National Pharmacovigilance (PV) System in Myanmar: A review

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Abbreviations

3S	Smart Safety Surveillance
ADE	adverse drug event
ADR	adverse drug reaction
aDSM	active TB drug-safety monitoring and management
AE	adverse event
ASEAN	Association of Southeast Asian Nations
CA	clinical assessment
CST	Core Structural Indicator
DFDA	Department of Food and Drug Administration
DoMS	Department of Medical Service
DR	drug-resistant
FDA	Food and Drug Administration
HR	human resources
ICSR	Individual Case Safety Report
MDR	multidrug-resistant
MOHS	Ministry of Health and Sports
NCCA	National Core Committee for aDSM
NPVC	National Pharmacovigilance Center
NTP	National Tuberculosis Programme
PIDM	Programme for International Drug Monitoring
PMDT	Programmatic Management of DR-TB [drug-resistant tuberculosis]
PV	pharmacovigilance
SAE	serious adverse event
TB	tuberculosis
WHO	World Health Organization

1. Introduction

1.1. Pharmacovigilance terminology

The World Health Organization (WHO) defines “pharmacovigilance” (PV) as “the science and activities related to the detection, assessment, understanding and prevention of adverse drug effects or any other possible drug-related problems.”[1] PV, previously known as “drug safety,” is an essential part of the health care system. It basically relates to understanding drug effectiveness and issues in a real-world setting.

PV is more than just a science of adverse drug reactions (ADRs); it deals with protecting patient’s well-being and identifies drug- or patient-related problems that result in adverse events (AEs) or reactions. PV is an important aspect of the overall drug-development process that involves health care professionals and post-marketing research as essential components in determining overall safety of the drug. It is not possible for a drug to be approved and authorized for use without undergoing assessment of PV data. Safe and effective use of drugs is fundamental in clinical policy. It is possible that drug-related problems can increase as more and new drugs are introduced to treat the burden of disease in a country; subsequently, it is necessary to have an effective PV system that, in turn, helps to ensure patient’s safety from ADRs. The PV system is developed to safeguard citizens of the region or country through timely, efficient, and effective identification, assessment, and communication of risks to help in decision-making for various actors and stakeholders in the health system.[2,3,4]

Various terminologies are used within the PV system to denote drug-related outcomes (Table 1).

Table 1. Pharmacovigilance terms and their standard definitions.

	Standard definition
Adverse drug reaction (ADR)	A response which is noxious and unintended and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.*
Adverse drug event (ADE)	Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.†
Serious adverse event (SAE)	A serious adverse event or reaction is any untoward medical occurrence that at any dose [does any of the following]: results in death; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; or is life-threatening.†

Sources: *WHO (1972)[4] and †Gupta (2011).[5]

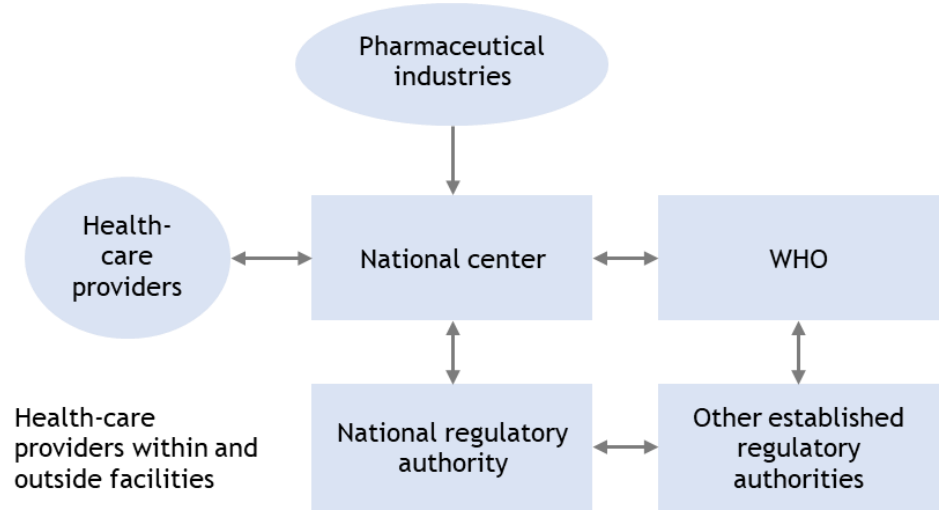
1.2. PV system

To perform any PV activities, it is necessary to establish a PV system. A PV system is defined as “a system used by an organization to fulfill its legal tasks and responsibilities in relation to pharmacovigilance and designed to monitor the safety of authorized medicinal products and detects any changes to their risk-benefit balance.”[2] The PV system represents structures, processes, and outcomes of PV that help to comply with legal frameworks and responsibilities, preventing ADR-related detriment, providing timely and accurate information about the safety and effectiveness of

medicinal products, and contributing to the overall protection and well-being of the patients.[2,4,Error! Bookmark not defined.]

Figure 1 represents the relationships among various levels of actors and centers for a functioning PV system. The suspected reports of ADR are generated and sent by local health care providers to regional or national centers for collation and assessment. The WHO network helps to report any ADR at the global level, which can be important information for other nations to follow-up with or monitor. Currently, the WHO Collaborating Centre for International Drug Monitoring (or the Uppsala Monitoring Centre) in Uppsala, Sweden, provides feedback to the National Pharmacovigilance Centers (NPVCs) as ADRs are reported to it.[6]

Figure 1. Diagrammatic representation of the pharmacovigilance system.



Source: World Health Organization (2015).[6]

WHO describes the functions of a national PV system as follows (taken from Annex 1 of the *WHO Pharmacovigilance Indicators*[7]):

1. To promote pharmacovigilance in the country, notably, to collect and manage adverse drug reaction (ADR) reports, reports of medication errors and suspected counterfeit/substandard drugs.
2. To collaborate and harmonize with existing ADR report collection activities within the country (e.g. national disease control programmes, ministry of health) as well as international studies that are monitoring ADRs in defined patients or populations (cohorts).
3. To identify signals, i.e. unknown or poorly characterized adverse events in relation to a medicine or a combination of medicines and/or its use.
4. To undertake assessment of risk and options for risk management.
5. To identify quality problems in medicines resulting in ADRs; and more generally, to support the identification of medicine quality issues.
6. To provide effective communication on aspects related to medicine safety, including dispelling unfounded rumours of toxicity attributed to medicines and/or vaccines.
7. To apply information resulting from pharmacovigilance for the benefit of public health programmes, individual patients and national medicines policies and treatment guidelines.
8. To develop and maintain drug utilization information.
9. To identify issues associated with unregulated prescribing and dispensing of medicines.

1.3. Global and regional scenario of ADRs and the PV system

According to European Commission's working document of 2008, 3.0 to 10.0 percent of the EU region hospital admission was attributed to ADR, or 2.5 to 8.4 million people, whereas 2.1 to 6.5 percent of patients develop ADR during their hospital stay. ADR was the cause of hospital admission for 8.1 percent of patients in Singapore, 4.2 to 30.0 percent in the United States and Canada, and 5.7 to 18.8 percent in Australia.[8,9] A study by Lazarou et al. estimated that, for hospitalized patients, the overall incidence of serious ADRs was 6.70 percent and that of fatal ADRs was 0.32 percent.[10] However, it was also estimated that around 70.0 percent of the ADRs leading to emergency department visits were preventable.[11] A meta-analysis revealed that ADRs in primary care settings (first point of health care) stood at 8.32 percent, with preventable ADRs being almost 23.0 percent. The incidence of ADR could be attributed to various causes, such as drug- or dose-related errors, prescription errors, use of multiple medications, and off-label use of uncommon medications.[12,13,14,15]

Medication errors in general practice had a prevalence rate of 5 percent in England. In addition, the combination of multimorbidity and number of medications was found to be one of the strongest predictors of ADR in one of the systematic reviews.[16] A multicenter study in Pakistan revealed that 58 percent of the adverse drug events (ADEs) due to antibiotics (among 486 ADEs) were preventable. These preventable ADEs were mostly due to medication errors (wrong drug, 40 percent; wrong dose, 14 percent). The study also found that errors were caused due to lack of knowledge about the patients (17 percent), lack of information about antibiotics (32 percent), and nonadherence to policies and procedures (38 percent).[17] Inadequate monitoring was also reported as one of the major contributing factors in preventable ADRs.[18,19,20,21]

There have been number of innovations, programs, and new applications that support improvements to in-country monitoring of drug/medical product safety and strengthening of regulatory mechanisms and authorities. Given the limitation of the resources, WHO has conceptualized a PV risk prioritization strategy known as Smart Safety Surveillance (3S) that essentially supports a country in establishing a focused rather generalized PV system. For instance, any novel drug introduced in a country might be monitored through the 3S strategy, which would allow for more efficient and meaningful use of limited resources, especially in low- and middle-income countries. The concept of "smart" relates to mutual collaboration, learning, and sharing of resources based on the combined expertise among countries.[22] Currently, this concept is being applied as a pilot project in six countries, which has shown that the system can be used across countries with varying capacity of PV systems.[23]

Likewise, the Centre for Health Security and the Australian Department of Health's Therapeutic Goods Administration have been supporting countries in the Indo-Pacific region, including Myanmar, in strengthening the capabilities of National Regulatory Authorities to increase the availability of "safe and effective" medical products, particularly for tuberculosis (TB) and malaria. Related to post-authorization safety studies, a new application of event monitoring called Specialist Cohort Event Monitoring has evolved that helps "a cohort of patients prescribed a medicine in the hospital and secondary care settings to be monitored." The method is unique in the sense that it enables a comparator cohort to apply "standard care or other medication concurrently."[24] Finally, WHO's Global Benchmarking Tool is a self-assessment tool for National Regulatory Authorities that enables exploration and identification of strengths and areas of improvement. There are four maturity levels that represent the extent to which the regulatory systems of the country have been stabilized and are functioning well to ensure safety, a high quality, and efficacy of medical products.[25]

2. Objectives of the Review

A review of PV systems was conducted from 2014 to 2015 among eight Association of Southeast Asian Nations (ASEAN) countries. However, the assessment did not include Myanmar. The PV system review showed that half of the countries had met the minimum requirements of a functional national PV system that was developed by WHO.[26] The three pillars of PV—capacity, legislative framework, and functionality—varied across the countries, especially in terms of presence of human resources (HR), reporting requirements, and risk communication. Lack of appropriate HR (both quality and quantity) have been one of the barriers to functional PV, as was found to be true across Laos PDR and Cambodia. A similar trend is observed in other low- and middle-income countries, too.[27]

There have been limited number of studies in Myanmar to understand, explore, and document its national PV system and its functionality, strengths, challenges, and gaps in implementation. This literature review attempts to collate evidence from the present limited evidence following three objectives:

- Clarify current AE reporting mechanisms and tools.
- Review and assess current PV system in close collaboration with the Department of Food and Drug Administration (DFDA) to understand the AE recording and reporting mechanism.
- Identify gaps to strengthen DFDA's PV system for introduction of a optimized radical cure with tafenoquine and ways to get it into the malaria surveillance system.

3. Methodology

This review assessment used an exploratory approach with use of available evidence in PV in Myanmar. We used a combination of reviewing existing documents and assessing the status of the PV system using the available evidence and information.

Review of documents

We used electronic databases (e.g., PubMed, Cochrane Library) and visited relevant websites (e.g., https://www.fda.gov.mm/) to extract information on PV in Myanmar. Search queries have been provided in the appendix, including summary of findings from the relevant published articles. Myanmar-specific studies, review article, reports, and other anecdotal information were explored through the electronic means. However, only PubMed yielded relevant studies that matched our search criteria. We also reviewed WHO guidelines and national manuals/guidelines relevant to PV. Published documents that are relevant to the subject were reviewed and summarized in the review findings (see section 4 below) under five headings:

1. PV process/guidelines in Myanmar.
2. National PV system's performance measurement in terms of WHO criteria and indicators.
3. Active TB drug-safety monitoring and management (aDSM).
4. Research on ADR.
5. Awareness of ADR system (PV system).

Key informant interviews

A guide was developed and used to interview five personnel who are key to the PV system. Further information of the interviewees are provided in the appendix.

Review of information to assess PV system

Using the available information, we assessed the PV system based on WHO's criteria for a functional PV system[28] and WHO's PV indicators.[2] WHO and partners suggest the following five minimum requirements related to activities, functions, and structures for any national PV system (taken from Annex 1 of the *WHO Pharmacovigilance Indicators*[7]):

1. An national pharmacovigilance centre with designated staff (at least one full-time), stable basic funding, clear mandates, well-defined structures and roles, and collaborating with the WHO Programme for International Drug Monitoring [PIDM];
2. A national spontaneous reporting system with a national individual case safety report (ICSR) form, i.e. an ADR reporting form;
3. A national database or system for collating and managing ADR reports;
4. A national ADR or pharmacovigilance advisory committee able to provide technical assistance on causality assessment, risk assessment, risk management, case investigation and, where necessary, crisis management, including crisis communication;
5. A clear communication strategy for routine communication and communication during crises.

To assess the PV system, the five requirements were scored with three possible scores for each: "1" if the system is in place and fulfills the criteria; "0.5" if there is any ambiguity in the system or processes; and "0" if there aren't any systems in place corresponding to the criteria. The routine communication domain included regular communication activities for both public and health care professionals using various media platforms, such as newsletters, conferences, emails, or social media. This scoring criteria was used previously in ASEAN countries[26] and has been adapted for the purpose of understanding the status of the PV system in Myanmar.

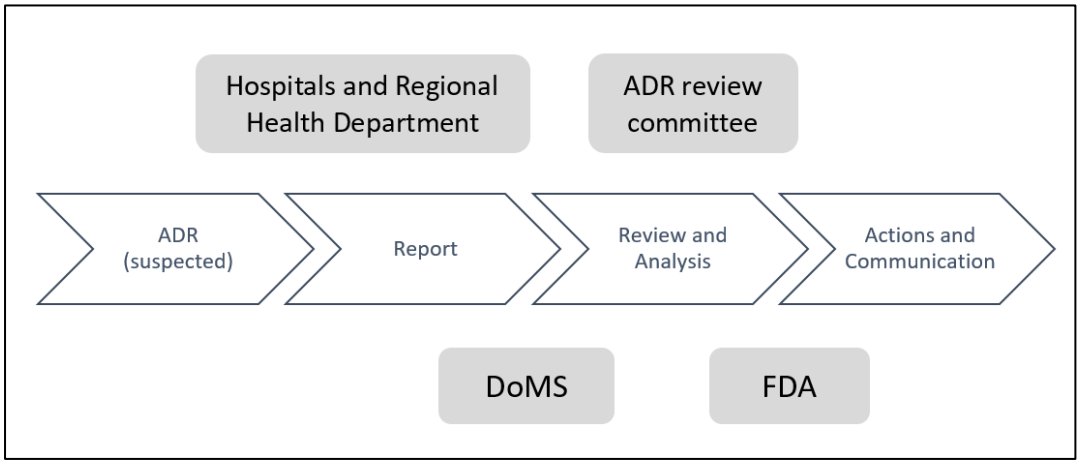
We also used WHO's PV indicators to assess and review the system. These indicators were mostly answered with binary response (yes/no), and in some instances, additional narratives had to be used to clarify the status of the indicators. These indicators were applied to the overall PV system and to PV systems at health facilities.

4. Review findings

4.1. PV process/guidelines in Myanmar

Myanmar became the associate member of WHO's PIDM in 2018. The PIDM, however, was established almost five decades ago in 1968 as a response to the thalidomide disaster. Hence, Myanmar's PV program is at the earliest phase of its implementation.

Figure 2**.** Adverse drug reaction (ADR) reporting components in Myanmar.

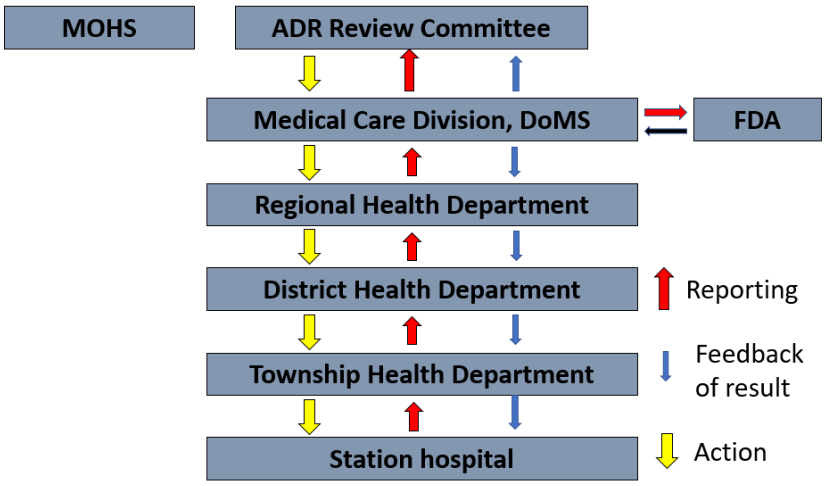


Source: Adverse Drug Reaction (Dr. Lwin Moe May)[43]

Abbreviations: DoMS, Department of Medical Service; FDA, Food and Drug Administration.

Nonetheless, in Myanmar, the ADR reporting system has been established at the Food and Drug Administration (FDA) since 2002. The guideline/policy lays out the ADR reporting process and flowchart (Figure 2 and 3). There are guidelines in place for reporting, reviewing, analyzing, taking necessary action, and communicating accordingly. Hospitals and regional health departments, an ADR review committee, the Department of Medical Service, and the FDA serve as implementing and governing bodies for smooth function of the PV system in Myanmar. However, in practice, the actual implementation has not been up to par with the set standards due to a lack of HR within the FDA. The FDA has distributed an ADR reporting form to central, state, and regional hospitals, as well as to health offices and drug advisory committee members. Any serious adverse event (SAE) is reported is reported directly to the FDA by the district and regional health departments, which are informed by the station and township hospitals, respectively. At this time, the FDA sends the report to the ADR review committee and the drug advisory committee for their opinion. And then a causality assessment is done. Any action taken or feedback from the report is announced by the FDA.

Figure 3. ADR reporting, action, and feedback flow and associated departments



Source: Adverse Drug Reaction (Dr. Lwin Moe May)43

Abbreviations: ADR, adverse drug reaction; FDA, Food and Drug Administration; DoMS, Department of Medical Service; MOHS, Ministry of Health and Sports.

4.2. National PV system's performance measurement in terms of WHO criteria and indicators

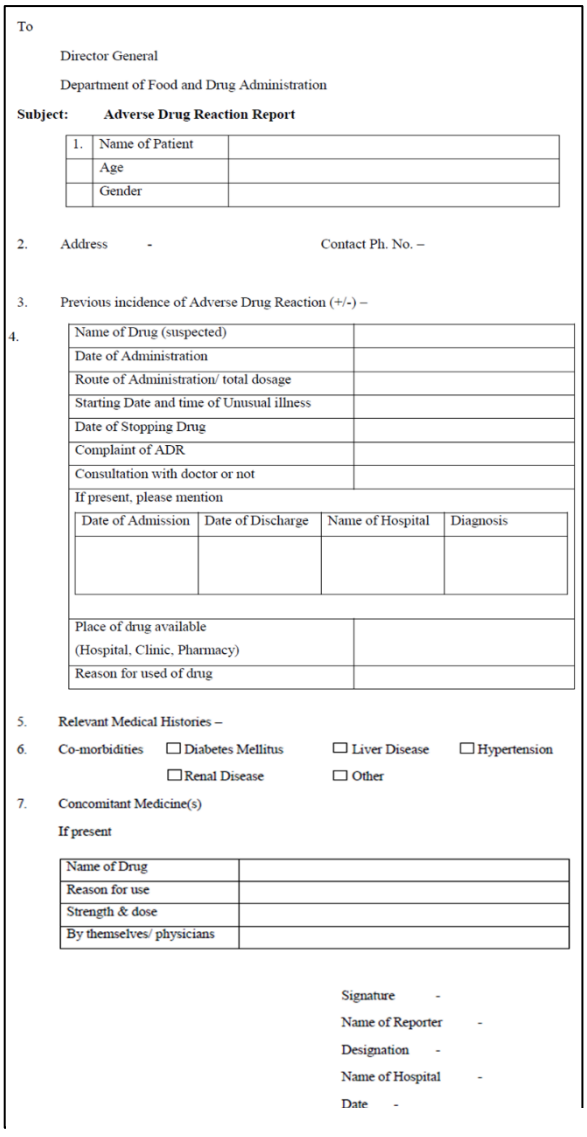
According to WHO, "an effective pharmacovigilance system ensures the monitoring of medicines, their availability, and safe use."[1] A PV system involves the systematic collection, collation, and analysis of reports of suspected ADRs, enabling detection of signals, their communication, and risk management. Myanmar joined WHO's PIDM in 2018 and currently has the status of associate member. Hence, Myanmar has its own national PV system for monitoring and responding to ADRs.

4.2.1. Assessment of the national PV system

There is a national policy and a legal framework in place for Myanmar's PV system which are consistent with other ASEAN countries in the region.[26] There are fewer than 50 full-time equivalent employees at the NPVC in Myanmar; additionally, proper management of HR is in question. There

are both active and passive surveillance systems in place, and both health care professionals and marketing authorization holders are mandated to report ADRs. Myanmar's PV system incorporates drugs and vaccines but does not monitor and report on herbal/complementary medicines and other products, like food and cosmetics. The system is set up to collect and collate ICSRs or ADR reporting forms, as well as assess causality (Naranjo probability scale and Liverpool algorithm),[29,30] types (Rawlins and Thompson),[31] severity (Hartwig severity scale),[32] and preventability (Schumock and Thornton scale)[33] of ADRs. However, Myanmar's PV system lacks a national/local database for collating and managing ADR reports, unlike other countries in the ASEAN region, such as Thailand.

As Myanmar is an associate member country of WHO's PIDM, it has access to a system called VigiFlow, a web-based report management tool that enables the online transmission of ICSRs to the WHO VigiBase at the Uppsala Monitoring Center. However, in-country, paper-based systems are used to report ADRs, as seen in figure 4. While a system exists to collate and compile the forms, it lacks an electronic database for recording and reporting them. Since there is a national aDSM database specific to TB-related SAE reporting, Myanmar's PV system was scored 0.5 for this component (see Table 3). Thus, the system/database for collation and collection of ADRs is not a complete one, as the general PV system still lacks the electronic database, including an electronic reporting and recording system at the health facility level.



To

Director General

Department of Food and Drug Administration

Subject: Adverse Drug Reaction Report

1.	Name of Patient	
	Age	
	Gender	

2. Address - Contact Ph. No. –

3. Previous incidence of Adverse Drug Reaction (+/-) –

4.

Name of Drug (suspected)	
Date of Administration	
Route of Administration/ total dosage	
Starting Date and time of Unusual illness	
Date of Stopping Drug	
Complaint of ADR	
Consultation with doctor or not	
If present, please mention	

Date of Admission	Date of Discharge	Name of Hospital	Diagnosis

Place of drug available (Hospital, Clinic, Pharmacy)	
Reason for used of drug	

5. Relevant Medical Histories –

6. Co-morbidities ☐ Diabetes Mellitus ☐ Liver Disease ☐ Hypertension ☐ Renal Disease ☐ Other

7. Concomitant Medicine(s)

If present

Name of Drug	
Reason for use	
Strength & dose	
By themselves/ physicians	

Signature -

Name of Reporter -

Designation -

Name of Hospital -

Date -

Figure 4. ADR Reporting Form

Furthermore, there is an absence of a risk communication strategy (e.g., regular published media, such as bulletins and annual reports, and crisis communication platforms for special announcements, such as letters, e-mails, meetings, and conferences) especially for the public. There is practice of holding conferences, seminars and meetings to provide updated information of medicine safety for health care professionals; however, the review could not identify any specific communication plan at the present. A few ASEAN countries, such as Thailand and Singapore, have clear communication strategies (having both routine communication, such as bulletins and annual reports, and platforms for conveying crisis announcements); however, other countries, such as Cambodia, Philippines, and Vietnam, have unclear communication strategies.2

Table 2 summarizes the assessment of the PV system in Myanmar.

Table 2. Characteristics of Myanmar's PV System.

	Criteria/Questions	Status of Myanmar
General	Year joined WHO Programme for International Drug Monitoring	2018
	No. of staff (full time equivalent) at the NPVC	<50 (work together with FDA)
	No. of staff per population	<0.92 per one million
	National policy or legal framework	Yes
Process	Surveillance system	Active and passive
	Mandatory reporting (health care professionals)	Yes
	Mandatory reporting (marketing authorization holders)	Yes
Scope of products	Drugs	Yes
	Vaccine	Yes
	Herbal/complementary medicines	No
	Others, like cosmetics, food, unregistered products	No
Pharmacovigilance-related activities	Collection/collation of ICSRs or ADR reporting forms	Yes
	ICSR causality assessment	Yes
	National database or system for collating and managing ADR report	No
	Risk management plans	Yes
	Risk communication	Partially (for health care professionals only)

Abbreviations: ADR, adverse drug reaction; FDA, Food and Drug Administration; ICSR, Individual Case Safety Report; NPVC, National Pharmacovigilance Center; WHO, World Health Organization.

Myanmar's PV system assessment revealed some gaps in characteristics that a functional PV system should have. Based on WHO's criteria, 28 Myanmar's PV system scored 3.5 out of a possible 5 points (Table 3), assuming the fulfilled criteria have actually been functional and able to monitor, report, and assess ADR in the country. Comparatively, a study showed that half of the eight participating ASEAN countries had fulfilled adequate PV functionality criteria, which means that they scored 5 out of 5 in the WHO criteria.26 However, the study was conducted in 2015, and the results might have changed since then.

Table 3. Scoring for national PV system based on WHO criteria.

	WHO criteria	Score for Myanmar
1	An NPVC with designated staff (at least one full-time), stable basic funding, clear mandates, well-defined structures and roles, and collaborating with the WHO PIDM	0.5
2	A national spontaneous reporting system with a national Individual Case Safety Report form, i.e. an ADR reporting form	1
3	A national database or system for collating and managing ADR reports	0.5
4	A national ADR or PV advisory committee able to provide technical assistance on causality assessment, risk assessment, risk management, case investigation and, where necessary, crisis management, including crisis communication	1
5	A clear communication strategy for routine communication and communication during crises	0.5
	Total Score	3.5

Source: Adapted from WHO (2015).[7]

Abbreviations: ADR, adverse drug reaction; NPVC, National Pharmacovigilance Center; PIDM, Programme for International Drug Monitoring; PV, pharmacovigilance; WHO, World Health Organization.

4.2.2 Core indicators performance of the National Pharmacovigilance Center (NPVC)

There are set WHO indicators that help to characterize PV, which are divided into three categories: core, complementary, and public health program. Of these, the core and complementary indicators are further divided into subcategories: structural, process, and outcome.2 Here, we focus on understanding the NPVC's performance based on the core indicators, including the subcategories, in detail. For instance, the core structural indicators for NPVC status provide further insights into Myanmar's PV system: HR, a communication plan, and a proper establishment for adequate training/education of health care professionals are all missing from the system (Table 4).

Table 4. Status of NPVC based on WHO's core structural indicators.

Core Structural Indicators (CSTs)	Status
CST1. Existence of an NPVC, department or unit with a standard accommodation	Yes
CST2. Existence of a statutory provision (national policy, legislation) for PV	Yes
CST3. Existence of a medicines regulatory authority or agency	Yes
CST4. Existence of any regular financial provision (e.g., statutory budget) for NPVC	Yes
CST5. The NPVC has human resources to carry out its functions properly	No
CST6. Existence of a standard ADR reporting form in the setting	Yes
CST7. A process is in place for collection, recording and analysis of ADR reports	Yes
CST8. Incorporation of PV into the national curriculum of the various health-care professions	No
CST9. Existence of a newsletter, information bulletin or website for dissemination of PV information	No
CST10. Existence of a national ADR or PV advisory committee or an expert committee in the setting capable of providing advice on medicine safety	Yes

Source: Adapted from WHO (2015).[34]

Abbreviations: ADR, adverse drug reaction; NPVC, National Pharmacovigilance Center; PV, pharmacovigilance; WHO, World Health Organization.

Furthermore, when exploring the status of PV systems at health facilities, there were more gaps to be addressed. Currently, there are no NPVCs or departments at the hospital level with clear mandate and policies. However, there is ADR reporting in place. Hospitals also do not allocate any budget for PV activities, and they still use paper-based ADR reporting, which means that they do not have a database of ADRs reported from other health care facilities. The lack of skilled and trained HR could be attributed to the fact that only FDA staff received training on PV in the past year, which accounted for only 0.02 to 0.04 percent of health care professionals.

Though there is an ADR reporting form, the form does not include criteria such as medication errors, treatment failures, or poor product quality problems, nor is there a separate report form for patients. As a result, only 56 cases of ADR were reported in 2019. There have been active surveillance activities carried out at the hospital level; however, as with the NPVC, there are no communication plans or activities to inform about drugs and PV activities (see appendix for additional indicator status).

Table 5. Structural, process, and outcome indicator status for PV at health care facilities.

	Indicator type	Status
Structural	NPVC or PV department or unit at the hospital	No, there is not a PV department at the tertiary hospital level.
	Clear mandate, organizational structure, roles, responsibilities, and reporting lines for the NPVC	In Myanmar, there is a clear mandate for ADR, but the organizational structures, roles, responsibilities, and reporting lines are pending for the NPVC.
	Presence of general drug information center or a specific NPVC	No

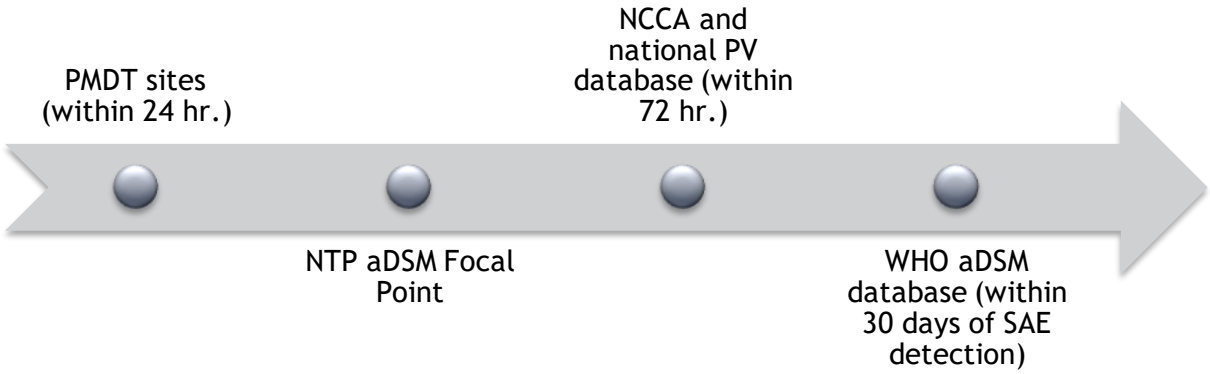
	Annual budgetary allocation for PV activities	No
	Availability of basic technologies at hospitals to support PV activities (e.g., telephones, fax machines, Internet, emails, projectors, desktops, laptops)	No
	Percentage of health care professionals / staff trained in PV in the past year	Only FDA staff (0.02%–0.04% of health care professionals)
Process Indicators	Separate report form for patients at hospital	No
	Patients in the hospital encouraged to report adverse events directly to NPVC	No
	Presence of form for reporting:	
	ADR at the hospital	Yes
	Poor product (drug) quality problems at the hospital	No
	Medication error at the hospital	No
	Treatment failure at the hospital	No
Outcome Indicators	Number of ADR reports received in the past year	56 cases in 2019
	Active surveillance activities by hospital in the last 5 years	Yes, the active surveillance is "Adverse Drug Reactions in Selected Wards of the Yangon General Hospital and Yangon Specialty Hospital During the First Quarter of 2019."[35]
	Number of patient education activities on ADR and medicine safety topics that have been carried out in the past year at the hospital	None, the patient education activities were done for the public by the General Practitioners' Society.

Abbreviations: ADR, adverse drug reaction; NPVC, National Pharmacovigilance Center; PV, pharmacovigilance.

4.3. Active TB drug-safety monitoring and management (aDSM)

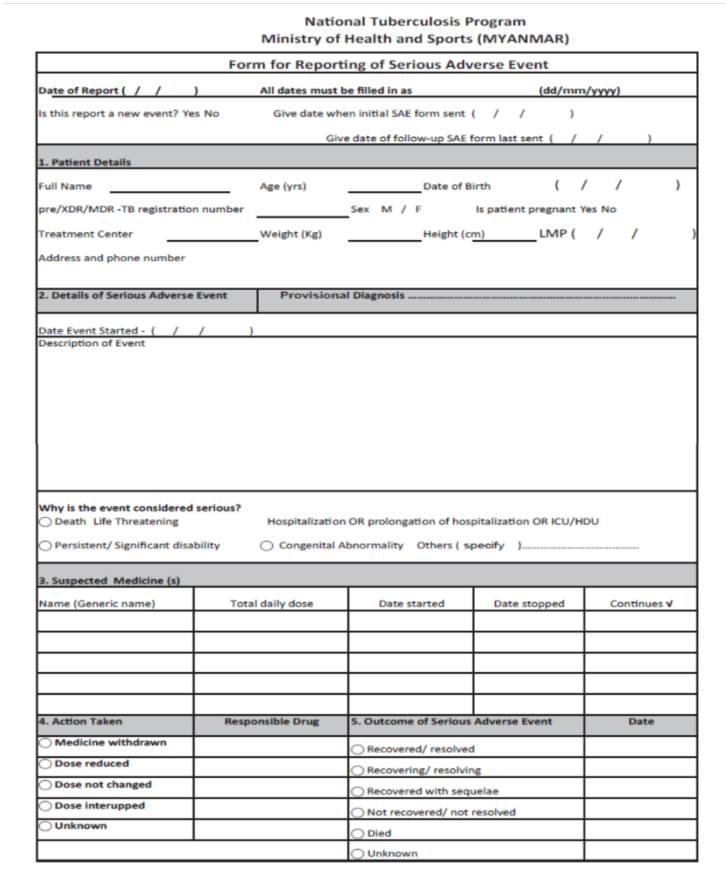
In Myanmar, the PV system for aDSM was established in 2017. Before the introduction of aDSM, Myanmar's NPVC was conducting spontaneous reports only, and there were low numbers of reports received per year. For example, in 2015 Myanmar received only 1.1 spontaneous reports per million population as opposed to 108 reports per million received in Vietnam during the same year.36 However, before the introduction of aDSM, the NPVC of Myanmar had not reported any AEs for the patients taking anti-TB drugs. This meant that there was lack of awareness in reporting of AEs related to TB drugs and its usefulness.

Figure 5. Reporting lines for aDSM in Myanmar.



Abbreviations: aDSM, Active TB drug-safety monitoring and management; NCCA, National Core Committee for aDSM; NTP, National Tuberculosis Programme; PMDT, Programmatic Management of DR-TB [drug-resistant tuberculosis]; PV, pharmacovigilance; SAE, serious adverse event; WHO, World Health Organization.

The system detects, manages, and reports suspected or confirmed drug-related toxicities in a timely manner. The Myanmar's general PV reporting system is being conducted voluntarily by health workers, with limited implementation. Also, there have been no TB-related AEs reported through the system. This is why establishment of aDSM was important, especially when new anti-TB drugs and new drug regimens were introduced in the country. Currently, Myanmar is implementing a core package of aDSM, which also means that the PV system will monitor and report only SAEs. SAE reports (see Figure 6) are generated at the Programmatic Management of DR-TB (drug-resistant tuberculosis) site and then sent to the National Tuberculosis Programme (NTP) aDSM Focal Point. The reports are then entered into the database of the National Core Committee for aDSM and the NPVC within 72 hours. Finally, the reports are forwarded to WHO, where they are entered into the WHO Global aDSM Database within 30 days of SAE detection (see Figure 5 above). A total of 234 SAE cases were reported from December 2017 to June 2019 in Myanmar.



National Tuberculosis Program
Ministry of Health and Sports (MYANMAR)

Form for Reporting of Serious Adverse Event

Date of Report (/ /) All dates must be filled in as (dd/mm/yyyy)

Is this report a new event? Yes No Give date when initial SAE form sent (/ /)

Give date of follow-up SAE form last sent (/ /)

1. Patient Details

Full Name _____ Age (yrs) _____ Date of Birth (/ /)

pre/XDR/MDR -TB registration number _____ Sex M / F Is patient pregnant Yes No

Treatment Center _____ Weight (Kg) _____ Height (cm) _____ LMP (/ /)

Address and phone number

2. Details of Serious Adverse Event | Provisional Diagnosis .....

Date Event Started - (/ /)

Description of Event

Why is the event considered serious?

◯ Death Life Threatening Hospitalization OR prolongation of hospitalization OR ICU/HDU

◯ Persistent/ Significant disability ◯ Congenital Abnormality Others (specify)

3. Suspected Medicine (s)

Name (Generic name)	Total daily dose	Date started	Date stopped	Continues ∨

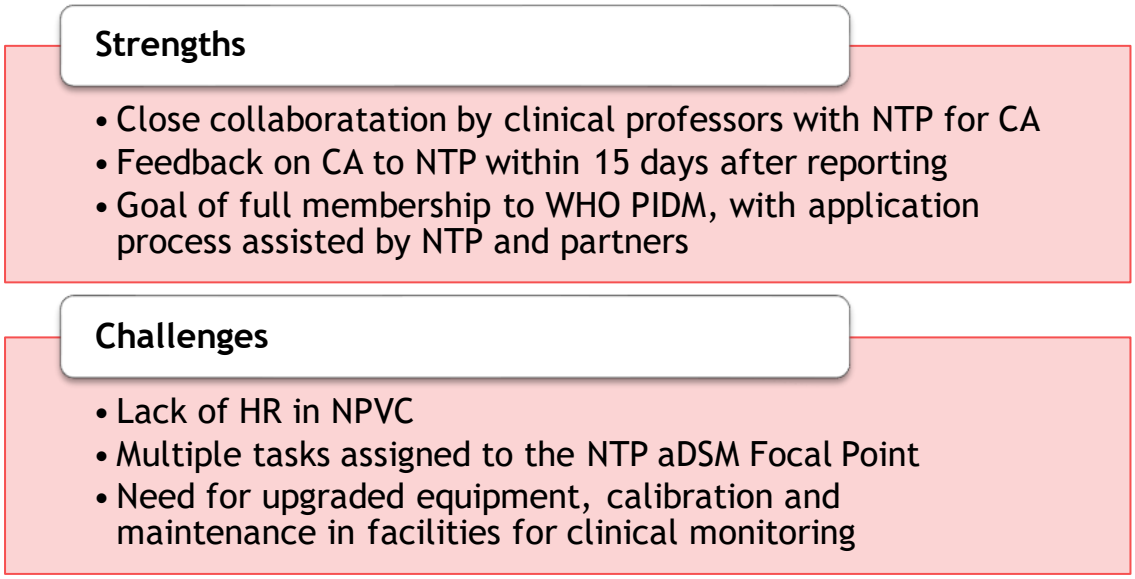
4. Action Taken	Responsible Drug	5. Outcome of Serious Adverse Event	Date
◯ Medicine withdrawn		◯ Recovered/ resolved	
◯ Dose reduced		◯ Recovering/ resolving	
◯ Dose not changed		◯ Recovered with sequelae	
◯ Dose interupped		◯ Not recovered/ not resolved	
◯ Unknown		◯ Died	
		◯ Unknown	

Figure 6. SAE Reporting Form

The aDSM in Myanmar has both strengths and limitations in its implementation (Figure 7). There has been proper collaboration between clinical professors and the NTP in conducting appropriate and timely clinical assessment (CA) of the reported SAEs. Myanmar is currently working on obtaining full

membership status in WHO's PIDM, up from the current associate member status, a move which the NTP and its partners are supporting. However, managing HR in both the NPVC and NTP as aDSM Focal Point has been one of the major challenges of the system. It is due to this limitation in human resources that Myanmar had to choose core aDSM package which is a bare minimum package that a country could choose out of three packages (next two being intermediate and advanced packages). Other challenges are high turnover of PV officers, lack of clarity in roles, and overload of responsibilities. In addition, there needs to be improvement in the setup and environment for clinical monitoring.[36]

Figure 7. Strengths and challenges in Myanmar's aDSM



Source: Tiemersma et. al. (2019)[36]

Abbreviations: aDSM, active TB drug-safety monitoring and management; CA, clinical assessment; HR, human resources; NTP, National Tuberculosis Programme; PIDM, Programme for International Drug Monitoring; WHO, World Health Organization.

4.4. Research on ADR

There have been very limited studies in Myanmar on occurrence of ADR. One such study was conducted in 2019 (published in 2020), where patients admitted to selected wards of Yangon General Hospital and Yangon Specialty Hospital were assessed. Of the 160 patients assessed, 65 ADRs were identified in 47 patients. Of these ADRs, one-fourth had led to hospital admission, whereas the rest appeared in 31 patients during their hospital stays. Compared to those patients without ADR, the patients who presented with ADR were younger, were on more medications, were more often female, and were more likely to have renal disease. However, the study also reported that more than half of the ADRs could have been prevented. The authors also pointed out 29% ADR prevalence reported in this study was on the higher side which may have been the result of active search for ADRs done for the study. Active search for ADRs is not practiced in the national PV system which limits the reporting of actual number of ADR in the country; hence, limiting the presence of accurate ADR incidence data.[35]

AEs and SAEs were also detected via the aDSM system while implementing a New Drugs and Regimen of bedaquiline and delamanid in Myanmar from 2017 to 2018, for which 126 patients were

enrolled for active PV monitoring. Over a period of nine months or less, 21 SAEs were reported, out of which 3 deaths occurred.[36]

Despite the limited evidence on ADRs or SAEs, it is apparent that drug-related reactions or events are prevalent in Myanmar. Other safety- and efficacy-related studies conducted (e.g., drugs and regimens related to treating malaria[37,38,39,40] and hepatitis C[41]) have reported mild or no AEs. Regionally, from 2013 to 2015, Thailand reported close to 781 ICSRs per year per million population, and Vietnam reported almost 85 ICSRs per year per million population, whereas countries like Cambodia, Indonesia, and Laos DPR reported less than 10 ICSRs per year per million population.[26] As reporting rates are one of the performance indicators of the PV system, this evidence suggests critical intraregional discrepancies in maintaining a functional PV system. Having a functional PV system is important in that ADRs are prevalent, and it is of utmost importance to detect, analyze, report, and communicate these events in a timely manner.

4.5. Awareness of ADR system (PV system)

Another important aspect of a functional PV system is awareness on the part of health care workers regarding ADR, SAE, and the overall system that is set up to manage such events.

A study conducted among post-graduate students and specialist clinicians from eight teaching hospitals under University of Medicine 1, Yangon (Department of Pharmacology)[44] in 2018 explored awareness of ADR among the respondents. A total of 256 respondents participated in the study, of which almost two-thirds were female, almost half (46 percent) were post-graduates, and more than 90 percent were bachelor of medicine, bachelor of surgery or master of medical science faculty (Tables 6 through 9).

Table 6. Characteristics of respondents (N=256): gender

Gender	Frequency	Percentage (%)
Male	66	25.80
Female	190	74.20

Table 7. Characteristics of respondents (N=256): designation

Designation	Frequency	Percentage (%)
Post-graduate	118	46.10
SAS/AL	85	33.20
JCS/L	28	10.90
SCS/AP/Professor	25	9.80

Abbreviations: AL, assistant lecturer; AP, associate professor; JCS, junior consultant; L, lecturer; SAS, staff grade, associate specialist, and specialty; SCS, senior consultant.

Table 8. Characteristics of respondents (N=256): department

Department	Frequency	Percentage (%)
Surgery	19	7.40
OG	27	10.50
Child	45	17.60
Others	143	55.90

Table 9. Characteristics of respondents (N=256): qualifications

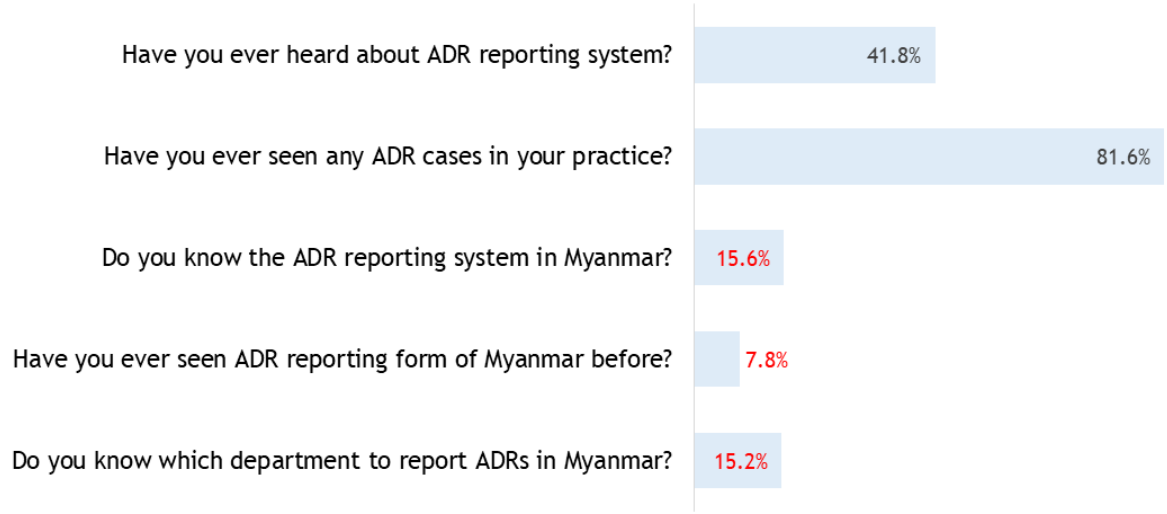
Qualifications	Frequency	Percentage (%)
MBBS	121	47.30
MMedSc	111	43.40

PhD or DrMedSc	19	7.40
Others	5	2.00
Total	256	100.00

Abbreviations: DrMedSc, doctor of medical science; MBBS, bachelor of medicine, bachelor of surgery; MMedSc, master of medical science.

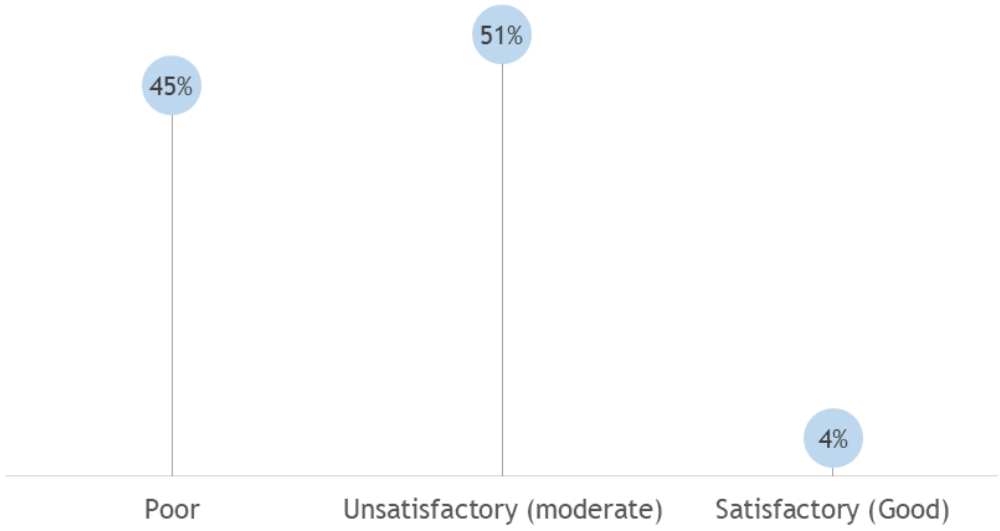
The respondents were asked about ADR reporting system. Only about four out of ten respondents had previously heard about the ADR reporting system, although eight out of ten respondents had seen ADR cases during their practice, which means that ADR occurrence is common. However, when asked about an ADR system as it relates to Myanmar, only a minority of the respondents had any awareness of it: approximately 16 percent knew about the ADR reporting system in Myanmar or about the department to which ADR gets reported, and a mere 8 percent had seen Myanmar's ADR reporting form before, which indicates very low awareness of Myanmar's ADR reporting system or PV system. Figure 8 summarizes the findings.

Figure 8. Awareness of respondents on adverse drug reaction (ADR) reporting (N=256)



The overall awareness score showed that only 4 percent of the respondents had a satisfactory level of awareness on ADR reporting, whereas approximately half of the respondents (51 percent) had an unsatisfactory level of awareness, and 45 percent of them a poor level of awareness (Figure 9).

Figure 9. Respondents' awareness, categorized by scoring (N=256)



Note: Awareness-related questionnaires were analyzed by sorting the respondents into three categories: *poor* (score of 0–11, or 0%–32%); *unsatisfactory*, (score of 12–22, or 33%–63%); and *satisfactory* (score of 23–35, or 64%–100%).

5. Conclusion

The review of the PV system in Myanmar revealed that the system is at the early phases of its implementation, and efforts are underway to improve it. While there are areas where Myanmar has performed strongly in terms of setting up a PV system, gaps remain that need to be addressed to establish a functional and effective PV system in the country. Some of the notable activities undertaken recently are as follows: being part of WHO's PIDM and applying for full membership, setting up an aDSM system, and striding toward establishment of an evidence base through research to support the strengthening of the PV system in Myanmar. Although a standard system with supporting policy is in place for a functioning PV system in the country, the practical side of it has shown issues with implementing the flow of information, setting up systems for proper recording and reporting of cases, and developing risk communication plans and then applying them. Recent studies have shown that Myanmar is no exception to the global occurrence of ADEs, which are, most certainly, expected to occur in the future, as well. Having a functional and appropriate PV system could help better investigate drug-related AEs whose evidence could help to better regulate access to drug, its use, and management of adverse events in future not only for Myanmar but for other countries too. Hence, this review of Myanmar's PV system adds to the scarce evidence available in the country.

Some of the weaknesses of the system include:

1. A clear gap between the written guidelines on PV and how it functions in field-level implementation.
2. A lack of adequately trained HR in the system who could work in a more focused and efficient manner, which has influenced some of the approaches (e.g., having to choose a core aDSM package as opposed to the intermediate package chosen by other countries in the region, such as Vietnam).

3. Other HR-related issues, such as high turnover of PV officers, lack of clarity in roles, and responsibility overload, which have hampered the smooth functioning of the PV system.
4. A substantial lack of awareness of the PV system among current and future health care practitioners in Myanmar.
5. Lack of clear communication practices and strategies, especially for the public.
6. Absence of an electronic ADR database at health facilities.
7. Lack of specific forms/tools for reporting medication errors, treatment failure, and poor product quality problems, as well as a separate report form for patients.

By contrast, some of the strengths of the system include:

1. The presence of national policy, processes, guidelines, and standards for a functioning PV system, incorporating all levels of health facilities in Myanmar's health system.
2. The presence of both active and passive surveillance systems and the mandate for both health care professionals and marketing authorization holders to report ADRs.
3. The presence of a well-established aDSM system which has improved reporting of AEs for anti-TB drugs.
4. A steady increment in research activities that relate to ADR and the PV system of Myanmar and that has supported the generation of evidence surrounding multiple aspects of the system.

6. Recommendations

6.1. Further improving the NPVC with proper implementation

Improving the NPVC will require the following:

1. Proper implementation of the system: Myanmar has established guidelines and processes for implementing a PV system. However, there is gap in their implementation. It is necessary to start dialogues with stakeholders at all levels of implementation to sort out implementation issues and transform them into actionable plans.
2. Adequate funding: The functionality of a PV system will depend on the funding aspect, as well. Adequate funding will help establish a support system for staff, develop infrastructure, and enable networking with stakeholders. A supportive regulatory system will only work if adequate funding is in place. As a matter of public safety, political commitment could be garnered to improve funding in PV systems.
3. Further strengthening of the PV database: A well-functioning database across all levels of the health system will be required to ensure efficiency in recording, reporting, and use of data over time. There is a need to continue current funding, or assess the need for funding, to expand the database to replace the paper-based reporting system. Furthermore, adequate training of health care professionals, including regular supervision, will be necessary.
4. Adequate supervision, monitoring, and timely action: A well-functioning PV system has a number of components that should work in synergy to achieve its objective. The whole process—from identifying the ADRs up through reporting the event and taking relevant actions—involves various personnel performing various tasks to reach a satisfactory and

actionable conclusion. Regular supervision of these actions is necessary in order to monitor and provide feedback to health care providers.

5. Adoption of current and proven programs and applications for specific monitoring of medical products: With the advent of new approaches and applications—such as the 3S concept, Cohort Event Monitoring approach, and WHO's Global Benchmarking Tool—there are proven options available for implementing more efficient and resource-friendly approaches that could be part of a national PV system. Whether to use these tools and applications, and which ones, will depend on the need and context. For instance, if there is a relatively new drug repurposed for use with a certain ailment, then applying the 3S concept, with learnings from countries that have already implemented it, may be the most effective and efficient option.

6.2. Addressing HR concerns in terms of quantity and quality

Resolving HR concerns will require addressing the following:

1. The HR aspect of PV: As the evidence clearly shows, there is a deep-rooted HR problem in the NPVC that needs some immediate attention. However, there is also the need for sustainable and long-term solutions, such as integrating PV education and training into the public health education system or using continuing medical education credits to achieve that for medical professionals. Attaching minimum continuing professional education credits to the renewal of a practice license could be one of the approaches to encouraging involvement of health care providers in the PV system.
2. Motivation for health care providers: The system should be able to acknowledge the effort of health care professionals in contributing to a well-functioning PV system. Being recognized and appreciated helps to maintain regular and high-quality reporting (for instance, spontaneous reporting). In addition, on-the-job training or step-down mentoring could encourage providers to be more sensitive toward this subject, which helps not only in developing a pool of personnel with adequate knowledge and awareness but also in retaining them as well.

6.3. Ensuring effective and increased awareness of the PV system

Creating awareness of the PV system will require the following:

1. Awareness of the PV system among health care professionals: The PV system and its processes are not well-known among health care professionals. It is important to strategize regular awareness activities at all levels of the health system and consider using multiple means and platforms (such as social media, emails, orientations) to sensitize health professionals in the importance and processes of PV. In addition, evidence suggests that regular feedback to health care providers on the reports they share is appreciated by them (e.g., using newsletters on a periodic basis to share an overview of the reports, disaggregated by type of AE, level of reporting, and so on).
2. An effective communication plan and implementation: Currently, no communication plan on PV exists in the country; though there are events (such as conferences, workshops, meetings) that communicate medicine safety to health care staffs/professionals. Information on drug safety, quality defects, counterfeiting, and so on is necessary and time sensitive, requiring communication to the public. Multiple platforms (e.g., social media, daily newspapers, emails, radio, etc.) could be strategically used to reach all ages of the population and various localities.

3. Effective media relations: Openness with the media will help to not only debunk rumors or false information to the public but also create an environment conducive to developing PV policies and legislation.

6.4. Strengthening data systems, data use, and learning

Strengthening data systems and use will require the following:

1. Use of AE data: Regular analysis and use of AE data should be in place to promote current treatment guidelines and improve policies.
2. Continuing research and regional learning: Currently, there is limited research conducted in the country to provide evidence for various aspects of the PV system. Academic research could be promoted in this area to bridge this gap. Other countries in the region have been successful in implementing PV systems, which could open the door for regional learning and sharing of events. In addition, not only quantitative explorations but also qualitative ones can help the decision-makers/policymakers understand the implementation issues and generate actionable plans to improve the PV system.

7. Appendix

List of key informant interviewees

The five personnel interviewed who are key to the Myanmar pharmacovigilance system are:

1. Dr. Lwin Moe May, Assoc. Professor, Department of Pharmacology, University of Medicine 1.
2. Dr. Nyein Chan Pyae, Lecturer, Department of Pharmacology, University of Medicine 2.
3. Dr. Ye Htut Linn, Assistant Lecturer, University of Medicine 1.
4. Dr. Nilar Nyein, Medical Officer, Department of Food and Drug Administration, Yangon.
5. Dr. Zayar Phyo, active TB drug-safety monitoring and management, World Health Organization.

Additional information on reporting of severe adverse events

Figure 10 demonstrates the flow of reporting for severe adverse events in Myanmar.

Figure 10. Reporting flow of SAE in Myanmar.

Abbreviations: aDSM, active TB drug-safety monitoring and management; DR, drug-resistant; FDA, Food and Drug Administration; MDR, multidrug-resistant; Medecins Sans Frontieres , ; NTP, National Tuberculosis Programme; SAE, severe adverse event; TB, tuberculosis.

Table 10. Summary of steps and timeline for SAE reporting in Myanmar.

STEP	Event description	Action taken	Responsible party	Forms sent to	Time frame
STEP 1	SAE event detected	SAE Form filled out and submitted	Hospital (treating) physician	NTP aDSM Focal Point adsm.ntp.myanmar@gmail.com (to send to NTP Program Manager)	Within **24 hours or 1 working day** of SAE detection
STEP 2	SAE Report Form received at the national level	SAE Form completed with all details, upon verification with the hospital/ MDR-TB Centre reporter; meeting for CA scheduled	NTP aDSM Focal Point	Clinical Professors and all members of the NCCA including FDA, and to the Department of Medical Services	Within **72 hours** of SAE detec-tion for initial reporting, then follow-up
STEP 3	SAE entry to National Database	All entries of SAE Form en-tered to National aDSM Database	NTP aDSM Focal Point	National aDSM Database	Within **72 hours** of SAE detection
STEP 4	Clinical Professors' meeting and causality consensus	Meeting conducted for CA, and Causality consensus made	NCCA Clinical Professors and other designated partners	NTP	Within **15 days** of SAE detection or during month-ly meeting
STEP 5	CA report completed	Feedback to the NTP and the hospital	NTP aDSM Focal Point	WHO Global aDSM database aDSM-database@who.int	Within **30 days** of SAE

Abbreviations: aDSM, active TB drug-safety monitoring and management; CA, clinical assessment; FDA, Food and Drug Administration; MDR-TB, MDR, multidrug-resistant tuberculosis; NCCA, National Core Committee for aDSM; NTP, National Tuberculosis Programme; SAE, severe adverse event; WHO, World Health Organization.

Additional information on indicators

Tables 11, 12, and 13 demonstrate the structural, process, and outcome indicator statuses, respectively, for hospitals in Myanmar.

Table 11. Structural indicator status at the hospital level.

Structural Indicators	Status
1. Is there an NPVC or department (e.g. to monitor, report ADRs) or unit (including monitoring, reporting ADR) located at the hospital?	No, there is not a PV department at the tertiary hospital level.
2. Is there a clear mandate, organizational structure, roles, responsibilities, and reporting lines for the NPVC?	In Myanmar, there is a clear mandate for ADR, but the organizational structures, roles, responsibilities, and reporting lines are pending for NPVC.
3. Is there a unit responsible for monitoring safety of medicines?	No, safety of medicines are the responsibility of the FDA and drug advisory committee.
5. Do hospitals have a a general drug information center, or does a specific NPVC exist that provides query-	No, hospitals do not have a drug information center, but there are plans to build a drug

response service on ADR and medicine safety information?	information center at the University of Medicine 1, Yangon.
6. Are there hospital staff who are specifically responsible for PV or medicines safety?	No, most of the hospital staff do not know about ADR. Therefore, education and awareness are required.
7. Does the job description indicate that the staff is charged with PV or medicine safety activities as a full-time function or as a part of other overall responsibilities?	There is no specific and designated staff for NPVC. Staff working for FDA are working for NPVC too.
8. Is there an annual budgetary allocation for PV activities or for the NPVC?	No.
9. Are standard operating procedures present for PV activities (e.g., the ADR reporting process)?	Yes.
10. Are there standard guidelines and protocols for monitoring medicine safety (e.g., the inspection process to ensure quality, the process of monitoring product quality)?	No, only standard operating procedures are present.
11. Is the hospital's drug and therapeutics committee responsible for providing advice to the regulatory authority on the safety of medicines?	Yes.
12. Is there a clear and intelligible guideline for the committee's decision-making process?	Yes.
13. Are there basic technologies available at hospitals to implement PV activities (e.g., telephones, fax machines, Internet, emails, projectors, desktops, laptops, etc.)?	No, there are only supplies for paper-based work.
14. Are they functional and currently being used for the above purposes?	Yes.
15. Are basic reference materials and related resources available and being used at hospitals?	No, basic reference materials and related resources are scarce.
16. What percentage of health care professionals on staff (doctors, pharmacists, nurses) have received PV training in the past year?	FDA staff only received PV training in the past year (0.02%–0.04% of health care professionals).
17. Does the hospital require coordination of PV activities (such as monitoring and reporting ADRs)?	Yes.
18. Does each department have a clearly defined task in the coordination scheme?	No.

Abbreviations: ADR, adverse drug reaction; FDA, Food and Drug Administration; NPVC, National Pharmacovigilance Center; PV, pharmacovigilance.

Table 12. Process indicator status at the hospital level.

Process Indicators	Status
1. Is the hospital connected to an external PV database (e.g., ADR report / National Drug Information & ADR Center Drug Safety Report)?	No, there is no PV department in the hospital.
2. How are the report forms collected and transferred to the NPVC?	The process is explained in the main body. Figures 2, 3 and 5 illustrate the flow of ADR reports
3. Does the hospital have a separate report form for patients?	No, the patients do not know about ADR.
4. Are patients in the hospital encouraged to report adverse events directly to the NPVC?	No.
5. Does a form exist for reporting ADR at the hospital? 6. Does a form exist for reporting poor product (drug) quality problems at the hospital?	Yes. No, there is only the ADR report forms.

7. Does a form exist for reporting medication error at the hospital?	No.
8. Does a form exist for reporting treatment failure at the hospital?	No.
9. Are PV and medicine safety data and pharmaceutical inspection cooperation schemes used in medicine procurement decisions?	Yes.
10. Do procurement policies require PV and medicine safety data to be used in procurement guidelines?	Yes.
11. Does the hospital have a strategy or plan to mitigate, limit, or monitor the use of high-risk medicines?	No, but Aung San (TB) hospital has a plan to mitigate, limit, or monitor the use of high-risk medicines.
12. Have the plans to mitigate, limit, or monitor the use of high-risk medicines for safety purposes been carried out?	No.
13. What activities have been carried out to mitigate risk of such high-risk medicines?	ADR reporting, and the drug information center and drug advisory committee plan to implement activities to mitigate risk of high-risk medicines.
14. Are health care staff and patients updated with medicine safety information?	Yes, via conferences, seminars and meetings that provide updated information.
15. Do advertisements reflect the update on medicine safety information?	Yes.
16. Are there measures to report inappropriate or infringing pharmaceutical advertising materials and activities?	No.
17. What sources of information are used by the hospital to make the above decisions (risk management decisions)?	ADR report.
- Other sources?	Clinical trial report, WHO/FDA/EMA safety warnings, literature, journals, databases, and microbiologist reports.
18. Does the Drug and Therapeutics Committee carry out PV activities or resolve drug safety issues?	Yes.
19. Is there a record of the meeting on the above issues?	Yes.

Abbreviations: ADR, adverse drug reaction; EMA, European Medicines Agency; FDA, Food and Drug Administration; NPVC, National Pharmacovigilance Center; PV, pharmacovigilance; TB, tuberculosis; WHO, World Health Organization.

Table 13. Outcome/impact indicator status at the hospital level.

Outcome or Impact Indicators	Status
1. How many ADR reports were received in the past year?	56 cases in 2019.
2. How many ADR reports were sent to the NPVC in the past year?	Not available
3. How many pharmaceutical product quality surveys were conducted in the past year compared to the proposed plans?	Not available
4. Has the hospital carried out review studies on medicine utilization?	Yes, at the tertiary hospital level..
5. Has the hospital carried out active surveillance activities in the last 5 years (e.g., epidemiological studies,	Yes, the active surveillance is “Adverse Drug Reactions in Selected Wards of the Yangon

incident monitoring through cohort event monitoring research, phase 4 clinical research)?	General Hospital and Yangon Specialty Hospital During the First Quarter of 2019."[35]
6. Have any patients reported experiencing drug-related adverse events in the past year?	No.
7. Were there any patients whose treatment was modified due to treatment failure or ADRs in the past year?	No.
8. Has the above information been reported to any units or individuals?	No.
9. How many PV-related information requests were received in the past year? What was the rate of requests received for information related to PV (e.g., asking about the ADRs) in the past year?	
10. What was the rate of requests processed and answered in the past year?	
11. Were any medicine safety bulletins (e.g., ADR issues) scheduled to be published in the past year?	No.
12. Were any medicine safety bulletins (e.g., ADR issues) published in the past year?	NA
13. How many medicine safety issues of hospital relevance identified from outside sources were acted on in the past year?	
14. Are safety signals and significant safety issues promptly communicated to health workers and the public?	No.
15. How long does it usually take from when a safety signal or significant safety issue is identified to when it is communicated to the health workers and the public?	
16. How many patient education activities on ADR and medicine safety topics have been carried out in the past year at the hospital?	None, the patient education activities were done for the public by the General Practitioners' Society.
17. Were any "dear health care professional" letters or any other type of regulatory safety alert letters developed and distributed in the past year?	No.
18. Were there any drug safety changes or certifications in treatment guidelines or drug lists due to the assessment of signs or safety issues in the past year?	
19. What was the number of recommended risk management activities (including phase 4 studies) due to new medicine safety data in the past year?	The exact number is not available, although Phase 4 studies were done for Anti-TB drugs.
20. Is there documentation that summarizes or reports on these activities in the past year?	Yes.
21. Did the hospital assess the management impact of making decisions to ensure drug quality and safety in the past year?	Yes.

Abbreviations: ADR, adverse drug reaction; NPVC, National Pharmacovigilance Center; PV, pharmacovigilance.

Search Query

Table 14 shows the parameters of the search query for the assessment.

Table 14. Search query parameters for the assessment.

(((Drug) AND
(adverse AND (event or events)) OR
(adverse AND (reaction OR reactions))) OR
(OR pharmacovigilance OR pharmacovigilance system OR PV system))
AND (Myanmar OR Yangon)

List of studies relevant to pharmacovigilance or adverse events of drug use in Myanmar

Table 15 summarizes some key studies that are relevant to the Myanmar assessment.

Table 15. Summary of studies relevant to PV or drug related AEs in Myanmar.

Author and year of publication	Study design	Study's focus	Population with drug-related event
May et al., 2020[35]	Prospective observational study	To study ADRs in patients admitted to selected wards of Yangon General Hospital and Yangon Specialty Hospital, Myanmar	47 out of 160 patients
Tiemersma et al., 2019[36]	Literature review	To discuss early experiences with aDSM and similar methods of active PV for New Drugs and Regimen in TB programs	NA
Suwankesawong et al., 2016[26]	Cross-sectional survey	To explore the current landscape and identify challenges of PV among Association of Southeast Asian Nations countries	NA
Han et al., 2020[37]	Prospective efficacy study	To study the efficacy of pyronaridine–artesunate for the treatment of uncomplicated *P. falciparum* and *P. vivax* malaria in southern and northern Myanmar to support a review of the national malaria treatment policy and to inform the design of malaria elimination programs in the context of artemisinin resistance	0
Landier et al., 2017[38]	Pilot phase of a multicenter cluster-randomized control trial	To study safety and effectiveness of mass drug administration in reducing *P. falciparum* incidence and prevalence in four villages with high prevalence of sub-microscopic infections located on the Thailand–Myanmar border	212 out of 3,931 (mild to moderate AE)
Smithuis et al., 2010[40]	Open-label randomized trial	To compare effectiveness of four fixed-dose artemisinin combination therapy and a loose tablet combination of artesunate and mefloquine and assess the addition of a single gametocytocidal dose of primaquine	599 out of 808 (mostly vomiting and dizziness)
McLean et al., 2021[42]	Cluster-randomized controlled trial	To study safety, effectiveness, and potential resistance selection of dihydroartemisinin–piperaquine mass drug administration in a region with artemisinin resistance in Myanmar	151 out of 4,173 (mostly dizziness and rash or itching)
Sun et al., 2011[39]	Clinical trial	To study efficacy and safety of compound dihydroartemisinin/piperaquine (DHAPIP) for treating uncomplicated falciparum malaria in Laiza city of Myanmar	7 out of 71 (mild)

Abbreviations: ADR, adverse drug reaction; aDSM, active TB drug-safety monitoring and management; AE, adverse event; NPVC, National Pharmacovigilance Center; PV, pharmacovigilance.

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