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Pharmacovigilance in the Caribbean Countries: an Overview

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Abstract

Purpose of overview The constant surge in accessing essential medicines creates a greater need for continuous monitoring of usage. The inability to source active pharmaceutical ingredients during the COVID-19 pandemic resulted in drug shortages that increased online requests for medications. E-commerce and social sites have opened the floodgate for the marketing of falsified, substandard, and unregistered pharmaceuticals, making them easily accessible to consumers with the click of a button. A high prevalence of such products with compromised quality highlights further the need for enhanced post-marketing vigilance of safety and quality within the pharmaceutical industry. This review aims to assess the extent to which pharmacovigilance (PV) systems in selected Caribbean countries conform to the minimum World Health Organization (WHO) requirements, highlight the importance of PV in ensuring the safer use of medicines across the Caribbean region, and identify opportunities and challenges in building comprehensive PV systems.

Recent Findings The review finds that while major advancements in PV and adverse drug reaction (ADR) monitoring have occurred in Europe and other parts of the Americas, little has been done in the Caribbean region. Only a few countries in the region are active members of the WHO's global PV network, and ADR reporting is minimal. The reason for low reporting includes a lack of awareness, commitment, and participation of healthcare professionals, manufacturers, authorized distributors, and the general consumers.

Summary Nearly all established national PV systems do not fully conform to the minimum PV requirements by the WHO. Legislation, regulatory framework, political commitment, adequate funding, strategies, and incentives to encourage reporting of ADRs are needed to build sustainable PV systems in the Caribbean.

Keywords Pharmacovigilance · Adverse drug reaction reporting · Regulatory framework and legislation · Pharmaceutical policies · Caribbean countries · West Indies

Introduction

The World Health Organization (WHO) defines pharmacovigilance (PV) as "the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any medicine-related problem" [1]. It monitors the occurrence of adverse drug reactions (ADR) and the occurrence of adverse events (AE). ADR is defined as "an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product." [2]. AE refers to the untoward medical occurrence in a patient receiving drug therapy, but which does not necessarily have a causal relationship with the treatment [2]. This article focuses mainly on ADR reporting, although the information

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collected via PV systems can aid in distinguishing ADRs from AEs.

Pharmacovigilance is a fundamental component of effective drug regulation systems, public health programs, and clinical practice, which represents an integral part of clinical research. It involves the systematic collection, analysis, and interpretation of information regarding pharmacotherapy to ensure the safe and effective use of a drug. Post-marketing PV is critical throughout the product life cycle to ensure the safety and efficacy of a product with long-term use [3, 4]. This is achieved through the collection and evaluation of adverse event reports, signal detection, risk management, and communication with healthcare professionals and the public. Pharmacovigilance also involves collaboration between stakeholders such as drug regulatory authorities, healthcare professionals, and pharmaceutical companies. This collaborative effort helps to ensure the timely identification of any drug-related issues and the development of appropriate measures to mitigate them.

In the 1950s, thalidomide was introduced and marketed as a sedative to treat morning sickness in pregnant women. In 1961, it was linked to congenital malformation of newborns, causing several birth defects in over 10,000 babies by causing phocomelia, a rare deformity characterized by shortened and underdeveloped limbs [5]. In addition, it caused severe sensory peripheral neuropathy in adults [6] and was withdrawn from the global market in 1962. The thalidomide disaster raised numerous questions about the reliability of animal tests, quality assurance, and the importance of continuous post-market surveillance (PMS) of drugs. The mechanism of the adverse effect of thalidomide has been uncovered, 60 years after it was first acknowledged [7].

PV involves the detection, assessment, and prevention of adverse effects or any other drug-related problems. The objective of PV is to identify and minimize the risks associated with medicines while maximizing their therapeutic benefits. ADR reporting is the process of collecting and reporting information about adverse reactions that occur after a medication has been administered. This information is used to identify new and unexpected ADRs and to monitor the safety of drugs already on the market.

PV, ADR reporting, and drug monitoring are of great significance as these activities help to ensure that medicines are safe and effective, and that patients are receiving the best possible care. They also provide valuable information to healthcare professionals and regulatory agencies, allowing them to make informed decisions about drug safety and effectiveness.

This article reviews the PV systems and legislations in selected Caribbean countries, with the aim to analyze the extent to which they conform to the minimum PV requirements by the WHO and to highlight the importance of PV in ensuring safer use of medicines across the region. In addition, it identifies potential areas of opportunities, challenges, and strategies that can be implemented across the region to create a comprehensive PV system and encourage the reporting of ADRs.

Background

PV has expanded and developed significantly over the years, and its importance in the healthcare system has been acknowledged worldwide. Its scope covers ADRs, medication errors, counterfeit/substandard medicines, lack of efficacy of medicines, misuse and/or abuse of medicines, and interactions between medicines [8]. With an exponential increase in access to medication comes a greater need for routine monitoring of usage. Reporting of adverse drug reactions (ADRs) is an essential aspect of pharmacovigilance, as it allows for the continuous monitoring of drugs and helps to identify new safety concerns or risks associated with their use.

ADRs have a global reputation for being one of the most common causes of patient harm. The high prevalence of ADRs in both institutional and community settings has caused a notable surge in morbidity and mortality. Onakpoya et al. [9] revealed that 462 post-marketing withdrawals of pharmaceuticals were made globally between the periods 1953 and 2013 because of ADRs. The collating and analysis of suspected ADR reports is a valid strategy to increase awareness of previously unknown ADRs and to detect the nature, severity, or frequency of ADRs, resulting in therapy optimization and ADR minimization.

Adverse drug reactions (ADRs) can occur due to various factors, including drug interactions, dosage errors, or individual variability. Drug monitoring also helps to identify potential drug interactions or contraindications, enabling healthcare professionals to adjust the drug regimen accordingly and minimize the risk of ADRs and detect previously unreported drug effects.

The scope of PV goes beyond monitoring ADRs and includes irrational drug use, drug addiction, and overdose, which are global epidemics, and lead to increased morbidity and mortality. The devastating impacts of drug abuse cost nations millions of dollars annually. According to the WHO, approximately 450,000 people died because of drug use in 2015, and of those deaths, 167,750 were directly associated with overdose [10]. The fight against drug abuse is one that requires strategic action and intervention. A robust PV system can give insight into the pattern of drug use within our societies. Routine screening and analysis of data can help detect the nature of abuse and trigger regulatory action. This helps to improve patient safety and identify areas in which special attention might be required. Drug monitoring plays a crucial role in reducing medication errors, which can result in adverse drug events or harm to patients. By

closely monitoring drug therapy, healthcare professionals can detect and prevent medication errors, such as incorrect dosing, drug interactions, or adverse drug reactions. This can ultimately improve patient safety and ensure that medication use is safe and effective.

Health care professionals (HCP), patients, and manufacturers are no strangers to medication errors (ME). It is a daily occurrence, which may result in prolonged hospitalization, morbidity, or mortality. Errors during prescribing, transcribing, dispensing, administration, packaging, and labeling can cause ME. In 2011, the WHO and the Moroccan PV Center joined to collaboratively and systematically address the components of the extended duties for national centers including the collection and analysis of ADRs related to ME [4]. PV centers aim to determine root causes by screening, analyzing, identifying, and classifying ME based on individual case safety reports (ICSRs). Regulatory action can be triggered if errors stem from labeling or packaging. Information derived can be vital in educating HCP about the importance of reporting and creating awareness of the root causes, and encouraging them to develop appropriate practices. This will improve patient care and minimize ADRs and mortality by ME.

Medication errors are often linked to the use of substandard and falsified (SF) medicinal products and unregistered medicinal products. These products may contain incorrect ingredients, incorrect doses, or no active ingredients at all, leading to ineffective treatment or harm to the patient. Proper regulation and oversight are essential to ensure the safety and effectiveness of the medication. There are ongoing efforts to combat SF medicines through legislation, manufacturing practices, and supply chain management. WHO defines "substandard" as authorized products that fail to meet their quality, specification, or both, whereas "falsified" are products that intentionally or fraudulently misrepresent their identity, composition, or source [11]. PV is pivotal for detecting SF products through the identification of ADRs caused by such products and signals from these can trigger regulatory decisions. Unregistered medicinal products refer to preparations that have not undergone the necessary regulatory approval processes required for them to be legally registered, marketed, and sold in a particular country or region. These products may be unlicensed or counterfeit, and they often do not meet the required standards for safety, efficacy, and quality. Without effective post-market surveillance and enforcement, SF and unregistered products can enter the market undetected, leading to harm to patients. Improved post-marketing legislation and stronger regulatory frameworks are needed to prevent these dangerous products from reaching patients.

PV is key for a strong regulatory system both at the national and international levels. According to WHO, "sound drug regulatory arrangements provide the foundation for a national ethos of drug safety and for public confidence in medicines" [12]. There are possibilities that certain adverse events may go undetected in the pre-registration developmental phase of some drugs and may prove to be problematic post-registration. Post-marketing surveillance (PMS) is pivotal in ensuring continuous safety and detecting safety issues that may be relevant to future regulatory actions. Post-marketing legislation plays a crucial role in identifying and managing drug interactions. While pre-marketing clinical trials can identify many potential interactions, post-marketing surveillance can detect previously unknown interactions. This can update drug labels and provide clinicians with essential information to prevent adverse drug events resulting from drug interactions.

Concomitant use of multiple drugs is a common cause of drug interactions. Clinically significant drug-drug interactions may result in severe adverse effects that can worsen a patient's health, prevent achievement of treatment outcomes, and prolong hospitalization stays [13, 14]. Drug-food and drug-herbal product interactions [15] and genetic predisposition are other factors for undesired effects, many of which are currently undocumented. Analysis of spontaneous reports (SR) may help detect and identify previously unknown interactions [16]. Drug interactions can lead to adverse drug reactions (ADRs), which contribute to the economic burden of healthcare systems. ADRs require additional medical interventions and hospitalizations, thereby increasing costs. Proper management of drug interactions through post-marketing surveillance and effective communication between healthcare providers can reduce the incidence of ADRs, leading to a decrease in healthcare costs.

ADRs can generate substantial costs in the millions of dollars annually to manage. Globally, a significant percentage of health budgets is spent on complications due to ADRs. In 2000, a study conducted in the USA estimated the overall cost associated with drug-related morbidity and mortality in ambulatory care to exceed US$177.4 billion, with hospital admissions accounting for 70%, while prolonged hospitalization accounted for 18% of the cost [17]. The estimate was equivalent to 13% of the total health expenditure for the same year (US$1.369 billion). PV can be a crucial tool for early detection and identification of drug safety signals, thus minimizing potential clinical and economic costs of ADRs. International pharmacovigilance plays a crucial role in reducing the economic burden of adverse drug reactions (ADRs). By collecting and sharing information on ADRs, pharmacovigilance systems can identify and manage safety signals and facilitate the timely withdrawal of unsafe medicines from the market. This helps to reduce the costs associated with ADRs and improve patient safety worldwide.

Due of the thalidomide tragedy, WHO established a collaborative system in 1968 for the international collection of individual reports of suspected ADRs [18]. This was a swift action to prevent a repetition of a medical disaster of such a magnitude. As of 2022, there are 172 member countries, 151 full members, and 21 associate members who endeavor to upgrade their status by establishing and implementing systems to promote PV at their country's level. Barbados, Cuba, the Dominican Republic (2020), and Jamaica, St. Vincent and the Grenadines (2022), and Suriname (2007) are the six Caribbean countries with full membership. Anguilla, Antigua and Barbuda, British Virgin Islands, Dominica, Grenada, Haiti, St. Kitts and Nevis, St. Lucia, St. Vincent and the Grenadines, and Montserrat are all associate members preparing for full membership [19].

Pharmacovigilance in the Caribbean

Geography and Demography

The Caribbean is a region of the Americas consisting of 30 nations and is ethnically heterogeneous with a population of about 40 million people. The Afro-Caribbean and Indo-Caribbean are the largest groups of people in the region. English remains the dominant language among Spanish, French, and Dutch. In this review, the mainland countries of Belize, Suriname, and Guyana will be considered Caribbean territories due to their strong economic, political, and cultural ties with the region, with the capital city of Guyana housing the headquarters of the Caribbean Community Secretariat (CARICOM).

Regional Health Organizations

There are organizations established to harmonize healthcare in the region. Some of these institutions are committed to forming a collaboration to create integrated health systems between the Caribbean and the rest of the Americas. Other activities include regulatory harmonization and PV. Such organizations include the Caribbean Public Health Agency (CARPHA), the Organization of Eastern Caribbean States Health Unit (OEC), and the Pan American Health Organization (PAHO).

PAHO

PAHO is the regional office of the WHO for the Americas. It also functions as a specialized health agency for Latin America and the Caribbean to improve the health and quality of life in the region and currently has approximately thirty (30) member states from the Caribbean. It held a series of PV workshops and educative seminars designed to highlight the importance of routine PMS of pharmaceuticals marketed in the region that can lead to an improved understanding of the trends, challenges, and opportunities of healthcare systems and provide an evidenced-based rationale to support decision-making across the region [20].

CARPHA

It currently involves 24 member states that also include Guyana, Suriname, and Belize. CARPHA functions as a critical part of robust mechanisms for drug regulation in CARICOM. The institution's commitment toward PV is evident from their 2017 launch of "VigiCarib," a regional online reporting and surveillance system for the Caribbean Regulatory (CRS) to report ADRs and SF products, with a mission to promote PV and PMS in the Caribbean [21]. The system allows HCP, consumers, patients, and other stakeholders to report ADR events to the CRS for analysis. After completion of the analysis, details of detected signals are shared with CARICOM member states and national RA for regulatory actions. Reports can be made via email or a web domain. CARPHA forwards signals and ICSRs to WHO-UMC-PIDM and reports safety issues to the Global Surveillance and Monitoring System (GSMS) on behalf of CARICOM states [21]. Reports to VigiCarib by member states during the period October 2017–November 2020 revealed 233 ADRs from participating countries [22].

OECS Health Unit

It works closely with Health Ministries (MOH), Regulatory Authorities (RA), communities, and other health organizations in delivering health care to its member states. The Pharmaceutical Procurement Service (PPS) is a department within the Health Unit that acquires pharmaceuticals and regulates and performs PV activities on behalf of member countries. All OEC states use a principal ADR report form created by the PPS.

Systems Established in Selected Caribbean Nations

The quality of the procedure for collating and analyzing reports is a decisive factor in the effectiveness of any PV system. Therefore, we will evaluate some systems in the Caribbean according to WHO minimum requirements. The Caribbean is a region composed of numerous small island states, each with unique healthcare systems resources and challenges. Major obstacles include a lack of resources, inadequate training, and limited public awareness of the importance of reporting ADRs [23]. These challenges can hinder the timely detection and reporting of ADRs, leading to adverse health outcomes for patients. Furthermore, the Caribbean region is prone to natural disasters, and

pharmacovigilance systems can be severely affected during such times, as observed during Hurricane Maria in 2017, which disrupted drug safety monitoring systems in Puerto Rico [23]. Despite the setbacks faced by the region, efforts have been made to strengthen pharmacovigilance in the region. This has been facilitated by CARPHA, which established a regional pharmacovigilance program to facilitate the sharing of drug safety information among member states and conducts training programs for healthcare professionals on pharmacovigilance and ADR reporting, leading to the establishment of pharmacovigilance centers in some countries.

The minimum requirements that the WHO and partners agree should be present in any national pharmacovigilance system, which include [24]:

1. A national pharmacovigilance center with designated staff (at least one full time), stable basic funding, clear mandates, well-defined structures and roles, and collaboration with the WHO Programme for International Drug Monitoring
2. The existence of 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 crisis communication

Barbados

The country joined WHO-UMC-PIDM in 2008, but PV monitoring was established at the Barbados Drug Service (BDS) in 2011 [25]. The BDS is the national RA and procurement body responsible for PV and PMS of drugs marketed and utilized in the country. However, there are no legal provisions in the Medicines Act that cover PV activities as part of the RA mandate, and no legal framework obligates routine monitoring of ADRs or PMS by marketing authorization holders (MAH). There is no national PV center or national database to store and analyze information pertaining to ADRs, and no national pharmacovigilance advisory committee (PAC) to provide technical recommendations on safety issues and regulatory actions and to perform causality assessment, risk management, or case investigation. An official standardized form for reporting ADRs is provided and is available online. Official forms are also available to report SF products. Submissions can be done via hard copy, online, or by email. The BDS revealed 124 ADR report submissions from various polyclinics nationwide during 2015 to 2016 fiscal year [17]. ICSRs are shared with WHO-UMC, and Barbados can utilize the PV services offered by CARPHA's "VigiCarib" [21].

The Bahamas

There is no legal framework that provides for formal regulation of pharmaceuticals by the National Drug Agency. In addition, there are no legal provisions that obligate PV, ADR monitoring, or PMS as part of RA responsibility. Moreover, a national center for PV is yet to be established and does not conform to any of the minimum requirements for PV. However, a handful of discussions and workshops have been held in the past as part of the broad scope that will lead to the introduction and establishment of a PV system in the country. Being a CARICOM state, the Bahamas can utilize the PV services offered by CARPHA's "VigiCarib" to member states [21].

Belize

Despite being situated in Central America, Belize shares similar heritage with some Anglophone Caribbean territories and has very strong ties to the region. It is part of CARICOM and a participant of the CARICOM Single Market and Economy (CSME). The newly created Food and Drug Act provides the legal framework and standard operational procedures that govern the regulatory activities of the Drug Inspectorate Unit (DIU). In 2020, Belize became an associate member of the WHO Program for International Drug Monitoring (WHO PIDM). The WHO PIDM assists countries with PV by providing software and analytical tools to report and analyze adverse events [26]. As part of its ongoing initiatives to provide quality medications in the public sector, the MOH sent five generic drugs for evaluation at CARPHA's testing laboratory in 2019, and the five medications passed the quality tests as per global standards. These steps show the commitment of the Ministry to the continuous monitoring of pharmaceuticals through the public reporting any suspicious medication to the Drug Inspectorate Unit [27]. Belize's utilizes CARPHA's Caribbean Regulatory System and its market surveillance reporting platform, "VigiCarib" [21].

Cuba

PV in Cuba is governed by legal provisions (Law of Public Health 1988) and is managed by the National Pharmacovigilance Coordinating Unit (UCNFv) within the Department of Pharmacoepidemiology. It is a member of the WHO-UMC-PIDM since 1994, becoming the first Caribbean nation to join UCNFv that is located within health institutions and

functions as the national center for all PV activities [28]. ADRs caused by natural and traditional medicine (MNT) are also monitored, but their responsibilities exclude monitoring vaccines. A pharmacotherapeutic committee is formed at various health institutions to serve as a national PV advisory committee to review cases and provide causality assessment, risk management, case investigation, and management. Reporting of ADRs is done with a standardized form provided by the Ministry of Public Health (MPH). HCP reporting forms differ slightly from the one allocated to patients. Entries are captured and analyzed in "FarmaVigiC," an electronic database that feeds to the national center. RA and MPH are notified of all detected signals. In addition, information is shared on a quarterly basis with the Collaborating Center of WHO in Uppsala (Sweden). Cuba is among the top twenty (20) countries with the highest reporting rate of ADRs per million inhabitants globally and is one of the highest reporting in the region. Cuba also occupies a high level within PAHO ratings and qualifies as a reference PV system for the region [29, 30].

Guyana

Guyana is among the founding members of the CARICOM and is home to the organization's headquarters and, as such, makes it a participant of the CSME and an associate member of the WHO-UMC-PIDM. There are legal frameworks provided by the Food and Drugs Act that authorizes the Government Analyst–Food and Drug Department (GA-FDD to regulate pharmaceuticals for requisite quality and safety. The 2007 Guyana National Medicines Policy provides for the establishment of a national center for PV as a unit within the GA-FDD. Guyana has collaborated with CARPHA in an effort to fight SF products by signing a Memorandum of Understanding with the CRS in 2017, allowing medicines to be submitted to CARPHA for pre-registration evaluation and testing. Under this agreement, Guyana also receives assistance from CARPHA's Medicine Quality Control and Surveillance Department with PMS. As a CARICOM member, Guyana has access to CARPHA's Caribbean Regulatory System and its market surveillance reporting platform, VigiCarib [21].

Haiti

Haiti is an associate member of the WHO-UMC-PIDM. The Department of Pharmacy, Medicine, and Traditional Medicine is responsible for enforcing the National Pharmaceutical Policy, which strategically focuses on the procurement of essential medicines and the regulation of imported drugs, manufacturing companies, distribution, and dispensaries. Due to a loosely structured regulatory system, a free market for the sale of SF products has been created. At present, there is no PV system implemented, and no ADR reporting and monitoring program exists in the country. The laws and policies that regulate the pharmaceutical sector were implemented in 1948. A revision to the law on pharmacy and medicines was debated and passed by the Chamber of Representatives in 2003 but has not been adopted by the Senate [31].

Jamaica

Jamaica became a full-time member of the WHO-UMC-PIDM in 2012, becoming the latest Caribbean country to join Cuba and Barbados. The Standards and Regulation Division (SRD), a unit within the Pharmaceutical and Regulatory Affairs Department, is the national center that coordinates the PV activities, along with SF surveillance. Jamaica became an associate member of the WHO Programme for International Drug Monitoring in 2009, the second country in the English-speaking Caribbean. The legal framework governing the reporting of ADRs is outlined in the Food and Drugs Act, Regulation 70, 1975 [32]. The SRD's "PharmWatch Jamaica" program was introduced in 2006 to facilitate and encourage ADR reporting. A collaborative effort involving the MOH and the University of the West Indies Pharmacology department helped revise and redesign the old ADR reporting form to a much more modernized form as a renewed effort to encourage spontaneous ADR reporting [33]. The "PharmWatch" form was created and is made available online and directly at MOH to all healthcare professionals and consumers Although there is no legal framework that obligates ADR reporting by MAH, there are measures that require the submission of ADR reports involving their products via PharmWatch or the Council for International Organizations of Medical Sciences (CIOMS) form for reporting ADRs, and reports are shared with WHO-UMC [32].

Trinidad and Tobago (T&T)

In T&T, there are legal provisions in the Medicines Act that mandates PV and ADR monitoring by the Drug Inspectorate Division and the Chemistry, Food, and Drugs Division. A legal framework obligating the routine monitoring of the safety of products by MAH also exists but is not enforced. T&T system for PV is not comprehensive, and there is an official standardized form provided by the MOH for reporting ADR and SF; however, in practice, it is not customarily used, and reporting is less common. Moreover, there is an absence of a computerized national database to collate and analyse ADR reports. Reporting can also be done via the CFDD web platform and CARPHA's VigiCarib [21].

The OEC States

OEC nations are all associate members of the WHO-UMC-PIDM. The PPS form is used across member states to report ADRs. In addition, PPS submit to WHO-UMC on behalf of member states. At present, PV systems in nearly all of the countries within this territory are not backed by legal frameworks or legislation and do not fully conform to the WHO minimum requirements for PV, with the exception of St. Vincent and the Grenadines.

In St. Vincent and the Grenadines, there is no legal framework that provides for PV or mandates ADR monitoring. However, a national PV center exists and is equipped with a computerized database for storing received case reports. ICSRs are sent to WHO-UMC. Meanwhile, in Grenada, the Medical Products Act provides the legal frame that obligates the RA to perform PV and mandates MAH to routinely monitor the safety of their products, although the PV system does not exist at national level.

Discussion

The Challenges Faced

PV in the Caribbean is still in the infancies, needs strengthening, and is not fully implemented in practice when compared to PV in the European Union and the rest of Americas. The absence of a comprehensive PV system across the region is due to challenges that may be political, economic, financial, and lack of resources. Moreover, there are no legal provisions with corresponding regulations in place, which mandate PV activities or ADR monitoring, and, therefore, its compliance and enforcement is not guaranteed. On the other hand, countries that have legislations for PV and ADR monitoring lacked adequate capacity to perform the task effectively due to lack of funding and resources. Greater attention to funding, infrastructure, training programs, and adequate number of trained staff is necessary to coordinate and sustain PV. The ADR reporting rate in the region is low and makes it challenging for the effective detection of signals, which directly hinders possible and necessary regulatory actions. A complex spontaneous reporting system, lack of awareness and knowledge, underreporting by HCP, and lack of feedback and confidentiality are some of the common factors that contribute to low reporting of ADRs. The absence of PV teaching and training in medical, pharmacy, and nursing schools and training institutions has resulted to the dearth of PV competencies among HCP to monitor drugs and meet their PV obligations. Therefore, they are unclear about the vital role they play in PV. Capacity building in the Caribbean has improved ADR reporting, and, while each country has its own unique approach, they share common themes related to WHO requirements for pharmacovigilance, (Table 1) including adverse drug reaction reporting, monitoring of medicine safety, capacity building and training, collaboration and information sharing, and regulatory oversight. The provision of PV services is much more complex and depends on many intertwining factors such as population density, GDP, gross national income per capita, physician density per population, and total expenditure on health (Table 2).

"VigiCarib" is an improvement to PV in the region, but its service is limited to CARICOM member states. Although the pooling of resources, sharing of information, and harmonization of activities among regional territories can lead to a stronger system, national PV centers for monitoring are essential and pivotal in ensuring complete PV coverage and signal detection in a timely manner. "VigiCarib" is a major initiative but does not invalidate the importance and the need for the establishment of national PV centers to monitor medicines and ADRs proficiently. The Substandard and Falsified (SFF) Classification Framework can be utilized

Table 1 Caribbean country's checklist for the minimum requirement of PV by WHO

Country	World Health Organization minimum requirement checklist				
	National PV center	National spontaneous reporting system	National Database	National PV advisory committee	Communication strategy
Barbados	x	*	x	x	√
Bahamas	x	*	x	x	√
Belize	x	*	x	x	√
Cuba	√	√	√	√	√
Guyana	√	*	x	x	√
Haiti	x	*	x	x	x
Jamaica	√	√	√	x	√
Trinidad and Tobago	x	*	√	x	√

*Vigicarib

Table 2 Factors that can influence the ability to provide adequate pharmacovigilance services in Caribbean countries

Parameters	Barbados	Bahamas	Belize	Cuba	Guyana	Haiti	Jamaica	Trinidad and Tobago
[1]Population (2021)	281,200	407,906	4,000,031	11.26M	804,567	11.45M	2.828M	1.526M
[2]G.D.P per capita USD (2021)	4.868M	11.209M	2.492M	107.4M	7.658M	21.017	14.674M	24.46M
[3]Gross national income per capita USD (2021)	16.9M	26.49M	6.07M	8.92M	9.41M	1.43M	5.19M	15M
[4]Physician density per 1000 population (2021)	2.5 (2017)	1.9 (2017)	1.1 (2018)	8.4 (2018)	1.4 (2020)	0.2 (2018)	0.5 (2018)	4.5 (2019)
[5]Total expenditure on healthcare per capita USD (2019)	1.143M	2.004M	293,410	1.032M	325,890	56,990	327,400	1.17M

[1] https://data.worldbank.org/indicator/SP.POP.TOTL?locations=BB

[2]https://data.worldbank.org/indicator/NY.GDP.MKTP.CD?locations=S3

[3] https://data.worldbank.org/indicator/NY.GNP.PCAP.CD

[4] https://data.worldbank.org/indicator/SH.MED.PHYS.ZS

[5] https://data.worldbank.org/indicator/SH.XPD.CHEX.PC.CD

for post-marketing surveillance of drug quality [34]. This framework attempts to identify and characterize SF medicines before they cause harm to consumers.

Another important aspect of post-marketing surveillance of quality is the identification of unregistered medicines. These are medicines that have not been registered with the regulatory authority and are not authorized for use in a particular country. Unregistered medicines can be particularly dangerous because they have not undergone the same level of scrutiny and testing as registered medicines. The WHO has developed a set of guidelines for the surveillance of unregistered medicines, which provides a framework for the identification, reporting, and management of these products [34]. For this initiative to be successful, there is a need for more frequent random sampling of products for testing and greater collaboration between nation states.

The small population sizes and financial constraints of Caribbean countries influence the resources that can be channeled into PV and drug monitoring. Their small market size, human resources constraints, limited resources, and geographic dispersion are all factors that hinder the development of effective systems. This may be mitigated by regulatory collaboration and work sharing. Small states may lack the human resource capital to assign designated staff for medication regulation in the private sector but may be involved in quality assurance exercises linked to public procurement. The low user fees and small public investment often mean that the regulatory systems are severely underfunded and, therefore, lack basic resources required to perform their functions with full accountability [35].

The Caribbean nations can build a regional regulatory system with a defined scope for the region, and, through sharing of responsibilities, create a system that is less resource intensive but which will still be effective to achieve adequate regulation and oversight of their health systems. The functions that may be shared for enhanced efficiency include marketing authorization, market control/surveillance/vigilance, and licensing of regulatory establishments [35].

Regulatory collaboration among nation states for pre-registration approval and assessments of pharmaceuticals can possibly compensate for the scarce technical, financial, and human resources for PV and post-marketing quality surveillance. The Caribbean Regulatory System CRS is a harmonized regulatory system that coordinates the registration and surveillance of pharmaceutical products in the Caribbean Community (CARICOM) member states [36]. The system enables CARICOM countries to share resources, expertise, and information, which enhances regulatory efficiency and effectiveness. Another opportunity for regulatory collaboration in the Caribbean is work sharing. Work sharing involves the sharing of regulatory responsibilities and workloads between regulatory authorities to avoid duplication of effort and optimize resources. Work sharing can be particularly useful for Caribbean islands with limited resources, as it can reduce the burden of regulatory activities and improve efficiency.

Another important factor is reference regulation, which offers opportunities for Caribbean countries to leverage the regulatory decisions of other countries or organizations to support their own regulatory decisions. This approach can help to streamline the regulatory process and improve patient access to safe and effective medicines. This presents an opportunity for other nations within the region who are not CARICOM members to be incorporated into the Vigi-Carib arrangement for improving their individual PV reporting and that of the region.

This monitoring system is significant as it can feed directly into the WHO-UMC VigiBase, a global pharmacovigilance database managed by the Uppsala Monitoring

Centre (UMC) in Sweden, in collaboration with the World Health Organization (WHO) [37]. VigiBase collects and stores reports of suspected ADRs from around the world, submitted by national pharmacovigilance centers, regulatory authorities, pharmaceutical companies, and healthcare professionals. This signifies the role of VigiCarib as a regional source for collecting data from the Caribbean. It is a Caribbean-driven initiative, which may be more likely to attain support due to its regional monitoring by CARPHA.

Many Caribbean countries face challenges in securing sufficient funding for PV activities. Funding for these activities may come in part from individual governments, donor organizations, such as the World Health Organization (WHO), regional organizations, such as the Caribbean Community (CARICOM), or the Pan American Health Organization (PAHO). In addition to financial support, these organizations may provide support for training, capacity building, and infrastructure development. However, securing sufficient funding remains a challenge in many Caribbean countries, and ongoing efforts are needed to ensure that pharmacovigilance activities are adequately funded and resourced.

In conclusion, post-marketing surveillance of quality is essential to ensure the safety and efficacy of pharmaceutical products. The use of standardized frameworks, such as the SFF Classification Framework and the WHO guidelines for the surveillance of unregistered medicines, can help to identify substandard, falsified, and unregistered medicines before they cause injury or harm to consumers.

What Must Be Done?

Legal framework: A robust national PV system will require solid legislation and political commitment. As such, there is a need for clear, modernized legislation and national policies for PV to guide and regulate its development, implementation, and sustainability. The inception of legislation that obligates all HCP to report ADRs as part of their professional duty and formalizes PV and PMS as ultimate responsibilities of MAH will be essential in nurturing a culture that prioritizes ADR reporting.

Infrastructure and human resources: PV should be considered an integral aspect of healthcare and public safety and must be sufficiently funded to sustain its operations and improve infrastructure and technological tools. Improvements must be done to the process for reporting ADRs to remove any barriers.

Awareness among consumers and HCPs: Technology has opened the floodgate for SF. Public awareness of medicine safety needs to be raised, and consumers must be brought to the speed of their value in PV. National campaigns and educational initiatives must be deployed to raise awareness of the significance and process of reporting ADR. All HCP should be motivated and apprised of their professional duty to report ADRs and encouraged to adopt a culture of safe healthcare practices to minimize ME and AEs.

PV in academia: It is essential that future HCP be exposed to active PV training to initiate awareness and build competence in reporting and handling ADRs in clinical practice. PV should ideally be made a part of the basic training of HCP and integrated with the curriculums.

PV at facility level: To encourage ADR monitoring at the facility level, it is crucial that manufacturers and MAH are held accountable and insisted upon to comply with the regulatory requirements for ADR reporting. Policies bound by legislation that mandate continuous PMS must be implemented and enforced.

Incentives to Encourage ADR Reporting

Spontaneous ADR reports form the cornerstone of PV systems and function as early alert, which is critical in the monitoring of the safety of medicinal products and safeguard patients from preventable adverse events. Therefore, incentives can be utilized to encourage and increase reporting of ADRs. These include:

- Feedback and acknowledgment letters to reporters and HCP and PV staff to officially compliment them on their valuable involvement and services. This simple gesture will increase dedication among reporters and staff.
- E-reporting platforms: Smart mobile devices with internet connectivity are widely used among consumers and HCP. An online or mobile platform for reporting ADR will be more convenient and faster.
- Charges by network providers may be costly and can discourage reporters. Therefore, toll-free numbers for reporting will remove such barriers.
- License renewal points: As an incentive to encourage reporting by HCP, the licensing and registration boards for healthcare staff should reward their members with license renewal points for reporting ADRs.

Conclusion

The national PV systems in the Caribbean region do not conform to the minimum requirement laid out by WHO for national PV. Lack of government funding and the absence of legislations or policies to govern PV operations and mandate ADR monitoring by all healthcare professionals and market authorization holders are factors that contribute to the low reporting of ADRs in the region. To strengthen PV in the Caribbean, special attention must be given to funding and creating awareness among consumers and HCPs on the significance of ADR reporting. Some feasible strategies that

can be implemented to encourage and increase the number of ADR reporting include increased awareness, standardizing and simplifying the reporting process through the use of smart/mobile devices, use of toll-free numbers, and provide incentives to health care providers such as financial/awards/recognition or allocating credit/points for their license renewal. It is also important to enhance training and publicize and establish/foster a culture of ADR reporting.

Compliance with Ethical Standards

Conflict of Interest The authors have no conflict to declare.

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