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Evaluation of Adverse Drug Reaction Reporting on the Badan POM Website in Yogyakarta Special Region

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ABSTRACT

Background: Adverse Drug Reaction (ADR) is defined as a harmful and unintended response to a drug, as a part of the pharmacovigilance system to identify drug safety-related issues. As a regulatory, the Indonesian Food and Drug Authority (BPOM) has facilitated an online reporting platform for healthcare professionals via the website www.e-meso.pom.go.id.

Objectives: The objective of this study is to characterize Adverse Drug Reaction (ADR) reporting within the Special Region of Yogyakarta, serving as an early detection mechanism for potential drug safety hazards.

Methods: This observational cross-sectional survey study utilized ADR reporting data obtained from the MESO website of the Indonesian Food and Drug Authority in the Special Region of Yogyakarta (DIY). The collected data were subjected to descriptive analysis. A total of 169 reports were analyzed, encompassing 255 suspected drugs and 255 ADR events.

Results: The report identifies three predominant groups of patient disease characteristics: diseases of the circulatory system (15.38%), certain infectious and parasitic diseases (11.24%), and diseases of the respiratory system (9.47%). Regarding the type of ADR based on its Sub Organ Class (SOC), Skin and subcutaneous tissue disorders is most frequently involved (21.57%). The antibiotic group is the most commonly suspected type of drug (34.90%), with Levofloxacin and Ceftriaxone being the most implicated in causing ADR (11.24%). Oral administration is the most common route associated with ADR, followed by intravenous administration.

Conclusion: In 2023, the monitoring of ADR in the Special Region of Yogyakarta revealed that antibiotics were the most frequently suspected drug class in relation to ADR. The dermatological organ system was also identified as the predominant organ affected by these reactions.

Keywords: Antibiotics; Adverse Drug Reaction Reporting; Badan POM; e-Adverse Drug Reaction Monitoring (e-MESO); Pharmacovigilance;

INTRODUCTION

Adverse Drug Reaction (ADR) is defined as a harmful and unintended response to a drug. ADRs are a significant cause of morbidity and mortality, contributing to increased healthcare costs[1]. In the United States,

ADRs are estimated to be the fourth to sixth leading cause of death [2]. The reporting rate of ADRs is relatively low; a systematic review indicated that the proportion of hospitalized patients experiencing ADRs ranges from 1.6% to 41.4%. According to Aagaard et al., high-income countries exhibit higher ADR reporting rates compared to low-income countries [3]. In Europe, the reporting of non-serious ADRs ranged from 25% to nearly 60% as of November 2017 [4]. The incidence of ADRs has remained relatively unchanged over time, with studies suggesting that 5% to 10% of patients may experience an ADR upon admission, during hospitalization, or at discharge, despite various prevention efforts [5]. It has been asserted that the healthcare system can promote reporting, ensure appropriate medication use, and enhance patient care safety [6].

In Indonesia, the prevalence of Adverse Drug Reactions (ADRs) ranges from 0.9% to 99%, contingent upon drug usage, therapy duration, and dosage. Insulin, cardiovascular agents, and anti-inflammatory drugs exhibit the highest incidence of ADRs, with prior studies reporting a maximum percentage exceeding 60% [7]. As the National Pharmacovigilance Center (Pusat Farmakovigilans/MESO Nasional), the Indonesian Food and Drug Authority (BPOM) plays a crucial role in the oversight and supervision of the safety of drugs, including vaccines circulating within Indonesia. Consequently, continuous pharmacovigilance activities are essential to ensure the ongoing safety of drugs in circulation [8].

The pharmacovigilance reporting system in Indonesia is entirely centralized at the National Pharmacovigilance Center under the Indonesian Food and Drug Authority [9]. The reporting system for adverse drug reactions can be conducted through the following methods: 1) ADR Online: Reporting of Adverse Drug Reaction (ADR); 2) Yellow Card Form: (ADR Reporting Form) - A form for reporting Adverse Drug Reaction by healthcare professionals. In 2023, the Indonesian Food and Drug Authority (BPOM) received a total of 13,156 reports from healthcare professionals and the pharmaceutical industries. Over the past five years (2019-2023), there has been a notable increase in the number of Adverse Events, Adverse Drug Reaction (ADR), and Adverse event following immunization (AEFI)/ Kejadian Ikutan Pasca Imunisasi (KIPI) reports submitted to BPOM. Despite this upward trend, the volume of reports remains relatively low compared to Indonesia's overall population. In 2023, the Indonesian provinces with the highest number of ADR reports were West Java, DKI Jakarta, Central Java, East Java, South Sumatra, Banten, DI Yogyakarta, Bali, West Nusa Tenggara, and South Sulawesi [8].

Reporting Adverse Drug Reactions (ADRs) is critical to prevent further detrimental effects of drug prescriptions received by patients [10]. The completeness and accuracy of ADR reports are paramount to enable proper analysis of the causal relationship between suspected treatments and adverse events. Immediate measures should be taken to enhance the quality of these reports [11]. The involvement of healthcare professionals is vital. Pharmacovigilance generally necessitates close collaboration among various stakeholders, including politicians, policy makers, health administrators, the pharmaceutical industry, healthcare professionals, and the general public. One of the key successes of post-marketing drug safety surveillance hinges is the proactive role of healthcare professionals in reporting ADR events for patients under their care as part of their professional responsibility [12].

Globally, Adverse Drug Reactions (ADRs) constitute a significant cause of morbidity and mortality among patients, in addition to escalating healthcare costs. Published data reveal that approximately 2 million ADRs occur annually, including 100,000 fatalities, positioning ADRs as the fourth leading cause of mortality. This imposes an estimated financial burden of $136 billion on the global healthcare system. Clinical evidence demonstrates that drugs effective in some patients may be ineffective or induce adverse reactions, potentially fatal, in others who are intolerant. Consequently, the reporting of ADRs is crucial to ascertain the full extent of their impact on public health [13].

The characteristics of Adverse Drug Reaction (ADR) reporting exhibit substantial variability across countries, influenced by local health systems, drug utilization patterns, and sociodemographic factors. ADR reporting is essential for identifying and managing adverse drug reactions, thereby enhancing patient safety and the quality of care. In India, the Pharmacovigilance Programme of India (PvPI) oversees reporting via VigiFlow. The Food and Drug Administration (FDA) manages ADR reporting through the Adverse Event Reporting System (FAERS) in the United States. The European Medicines Agency (EMA) coordinates ADR reporting through EudraVigilance within the European Union. Common challenges across regions include underreporting, data quality, and language diversity [14]. Frequent ADRs reported in Europe encompass those affecting the central nervous system, gastrointestinal, and cardiovascular systems [15]. In the United States, hepatotoxicity is a significant cause of morbidity and mortality and is a major driver of post-marketing regulatory actions [16]. Antibiotics and radiocontrast agents were the most frequently implicated agents in ADRs [17]. In Japan, commonly reported adverse events include interstitial lung disease, abnormal hepatic function, and decreased platelet

count [18]. In India, antibiotics, other drug classes, and nonsteroidal anti-inflammatory drugs were identified as the most frequent causes of adverse drug reactions [19].

Due to the different characteristics of ADR reporting across different countries, performing a descriptive assessment of ADR reporting is imperative, particularly within the Special Region of Yogyakarta. The objective of this research study is to furnish a comprehensive description of the reporting characteristics of Adverse Drug Reaction Monitoring on the BPOM website in the Special Region of Yogyakarta, serving as an early detection tool for drug safety in Indonesia, with a specific focus on the Special Region of Yogyakarta.

METHODS

Study Design

This research was designed as a cross-sectional survey study, encompassing Adverse Drug Reaction (ADR) or Adverse Event case reports derived from the MESO BPOM website within the Special Region of Yogyakarta for 2023.

Population and Samples

The study population consists of Adverse Drug Reaction (ADR) reports submitted to the MESO BPOM website from January 1, 2023, to December 31, 2023, within the Special Region of Yogyakarta. The reporting used in this study consisted of reports that met the predetermined inclusion and exclusion criteria. In this study, the inclusion criteria were the ADR reports from January 1, 2023, to December 31, 2023, in the Special Region of Yogyakarta, while reports with incomplete record data were considered as exclusion criteria.

Study Instruments

There was no sample calculation in this study, all MESO reports on the BPOM website within the Special Region of Yogyakarta for the year 2023 that met the predetermined inclusion and exclusion criteria were included in the analysis. The inclusion criteria comprised ADR reports that reported from January 1, 2023, to December 31, 2023, in the Special Region of Yogyakarta**.** The results of data screening identified 169 reports with 255 suspected drugs that met the inclusion and exclusion criteria. These reports were subsequently used to evaluate the ADR characteristics of the date reports.

Data Collection

Data were collected retrospectively by pulling data from the MESO website on the ADR online subsite. In 2023, there were 205 MESO reports on the BPOM website, with the exclusion criteria being complete MESO reports; 169 reports were obtained with 255 suspected drugs.

Data Analysis

The analysis was performed utilizing descriptive statistical methods encompassing characteristic patient variables such as gender, age, patient disease characteristics, and therapy characteristics. Additionally, descriptive analysis was applied to data concerning the most common drug use groups, the predominant routes of drug administration, the most frequently reported types of ADRs, and the major categories of suspected drugs extensively reported in ADR reporting.

RESULTS AND DISCUSSION

Overview and Characteristics of Reports

Number of ADR reports

The total number of MESO reports submitted on the BPOM website within the Special Region of Yogyakarta from January 1, 2023, to December 31, 2023, amounted to 205 reports. Of these, 169 met the inclusion and exclusion criteria, and 255 were suspected of drugs.

Patient Characteristics: gender and age

The characteristics of patients in this study are based on the division of gender, age, diagnosis on admission, comorbidity, seriousness level, and characteristic of therapy, as shown in Table I.

Table I. Characteristics of patients categorized by demographic attributes, disease profiles, and treatment modalities.

Patients' Characteristics		Frequency Total = 169	Percentage (%)
Demographic Characteristics			
Gender	Male	72	42.60
	Female	97	57.40
Age	Elderly (>65 yrs)	30	17.75
	Adults (18-65 yrs)	122	72.19
	Adolescence (10 – 17 yrs)	7	4.14
	Pediatric (1-9 yrs)	10	5.92
Patient Disease Characteristics			
Admission Diagnosis	ICD 10 – I. Certain infectious and parasitic disease	19	11.24
	ICD 10 – II. Neoplasm	13	7.69
	ICD 10 – IV. Endocrine, nutritional, and metabolic diseases	15	8.88
	ICD 10 – IX. Diseases of the circulatory system	26	15.38
	ICD 10 – V. Mental and behavioral disorder	8	4.73
	ICD 10 – X. Diseases of the respiratory system	16	9.47
	ICD 10 – XI. Diseases of the digestive system	15	8.88
	ICD 10 – XII. Diseases of the skin and subcutaneous tissue	8	4.73
	ICD 10 – XIX. Injury, poisoning, and certain other consequences of external causes	8	4.73
	ICD 10 – XVIII. Symptoms, Signs, and Abnormal Clinical and Laboratory Findings, Not Elsewhere Classified	13	7.69
	Others	28	16,56
Comorbid disease	ICD 10 – I. Certain infectious and parasitic disease	1	0.59
	ICD 10 – IV. Endocrine, nutritional, and metabolic diseases	7	4.14
	ICD 10 – IX. Diseases of the circulatory system	5	2.96
	ICD 10 – X. Diseases of the respiratory system	6	3.55
	ICD 10 – XI. Diseases of the digestive system	2	1.18
	ICD 10 – XIV. Diseases of the genitourinary system	5	2.96
	ICD 10 – XIX. Injury, poisoning, and certain other consequences of external causes	3	1.78
Patient's Therapy Characteristics		**Frequency Total = 255**	**Percentage (%)**
Seriousness	Serious	71	27.84
	Not serious	184	72.16
Route of administration	Per-oral	172	67.45
	i.v.	68	26.67
	subcutan. etc	7	2.75
	Unknown	8	3.13
Drug classes (6 largest groups)	Antibiotics	97	22.88
	Antihypertensive	39	9.20
	NSAID	36	8.49
	Drugs for acid-related disorders	17	4.01
	Antihyperlipidemic	17	4.01
	Other analgesic and antipyretics	17	4.01

Most reported cases involved female patients, constituting 57.40% of the total, while male patients accounted for 42.60%. Age-wise, the largest proportion of reported patients were adults (18-65 years) at 72.19%. Elderly patients (>65 years) comprised 17.75% of the reports, pediatric patients (1-9 years) made up 5.92%, and adolescent patients (10-17 years) represented 4.14% of the total cases. The results indicate that women have a higher risk of adverse drug reactions, although the gender-related differences remain partially incomplete and

contradictory. The complex interactions between exogenous and endogenous influences, particularly gender-specific and individual factors, can lead to unexpected effects. Drug selection should be tailored to individual circumstances and involve a benefit-risk assessment in collaboration with the female patients being treated. This is especially important in forensic contexts, where women often require long-term care due to various factors, such as fluctuations in drug levels during the menstrual cycle. Regular clinical monitoring and tolerability examination can enhance treatment safety and therapeutic success [20].

Another study reports that women experience adverse drug reactions (ADRs) nearly twice as frequently as men. The research findings reveal significant gender differences in pharmacokinetics: among patients given standard drug doses, women are exposed to higher drug concentrations in the blood and have longer drug elimination times than men. This likely contributes to the nearly twofold increase in adverse drug reactions in female patients, raising the possibility that women are routinely overmedicated. [21].

Admission Diagnosis Characteristic

The ADR reporting data indicates that the three predominant groups of patient disease characteristics are as follows: ICD-10 IX, encompassing diseases of the circulatory system (15.38%); ICD-10 I, encompassing certain infectious and parasitic diseases (11.24%); and ICD-10 X, encompassing diseases of the respiratory system (9.47%). Among the comorbidities, the most frequently observed groups are ICD-10 IV, encompassing endocrine, nutritional, and metabolic diseases (4.14%); ICD-10 X, encompassing diseases of the respiratory system (3.55%); ICD-10 IX, encompassing diseases of the circulatory system (2.96%); and ICD-10 XIV, encompassing diseases of the genitourinary system (2.96%).

There is a significant relationship between acute respiratory infections and the development of circulatory system diseases. Acute respiratory infections can trigger conditions such as angina pectoris, chronic ischemic heart disease, cerebrovascular disease, and atherosclerosis. Seasonal occurrences of acute respiratory infections are predictors of mortality due to cardiovascular diseases, highlighting the connection between respiratory infections and circulatory health [22].

Infectious diseases such as tuberculosis frequently cause adverse drug reactions (ADRs). Repeated administration or rechallenge can help identify the causative drug, but in some cases, it remains unidentified, and patients can complete treatment with individual components without experiencing ADRs. This may be due to the excipients added in fixed-dose combinations, which can trigger allergic reactions [23]. Antibiotics, commonly used to treat bacterial infections, are associated with numerous side effects, including gastrointestinal disturbances, rashes, and hypersensitivity reactions [24].

Infectious diseases frequently cause adverse effects through various mechanisms, including immune system response, drug toxicity, antibiotic resistance, and genetic factors. Infectious diseases can weaken the immune system, making patients more susceptible to adverse drug reactions. This is particularly evident in patients with HIV or those undergoing treatments that suppress the immune system [25]. Another factor is advanced age, which has the highest incidence of ADRs in infection cases [26].

Seriousness Characteristic

The majority of the reports fell under the non-serious reporting category, constituting 72.16% of the total. In contrast, the serious reporting category accounted for 27.84% of the reports. Reaction terms of serious occurrences including: bradycardia, tachycardia, palpitations, chest discomfort, rash, gingivitis, gastrointestinal hemorrhage, anaphylactic reaction, hepatotoxicity, apnea, and dyspnea

Route of Administration Characteristic

The predominant routes of drug administration reported were oral, accounting for 67.45 % of the cases, and intravenous, comprising 26.67% of the cases. The oral route is the most common method for drug administration due to its convenience, cost-effectiveness, and high patient compliance, [27] this widespread use also makes it the most frequently associated with adverse drug reactions (ADRs).

Drug Classes Characteristic

The drug classes most frequently documented were antibiotics (22.88%), antihypertensives (9.20%), nonsteroidal anti-inflammatory drugs (NSAIDs) (8.49%), Drugs for acid-related disorders (4.01%), Antihyperlipidemic (4.01%), and other Analgesic and antipyretics (4.01%).

ADR Based on Organ Systems and Suspected Drug

The 2023 ADR reporting profile in the Special Region of Yogyakarta categorizes the types of ADR affecting various organ systems. The highest prevalence was observed in the Dermatological organ system (21.57%), followed by Generalized (19.61%), Gastrointestinal (17.25%), Cardiovascular (9.80%), ENT/Oral (9.01%), and Neurological (8.63%) systems. The most commonly suspected drugs are antibiotics (34.90%), NSAIDs (10.20%), antihypertensives (7.06%), antiplatelets (6.27%), and drugs for obstructive airway diseases (4.31%). (Table II)

Table II. Overview of ADR reported based on organ system classification and suspected drugs

ADR by Organ System Classification and Suspected Drug		Frequency of ADR (total = 255)	Percentage (%)
ADR Based on Organ System Classification (6 largest groups)	Dermatological	55	21.57
	Generalized	50	19.61
	Gastrointestinal	45	17.25
	Cardiovascular	27	9.80
	Neurological	22	9,01
	ENT/Oral	20	7.84
Suspected drug (5 largest group)	Antibiotics	89	34.90
	NSAIDs	26	10.20
	Antihypertensive	18	7.06
	Antiplatelet	16	6.27
	Drugs for obstructive airway diseases	11	4.31

The most frequently suspected drug

Antibiotics are the most common cause of ADR occurrences. Among antibiotics, Levofloxacin and Ceftriaxone are most often suspected of causing ADR (11.24%), followed by Amoxicillin (10.11%), Metronidazole (7.87%), Cefixime trihydrate (7.87%), and Ciprofloxacin (6.84%). This distribution reflects the widespread use of these antibiotics in clinical practice, potentially increasing the likelihood of associated ADRs [28]. Adverse effects of Levofloxacin in patients include dyspnea, insomnia, rash, and pruritus. In contrast, Ceftriaxone causes adverse effects such as dyspnea, pruritus, urticaria, and angioedema.

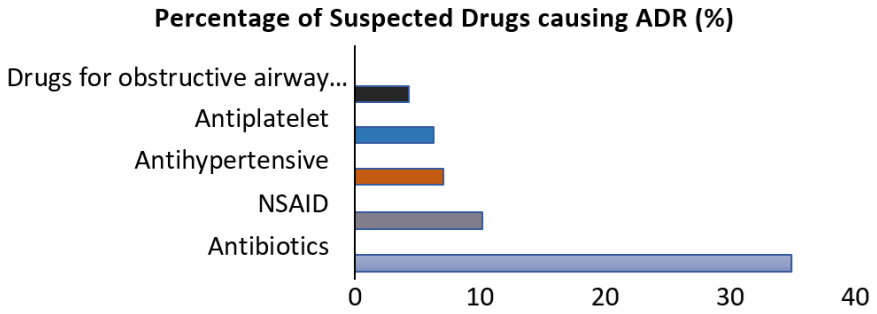

Figure 1. Overview of the most suspected drugs causing ADR (5 largest groups)

A 2021 study reported that adult patients using antibiotics also have the highest risk of experiencing ADRs [29]. Additionally, antibiotic resistance mechanisms contribute to adverse drug reactions. Anti-microbial resistance (AMR) control programs and pharmacovigilance data reporting, regulators play a crucial role as warning tools for suspected resistance [30]. Genetic factors also contribute to the occurrence of adverse effects in infection treatments. The extent of gene contribution to ADRs is unclear and varies according to the drug and type of ADR. Pharmacogenetics and pharmacogenomics have been applied to reduce the incidence of ADRs, particularly drug hypersensitivity reactions [31]. Another study also mentions that factors such as excessive use of antibiotics, high doses, and patient sensitivity contribute to the prevalence of ADR occurrences [32].

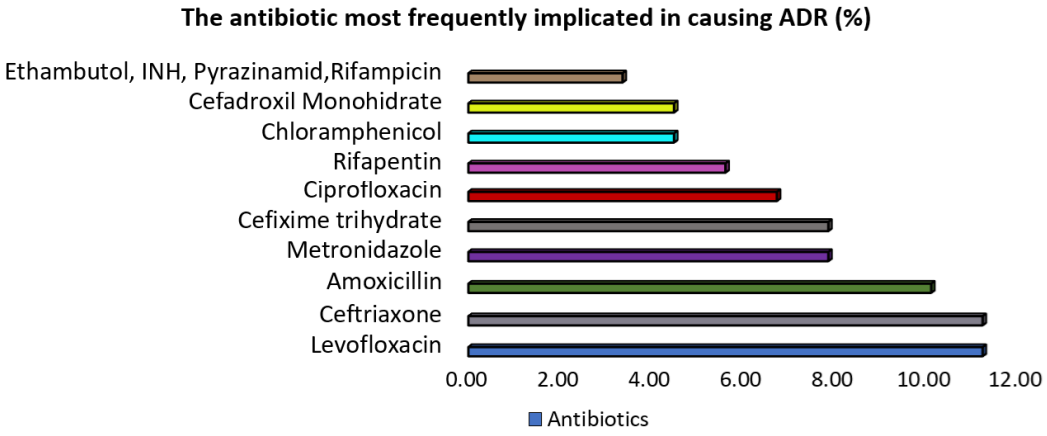

Figure 2. Overview of the most common antibiotics causing ADR (10 largest groups)

The second most frequently suspected drug class causing ADR is NSAIDs, with the most common being Ketorolac (5.10%), followed by Mefenamic Acid (1.57%) and Diclofenac Sodium (1.18%). Adverse effects of Ketorolac include abdominal discomfort, urticaria, pruritus, and periorbital swelling. The third most frequently suspected drug class causing ADR is antihypertensives, with the most common drugs in this class being Amlodipine (4.71%), Captopril (0.78%), and Valsartan (0.39%). Adverse effects of Amlodipine include peripheral edema, palpitations, angioedema, abdominal pain, and chest pain.

The most frequently affected organ system

The organ system most frequently implicated in causing ADR is the dermatological system, accounting for 21.57% of cases (figure 3). The associated symptoms and signs include urticaria, rash, and pruritus. This is followed by the generalized system, which accounts for 19.61% of cases, with symptoms such as angioedema, skin reactions, Stevens-Johnson Syndrome, fever, and anaphylactic reactions. The gastrointestinal system is affected in 17.25% of cases, with symptoms like nausea, vomiting, abdominal pain, and dyspepsia.

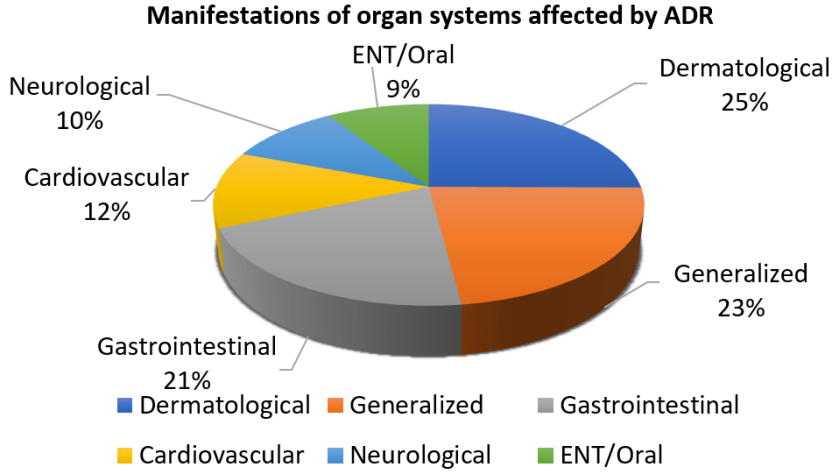

Figure 3. Overview of ADR occurrences based on the affected organ systems (6 largest groups)

Reaction Term

Table III lists the reaction terms reported based on the affected organ systems. In this study, the dermatological system is predominantly affected, with reaction terms including urticaria, rash, pruritus, erythroderma, and burning sensation.

Stevens-Johnson syndrome (SJS) is a severe adverse drug reaction, a life-threatening mucocutaneous condition characterized by widespread blistering and significant epidermal detachment. In this study, it was documented to arise following the oral administration of Lamotrigine (3 cases), Fluoxetine (1 case), Aripiprazole

(1 case), ocular application of Cendo Xitrol (1 case), and intravenous infusion of Paracetamol (1 case). Out of these, 6 cases were classified as serious, with 1 non-serious case. A study in Japan indicates that exposure to Lamotrigine is associated with an increased risk of Stevens-Johnson syndrome (SJS) [33]. Although another study indicates that the incidence of Stevens-Johnson syndrome (SJS) caused by Lamotrigine is relatively low, about 0.04%[34]. The pathogenesis of lamotrigine-induced SJS remains unclear; however, it is postulated that lamotrigine inhibits the voltage-dependent sodium channels, resulting in a stable neuronal membrane in high concentrations. Lamotrigine may also produce reactive metabolites, which could activate the immune system and cause tissue damage [35].

There were 3 cases of anaphylactic reaction observed in this study, associated with the oral administration of Cefadroxil (2 cases) and Paracetamol (1 case). The mechanism of anaphylaxis to cephalosporins like cefadroxil often involves an IgE-mediated response. Studies on similar cephalosporins, such as cefaclor, have demonstrated specific IgE responses to drug-protein conjugates, indicating that the immune system can recognize these drugs as allergens [36]. Paracetamol is a commonly used analgesic and is rarely associated with side effects. However, rare cases of anaphylactic reactions have been reported, In some cases, hypersensitivity reactions have been confirmed through skin tests and basophil activation tests (BAT) [37]. Excipient ingredients in Paracetamol formulations can occasionally trigger allergic reactions [38].

In this study, there were 3 cases of hemorrhage associated with the suspected drugs Acetylsalicylic acid (1 case) and Clopidogrel (2 cases). Acetylsalicylic acid is known to cause gastrointestinal bleeding due to its inhibition of cyclo-oxygenase (COX I) in the digestive tract mucosa. The incidence of GI bleeding in patients taking low-dose Acetylsalicylic acid is reported to be around 2.7%. Clopidogrel, although initially considered safer for the gastric mucosa compared to ASA, has been shown to increase the risk of gastrointestinal bleeding. This risk is particularly notable in patients with pre-existing silent gastric ulcers [39].

There were 27 reported cases of adverse drug reactions affecting the cardiovascular system, with suspected drugs being Amlodipine (8 cases), Salbutamol (3 cases), Procaterol HCl (2 cases), Amiodarone HCl injection (2 cases), and others. Several methodologies, such as Structure-Activity Relationship (SAR) models [40], drug interaction studies [41], cardiovascular risk assessment in drug development [42], and the evaluation of specific drug classes [43], have been developed to predict cardiovascular side effects. Although methods for predicting adverse drug reactions are available, some occurrences can be difficult to predict, for example, reaction terms such as chest discomfort during using Clopidogrel and Amlodipine. Chest discomfort is not listed as a common side effect of clopidogrel and amlodipine. The side effects of chest discomfort from the suspected drug Ondansetron is palpitations and shortness of breath. Literature mentions that Ondansetron has been linked to cases of ventricular arrhythmias, which can manifest as palpitations or a sensation of the heart racing [44].

The most frequently reported reaction term affecting the cardiovascular system was edema, which in this study was classified as a non-serious event. The suspected drugs associated with these cases were Amlodipine, Ketorolac tromethamine, Ceftriaxone, Omeprazole, and Lansoprazole. There is one reported case of a cardiovascular organ reaction in the form of bradycardia suspected to be caused by the drug amiodarone. Literature indicates that bradycardia is listed among the common side effects of amiodarone, along with other cardiovascular effects such as hypotension [45].

There are three reported cases involving the ENT/ oral organ system with the reaction term stomatitis. The suspected drugs in these cases are Griseofulvin, mefenamic acid, and cefixime trihydrate. There is a lack of specific evidence that these drugs can cause stomatitis. Gingivitis in the ENT/oral organ system has been reported in one patient who was concomitantly using three drugs: acetylsalicylic acid, clopidogrel, and streptokinase. Bleeding side effects are frequently observed in patients treated with this drug worldwide. The effect of acetylsalicylic acid varies individually, and it might be important to screen out patients who respond less effectively to the drug [46]. The use of aspirin, clopidogrel, and streptokinase concomitantly can indeed increase the risk of bleeding, but there is no direct evidence from the provided abstracts that this combination specifically causes gingivitis. As a thrombolytic agent, streptokinase also increases the risk of bleeding. When combined with antiplatelet agents like aspirin and clopidogrel, the bleeding risk is further amplified [47].

Dry mouth has been reported as a side effect of the suspected drug Ranolazine affecting the ENT/oral organ system. Although there is no direct literature indicating that dry mouth is a side effect of ranolazine, it is known that medications with anticholinergic potential inhibit saliva secretion, which can lead to symptoms of dry mouth [48].

Table III. Reaction terms for each organ system

Organ System (6 largest)	Reaction Term	Frequency
Dermatological (55)	Rash	19
	Pruritus	16
	Urticaria	11
	Burning sensation	6
	Erythroderma	3
Generalized (50)	Angioedema	23
	Skin reaction	14
	Steven-Johnson syndrome	7
	Fever	3
	Anaphylactic reaction	3
Gastrointestinal (45)	Nausea vomiting	22
	Abdominal pain	9
	Dyspepsia	6
	Hemorrhage	3
	Hiccup	3
	Diarrhea	1
	Constipation	1
Cardiovascular (27)	Oedema	12
	Tachycardia	5
	Palpitation	5
	Chest discomfort	3
	Hypotension	1
	Bradycardia	1
Neurological (22)	Dizziness	8
	Tremor	4
	Vertigo	2
	Restlessness	2
	Insomnia	2
	EPS	2
	Gait disturbance	1
	Delirium	1
ENT/Oral (20)	Eye pain	9
	Stomatitis	3
	Gingivitis	3
	Hypoesthesia oral	2
	Vision blurred	1
	Tinnitus	1
	Dry mouth	1

Several lines of evidence reported similar results, indicating that antibiotics are the most frequent drug class associated with adverse drug reactions (ADRs) [49–51]. The highest frequency of ADRs is observed in the skin and subcutaneous tissues [29,51].

The advantages of this study include its retrospective design using the BPOM ADR Database, which is easily accessible, and the information provided is quite comprehensive, utilizing the ADR reporting format with core variables that have been established and validated by BPOM. The disadvantages or limitations of this study are that some of the ADR reporting by reporters on the database have contradictory information between what was typed on the report and its description, incomplete data or information, leading to data incompleteness and potential misinterpretations. The study is also limited to 2023, which may not optimally capture annual trend analyses in reporting characteristics. The researcher suggests conducting descriptive profile assessments of ADR reporting for other periods to provide a more comprehensive understanding.

However, this study is important as it has never been conducted before within the Special Region of Yogyakarta. It provides an overview of the MESO reporting characteristics in 2023 in the Special Region of Yogyakarta, serving as an early detection tool for drug safety in the community. It offers insights for healthcare professionals and regulators to take follow-up actions against adverse drug reactions, supporting the circulation of safe, high-quality, and beneficial drugs within the Special Region of Yogyakarta.

CONCLUSION

Monitoring Adverse Drug Reactions (ADR) is a crucial aspect of drug safety surveillance in Indonesia. The MESO reports from the Special Region of Yogyakarta in 2023, published on the BPOM ADR database, indicate that antibiotics are the most frequently suspected drug class causing ADR, with the dermatological system being the most affected organ system, and the majority of reports are classified as non-serious. The 2023 MESO reporting data characteristics can serve as a valuable database to identify, document, and reduce the frequency of ADR occurrences, and as an early detection measure for drug safety by healthcare professionals and BPOM as the regulator

STATEMENT OF ETHICS

This study was approved by the Committee on Ethical Clearance Faculty of Medicine, Universitas Gadjah Mada, with ethical clearance number: KE/FK/1698/EC/2024, dated November 8, 2024.

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