Systematic Review

Healthcare Professionals' Knowledge, Attitude andPerception toward Adverse Drug Reaction Reporting in Saudi Arabia: A Systematic Review

. ABSTRACT

Aims: To systematically evaluate the currently available evidences about the knowledge, attitude and perceptions of healthcare professionals in Saudi Arabia towards reporting adverse drug reactions to the Saudi Food and Drug Authority (Saudi FDA) as the regulatory authority monitoring adverse drug reactions in the country.
Study design: Systematic Review
Methodology:A systematic search of the literature was conducted on ScienceDirect, PubMed, OVID databases as well as Google Scholar for all studies published in English up toJune 2023. Strengthening the Reporting of Observational Studies in EpidemiologyJoanna Briggs Institute (STROBE) checklist was used to appraise the quality of the cross-sectional studies included in this review.
Results:A total of 27 studies conducted in different healthcare institutions in Saudi Arabia were included in the systematic review. Overall, in the knowledge domain, the awareness of healthcare professionals toward the existence of a national pharmacovigilance adverse drug reaction reporting system ranged from10% to 95%. In the attitude domain, thebelief of the healthcare professionals that reporting adverse drug reaction is a professional obligation ranged from 12.80% to 90.20%. In the perception domain, 46.53% to 100% of healthcare professionals perceive adverse drug reactionreporting has a positive impact on healthcare system and improves patient's care and quality of life.
Conclusion: Despite having positive attitude toward reporting adverse drug reactions, the healthcare professionals require more education and training in utilizing the Saudi FDA provided adverse drug reaction form and online system to report on the adverse drug reaction the they encounter during their practice.

Keywords: Adverse Drug Reaction; Pharmacovigilance; Healthcare Professionals; Knowledge; Attitude;Perception; Saudi Arabia.

1. INTRODUCTION

Adverse drug reaction (ADR) is defined as an unintendedharmful effect of medication that is usually unpredictable, resulting from the utilization of otherwise normal drug doses intended for therapeutic or prophylactic effects, and it is a frequent cause of morbidity and mortality [1, 2]. Pharmacovigilance (PV) is a process that is concerned with assessing, detecting, and reporting ADR to ensure drug safety during the post-marketing surveillance (PMS) phase [3]. Thus, having active PV and well-established ADR reporting systems can reduce the economic burden and frequency of hospital admissions associated with ADR. The Saudi Food and Drug Authority (Saudi FDA) is the regulatory authority responsible for monitoring drug safety in Saudi Arabia. The Saudi FDA established the National Pharmacovigilance Center (NPC) with the aim of receiving and monitoring drug safety through the provision of a spontaneous ADR monitoring system known as the Saudi Vigilance System(SVS)[3-5].

The NPC receives spontaneous ADR reports from the Healthcare Professionals (HCPs) and the public through paper forms, online reporting forms, direct verbal communication, and via fax or phone. Awareness campaigns were conducted by the Saudi FDA toenhance the

knowledgeandawareness of the HCPs and the public of the importance of PV and ADR reporting, as the main stakeholders in this process [3, 6, 7].
Underreporting is a challenge facing different international drug regulatory authorities around the world and was also reported by national studies in Saudi [2, 3, 7, 8], due to the unfamiliarity of the stakeholders: HCPs and the Public in particularwith PV and ADR reporting. Thus, stakeholders' knowledge and perception of their roles in ADR reporting, and the implementation of an efficient electronic platforms that encourage their engagement in submitting any experienced ADR are amongthe major factors in improving the national performance of ADR reporting [2, 9].
The purpose of this systematic review is to evaluate the literature that focused on measuring the knowledge, attitude and perception (KAP) of HCPs practicing in Saudi Arabia toward PV and ADR reporting. This evaluation will help in describing the current status of the information provided to the NPC in terms of their frequency and quality, and to identify any gaps that need to be addressed to improve the quality of the ADR reported to the Saudi FDA by the HCPs.

2. MATERIAL AND METHODS

2.1 Study Protocol
A systematic review of the existing evidences related to KAP of HCPs in Saudi Arabia toward ADR reporting following thePreferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statements (Appendix Supplementary file 1) was conducted[10].

2.2 Eligibility Criteria
All studies that met the following inclusion criteria were included: 1) Cross-sectional studies(CSS); 2) investigating at least one component of the KAP model regarding ADR reporting; 3) study population consisting of HCPs in Saudi Arabia (Physicians, Dentists, Pharmacists, Pharmacy Technicians and Nurses); 4)published in English. No restriction was applied to the setting, time or the quality of the study.
Exclusion criteria: 1) Study population consisting of students, interns, postgraduates, patients or the public; 2) qualitative study design.

2.3 Search Strategy
Research articles were retrieved from three databases (Science Direct, PubMed and OVID). Studies that were not cited in the above-mentioned databases were retrieved from Google Scholar. The keywords used in the search were: knowledge, attitude, perception, awareness, pharmacovigilance, adverse drug reaction, adverse drug reaction reporting and Saudi Arabia. The full search strategy for the databases is provided in Appendix Supplementary file 2. After the completion of the search, the records were transferred to Endnote software (V. X8: Clarivate Analytics, Philadelphia, PA) and any duplicates were removed. Studies based on title, abstract, and full text were screened following the pre-specified eligibility criteria.

2.4 STUDY SELECTION
Literature screening of the extracted articles was carried by examining the titles and abstracts for relevant inclusion criteria was conducted. Full-text articles were then evaluated against the inclusion and exclusion criteria. The articles selection process resulted in twenty-seven studies that were included in the systematic review (Figure 1).

2.5 Data Extraction and Quality Assessment
Data related to study characteristics, methodological details, main outcome measures, and findings was extracted from the selected articles and organized in an excel table to facilitate the assessment of their quality using STROBE (Strengthening The Reporting of Observational Studies in Epidemiology) checklist [11]. STROBE covers twenty-two criteria for study design quality and biases in the study. For each criterion met, the study was given one point; the highest score indicates that the quality of the study was high. Also the five items risk of bias in cross-sectional surveys of attitudes and practice was used [12].

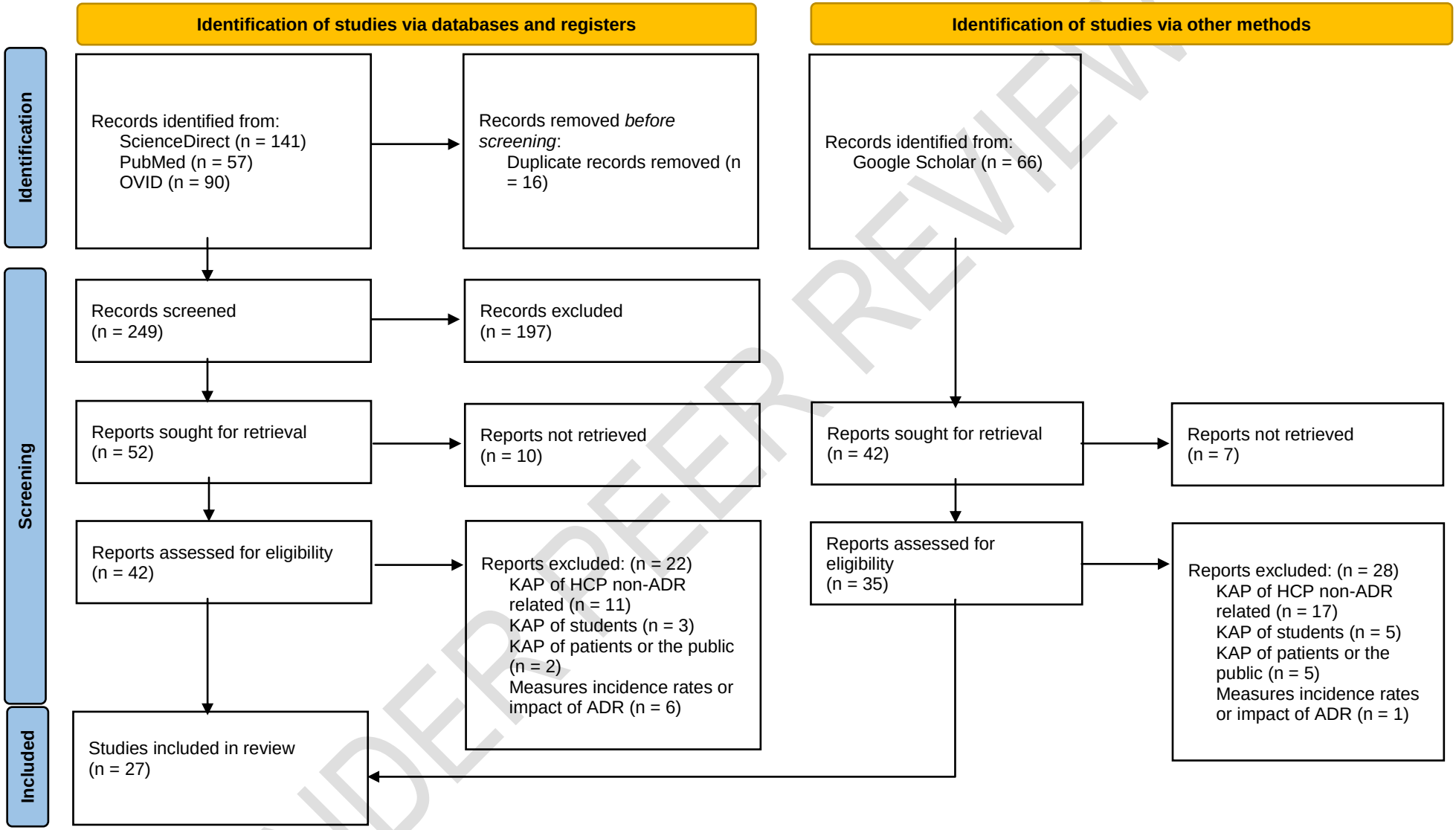

Fig 1. PRISMA 2020 Flow Diagram

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit:http://www.prisma-statement.org

2.6 Statistical Analysis

Qualitative analysis was conducted on the included published literature and the results (number and percentage) were reported in a narrative way, focusing on common findings that were observed across the included studies.

2.7 Patient and Public Involvement

Patients and the public were not involved in the design or conduct of this study.

3. RESULTS

3.1 Selection Process

A total of 354 articles were identified from all searches. After removal of duplicates; 338 records were screened by title and abstract, and full-text based on eligibility criteria, of which twenty-seven studies were included in the final review[13-39]. The PRISMA flow diagram for the complete study selection process is presented in Fig 1.

3.2 General Characteristics of the Included Studies

The 27 studies that are included in this systematic reviewwere published between 2013 and 2023. The characteristics of the included studies are displayed in Table 1. Ten studies included HCPs namely: physicians, dentists, pharmacists, pharmacy technicians and nurses[13, 16, 17, 21, 23-27, 39], 7 other studies focused on the KAP on community pharmacists[14, 15, 19, 30, 35, 36, 38], 3 focused on physicians[18, 22, 33], 3 focused on hospital pharmacists[20, 31, 34], 2 focused on hospital and community pharmacists[28, 37], 1 focused on physicians and dentists [33], and 1 focused on hospital pharmacists[32].

The total number of HCPs included in those studies was 6510, constituting sample sizes that ranged from 50 to 1172, the distribution of HCPs is presented in Fig 2. The response rates across the included studies varied from 40% to 97%. Twenty-five of these studies had evaluated the HCPs' knowledge toward ADR reporting [14-38], 17 had evaluated the attitude toward reporting ADR to theregulatory authority [13, 17-27, 32, 34-36, 39], while 4 had evaluated the perception of HCPs to report ADRs [14, 18, 31, 38]. All studies were cross-sectional studies that were conducted in different settings; hospitals (university hospitals, governmental or privatehospitals), community pharmacies and primary care centers around different cities and regions across Saudi Arabia.

3.3 Quality Assessment

Assessment of the quality of the included studies revealed that the study's design, rational, objectives, setting, descriptive data, outcome data, key results and interpretation were clearly stated in all included studies. Eligibility criteria, potential sources of bias, study size, missing data, potential confounders and unadjusted estimates information were not stated by many studies.

3.4 Main Findings

Knowledge, attitude and perception of HCPs in Saudi Arabia toward PV and ADR reporting were evaluated by 27 studies included in this systematic review and the most significant information is presented in Table 1.

Table 1. Characteristics of included studies that measured the knowledge, attitude and perceptions of healthcare professionals in Saudi Arabia toward ADR reporting

No.	Author, Publication Year	Setting / City or Region	Study Design	Data Collection Tool	Sample Size	HCP Category	Response Rate	Outcomes	Main Finding	Quality
1	Khan, 2013 [14]	7 CP/ Eastern Region, Alahsa	CSS	Self - administered Questionnaire	50	Community Pharmacists	71.43%	Knowledge and Perceptions	10% know of the existence of ADR reporting system	>75%
2	Mahmoud et al., 2014 [15]	14 IP, 68 CP 20 HP / Riyadh	CSS	Self - administered Questionnaire	104	Community Pharmacists	70.70%	Knowledge	22.1% aware of the ADR reporting process	<75%
3	Al-Hazmi, 2014 [13]	7 Hospitals / Holy City of Makkah	CSS	Self - administered Questionnaire	310	205 Physicians 25Dentists 49 Pharmacists 31Nurses	65.90%	Attitude	23.9% know to whom ADR should be reported	<75%
4	Abdel-Latif and Abdel-Wahab, 2015 [16]	9 Hospitals / Al-Madinah Al-Munawwarah	CSS	Self - administered Questionnaire	384	148Physicians 37 Pharmacists 41 Pharmacists Technicians 158 Nurses	65.64%	Knowledge	39.6 % aware of the regulatory body following ADR reporting	<75%
5	Alshammari et al., 2015 [17]	12 Hospitals / Riyadh, Dammam andJeddah	CSS	Self - administered Questionnaire	323	110Physicians 106 Pharmacists 104Nurses 3Others	72%	Knowledge and Attitude	36.9% know the regulatory body to whom the ADR should be reported	<75%
6	Rabba and Ain, 2015 [19]	Randomly selected CP / Al-Kharj	CSS	Self - administered Questionnaire	53	Community Pharmacists	81%	Knowledge and Attitude	21% know where to report ADRs	<75%
7	Al-Arifi et al., 2015 [18]	King Khalid UH / Riyadh	CSS	Self - administered Questionnaire	73	Physicians	81.09%	Knowledge, Attitude and Perception	41.4% unaware of the availability of the ADR reporting forms	<75%
8	Almandil, 2016 [21]	King Fahd UH / Khobar	CSS	Self - administered Questionnaire	331	161 Physicians 39 Pharmacists 21 Pharmacy Technicians 110 Nurses	82.75%	Knowledge and Attitude	43.8% did not know how to report ADR	>75%
9	Bakhsh et al., 2016 [22]	3 GH / Jeddah	CSS	Self - administered Questionnaire	337	Physicians	87.50%	Knowledge and Attitude	38.9 % aware of the existence of ADR reporting policy	>75%

10	Alharbi et al., 2016 [20]	4 Gov. H and 7 PCC/ Al Madinah Al Munawarah	CSS	Self - administered Questionnaire	103	Hospital Pharmacists	79%	knowledge and Attitude	48.5% know the ADR reporting process to the SFDA	>75%
11	AlShammari and Almoslem, 2018 [25]	9 TCH / Riyadh, Qassim and Eastern Region	CSS	Self - administered Questionnaire	336	55 Physicians 138 Pharmacists 110 Nurses	70%	Knowledge and Attitudes	67% unaware of the regulatory body monitoring ADRs	>75%
12	Moinuddin et al., 2018 [26]	King Saud Medical City / Riyadh	CSS	Self - administered Questionnaire	399	52 Physicians 4Dentists 32Pharmacists 301Nurses 10others (technicians)	88.60%	Knowledge and Attitude	34.8% unaware of how to report ADR	>75%
13	Tadvi et al., 2018 [27]	Hospitals, PHC, MC and other HCP / Majmaah	CSS	Self - administered Questionnaire	148	18 Physicians 25Pharmacists 42 Nurses	59.20%	Knowledge and Attitude	63.5% aware of the regulatory body to whom the ADR should be reported	>75%
14	Ali et al., 2018 [24]	Health Centers / Dammam	CSS	Self - administered Questionnaire	136	17 Physicians 41Pharmacists 59 Nurses 19Other HCPs	84.37%	Knowledge and Attitude	73.33% unaware of the regulatory body to whom ADR should reported	>75%
15	Abomughayedh and Ali, 2018 [23]	Aseer Central Hospital / Aseer Region	CSS	Self - administered Questionnaire	189	61Physicians 39Pharmacists 89Nurses	82.17%	Knowledge, Attitude	20.1% had reported the ADR to regulatory body	<75%
16	Al Doughan et al., 2019 [28]	HP and CP / Riyadh, Eastern Province, Jeddah and Other Cities	CSS	Hard copy or online distributed Questionnaire	263	208Hospital Pharmacists 55Community Pharmacists	-	Knowledge	26.62% aware of the period required to report serious ADR	<75%
17	Alshayban et al. 2020 [31]	MOH and Other Hospitals	CSS	Interviews and online Self - administered Questionnaire	234	Hospital Pharmacists	51.10%	Knowledge and Perception	80.8% aware of the regulatory body to whom ADR should be reported	>75%
18	Ali et al., 2020 [30]	CP / Dammam	CSS	Online Self - administered Questionnaire	101	Community Pharmacists	67.33%	Knowledge	46.53 believe it is important to report ADR	<75%
19	Al-Mutairi et al., 2021 [32]	Public, Private, and UH / Riyadh	CSS	Self - administered Questionnaire	289	Hospital Pharmacists	82.60%	Knowledge and Attitude	96.2% aware of the PV center in the country	>75%
20	Al-Abdulkarim et al., 2021 [29]	NGH / Riyadh	CSS	Self - administered Questionnaire	240	Physicians	40%	Knowledge	81% unaware of the ADR reporting system	>75%

21	Almasri, 2021 [38]	Community Pharmacies / Jeddah	CSS	Self - administered Questionnaire	144	Community Pharmacists	71.43%	Knowledge and Perception	56.4% did not know of the existence of the NPC program	<75%
22	Alomi et al., 2021 [33]	All geographical locations / Saudi Arabia	CSS	Online Self - administered Questionnaire	151	111Physicians 39Dentists	60.15%	Knowledge	45.33% knew the official form of ADR reporting system	>75%
23	Alshabi et al., 2022 [34]	5 GH/ Najran	CSS	Self - administered Questionnaire	102	Hospital Pharmacists	70.30%	Knowledge and Attitude	95% aware of the existence of the ADR reporting system	>75%
24	Alsheikh and Alasmari, 2022 [35]	CP/ Saudi Arabia	CSS	Self - administered Online Questionnaire	1172	Community Pharmacists	95.20%	Knowledge and Attitudes	70.8% knew about the ADR reporting form	>75%
25	Alqahtani et al., 2023 [39]	Social Media HCP related groups / Jazan Province	CSS	Online Self - administered Questionnaire	351	115Physicians 125 Pharmacists 21 Pharmacists Technicians 90 Nurses	76.30%	Attitudes	9.7% believe that attending workshops and having training related to ADR reporting is essential for HCPs	>75%
26	Alghazwani et al., 2023 [37]	38 CP, 57 HP 1 PMC,1 OPP / Asir Region	CSS	Self - administered Questionnaire	97	39Community Pharmacists 58Hospital Pharmacists	97%	Knowledge	41.2% did not regularly report the encountered ADR	>75%
27	Abdulsalim et al., 2023 [36]	CP / Qassim	CSS	Self - administered Questionnaire	209	Community Pharmacists	96%	Knowledge and Attitudes	85.6% do not know how to report ADRs	>75%

ADR: Adverse Drug Reaction. CSS: Cross-sectional Study. CP: Chain Pharmacy. GH: General Hospital. Gov. H. Governmental Hospital. *HP: Hospital Pharmacy. IP: Independent Pharmacy.* MC: MedicalColleges. PCC: Primary Care Center.NGH: National Guard Hospital. NPC: National Pharmacovigilance Center. OPP: Outpatient Pharmacy. PMC: Primary Medical Center. SFDA: Saudi Food and Drug Authority. TCH: Tertiary Care Hospital.UH: University Hospital.

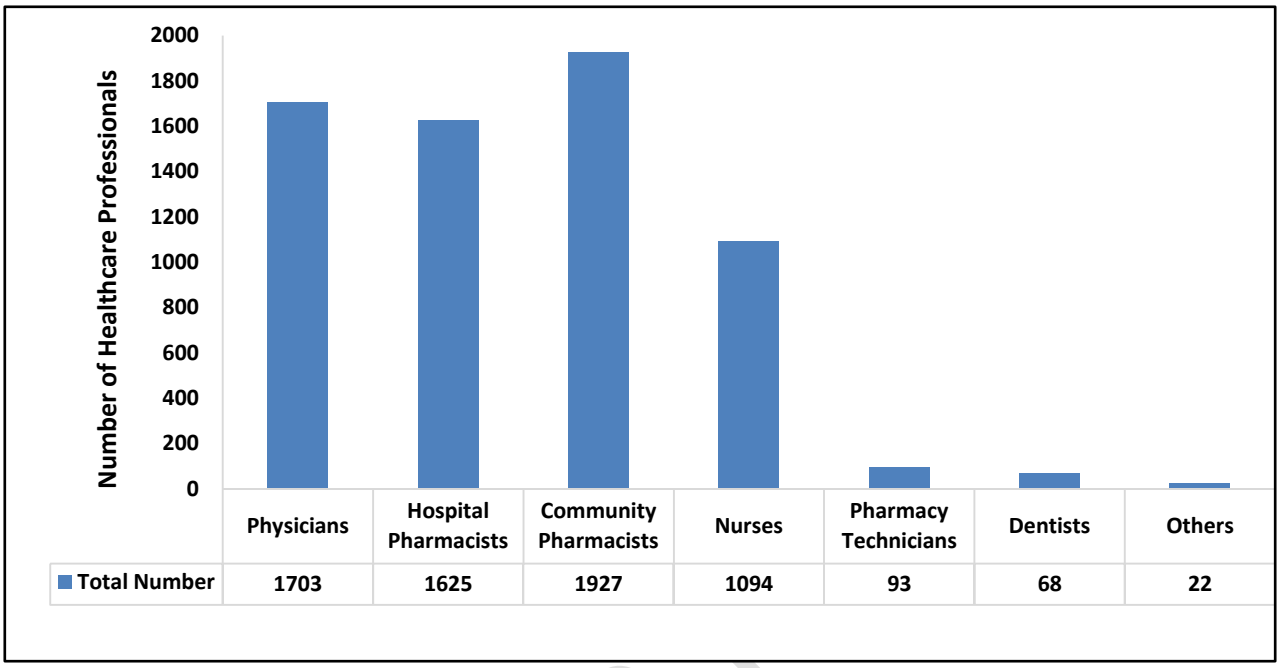

Fig 2. Healthcare Professionals Distribution

3.4.1 Adverse Drug Reaction Reporting Knowledge

Knowledge of HCPs toward PV and ADR reporting was evaluated by several questions and the most common question asked was about the knowledge of HCPs of the availability of the Saudi FDA vigilance system for ADR reporting in the country. The evaluation of participating HCPs in these studies revealed that their knowledge ranged from 10% to 95%[13-20, 22, 24, 25, 27, 29-31, 34, 37-39] . The second most frequently reported question was about the knowledge of the national regulatory body in Saudi Arabia responsible for receiving and following ADR reporting in the country. The knowledge of HCPs as reported by the reviewed studies ranged from 4.5% to 96.20% [13, 15, 18, 21-23, 25, 26, 28, 31-39]. Another question that was frequently asked was about the official ADR reporting form provided for HCPs to submit their reports to the NPC. Evaluation of the HCPs participating in these studies indicated that their knowledge ranged from 11% to 100% [18, 19, 22-24, 26, 28, 30, 32, 33, 35, 39]. Beside asking about the definition of PV and ADR few studies have evaluated the knowledge of HCPs of the International PV Center, its location, the WHO online database for ADR reporting and the common scale for establishing causality of ADRs (Appendix Supplementary file 3).

3.4.2 Adverse Drug Reaction Reporting Attitude

The attitude of HCPs toward ADR reporting and PV was evaluated by many studies and the most common questions asked were whether the HCPs believe that ADR reporting is their professional obligation and whether they did report ADR during their practice. Many HCPs believed that ADR reporting is a professional obligation and this belief ranged from 12.80% to 90.20%[13, 17, 19-21, 23, 25, 27, 30, 32, 34-36, 39]. The attitude of HCPs toward reporting ADR is indicated by their actual involvement in reporting ADR during their practiced and it ranged from 11.20% to 83%[15, 19-27, 31, 34, 36, 39]. Other studies have assessed the attitude of the HCPs toward the ease of using the online reporting system, the time

consumed in reporting ADR, andwhether having incentivesimpact their attitude of submitting more ADR reports (Appendix Supplementary file 3).

3.4.3 Adverse Drug Reaction Reporting Perception

Few of the included studies had evaluated the perception of HCPs toward ADR reporting and most of these studies evaluated theperception by asking whether the HCPs think that reporting ADR will positively impact the healthcare (HC) system, patient care, improves the quality of life, or contributes to drug safety. The perception of HCPs toward this question ranged from 46.53% to 100% [14, 18, 20, 26, 29, 30, 34-36, 39]. The studies also show that HCPs think that it is important to report ADR and their perception was from 11.34% to 97%[13, 17, 19, 21, 23, 24, 31, 34, 36, 38], and they believe it should be compulsory for HCPs to report ADR reaction with a perception ranged from 12% to 93.80%[13, 18, 19, 25, 26, 30, 31, 35, 39].The perception of HCPs toward whom among the HCPs they believe is responsible to report ADR to the Saudi FDA; the physicians, pharmacists or all HCPs are responsible was evaluated, also somestudiesevaluated the perception of HCPs toward the inclusion of PV training in undergraduate curriculum (Appendix Supplementary file 3).

4. DISCUSSION

This systematic review of the literature focusing on the KAP of HCPs toward ADR reporting and their contribution to PV in Saudi Arabia.It revealed an active interest among researchers in the country to assess the national PV status in different healthcareinstitutions and HCPs practices to ensuredrug safety and provide quality healthcare to patients and the public nationwide. Different healthcare institutions were included in the reviewed studies; governmental and private, tertiary care hospitals, primary care centers, outpatient, hospital and community pharmacies. These institutions were distributed in different regions and cities in the country which in hindsight served as a testament to evaluate the dissemination ofa standardized practice in these institutions in terms of PV and ADR reporting process.

The HCPs included in these studies are those who are in direct contact with patients and hence are in good position to witness, observe and thus report ADR when they are encountered. Community pharmacists were the largest group of HCPs that were evaluated in the included studies, followed by physicians, hospital pharmacists and nurses respectively.

The KAP questionnaires that were utilized by the reviewed studies differ to great extent among the included 27 studies and did not follow a standardized validated measures nor standardized question items. Very few studies had indicated the performance of pilot test or applied internal consistency measures, whichlimit the development of representative conclusion assessing the knowledge, attitude and perception of HCPs toward ADR reporting[33, 36-39].

In general knowledge assessment of HCPs toward PV and ADR reporting indicated that pharmacists had better knowledge of PV, ADR reporting, and related policies and guidelines compared to physicians and nurses[16, 21, 27, 33, 39].Knowledge comparison between hospital and community pharmacists revealed that hospital pharmacists are much more knowledgeable of the ADR reporting process, where and how to report ADR to the Saudi FDA PV system. Also, hospital pharmacists had the advantage of more clinical experiences and involvement in professional discussions about ADR reactions assessment and evaluation[28, 37]. Community pharmacists'knowledge of the NPC spontaneous reporting system was low, and indicated that they require more training from the Saudi FDA on utilizing the reporting system. Also they were unaware if they can submit ADR reports as community pharmacist, and they relate their low interest in reporting ADR to several factors such as: time consumption, workload, they believe that it is more of physician and hospital pharmacists duty than theirs, fear of reporting incorrect ADR, unawareof ADR reporting and availability of the ADR reporting form[14, 15, 19, 30, 35, 36, 38].

In terms of attitude, although many studies indicated that the participating HCPs believe that ADR reporting is their professional obligation[13, 17, 19-21, 23, 25, 27, 30, 32, 34-36, 39], ADR was reported by considerably few HCPs [15, 21-25, 36]. Also, very few HCPs indicated that they had attended Continuous Medical Education (CME) workshops and training sessions related to PV and ADR reporting[21, 22, 24, 25, 27, 28, 37]. In some studies, HCPs indicated that their lack of interest in reporting ADR was because they find it difficult to spontaneously report ADRs (55%) [39] and they believe that the reporting form was too complicated for them to fill (56.70%, 61%) [25, 35].

Many HCPs perceive that ADR reporting has a positive impact on healthcare, drug safety and improves the quality of patient's life [14, 18, 20, 26, 29, 34-36], and admit that it is important to report ADR [17, 19, 21, 23, 31], but underreporting seems very common among most of the studies when it comes to the practice of actual submission of ADR report to the Saudi FDA. Some HCPs are not aware of the NPC as the responsible regulatory body of receiving ADR reports [15, 26].Some studies had investigated the factors and barriers that might have contributed to underreporting by HCPs. The most common factors that were frequently reported by HCPswere workload and lack of time [13, 15, 17-20, 25, 26, 30, 32, 36, 37]. In terms of the utilization of the NPC provided ADR reporting system some HCPs indicated that not knowing how to report the ADR was the main factor for not reporting ADRs [13, 15, 18, 21, 22, 26], while other HCPs indicated the unavailability of the reporting form [13, 19]or thatthe report form was not clear [25].

The findings of this systematic review are consistent with similar studies like Balan[40], Anbeo and Abacoglu[41], Khan et al. [42], and Bhagavathula et al. [43], that had evaluated the KAP of HCPs toward PV and ADR reporting. Thus, it is recommended that HCPs participation and contribution toward PV and ADR reporting should be enhanced by providing continuous education sessions and workshops that should be conducted on a regular bases by the Saudi FDA and increase the awareness of HCPs of the importance of ADR reporting in PMS to ensure drug safety and provide quality healthcare practices to patients and the public.

Some interventional studies conducted in Saudi Arabia that have tested the effect of training and provision of incentives in stimulating the compliance of HCPs in ADR reporting. Ali et al. reported an increase in compliance of HCPs in which the number of ADR reporting increased by 40.6 (95% confidence interval: 26.1-55.1) after the provision of incentives to the reporting HCPs. The study also reported that this significant increase in ADR reports was associated with the profession of the reporting HCP and the seriousness of the reported ADR ($P < 0.001$)[44]. Cheema et al. conducted a randomized controlled trial to determine the effect of structured education in improving the knowledge of hospital pharmacists in Saudi Arabia toward ADR reporting, utilizing Saudi FDA guidelines. The group noticed a significant improvement in the mean knowledge score of participating hospital pharmacists from 7.67 ($\pm$ 2.1) at baseline to 11.22 ($\pm$ 0.4) (95% CI -4.5 to -2.5; $p < 0.0001$), compared to unchanged mean knowledge score in the control group (6.71 ($\pm$ 2.3))[45].

Although the results of the included studies were generated from different KAP assessment tools, they provided wealth of information about the status of PV and ADR reporting process available to the NPC in the country. One limitation of the study is its inability to provide useful data to conduct meta-analysis due to the heterogeneity of the utilized KAP items even though quality assessment measures were conducted to minimize the presence of potentialbias.

5. CONCLUSION

The knowledge, attitude and perception of healthcare professionals in Saudi Arabia toward adverse drug reaction reporting and pharmacovigilance was evaluated. The healthcare professionals had good knowledge of the main concepts of pharmacovigilance and adverse drug reaction reporting. Their attitude indicated professional obligation toward reporting, but it is affected by workload, lack of time and unavailability of the report forms. They perceive

the submission of any adverse drug reaction report as being very important and should be made compulsory by the drug regulatory authority. To improve the compliance of healthcare professionals to contribute to pharmacovigilance and adverse drug reaction reporting, it is recommended that continuous education and training sessions should be provided by the Saudi FDA to the healthcare professionals.

SUPPORTING INFORMATION

S1 APPENDIX.
The Search strategy. (PDF)

S2 APPENDIX.
PRISMA 2020 checklist. (PDF)

S3 APPENDIX.
Questions used to measure knowledge, attitude, and perceptions of HCPs toward ADR reporting. (PDF)

REFERENCES

1. Tan, X., et al., *Investigation of the characteristics of medication errors and adverse drug reactions using pharmacovigilance data in China.* Saudi Pharm J, 2020. **28**(10): p. 1190-1196.
2. Hadi, M.A., et al., *Pharmacovigilance: pharmacists' perspective on spontaneous adverse drug reaction reporting.* Integr Pharm Res Pract, 2017. **6**: p. 91-98.
3. Alshammari, T.M., M. Alshakka, and H. Aljadhey, *Pharmacovigilance system in Saudi Arabia.* Saudi Pharm J, 2017. **25**(3): p. 299-305.
4. SFDA. *SFDA. Overview of Saudi Food and Drug Authority. About SFDA. 2023*. 2023 accessed 27/5/2023; Available from: https://www.sfda.gov.sa/en/overview.
5. SFDA. *SFDA. Circulated to inform the pharmacovigilance center. SFDA Circulars. 2009*. SFDA Circulars 2009; Available from: https://www.sfda.gov.sa/sites/default/files/2019-09/Circulated_to_inform_the_pharmacovigilance_center_0.pdf.
6. Alharf, A., et al., *Saudi Vigilance Program: Challenges and lessons learned.* Saudi Pharm J, 2018. **26**(3): p. 388-395.
7. El-Metwally, A., *Current status, and future prospects of pharmaco-epidemiology and post-marketing surveillance in Saudi Arabia: A review of literature.* Saudi Pharm J, 2018. **26**(5): p. 629-633.
8. Biagi, C., et al., *Underreporting in pharmacovigilance: an intervention for Italian GPs (Emilia-Romagna region).* Eur J Clin Pharmacol, 2013. **69**(2): p. 237-44.
9. Aljadhey, H., et al., *A qualitative exploration of the major challenges facing pharmacovigilance in Saudi Arabia.* Saudi Med J, 2015. **36**(9): p. 1097-102.
10. Page, M.J., et al., *The PRISMA 2020 statement: an updated guideline for reporting systematic reviews.* BMJ, 2021. **372**: p. n71.
11. von Elm, E., et al., *The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies.* J Clin Epidemiol, 2008. **61**(4): p. 344-9.

12. Guyatt G, B.J. *Methods commentary: Risk of bias in cross-sectional surveys of attitudes and practices.* 2021 [cited 2023; Available from: https://www.distillersr.com.
13. IL, N.A.-H.a.N., *Attitude and Awareness of Adverse Drug Reaction Reporting by Health Professionals in Seven Hospitals in the Holy City of Makkah, Kingdom of Saudi Arabia.* Journal of Clinical Trials, 2013. **3**(3).
14. Khan, T.M., *Community pharmacists' knowledge and perceptions about adverse drug reactions and barriers towards their reporting in Eastern region, Alahsa, Saudi Arabia.* Ther Adv Drug Saf, 2013. **4**(2): p. 45-51.
15. Mahmoud, M.A., et al., *Community pharmacists' knowledge, behaviors and experiences about adverse drug reaction reporting in Saudi Arabia.* Saudi Pharmaceutical Journal, 2014. **22**(5): p. 411-418.
16. Abdel-Latif, M.M.M. and B.A. Abdel-Wahab, *Knowledge and awareness of adverse drug reactions and pharmacovigilance practices among healthcare professionals in Al-Madinah Al-Munawwarah, Kingdom of Saudi Arabia.* Saudi Pharmaceutical Journal, 2015. **23**(2): p. 154-161.
17. Alshammari, T.M., et al., *Knowledge and attitude of health-care professionals in hospitals towards pharmacovigilance in Saudi Arabia.* Int J Clin Pharm, 2015. **37**(6): p. 1104-10.
18. Idris, A., *Knowledge, Attitude and Perception of Physicians towards Adverse Drug Reaction Reporting at King Khalid University Hospital, Riyadh, Saudi Arabia.* Tropical Journal of Pharmaceutical Research, 2015. **14**: p. 907-911.
19. Rabba, A. and M.R. Ain, *Pharmacovigilance Study: Exploring the Role of Community Pharmacists in Adverse Drug Reactions Reporting in Alkharj City, Saudi Arabia.* LATIN AMERICAN JOURNAL OF PHARMACY, 2015. **34**: p. 901-6.
20. Alharbi, F., A. Bahnassi, and W. Alonazie, *Attitude, knowledge and experience of hospital pharmacists with pharmacovigilance in a region in Saudi Arabia: A cross-sectional study.* Tropical Journal of Pharmaceutical Research, 2016. **15**: p. 1773-1779.
21. Almandil, N.B., *Healthcare professionals' awareness and knowledge of adverse drug reactions and pharmacovigilance.* Saudi Med J, 2016. **37**(12): p. 1359-1364.
22. Bakhsh, T., et al., *Assessment of Hospital Physicians' Knowledge, Awareness, Attitude and Practice of Reporting Adverse Drug Reactions in Jeddah, Saudi Arabia.* British Journal of Medicine and Medical Research, 2016. **16**: p. 1-16.
23. Ali, A.M.A.a.M.S., *Evaluation of Knowledge, Awareness, and Practice of Adverse Drug Reactions at Aseer Central Hospital in Saudi Arabia.* Journal of Medical and Pharmaceutical Sciences, 2018. **2**(3): p. 48-66.
24. Ali, M.D., et al., *Knowledge, Practice and Attitudes Toward Pharmacovigilance and Adverse Drug Reactions Reporting Process Among Health Care Providers in Dammam, Saudi Arabia.* Curr Drug Saf, 2018. **13**(1): p. 21-25.
25. AlShammari, T.M. and M.J. Almoslem, *Knowledge, attitudes & practices of healthcare professionals in hospitals towards the reporting of adverse drug reactions in Saudi Arabia: A multi-centre cross sectional study.* Saudi Pharmaceutical Journal, 2018. **26**(7): p. 925-931.
26. Moinuddin, K., et al., *Knowledge and Attitude of Health-Care Professionals Toward Adverse Drug Reactions Reporting at King Saud Medical City.* Journal of Pharmacy & Bioallied Sciences, 2018. **10**: p. 29-34.
27. Tadvi, N., et al., *Knowledge, Attitude and Practice of Pharmacovigilance in Healthcare Professionals and Medical Students in Majmaah, Saudi Arabia Care Centre.* 2018.
28. Fatimah Fouad Al, D., A. Yousef Ahmed, and I. Mais Hasan, *Pharmacist's Awareness and Knowledge of Reporting Adverse Drug Reactions in Saudi Arabia.* International Journal of Pharmacology and Clinical Sciences, 2019. **8**(1).
29. alabdulkarim, D., et al., *Knowledge and Barriers Among Physicians Toward Adverse Drug Reaction Reporting at a Tertiary Care Hospital in Saudi Arabia.* Hospital pharmacy, 2020. **56**.
30. Ali, M., et al., *Community Pharmacist's Knowledge, Practice and Barrier towards Reporting of Adverse Drug Reactions in Dammam, Saudi Arabia: A Cross-Sectional Survey Based Study.* Journal of Young Pharmacists, 2020. **12**: p. 81-85.
31. Alshayban, D., et al., *Pharmacovigilance Perception and Knowledge Among Pharmacists and Interns in Saudi Arabia.* Risk Management and Healthcare Policy, 2020. **Volume 13**.

32. Al-Mutairi, A., et al., *Medication safety knowledge, attitude, and practice among hospital pharmacists in tertiary care hospitals in Saudi Arabia: a multi-center study.* 2021. **79**(1): p. 130.
33. Alomi, Y., N. Alamoudi, and A. Almasoudi, *Physician's Knowledge of Adverse Drug Reaction in Saudi Arabia.* International Journal of Pharmacology and Clinical Sciences, 2021. **10**: p. 6-12.
34. Alshabi, A.M., et al., *Knowledge, attitude and practice of hospital pharmacists towards pharmacovigilance and adverse drug reaction reporting in Najran, Saudi Arabia.* Saudi Pharmaceutical Journal, 2022. **30**(7): p. 1018-1026.
35. Alsheikh, M.Y. and M.M. Alasmari, *A National Survey of Community Pharmacists' Viewpoints About Pharmacovigilance and Adverse Drug Reaction Reporting in Saudi Arabia.* Frontiers in Pharmacology, 2022. **13**.
36. Abdulsalim, S. and M. Farooqui, *Evaluation of Knowledge, Attitudes, and Practices about Pharmacovigilance among Community Pharmacists in Qassim, Saudi Arabia.* 2023. **20**(4).
37. Alghazwani, Y., et al., *The perspective of pharmacist on pharmacovigilance and adverse drug reaction reporting in Asir region, Saudi Arabia.* Eur Rev Med Pharmacol Sci, 2023. **27**(4): p. 1667-1680.
38. Almasri, D., *Adverse Drug Reactions Reporting System: Perceptions and Awareness of Community Pharmacists' in Jeddah, Saudi Arabia.* Journal of King Abdulaziz University - Medical Sciences, 2023. **28**(1).
39. Alqahtani, S.S., et al., *Healthcare professionals' awareness, attitudes and practices towards pharmacovigilance and spontaneous adverse drug reaction reporting in Jazan Province, Saudi Arabia: A survey study.* Saudi Pharmaceutical Journal, 2023. **31**(6): p. 979-988.
40. Balan, S., *Knowledge, attitude and practice of Malaysian healthcare professionals toward adverse drug reaction reporting: a systematic review.* Int J Pharm Pract, 2021. **29**(4): p. 308-320.
41. Anbeo, Z.G. and N. Abacıoğlu, *A Systematic Review of Healthcare Professionals' Knowledge, Attitudes, and Practices Regarding Adverse Drug Reaction Reporting in Ethiopia.* 2023. **20**(3): p. 198-209.
42. Khan, Z., et al., *Knowledge, attitude, practice and barriers towards pharmacovigilance and adverse drug reactions reporting among healthcare professionals in Turkey: a systematic review.* Curr Med Res Opin, 2022. **38**(1): p. 145-154.
43. Bhagavathula, A.S., et al., *Health Professionals' Knowledge, Attitudes and Practices about Pharmacovigilance in India: A Systematic Review and Meta-Analysis.* PLoS One, 2016. **11**(3): p. e0152221.
44. Ali, S., et al., *Adverse drug reaction reporting in a large tertiary hospital in Saudi Arabia: results of an incentive strategy.* Ther Adv Drug Saf, 2018. **9**(10): p. 585-590.
45. Cheema, E., et al., *Assessing the impact of structured education on the knowledge of hospital pharmacists about adverse drug reactions and reporting methods in Saudi Arabia: an open-label randomised controlled trial.* Drugs Ther Perspect, 2019. **35**(6): p. 296-300.