment, 53 % held a bachelor's degree, 22 % held an associate degree, and 25 % had a master's degree or higher. Among all participating HCPs, 23 % were from the pharmacy department, 21 % from the internal medicine department, 17 % from the critical care department, 12 % from the surgery department, 10 % from the cardiology department, 9 % from the pediatric department, and 6 % from the oncology department.

3.2. Knowledge of drug hypersensitivity reaction

Knowledge of respondents regarding drug hypersensitivity reactions (DHRs) is depicted in Fig. 1a. Item precision varied from 13 % to 89 %, with a mean precision of 43 %. Half of the respondents recognized druginduced anaphylaxis as a type I hypersensitivity reaction, 63 % believed that the reaction was IgE-mediated, and 90 % expected that the reaction would occur within 6 h of drug administration. Among all participating healthcare professionals (HCPs), 45 % agreed that cutaneous symptoms were the most common manifestation of drug allergies. The employment of provocation and skin prick tests was endorsed by 17 % and 30 % of respondents, respectively. Furthermore, 80 % of HCPs considered the penicillin skin test more reliable than tests for other drugs, while only 13 % believed that antihistamines affected drug skin test outcomes. Epinephrine was identified by 76 % of HCPs as the first-line treatment option for an anaphylactic reaction. Sub-analysis of the results, presented in Fig. 1b, indicated that females, individuals with advanced levels of education, and physicians had higher knowledge scores compared to their male and nurse counterparts (p < 0.05). No significant difference was found between the knowledge scores of physicians and pharmacists. HCPs working at the acute care level (including critical care, pediatrics, oncology, pharmacy, and cardiology departments) in hospitals were associated with a higher median knowledge score.

3.3. Attitudes about drug hypersensitivity reaction

Overall, 33 % of respondents were satisfied with their knowledge of drug hypersensitivity reactions (DHRs), and 42 % believed that healthcare professionals (HCPs) should receive advanced training in this



Fig. 1b. Knowledge of participants based on the gender, level of education, healthcare specialty, and hospital department.



A: Current designation



C: Participants' level of education



B: Years at institution of participants



D: Participants' ages

Fig. 2. Attitudes about drug hypersensitivity reaction.

area. Additionally, 40 % of the participants acknowledged that drug allergies adversely affect a patient's quality of life. Half of the participants reported that DHRs occur frequently in their daily practice, and about 61 % agreed that in vivo or in vitro drug testing should be performed prior to drug administration. The sub-analysis of the results, presented in Fig. 2, considered a positive percentage when the health-care providers expressed satisfaction with their attitudes towards DHRs, answering questions with 'agree' or 'strongly agree'. Healthcare professionals with an advanced level of education and extensive experience (over 20 years) and those older than 50 years displayed a more positive attitude towards DHRs (p < 0.05).

3.4. Practice toward drug hypersensitivity reaction

The general practice patterns of healthcare professionals (HCPs) regarding drug hypersensitivity reactions (DHRs) varied. Only 22 % of respondents reported taking a history of drug allergies before administering medication. Additionally, seventy-one percent of the respondents were unable to interpret the results of drug skin tests and the positive/ negative controls used during these tests. Recognition of DHRs was consistently observed by 21 % of participants and often by 14 %. Nearly 19 % of participants were involved in continuous medical education on

drug allergies. The sub-analysis of the results is illustrated in Fig. 3. A positive response was defined as healthcare providers being satisfied with their practices and answering questions with 'agree' or 'strongly agree'. Both age and a higher level of education were found to significantly influence the practices of healthcare workers. However, there was no significant difference in scores when analyzed by current job title and years of service at the institution.

4. Discussion

Drug hypersensitivity reactions (DHRs) are globally recognized as significant contributors to patient morbidity and hospital readmissions, necessitating vigilant identification, management, and follow-up (McDonnell and Jacobs, 2002). These reactions often involve multiple organ systems and can range from moderate to severe, sometimes posing life-threatening risks (Thong and Tan, 2011). Our study delved into the understanding of DHR mechanisms, clinical presentations, diagnostics, and management among healthcare providers (HCPs), uncovering a median knowledge score of 43 %. This score points to an urgent need for enhanced DHR education among HCPs, a conclusion supported by other studies (Özdemir et al., 2020; McDonnell and Jacobs, 2002).

Knowledge disparities among HCPs are influenced by geography,













C: Participants' level of education

. -



training, practice settings, and experience. For example, one study reported that approximately 74 % of pediatricians accurately understood DHRs, while the general knowledge level in other studies varied between 35 % and 77 % (Ercan and Konukbay, 2021; Wang et al., 2016). Our findings are in line with those among primary care physicians in Taif, Saudi Arabia (Allehaiby et al., 2021). Furthermore, our research indicates a link between HCPs' knowledge and their professional and educational backgrounds, where higher education and advanced training correlated with better knowledge (Allehaiby et al., 2021).

In terms of treatment, a reassuring 76 % of participants in our study correctly identified epinephrine as the first-line response for anaphylaxis, consistent with various guidelines and paralleling other research findings (Demoly et al., 2014; Celik et al., 2014; Ercan and Konukbay, 2021; Wang et al., 2016). This underscores the importance of epinephrine in emergency care, which, if administered promptly, can be lifesaving. Our findings reinforce the notion that educational gaps exist among HCPs, as indicated by the World Allergy Organization's guidelines, which point to a lack of understanding of anaphylaxis as a primary barrier to effective intervention (Simons et al., 2012; Seid et al., 2018).

Our study also emphasizes the correlation between HCPs' knowledge and their attitudes and practices. A notable majority of respondents expressed dissatisfaction with their current level of DHR knowledge, with many showing a keen interest in advanced training. This attitude mirrors the sentiment in previous studies (Ercan and Konukbay, 2021; Wang et al., 2016; Ahmad et al., 2021). Despite the general recognition of the importance of skin tests for DHR diagnosis, our study found that adherence to guideline recommendations for these procedures was inconsistent, with attitudes towards in vitro/in vivo testing varying widely (Ercan and Konukbay, 2021; Wang et al., 2016).

Our findings suggest that advanced education and experience foster a positive attitude towards managing DHRs, which is in line with studies where increased age was associated with a more favorable view of DHR management (Ercan and Konukbay, 2021; Wang et al., 2016). This positive attitude is crucial, as our study also highlights the need for improvement in HCPs' practical application of their DHR knowledge. While some clinical environments have initiated training sessions, there is a need to extend these educational efforts more broadly to improve HCPs' familiarity with DHR management.

Furthermore, our study points to a potential disconnect between knowledge and practice, particularly in the area of allergy history assessment and the management of anaphylactic patients. The lowerthan-expected percentage of HCPs routinely taking allergy histories before prescribing medications may have critical clinical implications. Additionally, the infrequent checking of patient records for drug allergies suggests a need for heightened vigilance during clinical historytaking (Demoly et al., 2014; Celik et al., 2014). Lastly, while our study provides valuable insights, it is important to acknowledge its limitations, including potential sampling and response biases, which may limit the generalizability of the findings. The crosssectional design precludes causal inferences, and the geographic focus may not reflect broader practices. The questionnaire's scope and statistical assumptions also merit consideration. These limitations highlight the need for further research to comprehensively address DHR complexities in healthcare.

5. Conclusion

This study highlights that healthcare professionals have a moderate understanding of drug hypersensitivity reactions (DHRs) and lack consistent management strategies. While attitudes toward DHRs are generally positive, this does not translate into clinical practice. The findings underscore the need for advanced training and educational initiatives to align knowledge with practice, thereby improving DHR patient care.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jsps.2024.102042.

References

- Ahmad Hameed Allehaiby et al., Knowledge, attitude, and practices of drug allergy among primary healthcare physicians in Taif, Ksa, 2021. Indo Am. J. P. Sci. 08(08).
- Celik, G.E., Pichler, W.J., Adkinson, N.F., 2014. Drug allergy. In: Adkinson, N.F., Bochner, B.S., Wesley Burks, A., Busse, W.W., Holgate, S.T., Lemanske, R.F., O'Hehir, E.R. (Eds.), Middleton's. Allergy Principles and Practice, 8th ed. Elsevier Saunders, pp. 1274–1295.
- Demoly, P., Adkinson, N.F., Brockow, K., et al., 2014. International Consensus on drug allergy. Allergy. 69, 420–437.
- Demoly, P., Hillaire-Buys, D., 2004. Classification and epidemiology of hypersensitivity drug reactions. Immunol. Allergy Clin. North Am. 24 (3), 345–v. https://doi.org/ 10.1016/i.jac.2004.03.010.
- Ercan, N., Konukbay, D., 2021. The knowledge, attitudes and practices of healthcare workers on drug hypersensitivity reactions in children: a tertiary centre experience from Turkey. Int. J. Clin. Pract. 75 (9), e14444.
- Gastaminza, G., Ruiz-Canela, M., Andrés-López, B., Barasona Villarejo, M.J., Cabañas, R., García-Núñez, I., Goikoetxea, M.J., Laguna, J.J., Lobera, T., López-San Martín, M.,

Martín-Lázaro, J., Mielgo-Ballesteros, R., Moreno, E., Moya-Quesada, M.D.C., Ortega-Rodríguez, N., Rojas-Perez-Ezquerra, P., Rosado, A., Salas, M., Sánchez-Morillas, L., Vila-Albelda, C., Corominas, M., 2019. Quality of life in patients with allergic reactions to medications: influence of a drug allergy evaluation. J. Allergy Clin. Immunol. Practice 7 (8), 2714–2721. https://doi.org/10.1016/j. jaip.2019.05.017.

- Gaudin, C., Ryan, D., Demoly, P., Tanno, L.K., 2023. Drug allergy in primary care: systematic review to support quality improvement initiative of management and optimization of healthcare pathways. Curr. Opin. Allergy Clin. Immunol. 23 (4), 263–270. https://doi.org/10.1097/ACI.000000000000924. Epub 2023 Jun 21.
- Kalikyan, Z., Harutyunyan, S., Hakobyan, A., Tadevosyan, A., Aloyan, T., Kocharyan, S., Tadevosyan, N., 2022. The awareness, practical approaches and attitude of health care professionals to drug hypersensitivity reactions in Armenia. Bratisl. Lek. Listy. 123 (4), 304–310. https://doi.org/10.4149/BLL_2022_048.
- Lazarou, J., Pomeranz, B.H., Corey, P.N., 1998. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 279 (15), 1200–1205. https://doi.org/10.1001/jama.279.15.1200.
- McDonnell, P.J., Jacobs, M.R., 2002. Hospital admissions resulting from preventable adverse drug reactions. Ann Pharmacother. 36 (9), 1331–1336. https://doi.org/ 10.1345/aph.1A333.
- Mertes, P.M., Malinovsky, J.M., Jouffroy, L., , Working Group of the SFAR and SFA, Aberer, W., Terreehorst, I., Brockow, K., Demoly, P., ENDA, & EAACI Interest Group on Drug Allergy, 2011. Reducing the risk of anaphylaxis during anesthesia: 2011 updated guidelines for clinical practice. J. Invest. Allergol. Clin. Immunol. 21 (6), 442–453.
- Mirakian, R., Ewan, P.W., Durham, S.R., Youlten, L.J., Dugué, P., Friedmann, P.S., English, J.S., Huber, P.A., Nasser, S.M., Bsaci, 2009. BSACI guidelines for the management of drug allergy. Clin. Exp. Allergy: J. Brit. Soc. Allergy Clin. Immunol. 39 (1), 43–61. https://doi.org/10.1111/j.1365-2222.2008.03155.x.
- Pichler, W.J., 2003. Delayed drug hypersensitivity reactions. Ann. Intern. Med. 139 (8), 683–693. https://doi.org/10.7326/0003-4819-139-8-200310210-00012.
- Schnyder, B., Helbling, A., Kappeler, A., Pichler, W. J., 2008. Drug-induced papulovesicular exanthema. In: Allergy, vol. 53(8), Wiley, pp. 817–818. doi: 10.1111/j.1398-9995.1998.tb03985.x.
- Schultz, L.J., Ettling, M., Chitsulo, L., Steketee, R.W., Nyasulu, Y., Macheso, A., Nwanyanwu, O.C., 1994. A nation-wide malaria knowledge, attitudes and practices survey in Malawi: objectives and methodology. Trop. Med. Parasitol.: Off. Organ Deutsche Tropenmedizinische Gesellschaft Deutsche Gesellschaft Technische Zusammenarbeit (GTZ) 45 (1), 54–56.
- Seid, M.A., Kasahun, A.E., Mante, B.M., et al., 2018. Healthcare professionals' knowledge, attitude and practice towards adverse drug reaction (ADR) reporting at the health center level in Ethiopia. Int. J. Clin. Pharm. 40, 895–902. https://doi.org/ 10.1007/s11096-018-0682-0.
- Simons, F.E., Ardusso, L.R., Bilò, M.B., Dimov, V., Ebisawa, M., El-Gamal, Y.M., Ledford, D.K., Lockey, R.F., Ring, J., Sanchez-Borges, M., Senna, G.E., Sheikh, A., Thong, B.Y., Worm, M., World Allergy Organization, 2012. Curr. Opin. Allergy Clin. Immunol. 2012 (12), 389–399.
- Thong, B.-H., Tan, T.-C., 2011. Epidemiology and risk factors for drug allergy. Br. J. Clin. Pharmacol. 71 (5), 684–700.
- Wang, Y., Zhu, R., Huang, N., Li, W., Yang, L., Zhang, S., Liu, G., 2016. Knowledge, attitudes, and practices survey of drug allergy among healthcare practitioners in central China: a multicenter study. Asia Pac. Allergy 6 (2), 105–111.

Weiss, M.E., Adkinson Jr., N.F., 1998. Diagnostic testing for drug hypersensitivity. Immunology and Allergy Clinics of North America Vol. 18(4), 731–744.

Wilkerson, R.G., 2021. Drug Hypersensitivity Reactions. Emerg. Med. Clin. North Am. 40 (1), 39–55. https://doi.org/10.1016/j.emc.2021.09.001. Epub 2021 Oct 29.