

**KNOWLEDGE, ATTITUDE AND PRACTICE OF HEALTH PROFESSIONALS
TOWARDS ADVERSE DRUG REACTIONS REPORTING****Hager Ali Saleh^{1*}, Albert Figueras² and Annie Fourrier-Réglat³**¹Department of Health Services Management, Faculty of Public Health and Health Informatics, Umm Al-Qura University, Mecca, Saudi Arabia.²Fundació Institut Català de Farmacologia. Departament de Farmacologia, Terapèutica i Toxicologia, Universitat Autònoma de Barcelona, Spain.³Associate Professor, Université de Bordeaux, Bordeaux, France.***Correspondence for Author: Hager Ali Saleh**

Department of Health Services Management, Faculty of Public Health and Health Informatics, Umm Al-Qura University, Mecca, Saudi Arabia.

Article Received on 29/05/2016

Article Revised on 19/06/2016

Article Accepted on 09/07/2016

ABSTRACT

Background: Medicines related morbidity and mortality is one of the major health problems which is beginning to be recognized by health professionals. The effectiveness of post-marketing surveillance program is directly dependent on the active participation of health professionals. Health professionals are in the best position to report on suspected adverse drug reactions observed in their everyday patient care. **Objective:** To determine the current status of knowledge, practices, and attitudes towards adverse drug reactions reporting among healthcare professionals. **Method:** 27 studies which were published from 2010 to 2015 extracted from three databases (Medline, SCOPUS and Science Direct- Elsevier) were reviewed. **Results:** According to reviewed articles, Healthcare professionals have a poor knowledge and practice towards adverse drug reactions reporting, although their positive attitude. **Conclusion:** This review enforces the need for appropriate training to increase Healthcare professionals' awareness. It provides information about how to improve adverse drug reactions reporting status.

KEYWORDS: Adverse Drug Reactions, pharmacovigilance, Knowledge, Attitude, Practice.**1. INTRODUCTION**

The World Health Organization defines an adverse drug reaction (ADR) as "a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function." (World Health Organization, 1972). While an adverse drug event (ADE) is an injury resulting from the use of a drug, it includes harm caused by the drug (ADR and overdoses) and harm from the use of the drug including dose reductions and discontinuations of drug therapy (World Health Organization, 2011; Nebeker et al., 2004).

According to ASHP, adverse drug reactions (ADRs) are which results in temporary or permanent harm, disability, or death or that requires discontinuing the drug, changing the drug therapy, modifying the dose, necessitates admission to a hospital, prolongs stay in a health care facility, necessitates supportive treatment, significantly complicates diagnosis, and negatively affects prognosis (American Society of Health-System Pharmacy, 1995). ADRs are global problems in both developing and developed countries, they contribute to a significant number of morbidity and mortality (World Health Organization, 2002; Oshikoya KA, 2006; Classen et al.,

1997; Waller, 2010). A meta-analysis study was published in 1998, ranked ADRs to be between fourth to sixth causes of death in the US (Lazarou et al., 1998). A study in the UK published in 2004 suggested that 6.5% of hospital admission were caused by ADRs, lead to a median of eight days of hospitalization and estimated annual cost to the National Health Services around €466 million (Pirmohamed et al., 2004).

The main aim of documenting ADRs is to prevent future injuries for patients. New ADRs are often discovered when drugs are used in larger or in different populations than studied during initial clinical trials (Nebeker et al., 2004; Jasmine C. Gatti, 2012). Clinical trials do not detect all possible adverse effects because; Study period do not long enough to detect adverse events that take a long time to develop, do not include enough patients to detect adverse events that occur rarely, do not include all of the different types of people who might use the drug and who might be more susceptible to some adverse events, such as older people, children, pregnant women, or people with other medical conditions (Department of Health Therapeutic Goods Administration, 2015). Therefore, after medicines licensing documentation and reporting of ADRs becomes important in clarifying the side effect profile of a drug which may influence drug

labeling or alerts that has impact in prescribing practice and help in protecting public health (Nebeker *et al.*, 2004; Jasmine C. Gatti, 2012; Jones, 2008).

The effectiveness of a post-marketing surveillance program is directly dependent on the active participation of health professionals. Health professionals are in the best position to report on suspected ADRs observed in their everyday patient care. All healthcare providers (physicians, pharmacists, nurses, dentists and others) should report ADRs as a part of their professional responsibility, even if they are doubtful about the precise relationship with the given medication (World Health Organization, 2002; Faich, 1986). Therefore, it is important to increase their awareness about pharmacovigilance as it will be helpful in improving the status of ADRs reporting (Pimpalkhute *et al.*, 2012). Before establishing any intervention, it is necessary to evaluate their knowledge, attitude and practices regarding ADRs reporting (Palaian *et al.*, 2011). The objective of this article is to determine through a literature review the current status of Knowledge, Attitudes and Practices (KAP) towards ADRs reporting among healthcare professionals (HCPs).

2. METHODS

Data sources and keywords

The following databases (Medline, SCOPUS and Science Direct- Elsevier) were considered to identify relevant publications related to KAP of health professionals on ADRs reporting. The search terms are Knowledge AND attitude* AND practice* AND health professional* AND ADRs report* and Mesh terms (Drug Related Side Effects, Adverse Reactions, Health Personnel) were identified to be used in combination with keywords. All the articles found in the different bibliography databases are reviewed first according to the title, then according to the information provided by the abstracts and then according to the full text. At each step, articles were retained or excluded for analysis. (Table 1 and figure 1).

Study selection

The inclusion criteria were English studies published from 2010 to 2015, papers with clear objectives to assess KAP, studies that report the tools used and studies with precise results. The search was last performed on May 2015.

Table 1: Publication selection process from each database.

Database	Number of citation identified from search strategy	Number of citation excluded on the basis of title	Number of citation excluded on the basis of abstract	Full text obtained
Medline	900	873	6	21
SCOPUS	8	4	1	3
Science direct	1000*	995	1	4

*3870 potentially relevant publications from them only 1000 publications can be viewed.

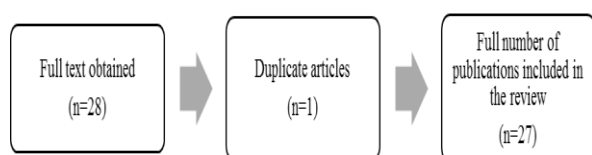


Figure 1: Overall Publications Selected.

3. RESULTS

Description of the articles included

A total of 27 articles met the inclusion and exclusion criteria. Figure 2 shows their distribution according to countries where the reviewed articles cover 16 countries, 8 developed countries (Canada, Italy, Oman, Saudi Arabia, Scotland, the UK, the US and Venezuela) and 8 developing countries (China, India, Iran, Jordan, Nigeria, Malaysia, Nepal, and Turkey). The highest number of studies was from India and Nigeria four studies for each. The (Table 2), summarize all the 27 articles according to the first author and publication year, study design, study participant, country and sample size. It revealed that two surveys were qualitative surveys using a structured interview (Walji *et al.*, 2011; Ting *et al.*, 2010) and the

other 25 surveys were quantitative surveys using self-administered questionnaire. Concerning healthcare professionals' categories were physicians, dental practitioners, hospitals and community pharmacists, herbal medicinal practitioners, nurses, non-medical prescribers and a mix of previous categories. The highest category was pharmacists (14 articles) followed by physicians (13 articles).

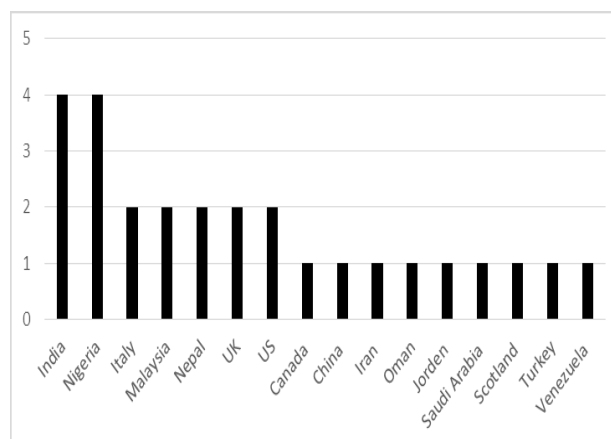


Figure 2: Distribution of Reviewed Articles according to Countries.

Table 2: Summary of the reviewed articles listed chronologically.

Studies	Study Design	Study participation	country	Sample size
(Pulford and Malcolm, 2010)	Cross-sectional using self-administered questionnaire.	Nurses, health visitor, GP and pediatrician	Scotland	91
(Ting et al., 2010)	Qualitative using structured audio recorded interview.	Community pharmacists	Malaysia	7
(Su et al., 2010)	Cross-sectional using self-administered questionnaire.	Hospital pharmacists	China	246
(Oreagba et al., 2011)	Cross-sectional using self-administered questionnaire.	Community pharmacists	Nigeria	332
(Chopra et al., 2011)	Cross-sectional using self-administered questionnaire.	Physicians	India	100
(Pérez García and Figueras, 2011)	Cross-sectional using self-administered questionnaire	Physicians and pharmacists	Venezuela	518 Physicians and 78 pharmacists
(Gavaza et al., 2011a) plus (Gavaza et al., 2011b)	Cross sectional using self-administered questionnaire.	Hospital and community pharmacists	The US	377
(Walji et al., 2011)	Qualitative using Semi-structured audio recorded interview	Community pharmacist	Canada	12
(Oreagba et al., 2011)	Cross-sectional using self-administered questionnaire.	Physicians	Nigeria	61
(Rehan et al., 2012)	Cross-sectional using self-administered questionnaire.	Resident Doctors and nurses	India	100 Physicians and 100 nurses
(Biagi et al., 2012)	Cross-sectional using self-administered questionnaire.	General Practitioners	Italy	168
(Khalili et al., 2012)	Cross-sectional using self-administered questionnaire.	nurses, physicians and pharmacists	Iran	82
(Pimpalkhute et al., 2012)	Cross-sectional using self-administered questionnaire.	Resident doctors in tertiary care teaching hospital	India	84
(Alan et al., 2013)	Cross-sectional using self-administered questionnaire.	Nurses and midwives	Turkey	329
(Osakwe et al., 2013)	Cross-sectional using mail and self-administered questionnaire.	physicians, pharmacists, nurses, medical lab scientists, radiographers and dentists	Nigeria	342
(Stewart et al., 2013)	Cross-sectional using self-administered questionnaire which sent by email.	Non-medical prescriber	The UK	613
(Hardeep et al., 2013)	Cross-sectional using self-administered questionnaire.	Physicians	India	61
(Yip et al., 2013)	Cross-sectional using self-administered questionnaire which sent by post.	General Dental Practitioners	The UK	130
(Awodele et al., 2013)	Cross-sectional using self-administered questionnaire.	Herbal Medicine Practitioners	Nigeria	378
(Pellegrino et al., 2013)	Cross-sectional using self-administered web questionnaire	Family Paediatricians	Italy	552
(Santosh et al., 2013a) plus (Santosh et al., 2013b)	Cross-sectional using self-administered questionnaire.	Physicians, nurses, and pharmacists	Nepal	162 doctor, 135 nurses and 32 pharmacist
(Jose et al., 2014)	Cross-sectional using self-administered questionnaire.	Community pharmacists	Oman	107
(Suyagh et al., 2014)	Cross-sectional using self-administered questionnaire.	Community and hospital Pharmacists,	Jorden	208
(Elkalmi et al., 2014)	Cross-sectional using self-administered questionnaire.	Community pharmacists	Malaysia	104
(Abdel-Latif and Abdel-Wahab, 2015)	Cross-sectional using self-administered questionnaire.	physicians, nurses, pharmacists', pharmacists' technicians	Saudi Arabia	384

Summary of results according to healthcare professionals' category

- Physicians

According to reviewed articles, 37% of physicians (Santosh *et al.*, 2013a), 59% (Hardeep *et al.*, 2013) and 73% (Chopra *et al.*, 2011) were aware of the existence of national pharmacovigilance Center, but 93.4% did not know its location (Hardeep *et al.*, 2013). Regarding their awareness about definitions of pharmacovigilance and ADRs, 38% (Chopra *et al.*, 2011), 64.3% (Pimpalkhute *et al.*, 2012), 77% (Hardeep *et al.*, 2013) and 82% (Pellegrino *et al.*, 2013) knew the pharmacovigilance definition while more than 50% of them were unable to identify the right definition of spontaneous ADR reporting (Pellegrino *et al.*, 2013), moreover 66% and 40% knew the definition of ADR and ADE, respectively (Chopra *et al.*, 2011), 42% and 32.7% were aware about type A and Type B ADRs, respectively (Santosh *et al.*, 2013a).

Regarding ADRs reporting, 94% agreed that spontaneous reporting is a part of their professional role (Biagi *et al.*, 2012), 74.4% would report reactions related to new drugs while 15% would report serious reactions, although all physicians agreed that the reporting is important, only 30% of them have reported an ADR before (Chopra *et al.*, 2011), 71% agreed that ADRs reporting should be obligatory and 90% agreed about establishing a pharmacovigilance Center in their institution (Hardeep *et al.*, 2013), 78.4% believed in the importance of ADRs reporting but 81% did not know the method to report (Santosh *et al.*, 2013a; Santosh *et al.*, 2013b), about one-third 35.7% thought the reporting should be only for newly marketed agents (Pimpalkhute *et al.*, 2012), 4.9% had reported ADRs and 95.1% were not aware about the existence of ADRs reporting system (Bello and Umar, 2011) and 61.95% has no knowledge of the reporting process (Pimpalkhute *et al.*, 2012). Regarding the reporting method, 47%, 31%, 13% and 9% preferred reporting to be by phone, drop box, email and personal visit, respectively and 93% expect to receive feedback after reporting (Rehan *et al.*, 2012).

- General Dental Practitioners (GDPs)

A study conducted in the UK indicated that, around three quarter of GDPs 74.9% were aware of the yellow card scheme, 88.5% indicated they never used the yellow scheme because they never see ADRs in their patients 58.5%. Only 2.3% said they made reports in the last two to four years. Furthermore, 26.2% stated they had a training in ADRs reporting (Yip *et al.*, 2013).

- Community pharmacists

According to the reviewed articles, 30% (Elkalmi *et al.*, 2014), 55% (Oreagba *et al.*, 2011) and 88.8% (Jose *et al.*, 2014) of pharmacists were aware of the existence of the national pharmacovigilance program. Regarding to the definition of pharmacovigilance and ADR, only 19% defined pharmacovigilance (Oreagba *et al.*, 2011) and 84% defined ADR correctly. Furthermore, 84.6% (Elkalmi *et al.*, 2014), 90% (Oreagba *et al.*, 2011) and 90.6% (Jose *et al.*, 2014) pharmacists considered ADRs

reporting as a part of their pharmaceutical care duties, in addition 73% believed that that they were the first point for ADR reporting by the public (Oreagba *et al.*, 2011).

Regarding the reporting of ADRs, 56% indicated that they had suspected an ADR without reporting it (Elkalmi *et al.*, 2014), 69.2% claimed that they reported to the regulatory authority (Jose *et al.*, 2014), while 85.9% stated they had never reported to the national pharmacovigilance Center (Pérez García and Figueras, 2011), furthermore, 68.3% were unaware of existing possibility of online reporting (Elkalmi *et al.*, 2014). 20.5% thought the reporting is only for events caused by new drugs and 42% said that events resulted from topical products should not be reported (Jose *et al.*, 2014) and almost all 99% were willing to practice pharmacovigilance if they trained (Oreagba *et al.*, 2011).

- Hospital Pharmacists

According to the reviewed articles, 84% and 65.6% were aware about the existence of the pharmacovigilance Center and its location, respectively (Santosh *et al.*, 2013a; Santosh *et al.*, 2013b). Regarding to pharmacovigilance and ADR definitions, 25.5% defined pharmacovigilance (Suyagh *et al.*, 2014), 69.5% (Su *et al.*, 2010) and 69.7% (Suyagh *et al.*, 2014) were able to define ADR, 62% were aware about type A and Type B ADRs (Santosh *et al.*, 2013a; Santosh *et al.*, 2013b). Regarding to reporting of ADRs, 67.9% had never reported any ADEs to FDA and 93.4% had not reported over last 12 months (Gavaza *et al.*, 2011a; Gavaza *et al.*, 2011b), 39.9% and 28.9% suggested the reporting for only serious and rare events, respectively. Most of them 97.6% agreed that ADRs represent an important problem in hospitals (Su *et al.*, 2010), 89.6% agreed that reporting to FDA help in educating others and improve patient safety (Gavaza *et al.*, 2011b).

Regarding their behaviour when facing patient with serious ADRs; 27% contact the physician, 24% direct patient to emergency room and only 6% report it although 95.2% agree that the reporting is their professional responsibility (Suyagh *et al.*, 2014).

- Herbal Medicine Practitioners

A study conducted in Nigeria revealed that, 26.2% respondents were pharmacists, 23.8% were Natural Health Practitioners and the remaining were traditional Herb Sellers. Most of them, 89.7% considered the herbal products as safe although, 91.2% of the pharmacist received some AE complained by users. These events were GIT problems, Skin Reaction, weight loss and others. And only 20.9% document these effects (Awodele *et al.*, 2013).

- Nurses

According to the reviewed articles, 30% of nurses were aware of the existence of the pharmacovigilance Center (Santosh *et al.*, 2013a; Santosh *et al.*, 2013b), 1.2% gave the name of that Center (Alan *et al.*, 2013) and 57.8%

knew its location (Santosh *et al.*, 2013a; Santosh *et al.*, 2013b). Regarding the definition of pharmacovigilance and ADR, 23% could correctly define pharmacovigilance (Alan *et al.*, 2013), 27% defined ADRs correctly (Rehan *et al.*, 2012), 50.4% and 67.4% were aware of type A and Type B ADRs, respectively (Santosh *et al.*, 2013a; Santosh *et al.*, 2013b).

Regarding the reporting of ADRs, 24.3% (Alan *et al.*, 2013), 63% (Santosh *et al.*, 2013a; Santosh *et al.*, 2013b) and 100% (Rehan *et al.*, 2012) of nurses agreed that ADRs reporting is important, 73% stated they reported ADRs to Center, 55% always record these reactions on the medical record, 27% did not inform anybody about this reaction as they thought it is a routine part of the treatment and 91% stated there was not any routine discussion on ADRs (Rehan *et al.*, 2012). Furthermore, 25% agreed that they can submit reports voluntary and 60% wanted reporting to be mandatory (Rehan *et al.*, 2012), 67% thought new drugs only need monitoring for ADRs (Rehan *et al.*, 2012). Regarding to the method of reporting, 83% did not know the method to report (Santosh *et al.*, 2013a; Santosh *et al.*, 2013b), 45%, 31%, 11% and 13% preferred reporting by phone, drop box, email and personal visit, respectively (Rehan *et al.*, 2012) and 82% expect to receive feedback after reporting (Rehan *et al.*, 2012).

- Non-medical prescribers

A study conducted in the UK revealed that, although 70.5% felt competent in all aspects of PV, only 57.3% received a PV training which its duration varied from 1 to 6 hours while 35.6% could not remember if they had been trained. Those who had training 13.9% said this training was not relevant to their practice and 34.2% agreed that they need further training. For their knowledge about the yellow card scheme, a seven true-false questions; only one-fifth, 22.8% answered questions correctly. For their attitudes and practice, 58.6% have submitted a yellow card, 22.1% agreed that they would not report unless they were sure the drug is the cause of reaction, most of them 98.6% disagreed that their reports make little or no contribution to pharmacovigilance and 16.2% agreed that they forgot the need to report. (Stewart *et al.*, 2013).

- Healthcare professionals (Mixed categories)

A study in Scotland, aimed to assess attitude and knowledge of HCPs mixing “nurses, physicians, health visitors, GP, community paediatricians”. It indicated that 90% were aware about their responsibility for ADRs reporting. However, less than 50% stated good knowledge about the yellow card and 9% did not know it. Around 90% felt they were confident in discussing suspected ADR with their colleagues (Pulford and Malcolm, 2010).

In Iran, a study was done to evaluate KAP of HCPs mixing “physicians, nurses and pharmacists” before and

after an educational program done by clinical pharmacists in teaching hospital. Before the intervention percentage of respondents ranged from 43.9% to 68.3% regarding identifying different goals of spontaneous reporting. After the intervention, percentages ranged between 53.7% and 85.4%. Regarding their believes, before intervention 67.0%, 23.2% and 4.9% agreed that reporting is a part of their professional role, yellow cards are complicated and were aware about what to report, respectively. After the intervention, those figures changed to 73.2%, 22% and 9.8%. Regarding the preferred method of reporting, 32%, 28.4% and 24.3% preferred to report yellow cards, online and by telephone, respectively. These figures were after the intervention 45.1%, 31.1% and 21.6%, respectively (Khalili *et al.*, 2012).

In Nigeria, a study aimed to evaluate Knowledge, Practice and impact of previous training for 341 healthcare professionals “physicians, pharmacists, nurses, medical lab scientists, radiographers, physiotherapists and dentists”. For the knowledge, 51% of the respondent who did not have training on pharmacovigilance defined pharmacovigilance correctly as compared to 77.7% among those who had training. Overall, 17% of those who had no training had good knowledge while those who had a training were 48.9%. Good practice score was found on 15.4% of those had not a training while it was 26.6% among those who had training (Osakwe *et al.*, 2013).

A study in Saudi Arabia, aimed to investigate Knowledge and awareness of 384 healthcare professionals “physicians, nurses, pharmacists and pharmacists’ technician”. It revealed that only one third 39.6% was aware about the existence of the national PV Center. The highest awareness 70.2% was found in pharmacists followed by pharmacists’ technician 61% then physicians 39.2% then nurses 27.2%. All respondents had a positive awareness of ADRs reporting and more than 80% of the physicians stated that they occasionally encountered ADR and 80% of the nurses stated they rare encountering ADR (Abdel-Latif and Abdel-Wahab, 2015).

Encouraging factors and barriers of ADRs Reporting

In five studies (Elkalmi *et al.*, 2014; Santosh *et al.*, 2013b; Stewart *et al.*, 2013; Pimpalkhute *et al.*, 2012; Su *et al.*, 2010), healthcare professionals stated factors that can encourage them to report. Almost of them stated they need for education and training, they need feedback after reporting and incentives (Table 3). Furthermore, in eight studies (Elkalmi *et al.*, 2014; Stewart *et al.*, 2013; Santosh *et al.*, 2013b; Pimpalkhute *et al.*, 2012; Biagi *et al.*, 2012; Chopra *et al.*, 2011; Walji *et al.*, 2011; Su *et al.*, 2010), indicated barriers faced by healthcare professionals. Almost agree on the lack of knowledge and lack of time (Table 4).

Table 3: Factors that can help in improving Reporting.

Studies	Healthcare professional	Encouraging factors
(Su et al., 2010)	Hospital pharmacists	- Education and training (n= 164, 66.7%). - More ward round (n= 108, 43.9%). - Encouragement by pharmacy department (n= 81, 32.9%). - Feedback (n= 54, 22%). - Fee for ADR reporting (n= 17, 6.9%).
(Pimpalkhute et al., 2012)	Resident Doctors	- Increasing awareness about PV through training and CMEs (n=28, 33.3%). - Make ADR reporting compulsory (n= 4, 4.8%). - Incentives (n = 5, 5.9%).
(Stewart et al., 2013)	Non-medical prescribers “pharmacists and nurses”	- Clear feedback, incentives, encouragement from pharmaceutical company (n= 515, 84%). - Receive a monthly reminder email (n= 293, 47.7%). - Clearly define responsibility, developing iPhone App to enable easy and rapid reporting (n= 216, 35.2%).
(Santosh et al., 2013b)	Healthcare Professionals (physicians, nurses and Pharmacists)	- Increasing awareness by training (n= 253, 76%). - Collaboration among healthcare professionals (n=223, 67%). - Involve pharmacists in reporting (n=210, 63.1%). - Make reporting as professional obligation (n= 184, 55.5%).
(Elkalmi et al., 2014)	Community Pharmacists	- Making ADRs reporting mandatory (n=59, 56.7%). - Receive feedback from relevant authorities (n=72, 72.1%). - Incentives (n=31, 27%).

Table 4: Barriers to reporting.

Studies	Healthcare professional	Barriers
(Su et al., 2010)	Hospital pharmacists	Lack of clinical knowledge (n =144, 68.6%) Lack of time (n=96, 45.7%) Non availability of ADRs reporting forms (n=64, 30.5%) Unknown reporting process (n=36, 17%)
(Chopra et al., 2011)	Physicians	Lack knowledge of what and where to report (n=45, 45%). Lack of time (n= 20, 20%). Nonavailability of ADRs reporting forms (n=15, 15%).
(Walji et al., 2011)	Community pharmacists	Lack of time. The perception that the process was complex.
(Biagi et al., 2012)	General Practitioners	Uncertainty whether the reason from the drug (n= 79, 47%). Lack of time (n = 37, 22%). Unknown reporting process (n= 28, 16.7%). Nonavailability of ADRs reporting forms (n=24, 14.3%)
(Pimpalkhute et al., 2012)	Resident doctors	Lack of knowledge about reporting process (n=52, 61.9%) Lack of time/ overburden (n= 19, 22.6%).
(Stewart et al., 2013)	Non-medical prescribers “pharmacists and nurses”	Time consuming and information needed not available (n= 484, 78.9% NMPs). Felt it is not their role to report (n= 269, 91.8% nurses) Lack of time (n= 12, 3.75% pharmacist)
(Santosh et al., 2013b)	Healthcare Professionals (physicians, nurses and Pharmacists)	Think that they have caused a patient harm (n=99, 30.7%). Think that a report will generate extra work (n= 97, 30.1%). Fear from legal liability (n=87, 27%). Lack of time (n= 74, 22.4%). Not confident in deciding ADR had occurred or not (n= 72,

		22.4%). Think report may be wrong (n= 68, 21.1%).
(Elkalmi et al., 2014)	Community pharmacists	Ignorance of where the report should be sent to (n= 46, 44.6%). Unavailability of reporting form (n= 44, 42.6%). Lack of knowledge on how to report (n= 36, 34.7%).

4. DISCUSSION

During the drug developmental phase, we get good information about its therapeutic activity but less about its safety because the clinical trials are conducted in a controlled environment in a limited number of patients and specific duration. After drugs licensing and marketing, it will be prescribed by hundreds of prescribers to thousands of patients belonging to different age groups. During the post-marketing phase, only unusual and rare ADRs are encountered. So, it will be useful to have a system which detects new safety information. ADRs' cost and burden on public health emphasize the importance of healthcare professionals' engagement in detecting and reporting them. The first step in engagement HCPs is evaluating the current situation and evaluating their knowledge attitude and practice regarding ADRs reporting.

Healthcare professionals' knowledge towards ADRs reporting

Based on various reviewed articles, HCPs have inadequate knowledge on defining ADR, ADE and PV, (range 16%-81%). They were unaware of the existence of pharmacovigilance centers in their countries and post-marketing surveillance activities, (range 16%-66%). In addition, they were unaware of ADRs reporting methods and process nor getting reporting forms. They think reporting is for new drugs related reactions (range 36% - 80%) and community pharmacists says there is no need for reporting reactions related to topical products (42%). It is clear that knowledge of ADRs reporting was not given much consideration in their education or training.

Healthcare professionals' attitude towards ADRs reporting

Almost of HCPs (range 79%-100%) agree that reporting is important and it is a part of their professional role (range 80%-92%) but one study the none medical practitioners (91.8% of nurses) stated it is not their role to report (Stewart et al., 2013). HCPs willing to participate in PV activities if they receive training, (range 78%-99%). The majority claim that reporting should be obligatory and few who will report voluntary, for their reporting method preference, it was clear they prefer reporting to be by phone (range 23%-47%).

Healthcare professionals' practice towards ADRs reporting

According to reviewed articles, HCPs' practice is poor, although they suspect reaction few who report it the majority did not report or inform anyone. Physicians and nurses don't discuss ADRs in their routine discussions, (60% and 91%, respectively). They enumerate many barriers that hinder their practice, those barriers are a

lack of knowledge, unaware about where and how to report, lack of time/ overburden and the perception that the process is complex, (Table 4).

KAP between different countries and specialties

From reviewed articles, it had been indicated that being developing or developed country did not affect the situation as all studies suggested the need for education and training. While when comparing results of different professionals, pharmacists have better knowledge than physicians then nurses, all have a good attitude but two studies (Gavaza et al., 2011a; Suyagh et al., 2014) emphasized that hospital pharmacists have better attitude than community pharmacists may because hospital pharmacists are in direct contact with other health professionals. While community pharmacists saw themselves the first point for ADRs reporting by publics (Oreagba et al., 2011). Regarding HCPs' practice, physicians' suspect more ADRs so who reported a little bit more than who reported between nurses and pharmacists. Dental practitioners claim they did not see reactions in their patients.

Assessing and improving KAP of healthcare professionals

All reviewed articles assessed KAP status by using self-administered questionnaires except two used structured interview. Healthcare professionals' KAP needs to be improved, education and training are coming first here starting from undergraduate courses till CME. Pharmacovigilance centers should play an active role in increasing awareness about their existence, location and activities in addition improving knowledge this may by lectures, workshops, newsletters, and posters. Hospitals' management also, should play their role by ensuring their HCPs staff have adequate PV training. Furthermore, HCPs need to be encouraged they stated some encouraging factors like receive feedback from relevant authorities, incentives and making reporting obligatory.

Strengths and limitation of this review

The strengths of this review are gathering information about KAP for different healthcare professionals' categories in one review, accessing to full text for all reviewed articles and reviewing the recent studies (last five years). While limitations are the most reviewed articles used self-administered questionnaire which causes low response rates "surveys did not come back", information bias especially if respondent misunderstood questions even studies which used qualitative method by structured interview its samples was very small sample size and publication bias where may there are some missed relevant publications or publications which referenced in others bibliographic databases.

Finally, the problem is not only in individuals who lack knowledge and have positive or negative attitudes but it the responsibility of healthcare systems as well. Top managements should address the ADRs reporting culture as a priority and ensure their healthcare personnel in an environment that help and encourage them to report. The commitment to the culture of reporting requires an organizational commitment of resources to address safety concerns, leaders should committee to change and enable staff to openly share safety information.

CONCLUSION

Based on the results of the present review the following may be concluded that this review provides data about KAP of different healthcare professionals' categories, it shows poor knowledge and practice but good attitude, it provides information about how to improve ADRs reporting status and it enforces the need for appropriate training of healthcare professionals.

ACKNOWLEDGMENT

The research leading to these results has been performed in the framework of the European training programme in Pharmacovigilance and Pharmacoepidemiology, Eu2P (see more information at www.eu2p.org). This research has received support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n°115014, resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA companies' in kind contribution.

REFERENCES

- Abdel-Latif, M.M.M., Abdel-Wahab, B.A. Knowledge and awareness of adverse drug reactions and pharmacovigilance practices among healthcare professionals in Al-Madinah Al-Munawwarah, Kingdom of Saudi Arabia. *Saudi Pharm. J. SPJ Off. Publ. Saudi Pharm. Soc.*, 2015; 23: 154–61. doi:10.1016/j.jsps.2014.07.005.
- Alan, S., Ozturk, M., Gokyildiz, S., Avcibay, B., Karataş, Y. An evaluation of knowledge of pharmacovigilance among nurses and midwives in Turkey. *Indian J. Pharmacol.*, 2013; 45: 616–8. doi:10.4103/0253-7613.121375.
- American Society of Health-System Pharmacy. ASHP guidelines on adverse drug reaction monitoring and reporting. *Am. J. Health. Syst. Pharm.*, 1995; 52: 417–9.
- Awodele, O., Daniel, A., Popoola, T.D., Salami, E.F. A study on pharmacovigilance of herbal medicines in Lagos West Senatorial District, Nigeria. *Int. J. Risk Saf. Med.*, 2013; 25: 205–17. doi:10.3233/JRS-130604.
- Bello, S.O., Umar, M.T. Knowledge and attitudes of physicians relating to reporting of adverse drug reactions in Sokoto, north-western Nigeria. *Ann. Afr. Med.*, 2011; 10: 13–8. doi:10.4103/1596-3519.76563.
- Biagi, C., Montanaro, N., Buccellato, E., Roberto, G., Vaccheri, A., Motola, D. Underreporting in pharmacovigilance: an intervention for Italian GPs (Emilia-Romagna region). *Eur. J. Clin. Pharmacol.*, 2012; 69: 237–44. doi:10.1007/s00228-012-1321-7.
- Chopra, D., Wardhan, N., Rehan, H.S. Knowledge, attitude and practices associated with adverse drug reaction reporting amongst doctors in a teaching hospital. *Int. J. Risk Saf. Med.*, 2011; 23: 227–32. doi:10.3233/JRS-2011-0543.
- Classen, D., Pestotnik, S., Evans, R., et al. The adverse drug events in hospitalized patients. *JAMA*, 1997; 277: 301–6.
- Department of Health Therapeutic Goods Administration, A.G., 2015. Reporting medicine and vaccine adverse events | Therapeutic Goods Administration (TGA). URL <http://www.tga.gov.au/reporting-medicine-and-vaccine-adverse-events> (accessed 6.3.15).
- Elkalmi, R.M., Hassali, M.A., Ibrahim, M.I.M., Jamshed, S.Q., Al-Lela, O.Q.B. Community pharmacists' attitudes, perceptions, and barriers toward adverse drug reaction reporting in Malaysia: a quantitative insight. *J. Patient Saf.*, 2014; 10: 81–7. doi:10.1097/PTS.0000000000000051.
- Faich, G.A. Adverse-drug-reaction monitoring. *N. Engl. J. Med.*, 1986; 314, 1589–92. doi:10.1056/NEJM198606123142427.
- Gavaza, P., Brown, C.M., Lawson, K.A., Rascati, K.L., Wilson, J.P., Steinhardt, M. Influence of attitudes on pharmacists' intention to report serious adverse drug events to the Food and Drug Administration. *Br. J. Clin. Pharmacol.*, 2011a; 72: 143–52. doi:10.1111/j.1365-2125.2011.03944.x.
- Gavaza, P., Brown, C.M., Lawson, K.A., Rascati, K.L., Wilson, J.P., Steinhardt, M. Examination of pharmacists' intention to report serious adverse drug events (ADEs) to the FDA using the theory of planned behavior. *Res. Social Adm. Pharm.*, 2011b; 7: 369–82. doi:10.1016/j.sapharm.2010.09.001.
- Hardeep, Bajaj, J.K., Rakesh, K. A survey on the knowledge, attitude and the practice of pharmacovigilance among the health care professionals in a teaching hospital in northern India. *J. Clin. Diagn. Res.*, 2013; 7: 97–9. doi:10.7860/JCDR/2012/4883.2680.
- Jasmine C. Gatti, 2012. Editorials: The Importance of Physicians Identifying and Reporting Adverse Drug Events - American Family Physician. *Am Fam Physician*, 85: 318.
- Jones, J.K., 2008. Medscape Pharmacists: Why Should I Report an Adverse Drug Event? URL <http://www.medscape.org/viewarticle/578160> (accessed 6.3.15).
- Jose, J., Jimmy, B., Al-Ghailani, A.S.H., Al Majali, M.A. A cross sectional pilot study on assessing the knowledge, attitude and behavior of community pharmacists to adverse drug reaction related aspects in the Sultanate of Oman. *Saudi Pharm. J. SPJ Off.*

- Publ. Saudi Pharm. Soc, 2014; 22: 163–9. doi:10.1016/j.jpsps.2013.07.006.
18. Khalili, H., Mohebbi, N., Hendoiee, N., Keshtkar, A.-A., Dashti-Khavidaki, S. Improvement of knowledge, attitude and perception of healthcare workers about ADR, a pre- and post-clinical pharmacists' interventional study. *BMJ Open*, 2012; 2: e000367, doi:10.1136/bmjopen-2011-000367.
 19. Lazarou, J., Pomeranz, B.H., Corey, P.N. Incidence of Adverse Drug Reactions in Hospitalized Patients. *JAMA*, 1998; 279: 1200. doi:10.1001/jama.279.15.1200.
 20. Nebeker, J.R., Barach, P., Samore, M.H. Clarifying adverse drug events: a clinician's guide to terminology, documentation, and reporting. *Ann. Intern. Med*, 2004; 140: 795–801.
 21. Oreagba, I.A., Ogunleye, O.J., Olayemi, S.O. The knowledge, perceptions and practice of pharmacovigilance amongst community pharmacists in Lagos state, south west Nigeria. *Pharmacoepidemiol. Drug Saf*, 2011; 20: 30–5. doi:10.1002/pds.2021.
 22. Osakwe, A., Oreagba, I., Adewunmi, A.J., Adekoya, A., Fajolu, I. Impact of training on Nigerian healthcare professionals' knowledge and practice of pharmacovigilance. *Int. J. Risk Saf. Med*, 2013; 25: 219–27. doi:10.3233/JRS-130605.
 23. Oshikoya KA. Adverse drug reaction in children: Types, incidence and risk factors. *Niger J Paediatr*, 2006; 33: 29–35.
 24. Palaian, S., Ibrahim, M.I., Mishra, P. Health professionals' knowledge, attitude and practices towards pharmacovigilance in Nepal. *Pharm. Pract. (Granada)*, 2011; 9: 228–35.
 25. Pellegrino, P., Carnovale, C., Cattaneo, D., Perrone, V., Antoniazzi, S., Pozzi, M., Napoleone, E., Filograna, M.R., Clementi, E., Radice, S. Pharmacovigilance knowledge in family paediatricians. A survey study in Italy. *Health Policy*, 2013; 113: 216–20. doi:10.1016/j.healthpol.2013.08.006.
 26. Pérez García, M., Figueras, A. The lack of knowledge about the voluntary reporting system of adverse drug reactions as a major cause of underreporting: direct survey among health professionals. *Pharmacoepidemiol. Drug Saf*, 2011; 20: 1295–302. doi:10.1002/pds.2193.
 27. Pimpalkhute, S.A., Jaiswal, K.M., Sontakke, S.D., Bajait, C.S., Gaikwad, A. Evaluation of awareness about pharmacovigilance and adverse drug reaction monitoring in resident doctors of a tertiary care teaching hospital. *Indian J. Med. Sci*, 2012; 66: 55–61. doi:10.4103/0019-5359.110902.
 28. Pirmohamed, M., James, S., Meakin, S., Green, C., Scott, A.K., Walley, T.J., Farrar, K., Park, B.K., Breckenridge, A.M. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ*, 2004; 329: 15–9. doi:10.1136/bmj.329.7456.15.
 29. Pulford, A., Malcolm, W. Knowledge and attitudes to reporting adverse drug reactions. *Br. J. Nurs*, 2010; 19: 899–904. doi:10.12968/bjon.2010.19.14.49048.
 30. Rehan, H.S., Sah, R.K., Chopra, D. Comparison of knowledge, attitude and practices of resident doctors and nurses on adverse drug reaction monitoring and reporting in a tertiary care hospital. *Indian J. Pharmacol*, 2012; 44: 699–703. doi:10.4103/0253-7613.103253.
 31. Santosh, K.C., Tragulpiankit, P., Edwards, I.R., Gorsanan, S. Knowledge about adverse drug reactions reporting among healthcare professionals in Nepal. *Int. J. Risk Saf. Med*, 2013a; 25: 1–16. doi:10.3233/JRS-120578.
 32. Santosh, K.C., Tragulpiankit, P., Gorsanan, S., Edwards, I.R. Attitudes among healthcare professionals to the reporting of adverse drug reactions in Nepal. *BMC Pharmacol. Toxicol*, 2013b; 14: 16. doi:10.1186/2050-6511-14-16.
 33. Stewart, D., MacLure, K., Paudyal, V., Hughes, C., Courtenay, M., McLay, J. Non-medical prescribers and pharmacovigilance: participation, competence and future needs. *Int. J. Clin. Pharm*, 2013; 35: 268–74. doi:10.1007/s11096-012-9739-7.
 34. Su, C., Ji, H., Su, Y. Hospital pharmacists' knowledge and opinions regarding adverse drug reaction reporting in Northern China. *Pharmacoepidemiol. Drug Saf*, 2010; 19: 217–22. doi:10.1002/pds.1792.
 35. Suyagh, M., Farah, D., Abu Farha, R. Pharmacist's knowledge, practice and attitudes toward pharmacovigilance and adverse drug reactions reporting process. *Saudi Pharm. J. SPJ Off. Publ. Saudi Pharm. Soc*, 2014; 23: 147–53. doi:10.1016/j.jpsps.2014.07.001.
 36. Ting, K.-N., Stratton-Powell, D.M., Anderson, C. Community pharmacists' views on adverse drug reactions reporting in Malaysia: a pilot study. *Pharm. World Sci*, 2010; 32: 339–42. doi:10.1007/s11096-010-9382-0.
 37. Walji, R., Boon, H., Barnes, J., Welsh, S., Austin, Z., Baker, G.R. Reporting natural health product related adverse drug reactions: is it the pharmacist's responsibility? *Int. J. Pharm. Pract*, 2011; 19: 383–91. doi:10.1111/j.2042-7174.2011.00150.x.
 38. Waller, P. *An Introduction to Pharmacovigilance*. Wiley Blackwell, UK: 2010.
 39. World Health Organization. *Glossary of Patient Safety*. Executive Board of the Health Ministers' Council, Riyadh, 2011.
 40. World Health Organization, 2002. *Safety of Medicines - A Guide to Detecting and Reporting Adverse Drug Reactions - Why Health Professionals Need to Take Action*. URL <http://apps.who.int/medicinedocs/en/d/Jh2992e/3.html> (accessed 6.3.15).
 41. World Health Organization. *WHO Technical Report No 498: 1972*.

42. Yip, J., Radford, D.R., Brown, D. How do UK dentists deal with adverse drug reaction reporting? *Br. Dent. J.*, 2013; 214: E22. doi:10.1038/sj.bdj.2013.426.