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Original Article

A Framework of National Pharmacovigilance System for Developing Countries

Maryam Nikookalam[a], Azamossadat Hosseini[b], Hamid Moghaddasi[b]*, Farkhondeh Asadi[b], Afshin Zarghi[c]

[a]PhD student of Health Information Management, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [b]Department of Health Information Technology and Management, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [c]School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Abstract

Pharmacovigilance is defined as "the science and activities related to the detection, assessment, understanding, and prevention of adverse drug reactions or any other drug-related problems". The framework of the national pharmacovigilance system illustrates the general pattern of how the health system approaches the care of health products, defines the philosophy of supervision and policy orientation, and outlines the structure and development priorities of pharmacovigilance. The present study was conducted with the aim of presenting a framework of the national pharmacovigilance system framework for developing countries. The present study is of an applied study that was conducted descriptively in 2023. To present a framework of the national pharmacovigilance system framework, the main components of the national pharmacovigilance system framework were first identified and determined through a review of valid scientific sources and texts and national pharmacovigilance systems of the countries under study, considering the conditions and requirements of these countries. Then, the proposed model was put to the opinion of 65 experts for validation, and the Delphi method was implemented with a three-point scale in two rounds. Based on the results of the present study, the main components of the national pharmacovigilance system framework include: functions, infrastructure, and network. Each component includes sub-components and related operations and was agreed upon by experts with an average agreement rate of 95%. The framework of the national pharmacovigilance system is essential as a guide for the implementation of the national pharmacovigilance system. This framework enables a comprehensive evaluation of the structures and national and regional institutions affecting pharmacovigilance and can lead to the optimal implementation of the national pharmacovigilance system in developing countries. The national pharmacovigilance system can reduce drug-related problems, and its ultimate result can be a reduction in mortality and morbidity rates.

Keywords: Pharmacovigilance; Drug monitoring system; Drug safety; Adverse drug events; Adverse drug reactions.

Corresponding Authors: Professor of Health Information Management and medical informatics, Faculty of Paramedical Sciences, Shahid Beheshti University of Medical Sciences, Darband St, Ghods Square, Tehran, Iran. E-mails: moghaddasi@sbmu.ac.ir.
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1. Introduction

Adverse drug reactions are one of the main causes of death in various societies [1-4] and impose significant costs on the country's health

system [5-12]. Numerous studies show that more than half of adverse drug reactions (45 to 90 percent) are preventable [5, 8, 9, 13-15]. An effective pharmacovigilance (PV) system ensures continuous monitoring of drugs and their safe use [16] and is one of the effective tools in preventing adverse drug reactions. Pharmacovigilance is defined as "the science and activities related to the detection, assessment, understanding, and prevention of adverse drug reactions or any other drug-related problems" [17-20]. The most important action to achieve a coherent pharmacovigilance system is to observe the guidelines and standards developed by the World Health Organization and the Uppsala Monitoring Centre (UMC), which describe the practical details of the information flow [21].

In the past 20 years, many countries have established national pharmacovigilance systems and joined the WHO network, but very few of these countries have the efficient national pharmacovigilance systems. Despite improved access to drugs, there has been no desirable progress in infrastructures and pharmacovigilance activities for monitoring adverse drug reactions and addressing safety issues. Most national centers are limited in terms of pharmacovigilance capacity, lack a supervisory framework, and structures governing laws and regulations [22-25]. The advancement of this system varies greatly in different countries [16, 26]. The lack of a functional and structured national pharmacovigilance system could be barriers to the supply of pharmaceutical products to countries and consequently create serious restrictions in patients' access to therapeutic options [24] and reduce the success of public health of related programs [22].

The pharmacovigilance framework serves as a guide for choosing an advanced pharmacovigilance system. The existence of a national system framework can help in the comprehensive evaluation of structures and national and regional institutions affecting pharmacovigilance [27]. The U.S. Agency for International Development (USAID 2009) in Strengthening Pharmaceutical Systems [SPS] presented a conceptual framework and operational approach for strengthening pharmacovigilance systems in developing countries [28]. Management Sciences for Health (MSH 2011) introduced a similar framework for this national system with minor changes in the mentioned framework [29]. This framework is essentially based on three prominent components: people, structures, and systematic functions [29, 30].

Chakrabarty and Thawani presented a framework for the national pharmacovigilance system in India, which includes two general parts: "manpower and the machinery" and "tasks of pharmacovigilance". Manpower include the staff of the National Pharmacovigilance Center (NPC), pharmacology experts, clinical medicine, epidemiology, toxicology, and advisory committee. Also, machinery includes hardware and as well as a few basic technological requirements in this center, for instance; uninterrupted power supply, telephone, computer, printer, fax, internet, photocopier. Pharmacovigilance duties in this framework include: information services, development and dissemination of information, evaluation,

secondary prevention of adverse drug reactions, reaching out, data processing, hypothesizing, and medicine regulation. Also, the items considered in the initial map of the establishment and launch of the pharmacovigilance system include; communication processes, how to collect data, disseminate information, system deployment needs, internal training, database, promotion of the pharmacovigilance system, and networking [31].

Also, Saha refers to the need for a pharmacovigilance network to manage data related to reports and identification of adverse drug reactions in a systematic way from different levels of community health care. Generally, in this framework, basic steps in setting up a pharmacovigilance network include: developing a general guideline, setting up of NPC, capacity building for it, data acquisition by ADR form, stimulation of ADR reporting, signal detection in an adverse drug event, and relations with other parties [30].

In addition, Tanja et al. state that some new and evolving national frameworks align with international standards, but others have added significant complexity and breadth to pharmacovigilance requirements, placing avoidable burden on stakeholders without necessarily benefiting patients [32].

Also, another systematic review study on the performance and activities of PV national system in developing countries using World Health Organization indicators showed that a multistakeholder approach towards strengthening national pharmacovigilance systems in developing countries is required, Furthermore, it highlights the need for applying a holistic approach that takes into account the resources and infrastructure available when addressing the policy and programmatic gaps in each [33].

Given that the advancement of national pharmacovigilance systems varies from basic facilities in low- and middle-income countries to the use of advanced technologies in developed countries [16], and unlike developing countries, most developed countries have structured organizations, frameworks, and strong pharmacovigilance systems [26], therefore, the present study was conducted with the aim of presenting a framework for the national pharmacovigilance system for developing countries.

2. Materials and Methods

The present study is an applied study that was conducted descriptively in 2023. It was conducted in two parts. Initially, electronic databases (EMBASE, MEDLINE, Google Scholar, and Web of Science) were searched for relevant, valid scientific texts published between 2004 and 2023. The search was initiated using the term 'pharmacovigilance system' and its synonyms, in combination with other groups of keywords that covered 'infrastructure'. The components of the national pharmacovigilance system framework, including policies, legal requirements, principles, standards, stakeholders, the communication network among them, and different processes in the national pharmacovigilance system, were identified and determined.

The results obtained were summarized through comparison and analysis, and the proposed framework was designed considering the conditions and requirements of developing countries and was put to the opinion of related experts. Final model was designed after considering the useful opinions of the experts. Finally, the validation of the proposed framework was carried out through the opinion of 65 experts, including faculty members of pharmacy colleges (15 people), faculty members of various medical fields (15 people), heads of drug research centers (9 people), pharmacists working in educational and therapeutic centers (15 people), executive managers of the Food and Drug Administration (4 people), managers of pharmaceutical companies (7 people) using the Delphi method and based on a three-point scale (unacceptable (0 -50 percent), relatively acceptable (50 to 85 percent), and acceptable (85 to 100 percent)) and in two rounds.

Validity of the data collection tool has been conducted through content validity through obtaining the opinions of relevant experts in this field. The reliability of this questionnaire was 0.81.

Data analysis in the first stage [identification of the components of the national pharmacovigilance system framework] was performed with a content analysis approach. Also, the analysis of the collected data in the validation stage of the framework was performed using descriptive statistics at the level of absolute and relative frequency distribution.

3. Results and Discussion

The framework proposed by the Management Sciences for Health serves as a foundational model for the development of a national pharmacovigilance system in various nations, with a particular emphasis on developing countries [34-39]. This framework is characterized by three key components: human resources, infrastructural elements, and systematic functions [29, 30]. The organization underscores the importance of a comprehensive and continuous pharmacovigilance system, which includes functions for monitoring, detecting, reporting, evaluating, and documenting medication safety data. Additionally, it emphasizes the need for intervention and information gathering from, and educational feedback provision to, reporters, prescribers, healthcare workers, other healthcare professionals, and consumers [28, 29, 40].

The national pharmacovigilance system framework in Canada is governed by the Federal Regulatory Post-Market Surveillance Strategy. This framework aims to optimize resources by prioritizing higher-risk products through standardized policies and implements a vigilance framework that consistently manages risks across product lines.

The pharmacovigilance framework presented by the Canadian Ministry of Health incorporates the continuous integration of new product vigilance tools into three functions that occur throughout the product lifecycle. These functions include data collection and processing, monitoring and evaluation, and risk management, and are based on the risk level of the product type. For the updating of the legal framework, it is necessary to develop new or improved regulations, guidelines, or policies. Additionally, the use of new or re-engineered processes and new information management and information technology tools is recommended [41].

In India, the Ministry of Health has designated the Indian Pharmacovigilance Commission with the aim of monitoring the specifications and benefits of drugs, the main goal of which is to create independent information about drug safety. This center focuses on the development of a database of drug information and adverse drug reactions and all medical institutions, hospitals, colleges, and public health programs in the country, both governmental and private, must report adverse drug reactions so that all product data are collected and analyzed in one place [42]. To ensure the quality of adverse drug reaction data, a quality review panel has been established to guarantee quality, and all centers are evaluated based on performance measurement criteria, completeness of the report, training provided, and other parameters mentioned in the pharmacovigilance program protocol [43]. The framework of the national pharmacovigilance system in India is based on the model presented by the Management Sciences for Health with three basic components: human resources, structure, and processes [44].

In Indonesia, from 2008 to 2011, a legal framework was established to strengthen pharmacovigilance, which makes the implementation of pharmacovigilance mandatory for pharmaceutical industries. The pharmacovigilance system in Indonesia includes voluntary reporting in hospitals and public health centers, public and private centers, through drug manufacturers by submitting a yellow form [45].

In many Asian countries such as Malaysia, the Philippines, Indonesia, South Korea, Saudi Arabia, the culture of reporting adverse drug reactions is distressingly low, and this may be partly because adverse drug reactions are not recognized. Sometimes adverse drug reactions are mistakenly perceived as part of therapeutic actions, and it is unlikely that doctors will report its [46, 47]. Also, the method of collecting, arranging, and reporting adverse drug reactions in each country has different problems. Also, in the pharmacovigilance systems of some countries, formal programs are held in the process of the national pharmacovigilance system framework for specific training programs for users and specialized forces of the system [48-50]. In most of the countries studied, the three components of human resources, structure, and processes are considered as the main components of the national pharmacovigilance system framework (**Table 1** and **2**).

Table 1. Components of the national pharmacovigilance system framework in the studied countries.

Country		H.R*	Structure	Processes
Developed	China	✓	✓	✓
	USA	✓	✓	✓
	United Kingdom	✓	✓	✓
	Canada	✓	✓	✓
	Japan	✓	✓	✓
	India	✓	-	✓
Developing	UAE	✓	✓	✓
	Saudi Arabia	✓	✓	✓
	S. Korea	✓	✓	✓
	Nepal	-	✓	✓
	Bangladesh	✓	✓	✓
	Pakistan	-	-	✓
	Malaysia	✓	✓	✓
	Thailand	✓	✓	✓
	Indonesia	✓	-	✓

* Human resource

Table 2. Processes of the national pharmacovigilance system in the studied countries.

Country		Data gathering	Signal detection	Risk assessment	Drug quality	Decision making	Relationships	Rules & regulation
Developed	China	✓	✓	✓	✓	✓	✓	✓
	USA	✓	✓	✓	✓	✓	✓	✓
	United Kingdom	✓	✓	✓	✓	✓	✓	✓
	Canada	✓	✓	✓	✓	✓	✓	✓
	Japan	✓	✓	✓	-	✓	✓	✓
	India	✓	✓	✓	✓	✓	✓	✓
Developing	UAE	✓	✓	✓	✓	✓	✓	✓
	Saudi Arabia	✓	✓	✓	✓	✓	✓	✓
	S. Korea	✓	✓	✓	✓	✓	✓	✓
	Nepal	✓	✓	-	✓	✓	-	-
	Bangladesh	✓	✓	✓	✓	✓	✓	-
	Pakistan	✓	-	✓	✓	✓	-	✓
	Malaysia	✓	✓	✓	✓	✓	✓	✓
	Thailand	✓	✓	✓	✓	✓	✓	✓
	Indonesia	✓	✓	✓	✓	✓	✓	✓

Based on the results of the study of various countries' pharmacovigilance frameworks and considering the conditions and requirements of developing countries, the main components of the national pharmacovigilance system framework, after considering the opinions of experts, were determined to include three components: work processes, infrastructure, and communication network.

The main work processes in this framework include data collection, data analysis, reporting, decision-making and appropriate actions, providing feedback to network components, and supervision of drug synthesis. The infrastructure component includes policies, principles, standards, and legal requirements, and the communication network includes the Food and Drug Administration (FDA) as the NPC, drug research centers, drug manufacturers, drug importing companies, drug distribution companies, drug prescribing centers, sources of adverse drug reaction collection, drug sales and delivery centers, patients and consumers of pharmaceutical products, and relationships between network components. Also, for each of the above sub-components, specific functions were determined.

According to the experts' opinions, the components 'providing feedback to network nodes' and 'supervising the modification of drug synthesis' (respectively with 74% and 57%) are proposed to be added as components of the work processes and 'patients and consumers of pharmaceutical products' as one of the network components within the framework of the national pharmacovigilance system considered in the final model.

After reviewing the suggestions of the experts and presenting them to the expert panel and their final approval, the necessary amendments were made in the model, the suggestions were considered, and the final model of the national pharmacovigilance system framework for developing countries was designed as Figure 1 and then put to the opinion in the second stage of Delphi (**Figure 1**).

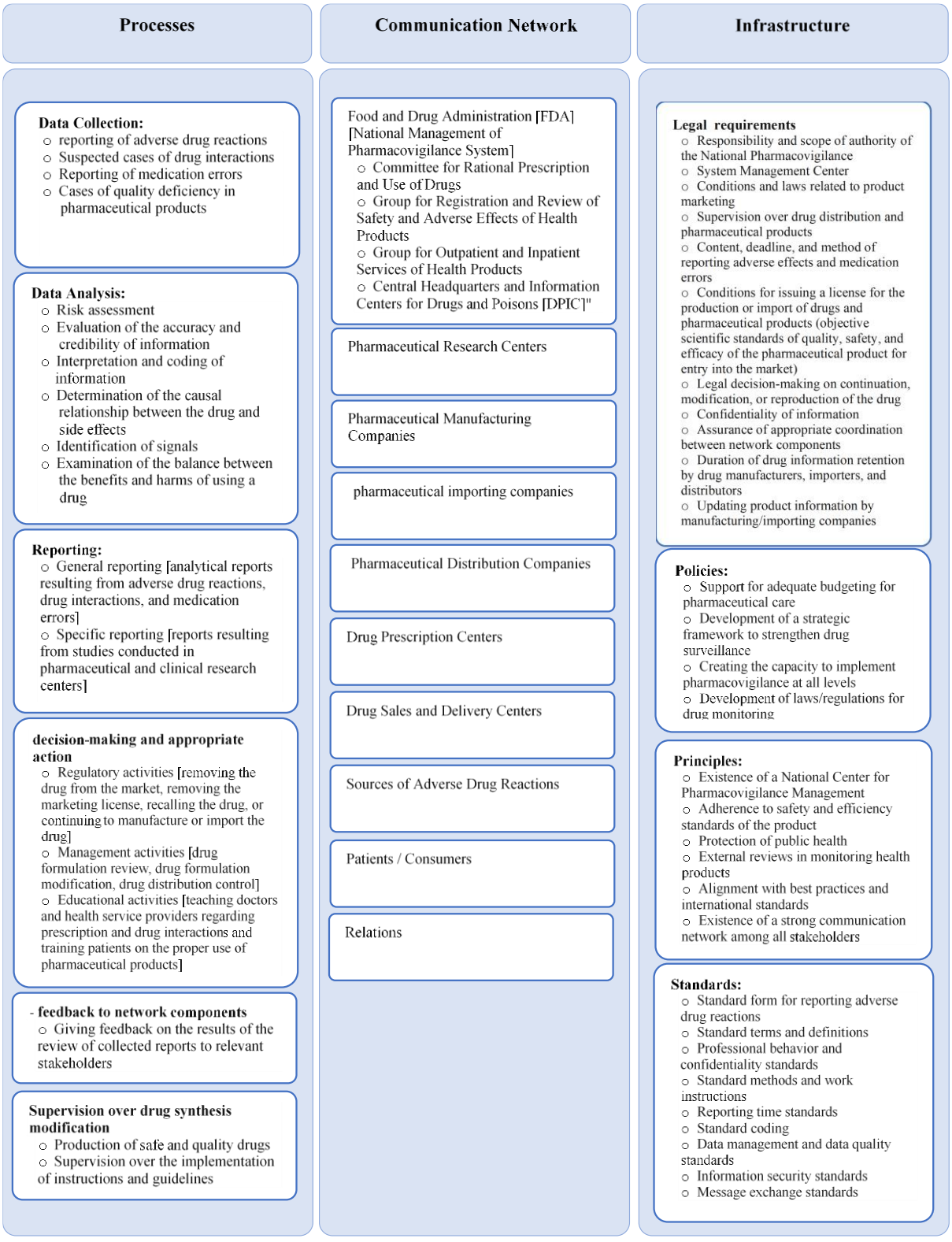

Figure 1. The national pharmacovigilance system framework for developing countries.

In the second stage of the Delphi method, the validation of the designed model was examined through the opinions of experts and was based on a three-point scale. All the components determined in the model of the national pharmacovigilance system framework

for developing countries were agreed upon by the experts with an average agreement rate of 95 percent (**Table 3**).

The national pharmacovigilance system framework in some countries, such as the European Union, has a multi-level nature and is defined at the European Union and national levels. These levels are interconnected through multiple relationships and collectively form the European Union's pharmacovigilance network. The framework of the Indian pharmacovigilance system is defined at four levels: regional, national, zonal, and environmental. Qualified colleges, hospitals, and medical centers have been selected as centers for monitoring adverse drug reactions. While the national pharmacovigilance system framework in some other countries such as Canada and Japan is regulated with federal regulatory post-market surveillance strategy.

The national pharmacovigilance system framework presented by the U.S. Agency for International Development (USAID) and Management Sciences for Health (MSH), which forms the basis for the development of the national pharmacovigilance system in various countries.

Table 3. Validation of the components of the national pharmacovigilance system framework of developing countries.

The main component	Components	Acceptable	Relatively acceptable	Unacceptable	Percent Agreement
Functions	Data collection	65	-	-	**100%**
	Data analysis	65	-	-	**100%**
	Reporting	23	35	7	**89%**
	Decision making	65	-	-	**100%**
	Feedback to network components	42	14	9	**86%**
	Supervising drug synthesis	26	19	20	**70%**
Infrastructure	Policies	65	-	-	**100%**
	Principles	52	9	4	**94%**
	Standards	65	-	-	**100%**
	Legal requirements	20	35	10	**85%**
Communication network	Food and Drug Organization	65	-	-	**100%**
	Pharmaceutical research centers	65	-	-	**100%**
	Drug Manufacturers	58	٥	2	**97%**
	Drug importing companies	43	11	11	**83%**
	Drug distribution companies	55	7	3	**95%**
	Drug prescribing centers [office, clinic, hospital]	65	-	-	**100%**
	Drug sales and delivery centers [pharmacies]	65	-	-	**100%**
	Sources of adverse drug reactions	65	-	-	**100%**
	Patients/consumers	65	-	-	**100%**
	Relationships	57	3	5	**92%**

Especially developing countries, is defined at the national level and is designed with three main components: people, functions, and structures.

However, an important point is that studies have shown that there is a low probability that an overly complex and heavy national pharmacovigilance system will be sustainable, especially in developing countries where there are limited infrastructures and resources [32].

Based on the results obtained from the present study, most of the countries under study had at least the processes expected by the World Health Organization. In the national pharmacovigilance system framework of the Management Sciences for Health organization, these processes include monitoring, identification, reporting, evaluation and documentation of drug safety data, as well as intervention and information collection and provision of educational feedback to reporters, healthcare providers, and consumers. Despite the fact that the mentioned framework is well-designed considering the requirements of the World Health Organization, it has not been effectively implemented in developing countries.

In the European Union's national pharmacovigilance system framework, the processes include collecting and managing data on drug safety, identifying signals, evaluating data and decision-making with regard to safety issues, proactive risk management, action to protect public health, establishing communication and informing stakeholders and people, auditing results and related key processes. Also, to ensure the uniform observance of pharmaceutical regulations, a set of technical principles in the form of documents, Good Manufacturing Practice (GMP), Good Distribution Practice (GDP), and Good Pharmacovigilance Practice (GVP) have been compiled. In Canada, the processes of the pharmacovigilance framework presented by the Ministry of Health, with the aim of continuous integration of surveillance tools in three process areas throughout the product life cycle, including data collection and processing, monitoring and evaluation, and risk management, are defined based on the product's risk level.

In most developing countries, pharmacovigilance activities are limited to reporting adverse drug reactions through a yellow form, and the implementation of superior pharmacovigilance guidelines requires extensive review and modification of processes in this area. Therefore, in the present study, considering the minimum processes expected by the World Health Organization and the conditions of such countries, the main processes in the framework of the national pharmacovigilance system include data collection, data analysis, reporting, legal decision-making, drug synthesis monitoring, and providing feedback to network components.

Also, based on the results of the present study, legal infrastructures were somehow considered in most of the studied frameworks. In some cases, it was mentioned as the main component of the national pharmacovigilance system framework, and in others, it was designed as a legal framework, guidelines, and superior action guides. For example, in the national pharmacovigilance system framework

of the Management Sciences for Health organization, legislative institutions are one of the components of the structure component. While in the European Union, Canada, Indonesia, and Saudi Arabia, a legal framework for drug safety surveillance has been determined and regulations, instructions, and policies are periodically reviewed and modified if necessary. In the drug governance framework, which has been designed based on the areas introduced as the characteristics of good governance by the United Nations Economic and Social Commission for Asia and the Pacific, policies, laws, and regulations are considered as the main components of the framework.

As a result, in this study, considering the importance of regulatory regulations for monitoring the safety of drug products and the wider term of infrastructures, it was determined as the main component of the national pharmacovigilance system framework, which includes sub-components of regulations and legal requirements, policies, principles, and standards.

One of the most important parts of the national pharmacovigilance system framework is determining the involved individuals, their roles, and their relationships in relation to the main processes of the framework. This component was mentioned in the studied frameworks with different names such as: people, structures, manpower, stakeholder coordination, those involved, etc., and each includes different individuals and organizations. In this regard, in many of the studied frameworks, two components of structure and manpower were mentioned. The structure includes the government, industry, hospitals, universities, professional, medical and pharmaceutical associations, poison and drug information centers, health professionals, patients and consumers, media, and manpower includes reporters of adverse drug reactions and evaluators.

The people involved in the national pharmacovigilance system framework of the European Union, in addition to the above, include regulatory authorities, pharmaceutical companies, and drug importers or distributors. In this study, the communication network, which has a wider comprehensiveness, was determined as the main component, which includes all the above-mentioned individuals and organizations and the communication network between them.

Given the above, the national pharmacovigilance system framework presented in this study, while having the characteristics and basic components of the effective national pharmacovigilance system frameworks in the world, considering the conditions and requirements of developing countries, has been designed with three main components of processes, infrastructures, and communication network and related sub-components.

4. Conclusion

The national pharmacovigilance system framework shows the general pattern of how the health system cares for health products, defines the philosophy of surveillance and policy orientation, and outlines the structure and priorities of pharmacovigilance

development. This study, considering the conditions, requirements, and needs of developing countries, has presented the national pharmacovigilance system framework for the establishment of an effective national pharmacovigilance system in these countries. This framework has three main components: processes, infrastructures, and communication networks. In general, after collecting information related to adverse drug reactions, drug interactions, or drug errors in various ways, the data are analyzed, the severity of the adverse event, the probable cause, and the preventability of it are determined. Also, research centers may obtain valuable data on the safe use of drug products through research studies. The results obtained are sent to the national pharmacovigilance centers (Food and Drug Administration) in the form of general and specific reports, which has the authority to take appropriate actions. The final activity in the framework is decision-making and taking appropriate action. Necessary interventions to reduce risk may be supervisory (such as revoking marketing authorization, recalling drugs), managerial (reviewing drug formulary, controlling drug distribution), or educational (training physicians on drug interactions or the proper use of the product for consumers). Finally, the actions taken are shared with reporters and other network components. Then, by following up on the collected and analyzed data, the effectiveness of the interventions should be measured. The outcome of this pharmacovigilance system reduces drug-related problems, and its final result is a reduction in mortality and morbidity rates.

Conflict of interest

The authors declare to have no conflict of interest.

References

[1] Campbell J, Gossell-Williams M, Lee M. A review of pharmacovigilance. The West Indian Medical Journal. 2014;63[7]:771.

[2] PI. P. Clinical perspectives in drug safety and adverse drug reactions. Expert Rev Clin Pharmacol. 2008;1[5]:695.

[3] Wiktorowicz M, Lexchin J, Moscou K. Pharmacovigilance in Europe and North America: Divergent approaches. Soc Sci Med. 2012;75[1]:165-170.

[4] World Health Organization. [2004]. Pharmacovigilance: ensuring the safe use of medicines. World Health Organization. https://iris.who.int/handle/10665/68782. [Accessed July, 2021]

[5] Gyllensten H HK, Jönsson AK, Sundell KA, Hägg S, Rehnberg C, et al. Modelling drug-related morbidity in Sweden using an expert panel of pharmacists. Int J Clin Pharm. 2012;34:548.

[6] Santoro A, Genov G, Spooner A, Raine J, Arlett P. Promoting and Protecting Public Health: How the European Union Pharmacovigilance System Works. Drug Saf. 2017 Oct; 40[10]: 855-869

[7] Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. Ann Pharmacother. 2008 Jul; 42[7]: 1017-25.

[8] Brvar M, Fokter N, Bunc M, Mozina M. The frequency of adverse drug reaction related admissions according to method of detection, admission urgency and medical department specialty. BMC Clin Pharmacol. 2009 May 4;9:8.

[9] Hakkarainen KM HK, Petzold M, Hägg S. Percentage of patients with preventable adverse drug reactions and preventability of adverse drug reactions - a meta-analysis. PLoS One. 2012;7[3]:11-3.

[10] World Health Organization. [2014]. Reporting and learning systems for medication errors: the role of pharmacovigilance centres. World Health Organization. https://iris.who.int/handle/10665/137036. [Accessed May, 2021]

[11] Schatz S, Weber R. Adverse drug reactions. Pharmacy Practice. 2015;1[1].

[12] Watanabe JH MT, Hirsch JD. Cost of Prescription Drug–Related Morbidity and Mortality. Ann Pharmacother. 2018;52[9]:829.

[13] Kant A BJ, Hopkins PM. Adverse Drug Reactions. In Elsevier Inc. 2019:130-143.

[14] Woo SA CA, Wickham ME, Peddie D, Balka E, Scheuermeyer F, et al. Methods for evaluating adverse drug event preventability in emergency department patients. BMC Med Res Methodol. 2018;18[1]:1-8.

[15] Gholami K, Shalviri G. Factors associated with preventability, predictability, and severity of adverse drug reactions. Ann Pharmacother. 1999 Feb; 33[2]: 236-40.

[16] World Health Organization. [2015]. WHO pharmacovigilance indicators: a practical manual for the assessment of pharmacovigilance systems. World Health Organization. https://iris.who.int/handle/10665/186642 [Accessed October, 2022]

[17] Harpaz R, DuMouchel W, Shah NH, Madigan D, Ryan P, Friedman C. Novel data-mining methodologies for adverse drug event discovery and analysis. Clin Pharmacol Ther. 2012 Jun; 91[6]: 1010-21.

[18] World Health Organization. [2002]. The importance of pharmacovigilance. World Health Organization. https://iris.who.int/handle/10665/42493 [Accessed June, 2021]

[19] World Health Organization. [2020]. Action framework to advance universal access to safe, effective and quality-assured blood products 2020–2023. World Health Organization. https://iris.who.int/handle/10665/331002. License: CC BY-NC-SA 3.0 IGO

[20] Rohilla A, Singh N, Kumar V, Kumar M, Sharma AD, Kushnoor A. Pharmacovigilance: Needs and objectives. Journal of Advanced Pharmacy Education & Research Oct-Dec. 2012;2[4].

[21] World Health Organization. Quality Assurance and Safety of Medicines Team. [2006]. The safety of medicines in public health programmes: pharmacovigilance, an essential tool. World Health Organization. https://iris.who.int/handle/10665/43384 [Accessed June, 2021]

[22] Nwokike J LE, Thumm M, An L. Comparative analysis of pharmacovigilance systems in five Asian countries. Pharmacoepidemiol Drug Safety. 2014:23-38.

[23] Olsson S PS, Dodoo A. Pharmacovigilance in resource-limited countries. Expert Rev Clin Pharmacol. 2015;8[4]:449-60.

[24] World Health Organization. [2018]. WHO Drug Information 2018, vol. 32, 2 [full issue]. WHO Drug Information, 32 [2], 187 - 282. World Health Organization. https://iris.who.int/handle/10665/330922 [Accessed Aug, 2021]

[25] Elshafie S RA, Zaghloul I. Pharmacovigilance in developing countries [part II]: a path forward. Int J Clin Pharm. 2018;40[4]:764-8.

[26] Sushma VK AS, SK, S. Pharmacovigilance in India: Present Scenario and Future Challenges. Drug Saf. 2019;42[3]:339-46.

[27] Moscou K, Kohler JC. Pharmacogovernance: Advancing pharmacovigilance and patient safety. In Social and Administrative Aspects of Pharmacy in Low-and Middle-Income Countries. Academic Press: 2018; 403-418.

[28] Strengthening Pharmaceutical Systems [SPS]. Supporting pharmacovigilance in developing countries: the systems perspective. Submitted to the US Agency for International Development by the SPS Program. 2009.

[29] Management Sciences for Health. MDS-3: Managing Access to Medicines and Health.

[30] Technologies. Management Sciences for Health: Arlington, VA [2012].

[31] Saha PS. Starting-up a pharmacovigilance network from scratch: A brief plan. Journal of

Pharmaceutical Research and Clinical Practice [JPRCP]. 2014;4[1]:58-66.

[32] Chakrabarty M, Thawani V. Starting a pharmacovigilance center: actions for implementation. Journal of pharmacology & pharmacotherapeutics. 2011;2[4]:295.

[33] Tanja Peters NS, Maya Abbas, Jabeen Ahmad, Jean‐Christophe Delumeau, Esteban Herrero‐Martinez MP, Johanna Piper, Fairouz Smail‐Aoudia, Willemijn van der Spuij TV, Gillian Winstanley Effective Pharmacovigilance System Development: EFPIA‐IPVG Consensus Recommendations. Drug Safety. 2021;44:17-28.

[34] Hamza Y. Garashi DTS, Ellen I. Schafheutle. A Systematic Review of Pharmacovigilance Systems in Developing Countries Using the WHO Pharmacovigilance Indicators. Therapeutic Innovation & Regulatory Science. 2022;56:717-43.

[35] Suke SG, Kosta P, Negi H. Role of pharmacovigilance in India: An overview. Online journal of public health informatics. 2015;7[2].

[36] Jha N, Rathore DS, Shankar PR, Thapa BB, Bhuju G, Alshakka M. Need for involving consumers in Nepal's pharmacovigilance system. The Australasian medical journal. 2014;7[4]:191.

[37] Sailakshmi BNS LT. Pharmacovigilance for Drug Safety Monitoring. J Pharm Nanotechnol. 2016;4:47-53.

[38] Sumit K AB. HARMACOVIGILANCE IN INDIA: PERSPECTIVES AND PROSPECTS. J Drug Deliv Ther. 2013;3:237-46.

[39] Mustansir MA- SD, Paul S, Rahim Z Bin, Hosen SMZ. Studies on Pharmacovigilance in Bangladesh: Safety Issues. Int J Pharm Teach Pract. 2013:613-21.

[40] Mohiuddin A. Pharmacovigilance: Present Scenario and Future Goals. Indian Journal of Pharmacy Practice. 2019;12.

[41] Strengthening Pharmaceutical Systems [SPS] Program. Indicator-Based Pharmacovigilance Assessment Tool: Manual for Conducting Assessments in Developing Countries. Submitted to the US Agency for International Development by the SPS Program. Arlington [2009[.

[42] Health Mo. Health Product Vigilance Framework. MedEffect TM Canada. 2012.

[43] Brashier DB, Sharma S. An adverse drug reaction clinic: Breathing fresh life into the pharmacovigilance programme. Journal of pharmacology & pharmacotherapeutics. 2012;3[1]:74.

[44] Biswas P, Biswas AK. Setting standards for proactive pharmacovigilance in India: The way forward. Indian Journal of Pharmacology. 2007;39[3]:124.

[45] Sanvidhan G Suke PK, Harsh Negi. Role of Pharmacovigilance in India: An overview. Online Journal of Public Health Informatics. 2015;7[2].

[46] Wangge G, Akbar W. Knowledge, attitudes and practice of pharmacovigilance among health care professionals in Indonesia. Health Science Journal of Indonesia. 2016;7[1]:59-63.

[47] Hartigan-Go K. Developing a pharmacovigilance system in the Philippines, a country of diverse culture and strong traditional medicine background. Toxicology. 2002;181:103-7.

[48] Biswas P. Pharmacovigilance in Asia. Journal of pharmacology & pharmacotherapeutics. 2013;4 [Suppl1]: S7.

[49] Alshammari TM, Alshakka M, Aljadhey H. Pharmacovigilance system in Saudi Arabia. Saudi pharmaceutical journal. 2017;25[3]:299-305.

[50] Elkalmi RM, Hassali MA, Ibrahim MIM, Widodo RT, Efan QM, Hadi MA. Pharmacy students' knowledge and perceptions about pharmacovigilance in Malaysian public universities. American journal of pharmaceutical education. 2011;75[5].

[51] Shin JY, Jung SY, Ahn SH, Lee SH, Kim SJ, Seong JM, et al. New initiatives for pharmacovigilance in South Korea: introducing the Korea Institute of Drug Safety and risk management [KIDS]. Pharmacoepidemiology and drug safety. 2014;23[11]:1115-22.