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EVOLVING TRENDS IN PHARMACOVIGILANCE AND MEDICINE SAFETY SYSTEM: A LITERATURE REVIEW

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Abstract:

For effective pharmacovigilance system, a strong linkage and coordination is needed with the regulators in order to keep them aware of the issues related to medicine safety so that appropriate regulatory actions can be ensured for safeguarding the public health. The aim of this study is to summarize research findings from developed and developing countries as well as from Pakistan regarding evolving trends and future prospects of pharmacovigilance and medicine safety system. A total of 63 studies were reviewed in terms of pharmacovigilance and medicine safety system operational in different countries. The review concluded that pharmacovigilance systems have been evolved from traditional practices of reporting towards online reporting system in many developed as well developing countries. Inadequate knowledge of healthcare professionals towards pharmacovigilance have been reported which can adversely affects the capacity of the system to monitor safety of medicines. Healthcare professionals have been involved in ADR monitoring in developed world, however this development must be replicated in developing countries to enhance the professional competence of the professionals to promote safe use of medicines

Key words: *ADR, pharmacovigilance, medicine safety system, healthcare professionals, Knowledge, Perceptions*

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INTRODUCTION:

The role of regulators in ensuring safety of medicines has attained a pivotal role as it has always remained one of the prime considerations for drug regulators across the globe. Public confidence in medicines can be enhanced by ensuring their safety which is primarily based on sound drug regulatory arrangements. Besides approval of new drugs, the drug regulators have to ensure safety of all medicines inclusive of complementary and traditional medicines, vaccines and biological [1]. Furthermore, they have to take measures for development of communication between all stakeholders having interest in the medicine safety. For effective pharmacovigilance system, a strong linkage and coordination is needed with the regulators in order to keep them aware of the issues related to medicine safety so that appropriate regulatory actions can be ensured for safeguarding the public health. The pivotal role played by pharmacovigilance in ensuring safety of medicinal products is well understood by regulators and they have to adequately support pharmacovigilance and medicines safety program in order to achieve objectives regarding medicine safety [2].

One of the essential components of the drug regulation is pharmacovigilance and medicine safety system, however, many developing countries are deficient in having basic pharmacovigilance systems in place for ensuring safety of medicines and even where basic systems exist at some level, it is deprived of the active support from healthcare professionals, regulators and other relevant stakeholders [3]. The regulatory authority is supposed to have an independent discipline of post-marketing surveillance to serve a distinct function within the regulatory framework. Such discipline must be segregated from the functions of evaluation and approval of new medicines. An exclusive source of information, infrastructure and expertise must be provided to the discipline of post-marketing surveillance enabling it to perform the desired functions, although, such system and resources can be shared with other disciplines for many good reasons [4]. For example, in order to determine harm and risk from any medicinal product, there should be access to the information so that proper pharmacovigilance process could be conducted. An ADR advisory committee is appointed in many countries by the national regulatory authority for giving technical approvals in pharmacovigilance and drug regulatory approvals [5, 6].

Methodology

The electronic databases Pub Med, Google Scholar and Science direct were searched for articles published from 2000 to 2015. The search terms used were pharmacovigilance, medicine safety, ADR and attitude. Full research papers and abstracts were searched and included in this review. A total of 63 studies were included in this review. Fifty nine studies were from developing and developed countries whereas only 4 studies were from Pakistan regarding prevalence of use, perceptions and knowledge of health care professionals mainly pharmacists regarding CAM. (Table 1)

Table 1: Details of Country and Number of Included Papers

Regions	Number of Studies	Countries
Developed & Developing Countries	59	USA, Australia, UK, Japan, Germany, Canada, Spain, South Korea, Ireland, Israel, West Indies, Turkey, Singapore, Ghana, Malaysia, India, Iran, Saudi Arabia, Qatar, Mascat, New Mexico, Africa.
Pakistan	04	
Total	**63**	

RESULTS AND DISCUSSION:

Safety of medicines relies on presence of effective pharmacovigilance system which can be ensured if all the relevant stakeholders play their due role. The relationship between these stakeholders is very crucial and of complex nature as well. A vibrant pharmacovigilance system can only flourish and develop if there is sustained collaboration and commitment among those partners who must collectively anticipate, comprehend and respond to the demands pertaining to safety of medicines which are rising in number with every passing day. Among the important partners of the pharmacovigilance system include the regulatory authorities, the pharmacovigilance cell, hospitals, public health programs, academia, healthcare professionals, patients, media, advocacy groups and the civil society. The role of healthcare professionals particularly the physicians, pharmacist and nurses is crucial in the entire system as they provide the foundation of medicine safety system by initiating the reports on potential ADRs and hence is accorded due importance around the globe. The healthcare professionals while serving in hospitals, clinics and public health programs can play a pivotal role in ensuring timely detection and reporting of ADRs which in turn leads to further actions like causality analysis, evaluation and remedial actions taking place in pharmacovigilance cell which is housed by the regulatory authority or academia [7].

Overview of Pharmacovigilance and Medicine Safety System in Developed Countries

The level of pharmacovigilance and medicine safety system in various developed countries has been assessed and many studies were designed for exploring the knowledge, attitude and perceptions of healthcare professionals like pharmacists, physicians, and nurses towards pharmacovigilance. Realizing importance of non-medical prescribers and patients in pharmacovigilance, their role has also been focused and ascertained through various studies.

Role of Healthcare Professional Regarding Pharmacovigilance and Medicine Safety System

A study designed to assess the knowledge and attitude of pharmacists serving in hospitals of United Kingdom towards ADR reporting demonstrated that they had a reasonable knowledge of ADR reporting and are supportive to the Yellow Card Spontaneous ADR Reporting Scheme (YCS). The study, however, recommended continuous education and training for increasing the ADR reports from hospital pharmacists [8]. Another study was conducted in Norway which aimed at exploring the attitude of pharmacists towards pharmacovigilance and their experience with ADR reporting. It was concluded that the pharmacists possess positive attitude towards pharmacovigilance, however, their experience with ADR reporting was found below the mark [9].

The role of physicians in pharmacovigilance also remained focus of various researchers. In Italy, a study aimed at assessing attitude of physicians to ADR reporting found that the physicians lack the knowledge regarding type of reactions to be reported preferably and the purposes of ADR reporting system. The study recommended consideration of various key measures particularly inclusion of pharmacovigilance related topics in pre- and post-graduation education programs, preparation of guidelines for ADR spontaneous reporting ensuring reporters feed-back information and implementation of the regional pharmacovigilance units [10]. The results of a survey conducted in European Union countries to explore the attitude of medical practitioners towards their national ADR spontaneous reporting systems demonstrated the need for further development of reporting techniques on larger scale in European Union countries [11].Another study carried out in Ireland to assess knowledge and attitude of physicians towards ADR reporting scheme highlighted that majority of the physicians were not aware of the ADR reporting criteria adopted by the National Drug Regulatory Agency and considerable disagreement existed among physicians in understanding of the meaning of common, occasional, rare and very rare ADRs. The study highlighted the need for continuous education and awareness programs to address these shortcomings [12]. In Italy, a study conducted for assessing the knowledge, attitude and behavior that could encourage the General Practitioners (GPs) to report more suspected ADRs demonstrated that education and training focusing on pharmacotherapy with emphasis on ADR reporting could improve the number of ADR reports. It was further recommended that communication among GPs could result in enhancement of ADR reporting [13]. The perceptions of physicians serving in Romania towards ADR reporting were also assessed and pharmacovigilance activities including ADR reporting was declared to be more of an accidental nature and the physicians were found ignorant of this activity. The study, however, found the physicians to have positive attitude towards ADR reporting as the majority believed that ADR reporting should be voluntary or mandatory [14]. A study carried out in Sweden to explore the role of nurses in ADR reporting observed that nurses who showed interest and are trained n ADR reporting could play an important role in ADR detection and reporting [15]. Another study aimed at investigating attitudes of nurses serving in Sweden to ADR

reporting recommended inclusion of hospital nurses as reporters as key measure to increase the reporting rate [16].

In Canada, a study carried out to determine the perceptions of physicians and pharmacists regarding pharmacovigilance and their role in reporting ADRs suggested for measures to re-define the expectations and targeted feedback in order to promote ADR reporting and awareness of the system. The study also recommended presence of an on-site professional for ADR reporting and education for further increase in ADR reporting[17]. In Scotland, a study was conducted with the objective to evaluate knowledge and attitudes regarding ADR reporting among the professional groups demonstrated that there were lower levels of knowledge about the purpose of the Yellow Card system specifically among healthcare professionals (physicians, pharmacist and nurses [18]. A study in Bosnia to investigates the role of healthcare professionals in ADR reporting demonstrated inadequate knowledge of ADRs and its procedure to report. The study found the perceptions of healthcare professionals toward ADR reporting as positive but it the actual practice of ADR reporting did not reflected it properly, probably because of inadequate knowledge and little experience of pharmacovigilance. The study recommended educational and training interventions with particular focus on the objectives and aims of pharmacovigilance [19]. The role of non-medical prescribers' (NMPs) in pharmacovigilance has also been ascertained and a study conducted in UK observed that NMPs participate and have required competence in adverse drug reaction reporting. The study however, indicated several key issues for consideration including the need for further training and support to optimize their role in pharmacovigilance [20].

Role of Patients in Pharmacovigilance Regarding Pharmacovigilance and Medicine Safety System

The patients can also pay a supportive role in ADR reporting and development of pharmacovigilance system.In developed countries, the role of patients in pharmacovigilance has also been has been focused and explored through few studies. It has been reported by a study that suspected ADRs reported by the patients may contribute to the functioning of the pharmacovigilance system by reporting type of drugs and reactions different from those reported by healthcare workers[21]. Another study conducted in United Kingdom to explore the contribution and role of patient reporting concluded that significant complementary contribution to the healthcare professionals can be made by the patients by identifying different serious drug reactions which could not be identified from HCPs reports alone [20]. In Netherlands, a study was conducted to determine and quantify the reasons of patient reporting of ADRs to pharmacovigilance center. The study indicated the severity of the adverse drug reaction as the main reason and motive for patients to report their adverse drug reactions to a pharmacovigilance center. [22]. To determine levels of public awareness regarding ADR reporting systems in for consumers in Australia, a study was conducted which concluded that consumers can play a pivotal role in enhancing monitoring and understanding of medicines safety, but there was low awareness about available reporting systems. The study also highlighted willingness of some consumers to use adverse drug reaction self-reporting systems, but promotion of such systems and training on how to use itwas required [23].

Overview of Pharmacovigilance and Medicine Safety System in Developing Countries

In order to assess and analyze the pharmacovigilance and medicine safety system in five Asian countries i.e. Bangladesh, Cambodia, Nepal, Thailand and Philippine, a study was conducted by strengthening pharmaceutical program (SPS) while using the Indicator Based Pharmacovigilance Assessment Tool (IPAT). This valuable exercise concluded that the capacity with regard to medicine safety of most of the medicine regulatory authorities (NRAs) of these Asian countries was limited. The regulatory framework and governance structures of these regulatory authorities which must be mandated by legislation and regulations was lacking to larger extent. Besides, considerable deficiencies existed in systems for accountability transparency and enforcement capacity required to ensure medicines safety monitoring by the pharmaceutical industry. The laws pertaining to pharmacovigilance were found un-focused, divergent and in-consistent with the applicable international standards. Furthermore, necessary measures to adopt relevant international standards were found at very preliminary and initial stage.The study observed that pharmacovigilance and its related structures in these five Asian countries were weak and the capacity of the system requiredfor generation and evaluation of signals and utilization of the information for risk management and communication was also deficient and limited. The study while putting question marks on the capacity of regulatory authorities (NRAs) of these countries suggested for taking immediate measures for strengthening the pharmacovigilance and medicine safety system besides recommending for assessment of pharmacovigilance system in other countries of

Asian region[24].A study conducted in India with the aim of assessing its pharmacovigilance system concluded that Drug Controller General of India should take immediate steps to make pharmacovigilance as mandatory function and put in place a mechanism of carrying out pharmacovigilance inspection in India[25].

The efficiency and reliability of any pharmacovigilance and medicine safety system, among other factors, largely depend upon the knowledge, attitude and practice of the healthcare professionals (community and hospital pharmacists, physicians and nurses)as they are the key players in detection and reporting of ADRs, which provides the foundation for flourishing of any sound pharmacovigilance system. Considering this key function performed by the healthcare professionals in supporting the development of effective pharmacovigilance and medicine safety system, various studies have been conducted in Asian countries to exploretheir knowledge, attitude and practice towards pharmacovigilance and ADR reporting so that the foundation of the pharmacovigilance system can properly be assessed and necessary interventions in this regard can be introduced to improve the situation.

Knowledge, Attitude and Practice of Community and Hospital Pharmacists Regarding Pharmacovigilance and Medicine Safety System

The pharmacists, being the custodian of medicines, play a central role in pharmacovigilance and ADRs identification and reporting and hence assessment of their knowledge, attitude and practice has always remained a focus for the researchers. Various studies have been conducted to assess their knowledge, attitude and practice particularly those working at community pharmacies. A study conducted in Turkey investigated the knowledge and attitude of community pharmacists working in Istanbul regarding pharmacovigilance and adverse drug reactions. The results of the study demonstrated that Turkish Community Pharmacists have poor knowledge regarding pharmacovigilance. The study suggested that there was an urgent need for educational interventions to train the community pharmacist on pharmacovigilance and ADR reporting (Toklu and Uysal, 2008). Knowledge, attitude and views of community pharmacist on adverse drug reporting were also investigated in Malaysia and it was found that there is a strong need for training of health professionals on adverse drug reactions and their reporting[26]. It Similar findings were recorded in Saudi Arabia where a study conducted to explore the knowledge, behavior and experience of community pharmacist concluded that majority of them possessed poor knowledge of adverse drug reaction reporting process. The study therefore suggested the pharmacovigilance authorities to take necessary steps to design interventional programs for increasing the knowledge and awareness of pharmacist regarding ADR reporting process[27].A similar study form Oman observed that although the pharmacists possessed an acceptable degree of knowledge, attitude and behavior regarding ADR reporting, but still a good number of them had below than acceptable level of knowledge on aspects related to drug safety[28]. The study further recommended that educational programs must be continued to generate awareness regarding reporting of ADRs and to ensure and persuade more active participation of pharmacists in the pharmacovigilance program [28].In Hong Kong, while assessing the attitudes and knowledge of pharmacists towards ADR reporting, it was highlighted that large majority of them agreed on the importance and need for reporting adverse drug reactions, however, it was noted that lack of knowledge of an adverse drug reaction reporting program might have led to under or non-reporting [29].

Hospitals play a central role in diagnosis and treatment and use of medicines. The hospital pharmacists are the key players in monitoring safety of drugs. Their role in the pharmacovigilance has always been recognized and thus assessment of knowledge, attitude and practice towards pharmacovigilance and medicine safety has remained prime concern for the researchers. In Thailand, it was observed that hospital pharmacists showed positive attitude towards ADR reporting and it was suggested that the potential role of hospital pharmacists in ADR identification should be investigated for the purpose of increasing reporting rates [30]. In China, knowledge and opinions of hospital pharmacists regarding spontaneous reporting of adverse drug reactions were also investigated in Inner Mongolia. It was demonstrated that hospital pharmacist serving in Mongolia had reasonable knowledge and positive attitude towards pharmacovigilance, however, majority of them had never reported and ADR in their professional career. The study further recommended that education of pharmacists on adverse drug reaction and their involvement in patient care would be important in improving adverse drug reaction reporting in hospitals [31]. The pharmacists from India were found to possess poor knowledge, attitude and practice towards ADR reporting and pharmacovigilance. The study suggested for imparting additional training to the pharmacists in order to make them effective part of ADR reporting system [32]. The results of the study conducted in Qatar indicated that pharmacists

working in different part of country had never submitted ADR report despite the fact that they possessed good knowledge of the purpose of pharmacovigilance and positive attitude towards this activity[33].

Knowledge, Attitude and Practice of Physicians and Nurses Regarding Pharmacovigilance and Medicine Safety System

Physicians enjoy a key position and importance in the health care system by providing healthcare services and ensuring use of appropriate and safe medicines to the public. The success of pharmacovigilance system largely depends upon their active participation in adverse drug reaction detection and its timely reporting to the quarters concerned which is based on possession of good knowledge and positive attitude by them towards this key function. Researchers focusing on assessment of pharmacovigilance and ADR reporting have always paid particular emphasis on investigation of knowledge, attitude and practice of physicians towards this crucial activity. A study was conducted in India for assessment of attitude and perceptions of medical practitioners towards ADR reporting and factors that influence it. It was concluded that imparting knowledge and creating awareness of ADR reporting would bring the reporting culture and increase the reporting rates [34]. A similar study conducted in Ahmadabad, India highlighted that prescribers were aware of the ADRs and importance of their reporting, however, lack of knowledge about ADR reporting system was clearly evident which resulted in under-reporting. It was suggested that creating awareness about adverse drug reaction reporting system and making it easy and convenient may aid in improving spontaneous reporting [35].Many other studies conducted in India in this regard demonstrated inadequacy of the knowledge among doctors regarding ADRs and its reporting and highlighted the importance of increasing awareness about pharmacovigilance [36]-[37]. Knowledge, awareness and practice of physicians on pharmacovigilance and medicine safety system have also been assessed in Malaysia. A study conducted in this regard concluded that there exists an urgent need to improve knowledge, attitude and practice of physicians regarding pharmacovigilance and suggested that it was imperative for World Health Organization (WHO) and National Pharmacovigilance Centers to take proactive measures to address the issue of ADRs for safeguarding the patients' lives. It was further recommended that the curriculum of all health related schools must be restructured with regard to pharmacovigilance without any delay and hesitation [38].

Nurses are one of the key players in healthcare triangle and their role in pharmacovigilance and medicine safety system cannot be undermined at all. To ascertain their knowledge, attitude and practice towards pharmacovigilance and adverse drug reaction reporting, various studies have been conducted. In Iran, it was found that they had little knowledge and poor practice regarding the pharmacovigilance and spontaneous reporting system[39]. Another study conducted in Tehran to assess their knowledge, attitude and practice (KAP) towards Iran's national adverse drug reaction reporting schemes and to identify reasons for under-reporting, demonstrated that they had insufficient knowledge regarding operation, purposes and usefulness of adverse drug reaction reporting system [39]. A study with similar objective was also carried out in United Arab Emirates which pointed out the need for interventional program among nurses focusing on the importance of adverse drug reaction reporting and its procedure to encourage their active and voluntary participation in drug safety surveillance [40].

Knowledge, Attitude and Practice of Medical and Para-Medical Professionals and Students Regarding Pharmacovigilance and Medicine Safety System

In India, a study conducted to explore knowledge, attitude and practice of healthcare professionals (both medical and para-medical) towards adverse drug reaction found poor knowledge of HCPs and recommended that continuous medical education and training of adverse drug reaction reporting would help in improving their knowledge about reporting of adverse drug reactions [41]. A similar study conducted with the aim to assess and compare the adverse drug reaction reporting beliefs of HCPs involved in the National Malaria Control Program of India recommended that a specific and targeted in-service education with hands-on training on adverse drug reaction monitoring and reporting needs to be designed to boost real time pharmacovigilance in India [42].Another study demonstrated that knowledge and attitude towards pharmacovigilance was gradually improving among healthcare professionals in India, but the actual practice of adverse drug reaction reporting was still deficient among them [43].In Kingdom of Saudi Arabia, the knowledge and awareness of adverse drug reactions reporting and pharmacovigilance system among healthcare professionals serving in Al-Madinah Al-Munawwarah hospitals was also assessed which demonstrated lack of knowledge and awareness of pharmacovigilance and adverse drug reactions reporting among them[44]. In Nepal, the knowledge, attitude and practices (KAP) of the healthcare

professionals (medical and para-medical) towards adverse drug reactions and pharmacovigilance was also explored which demonstrated similar results showing that healthcare professionals had a poor knowledge, attitude and practice towards adverse drug reactions and pharmacovigilance and there is a need for educational and awareness intervention for these professionals [45]. In Wuhan city of China, the knowledge and attitudes of healthcare professionals (doctors, nurses and administrators) to adverse drug reactions and the reasons for poor reporting were also studied which indicated that they had little knowledge on the basic adverse drug reaction reporting. The study concluded that address of ADR reporting centers and unavailability of the ADR reporting forms are the main reasons for underreporting and suggested that education and training of doctors, nurses and administrators to enhance their awareness regarding pharmacovigilancecan improve the reporting system [46].In Philippines, it was observed that healthcare professionals are generally familiar with the basic concepts of adverse drug reactions reporting and consider adverse drug reactions reporting as beneficial when a study was conducted to determine their awareness and attitudes towards adverse drug reactions reporting. The study suggested that adverse drug reactions reporting may be further enhanced through appropriate educational campaign [47].

Students are the future professionals who have to play an important role in supporting the development of the pharmacovigilance system and monitoring of medicine safety. Their knowledge and attitude towards pharmacovigilance and ADR reporting has considerable link with flourishing of medicine safety system. Assessment of their knowledge regarding pharmacovigilance also indicates the level and quality of pre-service training and suitability of curricula with regard to presence of core topics on pharmacovigilance and medicine safety. Considering the importance of this aspect, their knowledge, attitude and practice regarding pharmacovigilance has been explored by many researchers. In Malaysia, a study examined and compared the knowledge and perception of medicine and pharmacy students in a private university towards pharmacovigilance and adverse drug reactions reporting which demonstrated that the pharmacy students have more awareness and knowledge about pharmacovigilance and adverse drug reaction reporting as compared to medicine students [47].Assessing knowledge of first-year medical resident doctors regarding adverse drug reaction reporting, a study conducted in India demonstrated that their knowledge regarding adverse drug reaction reporting was quite poor and a need to incorporate adverse drug reaction reporting into undergraduate teaching, and its re-enforcement during internships was recommended [48].A recent study conducted in India concluded that the postgraduate resident doctors had a relatively better attitude but knowledge and practices towards adverse drug reactions and pharmacovigilance was found lacking. The study demonstrated that majority of them realized the importance of adverse drug reaction reporting and monitoring, but only a few had ever reported an adverse drug reaction owing to lack of motivation and training toward adverse drug reaction reporting and pharmacovigilance. The findings of the study also suggested that there was need for continuous education and sensitization regarding pharmacovigilance and adverse drug reaction reporting system for residents and improving the ongoing pharmacovigilance activities in hospital [49].

Pharmacovigilance and Medicine Safety System in African Region

Pharmacovigilance and medicine safety system of various African countries has been assessed. In Rwanda, the medicine safety system was assessed in 2009by using the IPAT and it was observed that majority of the structural, process and outcome indicators of functional pharmacovigilance system are missing. It was found that the pharmacovigilance policy in Rwanda had not been approved and relevant laws requiring regulation of medicines were missing. Furthermore, pharmacovigilance center and its guidelines were not approved and pre-service and in-service training on pharmacovigilance are deficient in many respects. No formal mechanism of medicine safety information was found in place whereas pharmacovigilance activities were found isolated and un-coordinated lacking any organized system to monitor patient safety. The assessment of system recommended that the Ministry of Health (MoH) of Rwanda must be supported towards the establishment of National Pharmacovigilance and Medicine Information Center (NPMIC), implementation of the training of trainers, development of systems for safety monitoring in the Community Health Workers (CHW) Program, and coordination of efforts for the initiation of active surveillance studies [50]**.**Assessment of pharmacovigilance and medicine safety system in Ghana identified that basic structures existed for improving the pharmacovigilance system. However, processes and outcomes indicators that mark well-functioning pharmacovigilance systems were found to be deficient[51].Another important study using the IPAT was conducted for comparative analysis of pharmacovigilance and medicine safety system in Sub-Saharan Africa. The findings of this study demonstrated that pharmacovigilance activities

were already taking place in most of these countries, however, it was suggested that pharmacovigilance systems in these countries can further be developed with the interest and support from global health initiatives. The study also pointed out that there is lack of coordination among all the components of the pharmacovigilance system that results in its fragmentation thereby affecting its capacity to ensure quality, efficacy and safety of medicines. The study recommended for strong coordination and linkage of existing activities for establishment of comprehensive medicine safety system and to improve quality of care and patient safety [52].Assessment of pharmacovigilance system of another country of African region i.e Burkina Faso suggested strengthening of the legal framework and structures for medicines safety activities, enhanced coordination between relevant stakeholders for development of effective medicine safety system enabling it to collect its own data, generate signals, evaluate and manage local medicine-related risks [53].Assessment of pharmacovigilance activities in low- and middle-income countries, while highlighting deficiencies regarding structural, process and outcome indicators, emphasized for urgent need for identification and implementation of feasible systems, governance, infrastructures, human resource, training and capacity building, sustainable methodologies, and innovations in pharmacovigilance. The study recommended that medicine safety information must be shared with the policy makers and regulators and knowledge of healthcare professionals must be enhanced through quality informatics and learning tools and rational use of medicines and patient safety must be kept as ultimate goal of pharmacovigilance [54].The pharmacovigilance system of Republic of Benin was also assessed which identified deficiencies in structural, process and outcome indicators and suggested for a need to identify and utilize adequate human resource for capacity building and maintaining the drug safety system for essential medicines. The study recommended involvement of all relevant stakeholders including Faculty of Medicine and Researchers for discussion on possible strategies and development of required interventions for successful implementation of pharmacovigilance and medicine safety system in the country [55]. Assessment of pharmacovigilance and medicine safety system of various African countries has highlighted deficiencies relevant to structural, process and outcome indicators and recommended urgent need for training and awareness of healthcare professionals for improving their knowledge regarding pharmacovigilance. Various other studies have also indicated poor knowledge and attitude of healthcare professionals towards pharmacovigilance which adversely affects the capacity of the system to monitor safety of medicines. In Lagos state of South Nigeria, a study conducted to investigate knowledge of pharmacists working at community pharmacies observed that they had poor knowledge about pharmacovigilance. It was also suggested that there was an urgent need for educational programs to train pharmacists about pharmacovigilance and adverse drug reaction reporting [56]. Another study aimed at investigating the knowledge and attitude of doctors in a teaching hospital of Lagos, Nigeria on spontaneous adverse drug reaction reporting and to suggest possible ways of improving method of reporting concluded that the knowledge of adverse drug reactions and how to report them are inadequate among doctors. The study recommended continuous medical education, training and integration of adverse drug reaction reporting into the clinical activities of the doctors [57].In Amhara region of Africa, a study conducted for assessing the knowledge, attitude and practice of healthcare professionals towards adverse drug reaction reporting and factors associated with reporting concluded that the level of knowledge and practice towards adverse drug reaction reporting was low. The study recommended for steps to create awareness among health professionals towards adverse drug reaction reporting [58]. In Nigeria, a study focused at examining and analyzing various pharmacovigilance studies conducted among healthcare professionals, medical and pharmacy students highlighted the need to improve knowledge, awareness and practice of health workers, medical and pharmacy students about pharmacovigilance. It was recommended that the curriculum of all health and health related schools should be restructured with respect to pharmacovigilance and medicine safety system [38]. In Zimbabwe, a pilot study was undertaken to investigate willingness of doctors and pharmacists working in the private sector to undertake adverse drug reaction reporting, to analyze their perceptions with regard to adverse drug reaction reporting. The study highlighted that healthcare professionals were willing to report ADRs[59]. A study undertaken to determine health care leaders' and policymakers' knowledge, attitudes, and policies related to adverse drug reactions at eight hospitals in Wad Madani, Sudan observed low awareness toward adverse drug reactions among health care professionals which reflected lack of basic knowledge and vigilance. The study suggested need for education and training of health professionals regarding adverse drug reactions [60].

Overview of Pharmacovigilance and Medicine Safety System in Pakistan

According to the literature searched, the pharmacovigilance and medicine safety system of Pakistan has not been assessed so far; however, few researchers have explored knowledge, attitude and practice of physicians and students towards ADR reporting which provides basis for the medicine safety system. All these studies emphasized on regular education and training, both pre-service and in-service, of the healthcare professionals so that quality of pharmacovigilance in Pakistan can be improved with generation of high quality treatment outcomes[61], [62]. In Karachi, a study conducted to assess the knowledge and attitude of physicians' towards ADR reporting concluded that the knowledge of ADRs among physicians serving in different hospitals of Karachiwas quite sufficient but their perceptions toward ADR reporting was found poor[63].Another study conducted to evaluate the knowledge, attitude and perceptions of senior pharmacy students towards pharmacovigilance and ADR reporting concluded that they were motivated to practice pharmacovigilance during their clerkship as well as during professional career. The study recommended that consistent monitoring of ADRs and appropriate documentation of the drug safety data was needed to generate high-quality treatment outcomes [64]. A similar study conducted to evaluate the knowledge, attitude and perception of adverse drug reaction reporting among the medical and dental students emphasized on creation of awareness through regular training, re-enforcement of guide-lines and promotion of reporting of adverse drug reactions amongst health professionals so that quality of pharmacovigilance can be improved in their future practices [61]. A recent study conducted in Abbottabad aimed at evaluating the knowledge, attitude and practice of pharmacy and medical students towards pharmacovigilance and ADRs reporting demonstrated that both pharmacy and medical students have low KAP scores which indicated a dire need for education and regular training of the students regarding pharmacovigilance and ADR management [62].

CONCLUSION:

Pharmacovigilance systems have been evolved from traditional practices of reporting towards online reporting system in many developed as well developing countries. Inadequate knowledge of healthcare professionals towards pharmacovigilance have been reported which can adversely affects the capacity of the system to monitor safety of medicines. Healthcare professionals have been involved in ADR monitoring in developed world, however this development must be replicated in developing countries to enhance the professional competence of the professionals to promote safe use of medicines. Effective measures particularly inclusion of pharmacovigilance related topics in pre- and post-graduation education programs, preparation of guidelines for ADR spontaneous reporting ensuring reporters feed-back information and implementation of the regional pharmacovigilance units must be implemented in order to reinforce the conception of effective pharmacovigilance and medicine safety system.

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