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Implementation Status and Challenges of Pharmacovigilance Program in Ethiopia: A Mixed-Methods Study

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Abstract

Functional pharmacovigilance systems are vital to ensure patient safety. There is a paucity of information on the organizational functionality of pharmacovigilance program in Ethiopia. This study assessed the pharmacovigilance programs and its implementation status in Ethiopia. A mixed study design was employed to assess pharmacovigilance functionality in hospitals, pharmaceutical companies, and the National Regulatory Authority. World Health Organization's Pharmacovigilance Indicators and Key Informant Interview Guide were used for data collection. Quantitative data were analyzed using Microsoft Excel (2013), while thematic analysis was used for qualitative study. Of the 30 hospitals covered, only one had a Pharmacovigilance Unit with a dedicated budget, three (10%) had assigned staff, and seven (23.3%) had implemented Standard Operating Procedures. Similarly, 4 (12.5%) of the 32 pharmaceutical companies had separate pharmacovigilance divisions, 12 (37.5%) had a regulatory affairs unit, and 5 (15.6%) had a pharmacovigilance budget. The National Pharmacovigilance Center has the most structure, process, and pharmacovigilance practices. Resource constraints and a weak reporting system were identified as major challenges, while patient harm, loss of confidence, increased circulation of unsafe products, and economic costs were reported as consequences. Increasing training, engaging stakeholders, and improving the regulatory system were recommended as key interventional strategies. Most hospitals and pharmaceutical companies lack most of pharmacovigilance system indicators. However, the national regulatory authority fulfilled most of the elements of Pharmacovigilance systems.

Keywords

adverse drug events, pharmacovigilance system, Ethiopia, patient safety, regulatory system

What do we already know about this topic?

- Healthcare professionals (HCPs) have a low level of knowledge, negative attitude, and less practice toward pharmacovigilance
- The number of reports received from HCPs to the national pharmacovigilance center (NPC) has been low
- In the WHO global benchmarking tool for evaluating the national regulatory system, Pharmacovigilance (PV) is one of the main tools.

How does your research contribute to the field?

- Advances the country's PV frameworks and system
- Enhance understandings of Adverse Drug Event (ADE) reporting through identification of influencing factors
- Improve ADE reporting through identification of barriers and enablers
- Strengthen regulatory decision-making
- Inform the need for development of PV specific policy in the country

What are your research's implications toward theory, practice, or policy?

- Expansion of training, and awareness creation campaign
- Undertake a high level of discussions with various stakeholders
- Incorporation of PV into procedures and clinical practices
- Inclusion of PV specific policies to adequately address PV
- Expanding active surveillance activities and integrate into the national PV system

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Introduction

Promoting patient safety is the main target of a healthcare system. Medicines play essential roles in the protection and promotion of public health. However, critical incidences and tragedies have been associated with medicines, often called adverse events.[1,2] Implementation of effective Pharmacovigilance (PV) system has been praised as an essential tool for the timely detection and management of Adverse Drug Events (ADEs). The World Health Organization (WHO) defined PV as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problems."[3,4] A robust *PV* system requires coordinated, interdependent activities, resource mobilization, and stakeholders' involvement to improve medicine safety.[5]

The global demand and access to new and effective medicines are rising with potential benefits and harms to end-users.[6] About 96% of the developed countries have functional local PV systems, while only 27% of low and middle-income countries (LMICs) have such systems.[7] The hindrances are the shortages of requisite infrastructures, resources, and coordination platforms.[8] Most LMICs lack a proper system to ensure the safety of medicines, and the PV system in these countries is still fledgling, characterized by inadequate funding, shortage of human and technical resources, and lack of adequate legal and regulatory provisions.[9,10]

Even though most African countries, including Ethiopia, are members of the WHO's collaborative drug monitoring Center, few have fully functional systems. Evidence showing the continent's burden of harm related to the safety of medicines is quite scarce.[10] There is a high underreporting of Adverse Drug Reactions (ADRs).[11,12]

A study in Ethiopia underlined that few reports are being submitted to the national PV Center (NPC).[13] There is little data on the PV system's effectiveness, functionality, and implementation status. Therefore, this study aimed to assess the PV system concerning the existence of structures, instruments, and implementation status in the selected pharmaceutical companies, hospitals, and the National Regulatory Authority (NRA).

Methods

Study Design

A mixed study design using both quantitative and qualitative techniques was employed for the study. The study was conducted from October 2019 to April 2020.

Study Setting, Source, and Study Population

For the quantitative survey, all available public and private hospitals in Addis Ababa, pharmaceutical companies (local medicine manufacturers, importers, and multinationals) in the country, and the NRA were used as a source population. The study population was general and specialty hospitals in Addis Ababa, local medicine importers registered as primary agents, local manufacturers which are not newly established, and multinationals having marketing and sales coordinating offices in Ethiopia.

For the qualitative study, the source population was all professionals working at hospitals, pharmaceutical companies and NRA. The study population were those purposively selected experts having experience, role, responsibility, understanding of PV, and position in their respective institutions. Key informants (KIs) were selected from the NRA, hospitals in Addis Ababa and pharmaceutical companies including local medicine manufacturers, multinational manufacturers, and importers registered as primary agents.

Data Collection Instruments

The WHO PV indicator checklist (2015) which is a practical manual for the assessment of PV systems was used to collect structure, process, and outcome level PV data.[14] The PV indicators were contextualized to local situations to collect data to measure the presence or absence of structure, process, and outcome level PV activities and practices from pharmaceutical companies, hospitals, and the NRA. Both core and complementary PV indicators were selected and used for objective measurement for the presence or absence of key infrastructures, activities, and outcomes. In addition, a semi-structured interview guide with probing questions was developed and used for qualitative exploration. The interview guide was developed by the research team based on the objectives and depth of the study. The interview guide was first prepared in English and then translated to the official language called Amharic.

Sampling and Sample Size

For the quantitative study, all government and private hospitals in Addis Ababa were approached to participate in the study. Of the total 33 general and specialized hospitals, 30 hospitals (12 government and 18 private) were willing to participate in the study. The three hospitals (1 government

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and 2 private) were not willing for an undisclosed reason. To determine the final sample size of local medicine importers, one-fourth (25%) of the total local medicine importers registered as a primary agent and accessible in the NRA's medicine registration information system (MRIS) database were used to calculate the final sample size. Accordingly, a total of 83 importers with registered products as primary agents were retrieved from the MRIS database. Of these, 21 (25%) importers were included. On the other hand, all the total 11 local medicine manufacturing companies in Ethiopia were included in the study. However, two of the new manufacturing plants were intentionally excluded from the study, and the remaining (n = 9) local medicine manufacturers were approached and six of them participated in the study. Two companies were not willing to participate and one was under the process of closing the plant. In addition, five of the six multinationals (having marketing sales office in Ethiopia) were included. One company was excluded as it was unable to get the focal person in charge responsible for the provision of data during data collection.

For the qualitative study, KIs were purposively selected from EFDA, pharmaceutical companies (local medicine importers, manufacturers and multinationals), and hospitals. The final sample size was based on data saturation (the point at which the data collection process no longer offers any new or relevant data). Accordingly, saturation was reached after 18 KIs interviews, and three additional interviews were included to check whether additional new ideas emerge or not making a total of 22 KIs.

Sampling Procedure

For the quantitative study, the researchers approached all general and specialized government and private hospitals in Addis Ababa, local medicine manufacturers and multinational suppliers. On the other hand, local medicine importers (registered as primary agents) were randomly selected until it reaches the final size. On the other hand, the key informants were purposively selected until it reaches point of saturation. **Interviews were made individually with KIs**.

Data Collection Procedure

Before commencing the study, an explanatory statement detailing the objective of the study was given to the respective institutions and individual KIs. Heads of the respective study institutions were contacted for their approval and access to data. The checklist was completed by data collector by interviewing the PV focal person in charge. During filling of the checklist for a quantitative study, the interviewer cross-checked the presence of evidences for the objective assessment by asking the focal person to show evidence for the claim. For the qualitative study, an in-depth KI interviews were conducted at their workplace. An interview took an average of 50 to 90 min and an audio record was used for those who are willing and a note was taken for those who refused to record their voice. Interviews were conducted face to face by the two research team members (SE and TM). KIs were invited to describe their opinions in the national working language (Amharic) to give them freedom, and any ambiguity from the interviewee was cleared at the time of the interview.

Data Quality Assurance Process

Before data analysis for the quantitative study, all checklists were cross-checked for their completeness. Some PV indicators which are not relevant or not applicable to the study organizations were removed. For **the qualitative exploration**, three pilot interviews were conducted to check the relevance of the interview guide questions in terms of addressing study objectives and research questions. The pilot test led to minor amendments of the interview guide such as inclusion of additional probing questions, and removing of vague and leading questions.

The transcripts of the interviews were generated from audiotapes and notes were taken and transcribed verbatim in Amharic, translated to English, and analyzed for issues and themes emerging from the text were independently coded and verified by two independent individuals (SE and TM). The interview result was back-translated to compare translations with the original text for quality, accuracy and evaluate the equivalence of meanings between the source and target texts. Also, interview data were analyzed as they were collected through the process of color-coding. Discrepancies during transcription, translation, back translation, and coding were reached into consensus through discussion among the research team members. Moreover, transcripts of the interviews were shared to some selected key informants for member checking.

Data Analysis

Quantitative data were analyzed using Microsoft Excel (2013), and results were expressed descriptively using frequency and percentages. Qualitative data were analyzed using themes with verbatim quotes. The thematic analysis mainly followed a deductive approach where analysis started with predetermined codes to the data set and then find excerpts that fit those codes from the row data set (text from the interviews). Those issues not captured in the deductive analysis or those not fit with themes used in the deductive approach were coded inductively in which themes generated by looking at patterns from the data set. In this approach, the researchers read through texts from interviews and allows codes to emerge. The codes were revised iteratively, and similar codes were grouped into themes. As the process continued, new themes emerged, and groups of related themes (sub-themes) were placed together under larger ones. Following thematic analysis, four core themes emerged:

Table 1. Analysis of core structural Pharmacovigilance indicators in hospitals, Addis, Ababa, Ethiopia, 2020 (N = 30).

		Government (N = 12)		Private (N = 18)		Total (N = 30)	
S/N	Core structural indicators	Yes	No	Yes	No	Yes	No
1	Presence of PV unit/department/	1 (8.3)	11 (91.7)	0 (0)	18 (100)	1 (3.3)	29 (96.7)
2	Availability of human resources to carry out PV functions	3 (25)	9 (75)	0 (0)	18 (75)	3 (10)	29 (90)
3	Availability of regular financial provision for PV unit	1 (8.3)	11 (91.7)	0 (0)	18 (100)	1 (3.3)	29 (96.7)
4	Presence of written SOP for PV	4 (3.3)	8 (66.7)	3 (16.7)	15 (83.3)	7 (23.3)	23 (76.7)
5	SOPs signed, documented and officially adopted	3 (25)	9 (25)	3 (16.7)	15 (83.3)	6 (20)	24 (8)
6	Presence of medicine safety information dissemination tool	4 (3.3)	8 (66.7)	0 (0)	18 (100)	4 (13.3)	26 (86.7)
7	Availability of ADR reporting form in the setting	11 (91.7)	1 (8.3)	16 (88.9)	2 (11.1)	27 (90)	3 (10)
8	Process in place for collection and recording of ADR	11 (91.7)	1 (8.3)	10 (55.6)	8 (44.4	21 (70)	9 (30)
9	Existence of newsletter/bulletin for PV information dissemination	5 (41.7)	7 (58.3)	0 (0)	18 (100)	5 (16.7)	25 (83.3)

Perception of current PV status; Factors influencing the implementation of PV; Impacts on the healthcare system; and Suggested strategies for effective implementation of PV. Under these four major themes, eleven subthemes were identified to describe the context better.

Ethical Considerations

The Ethical Review Board (ERB) of School of Pharmacy, Addis Ababa University approved the study (ERB/SOP/67/04/2019). Before data collection, permission was granted from all participating hospitals, pharmaceutical companies, and the NRA based on the letter of support and ethical clearance. Informed consent was obtained from all study organizations and individual participants before data collection.

Results

Quantitative Results

Background information on study organizations. In the study, 30 general and specialty hospitals, 32 pharmaceutical companies (6 local medicine manufacturers, 21 local importers, and five multinationals), and the NRA were included. Twelve hospitals were government-owned, and 18 were private. Six of the hospitals were teaching hospitals.

Structure, process, and outcome of pharmacovigilance practices and activities in hospitals. Except for one public hospital, no hospitals in the study have established effective PV units, and core PV structural indicators are not sufficiently organized (Table 1).

Regarding the process indicators, it was identified that 17 (56.7%) of the 30 hospitals claimed that they had reported ADR in the previous calendar year to the NPC. Similarly, 9 (30%) hospitals indicated they had reported in the hospital database. However, they could not substantiate their claim with recorded proof. Except for one hospital, none hospitals had active surveillance activities in the last 5 years.

Structure, process, and outcomes pharmacovigilance activities in pharmaceutical companies. Most of the structural elements of PV, such as the presence of PV units, budget, personnel, etc., were not in place in the pharmaceutical companies (Table 2). Like hospitals, most of the pharmaceutical companies in the study did not keep records for process-level PV indicators. For example, 14 (43.7%) pharmaceutical companies reported receiving ADRs in the previous calendar year but could not verify with recorded data. Furthermore, 13 (40.5%) pharmaceutical companies reported the presence of reports in their database, but the authors could not verify with documented evidences. Most of the outcome indicators used did not apply to pharmaceutical companies, and such indicators were excluded from the analysis.

Pharmacovigilance functions at the National Regulatory Authority. Except for the inadequate regular budget and standard ADR reporting form for the public, all other core PV structural requirements are available at the national level (Table 3). However, libraries or references for safety information and web-based training tools were unavailable at the NRA. The NPC under NRA exercises process indicators such as receiving and recording reports, conducting causality assessments, and PMS activities (Table 4). The authority, however, did not have documented data on the number of signals generated in the past 5 years and the percentage of preventable ADRs. However, it claimed that it had taken actions based on reports; of these, one was on safety issues, warnings on the restriction of use, and two withdrawal decisions.

Table 2. Analyzes of core structural Pharmacovigilance indicators in selected pharmaceutical companies, Addis Ababa, 2020, Ethiopia (n = 32).

S/N	Core structural indicators	Local manufacturer		Importer		Multinational manufacturer		Total	
		Yes	No	Yes	No	Yes	No	Yes	No
1	Presence of regulatory unit	3 (50)	3 (50)	6 (28.6)	15 (71.4)	3 (60)	2 (40)	12 (37.5)	20 (62.5)
2	Presence of PV unit/department/	0 (0)	6 (100)	1 (4.8)	20 (95.2)	3 (60)	2 (40)	4 (12.5)	28 (87.5)
3	Presence of human resources for PV unit	0 (0)	6 (100)	2 (9.5)	20 (90.5)	2 (40)	3 (60)	4 (12.5)	28 (87.5)
4	Presence of financial provision for PV	1 (16.7)	5 (83.3)	0 (0)	21 (100)	4 (80)	1 (20)	5 (15.6)	27 (84.4)
5	Presence of written SOP for PV	3 (50)	3 (50)	3 (14.3)	18 (85.7)	4 (80)	1 (20)	10 (31.2)	22 (68.8)
6	Presence of information dissemination tool for PV	1 (16.7)	5 (83.3)	2 (9.5)	19 (90.5)	4 (80)	1 (20)	7 (21.9)	25 (78.1)
7	Presence of safety database support	0 (0)	6 (100)	1 (4.8)	20 (95.2)	4 (80)	1 (20)	5 (15.6)	27 (84.4)
8	Presence of ADR reporting form	1 (16.7)	5 (83.3)	7 (33.3)	14 (66.7)	2 (40)	3 (60)	10 (31.2)	22 (68.8)
9	Process in place for collection, recording, and analysis of ADR	3 (50)	3 (50)	8 (38.1)	13 (61.9)	5 (100)	0 (0)	16 (50.0)	16 (50.0)

Table 3. Analysis of core Pharmacovigilance structural indicators at the national regulatory authority of Ethiopia, Addis Ababa, Ethiopia, 2020.

S.N	Core structural indicators	Yes	No	Remark
1	Availability of statutory provision for PV	√		Incorporated within the Proclamation
2	Presence of PV center or unit	√		Organized as a separate directorate
3	Availability of regular financial provision for the PVC		√	Considered with other budget plans of the authority
4	Presence of human resources to carry out PV functions	√		A mix of professionals in medicine, medical device, food, and laboratory
5	Presence of SOP for PV	√		SOP for receiving and processing ICSRs
6	Presence of national ADRs database	√		Directly adapted from WHO
7	Digitalization of ADR database	√		Shared with WHO
8	ADR reports sent to the WHO database	√		For reports with completed data
9	Presence of publication of ADR bulletin (newsletter) by PV center	√		Newsletter published every 4 months (quarterly)
10	Availability of clear communication tools	√		Fax, E-mail, website, Toll-free line (8482)
11	Presence of standard ADR reporting tool	√		Manual and electronic yellow form, mobile application (Med-safety)
	11a: Presence of relevant fields in the standard ADR form to report suspected medication errors	√		
	11b: Presence of relevant fields in the standard ADR form to report suspected counterfeit/ substandard medicines	√		
	11c: Presence of relevant fields in the standard ADR form to report therapeutic ineffectiveness	√		
	11d: Presence of relevant fields in the standard ADR form to report suspected misuse, abuse and/or dependence on medicines	√		
	11e: Availability of standard ADR reporting form for the general public		√	
12	Presence of mechanism in place for collection, recording, and analysis of ADR reports	√		
13	Presence of tools for PV information dissemination	√		PV Newsletter, website, email, phone
14	Availability of PV advisory committee or an expert committee in the setting	√		Transformed the Adverse Event Following Immunizations committee to a general safety advisory committee

Table 4. Analysis of core Pharmacovigilance process indicators at the NRA, Addis Ababa, Ethiopia, 2020.

S/N	Core process indicator	Result	Remark
1	Total no of ADR reports received in the previous year	1416	1329 ADR, 87 product quality defects
2	Current total number of reports in the NRA's database	4019	Total no of report during data collection period
3	Percentage of total reports acknowledged/issued back to reporters	100	Using either email or post but not sure whether it is reached or not to a reporter
4	Percentage of total reports subjected to causality assessment in the past year	2	Only conducted for serious ADEs. 2 serious ADEs/800 total reports.
5	Percentage of total annual reports satisfactorily completed and submitted to NPC in the previous year	-	No documented data
6	Percentage of reports of therapeutic ineffectiveness received in the last year	1	1/800 reports
7	Percentage of reports on medication error reported in the previous year	0	Not frequently detected and reported
8	No of active surveillance activities are or were initiated, ongoing, or completed in the past 5 years	03	Cohort event monitoring on ARV medication, HPV vaccine

Qualitative Results

Socio-Demographic Characteristics of Key Informants: Purposively selected 22 KIs from pharmaceutical companies, hospitals, and NRA were interviewed. Regarding gender and age, 63.6% were males; and 45.4% were between 31 and 35 years old. The majority of them were from hospitals (Table 5).

Experiences and Opinions on Pharmacovigilance Implementation

Theme 1: Perception of Current Pharmacovigilance Status

Most participants rated and characterized the national PV system as weak, isolated, uncoordinated, focused on a reactive approach, and found at the infancy stage. The KIs also described the PV system as lacking trained professionals in the field, centralized activity, lack of commitment, and ineffective communication with stakeholders. The following account can substantiate the opinion of most of the KIs:

> *[. . .] Overall, the system is still young and reactive. It seems just a one-time campaign rather than continuous vigilant activity. When there are specific safety-related allegations, the regulatory authority responds to that problem. It is just working like 'put off the fire' [P8, Medical Representative, Multinational]*

Contrary to the above reflections, a few respondents described the country's current PV system is better than some other African countries. They indicated that the NRA tried to conduct PMS on targeted products, control custom entry points, take samples for further quality tests, accept reports, and send them to the UMC.

Table 5. Socio-demographic characteristics of key informants, Addis, Ababa, Ethiopia, 2020 (n=22).

Characteristics	Category	N (%)
Gender	Male	14 (63.6)
	Female	8 (36.4)
Age group (Years)	25-30	3 (13.6)
	31-35	10 (45.4)
	36-40	5 (22.7)
	≥40	4 (18.2)
Academic qualification	Bachelor's degree	7 (31.8)
	Master's degree	15 (68.2)
Profession	Pharmacist	22 (100)
Work experience (Years)	5-10	6 (27.3)
	11-15	12 (54.5)
	≥16	4 (18.2)
Work position	Hospital pharmacy head	8 (36.7)
	Medical representative	2 (9.0)
	Manager (General, Deputy, or/ and Technical)	3 (13.6)
	Directorate Director (EFDA)	3 (13.6)
	Inspector	1 (4.5)
	Quality Assurance and Regulatory Affairs Officer	3 (13.6)
	PV Coordinator	1 (4.5)
	Drug Information Service Head	1 (4.5)
Work area	Pharmaceutical Companies (Importer, Local and Multinational Manufacturers)	8 (36.4)
	Hospital (Government and Private)	9 (40.9)
	National Regulatory Authority	5 (22.7)

Theme 2: Factors Influencing the Implementation of Pharmacovigilance

To better understand the context, the factors influencing PV system implementation, as reported by the KIs, were

categorized under two general sub-themes resource-related and reporting-related.

Resource Related Factors

Finance, personnel, technical capacity, social, and legal/political support were cited by the majority of the KIs as the main contributing factors that impact the overall functioning of the PV system in the country. Most participants mentioned the lack of an adequate number of appropriately trained and skilled experts in the area, further compounding the challenges to running the PV system, as was corroborated by personal accounts of a KI.

> *[. . .] As a country, we do not have adequately trained professionals in Pharmacovigilance. [P5, Deputy General Manager, Local manufacturing]*

KIs also indicated that a shortage of qualified PV staff resulted in poor detection of medicines' adverse effects and inadequate capacity to understand, assess, prevent, and manage safety-related risks.

> *"We use the WHO method for causality assessment, but there were times that we could not analyze by ourselves due to a lack of experts in the area. As a result, we would be forced to spend most of the incoming safety reports to UMC without analyzing." [P 18, Management, NRA]*

Most KIs identified financial constraints as an important challenge for PV-related activities in their respective organizations and the country. Lack of budget for PV activities incapacitates the PV centers, hospitals, pharmaceutical companies, public health programs, and the NPC from conducting active and passive surveillance, staff training, and expanding PV centers.

> *"I think we do not have a problem with the legal framework. We lack funds to run the Pharmacovigilance system smoothly." [P4, Manager, Import]*

Lack of collaboration, cooperation, and communication was among the social resource constraints in the country's PV system. It was stressed that the existing weak relationships, disengagement, and uncoordinated communication among key stakeholders such as the NRA, health facilities, pharmaceutical companies, and public health programs are critical issues calling for strategic intervention.

> *"There is weak inter-institutional communication and collaboration. The relationship, communication, and information exchange between the regulatory authority, pharma companies, and hospitals still require improvements." [P9, Deputy Manager, Local Manufacturing]*

Technical constraints were inadequate technical resources, such as a lack of data analysis and communication tools, data management infrastructure, and reporting tools. Respondents also witnessed a shortage of well-equipped, accredited, and adequately functioning quality testing laboratories compared to the increasing demand to check the quality of marketed products.

> *"We do not have adequate certified laboratories. We have one laboratory at the regulatory authority. We cannot test all samples to check whether they are of standard or counterfeit when ADRs and other quality issues are reported." [P22, Technical Manager, Import]*

Inadequate legal infrastructure, such as weak regulatory enforcement capacity, lack of PV-specific policy, inaccessibility of legal instruments to stakeholders, and latency of provision of feedback and executive measures, are challenging the country's weak medicine safety systems.

> *"[. . .] Most of the time, the authority does not enforce and control pharmaceutical companies to have Pharmacovigilance units and qualified persons for Pharmacovigilance."[P11, Management, NRA]*

In contrast, few respondents acknowledged the commitment of the NRA such as establishing PV centers in university-based teaching hospitals to decentralize PV functions, organizing the PV unit as an independent directorate, increasing the professional mix of the NPC staff, introducing a mobile app, and undergoing discussion with the ministry of finance for a separate budget agreement for the NPC.

Reporting Related Factors

Insufficient knowledge and awareness of HCPs on PV functions and inaccessibility of reporting tools are among the influencing factors.

> *"Health professionals have low awareness of reporting and give less priority to PV. Most healthcare professionals neglect many unintended reactions by considering them a common side effect." [P19, DIS Head, Hospital].*

Some of the KIs indicated that the current paper-based reporting form is cumbersome and not easily accessible to reporters. Besides, respondents expressed that the NRA launched an ADE reporting mobile application that simplifies the drawbacks of the paper reporting form, but it requires a smartphone, internet access, proper promotion and advocacy, and sensitization of HCPs.

> *"[. . .] The new mobile Med-Safety reporting system requires the presence of the internet and smartphone. Due to this, its application is limited." [P15, Management, NRA]*

Theme 3: Impacts on the Healthcare System

Compromising quality of care, feeling of insecurity and loss of confidence, increased circulation of unsafe products, and

costs were among the commonly stated consequences of the un-matured PV system by most KIs.

> *"Supply of pharmaceutical products without a proper vigilance system may result in patient harm rather than the benefit." [P2, Regulatory and QA Personnel, Local Manufacturing]*

> *"In a society where there is a distorted perception about medicines circulating in the market, they may consider that unsafe and low-quality medicines are dispensed to them because the regulatory authority failed to do its job properly. This eventually may erode public trust and confidence in the country's authority and health care system."[P11, Management, NRA]*

Some of the KIs also explained that countries that trade pharmaceuticals with Ethiopia might lose confidence and decline in exporting their products to a country, affecting investment in the pharmaceutical sector.

> *"[. . .] Pharmacovigilance is a global agenda. If we do not have a well-functioning Pharmacovigilance system, the country's image regarding medicine safety will be questioned." [P4, Manager, Import]*

KIs also explained that medicines are an essential component of health care and an asset to the country's economy, which affects the overall national economy as spending on medicines accounts for the highest expenditure of the national health budget. Some experts indicated that the absence of a robust PV system might encourage the circulation of counterfeited/substandard products in the country and ultimately create an unhealthy market.

> *"[. . .] Products with compromised safety and efficacy will affect the pharmaceutical market in the country by discouraging the legal business firms and encouraging the illegal ones, thereby promoting bad practices." [P17, Management, NRA].*

Theme 4: Suggested Strategies for Effective PV Implementation

Sectional experts suggested strategies to implement systems-related strategies, improve the regulatory system and capacity, provision of training and advocacy, motivate reporters, and increase stakeholders' engagement and communication.

Integrating clinical care of patients with national PV activities was suggested as one of the system-related strategies. To this effect, making ADR reporting part of the HCPs' routine clinical practice and linking it to the performance appraisal of the HCPs was mentioned asa strategy.

The experts also indicated that the current PV is centralized and requires decentralization to different health institutions, as substantiated by the following.

> *"Ethiopia is a vast country. Having one national PV center to coordinate all the pharmacovigilance activities in the entire country could be challenging. It requires decentralizing the center to other parts of the country." [P21, PV and Clinical Trial Coordinator, NRA]*

The respondent also provided critiques regarding the inclusiveness of the current reporting platforms, citing that it is professional-centric and does not allow patient reporting. They underscored the inclusion of a patient reporting format that enables the NRA to get complete information and enrich reports from HCPs.

> *"[. . .]. We do not have a patient-reporting format, even if we expect them to report. Therefore, the regulatory authority should work to narrow these gaps." [P15, Management, NRA]*

Even though the current PV directive and guideline indicate the responsibility of each stakeholder, the ability to act, implement, and enforce the NRA is inadequate. In addition, incorporating regulations/guidelines for patient reporting and making reporting mandatory by HCPs were among the mentioned regulatory-related strategies.

> *"[. . .] One of the key activities should be working on the regulation part. Enforcing market license holders to follow the safety profile of their products is very important. This can be done through support by regulation." [P15, Management, NRA]*

Respondents suggested implementing different incentive schemes such as quick feedback on actions taken on the report's status, acknowledging, and recognizing best performers and reporters as a motivation strategy for self-initiated reporting.

> *"[. . .] Reinforcing the reporters is important though reporting ADR is their professional duty. A mechanism that allows reporters to know the status of their reports and actions made is critical." [P19, Hospital DIS Head, Hospital]*

The KIs recommend integrating the country's PV system with public health programs, research, and health institutions. To this end, experts from the NRA mentioned that the authority is working with the ministry of health to integrate these public health programs with the PV system. In addition, the NPC is working with other research and medical institutions with active cohort event monitoring centers in the country.

Discussion

This study assessed the PV system status, practices, challenges, and improvement strategies of hospitals, pharmaceutical companies, and the NRA. This study's quantitative and qualitative findings indicated that the PV system in the studied hospitals and pharmaceutical companies was below the expected performance level. Most hospitals and pharmaceutical companies did not have the vital core structure, process,

and outcome PV indicators. Only 1 (3.3%) hospital had a PV unit with a dedicated budget, while the staff was assigned (10%), and SOP for PV (23.33%) indicated critical structural elements are deficient. The findings are much lower than the study reported in five Asian countries where less than 50% of such institutions had a PV center or unit or dedicated staff for PV-related activities within their setting.[15]

The data recording and archiving practices were poor in almost all hospitals, challenging the evaluation of the vital PV process indicators. It was observed that there was a lack of proper recording and documentation practices in the studied organizations. Hospital findings indicated the presence of process and outcome-related PV activities, but they could not be retrieved and verified with documented evidence. A study conducted at Hiwot Fana Specialized University Hospital, Harar, Ethiopia, indicated that only 37.3% of HCPs recorded ADR in the patient follow-up chart indicating the poor practice of ADR documentation among HCPs.[16] Similarly, a study conducted in six health facilities in Nigeria reported a lack of recording and documentation practices for ADRs.[17,18]

Most pharmaceutical companies in the study also observed performance deficiencies in most core structure, process, and outcome PV indicators. Of 32 companies, only 4 (12.5%) had separate PV units, 12 (37.5%) had a regulatory unit, 5 (15.6%) had a regular budget for PV, and 4 (12.5%) had dedicated staff for PV. A study conducted on pharmaceutical companies in Nigeria indicated similar findings.[19] The lack of documented evidence for most process and outcome indicators due to poor record-keeping and documentation practices made retrieving most quantitative data from process and outcome PV indicators difficult. Similarly, a study on LMICs showed that process and outcome indicators were absent.[20]

The NPC has basic infrastructure and procedures for PV-related activities, unlike pharmaceutical companies and hospitals. The NPC has a clear mandate, dedicated staff, PV SOP, safety bulletin, and safety advisory committee. However, the lack of a regular annual budget for PV functions is a constraint. A review by Isah *et al.*[6] in other African countries found similar results. Another comparative study in four East African countries (Ethiopia, Kenya, Tanzania, and Rwanda) indicated that Ethiopia and Rwanda do not have such a budget for PV regulatory activities.[21]

The qualitative exploration identified resource constraints and reporting issues as the main contributing factors to ineffective and inefficient PV systems in the country. The shortage of qualified personnel, finance, technical expertise, legal/political commitment, and stakeholder engagement were mentioned as challenges. Similar challenges were reported in studies in other African countries.[6,19,21] It was indicated that the country did not have an adequately trained workforce for effective PV system implementation. None of the hospitals and pharmaceutical companies have qualified staff in PV. The NPC lacks well-experienced and qualified experts and cannot conduct causality assessments for most incoming reports. The WHO's World Medicines Situation publication series by Pal *et al.*[22] indicated that most national centers in developing countries were severely understaffed and underresourced. Such experiences may probably be associated with the low level of awareness of the role of PV or due to other compelling priorities to improve access and coverage for essential health services.

Lack of knowledge and awareness by HCPs about reporting and problems with existing reporting tools were among the frequently cited issues by respondents. In a country with insufficient knowledge and awareness by HCPs regarding the importance of reporting, relying on a passive surveillance system further contributed to a low reporting rate. Reports from other African countries similarly indicated meager reporting rates, and the number of reports received is insufficient to identify significant drug-related issues.[20] The qualitative exploration also indicated the presence of negligence from HCPs in reporting ADRs. A study conducted in Tigray Region, Ethiopia, revealed that ADR reporting practices among HCPs were abysmal, and 75% of respondents reported having encountered one or more ADRs in their daily practice, but only 32.1% of respondents reported ADRs.[23] Another study in Amhara Region, Ethiopia, showed that a tiny proportion of HCPs had encountered ADRs but were not reported to the regulatory body.[24]

The respondents claimed the current manual reporting form is cumbersome (complex) and not fully accessible for HCPs. The *NRA* launched a mobile application (Med-Safety) to report ADR and was praised by the KIs for its advantages and as an alternative platform for reporting, though the need for *smartphones* and uninterrupted internet access were cited as drawbacks. Effective use of this mobile app still requires intensive advocacy, awareness creation, and reliable internet access, at least in health facilities. Training and advocacy, providing incentive schemes, and increasing stakeholders' engagement were suggested strategies to strengthen the existing *PV* system.[25]

Overall, this study indicated the positive moves by the NRA and NPC regarding PV functions. However, there is still a noticeable gap in the overall functionality of the PV system in healthcare facilities and pharmaceutical companies, and calls for the active involvement of all stakeholders to build an effective PV system.

Even though this study provided an overall picture of the PV system implementation status and challenges in the country, it has some limitations. The study did not collect data from a representative number of hospitals found in the country and regulatory bodies at the regional level, which may

affect the generalizability of the study results. Moreover, the researchers of this study couldn't retrieve important process and outcome indicators of the PV program due to poor recording and documentation systems of the studied organizations which may not reveal the overall picture of PV activities in the study organizations.

Conclusion

The study has identified PV system status regarding the structures, processes, and outcome levels at the NRA, pharmaceutical companies, and hospitals. The NPC has the basic PV structures, procedures, and processes that can be a good foundation for implementing PV systems in the country, even though significant gaps were observed in the system implementation. Hospitals and pharmaceutical companies lack structure, processes, and outcome PV indicators. Resource constraints and issues related to reporting were claimed as contributing factors that impede the implementation of the PV system. Improving the regulatory system, providing training and awareness, encouraging stakeholders' engagement, and providing incentives were suggested for improvement. Active collaboration with critical stakeholders in the sector to achieve a robust, integrated, and consolidated medicine safety system in the country is essential.

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Authors' Contribution

Sisay E., Teferi G., and Tesfa M. contributed to the conceptualization and the study design. Collection and analysis of data done by Sisay E. and reviewed by Teferi G. and Tesfa M. Sisay E. drafted the manuscript, and all authors reviewed and agreed on the final manuscript for submission.

Data Availability Statement

The dataset used in this article is available from the first author on request.

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Ethical/Consent Statement

Ethical Review Board (ERB) of School of Pharmacy, Addis Ababa University (ERB/SOP/67/04/2019) approved the study.

Consent

All study organizations and individual participants gave informed consent and volunteered to participate in this study

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Supplemental Material

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