Journal of Pharmaceutical Policy and Practice

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/jppp20

Descriptive analysis of the national drug adverse events (AEs) database in Lebanon

Rita Karam, Sarah Reda El Sayed, Aya Ibrahim, Joya-Maria Karam, Souheil Hallit & Abeer Zeitoun

To cite this article: Rita Karam, Sarah Reda El Sayed, Aya Ibrahim, Joya-Maria Karam, Souheil Hallit & Abeer Zeitoun (2025) Descriptive analysis of the national drug adverse events (AEs) database in Lebanon, Journal of Pharmaceutical Policy and Practice, 18:1, 2473014, DOI: 10.1080/20523211.2025.2473014

To link to this article: https://doi.org/10.1080/20523211.2025.2473014

Published online: 14 Mar 2025.

JOURNAL OF PHARMACEUTICAL POLICY AND PRACTICE
2025, VOL. 18, NO. 1, 2473014
https://doi.org/10.1080/20523211.2025.2473014

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS

Descriptive analysis of the national drug adverse events (AEs) database in Lebanon

Rita Karam [a,b,c], Sarah Reda El Sayed [a], Aya Ibrahim [a], Joya-Maria Karam[d], Souheil Hallit [e,f,g] and Abeer Zeitoun [a]

[a]Quality Assurance of Pharmaceutical Products Department, National Pharmacovigilance Program, Lebanese, Ministry of Public Health, Beirut, Lebanon; [b]Department of Chemistry and Biochemistry, Faculty of Sciences, Lebanese University, Beirut, Lebanon; [c]Pharmacology Department, Faculty of Medical Sciences, Lebanese University, Beirut, Lebanon; [d]Faculty of Medicine, Lebanese University, Hadat, Lebanon; [e]School of Medicine and Medical Sciences, Holy Spirit University of Kaslik, Jounieh, Lebanon; [f]Department of Psychology, College of Humanities, Effat University, Jeddah, Saudi Arabia; [g]Applied Science Research Center, Applied Science Private University, Amman, Jordan

ABSTRACT

Background: Adverse Events (AE) including both Adverse Drug Reactions (ADRs) and Medication Errors (MEs) are worldwide health issues tackled by Pharmacovigilance (PV) systems. In Lebanon, ADRs and MEs are monitored by the Lebanese National Pharmacovigilance Program (LNPVP) implemented under the supervision of the Lebanese Ministry of Public Health (MoPH) to ensure the post-marketing surveillance of each authorised medication. The objective of this paper is to evaluate the prevalence of detected AEs within the Lebanese population in a descriptive analysis.

Methods: This is a retrospective analysis-based study that describes collected national AE cases for all marketed medications as well as medications in the pre-marketed phase as part of clinical studies in Lebanon, the LNPVP data system spontaneously received that from Marketing Authorisation Holders (MAHs) between 2018 and 2023.

Results: Since the initiation of the LNPVP programme, a total of 21,631 Individual Case Safety Reports (ICSRs) have been processed; 3,855 of which were excluded and the remaining 17,776 ICSRs are the subject of this paper and correspond to 37,768 AEs associated with medications authorised for use in Lebanon. Among respondents, 55.3% were females, whereas 37.9% were associated with males. In addition, the LNPVP has received a total of 1,961 cases of suspected medication errors, constituting 5.2% of the overall reported AEs.

Conclusion: Our results showed that Lebanon, a country that suffers from a turbulent economic and health context, was able to implement a PV system and operate with efficiency while evaluating a 5-year worth of ICSR reports.

CONTACT Abeer Zeitoun abeer.zeitoun@hotmail.com Quality Assurance of Pharmaceutical Products Department, National Pharmacovigilance Program, Lebanese, Ministry of Public Health, Beirut, Lebanon

The dissemination of this information promotes stakeholder awareness by encouraging a collaborative approach among patients, healthcare providers, and regulatory authorities in Lebanon. However, further research is warranted to investigate factors contributing to MEs in Lebanon.

ARTICLE HISTORY Received 11 July 2024; Accepted 23 February 2025

KEYWORDS Pharmacovigilance; adverse drug event; adverse drug reactions; medication errors; drug safety monitoring; public safety

Background

Adverse Drug Events (ADEs) involve both Adverse Drug Reactions (ADRs) and Medication Errors (MEs). Both are worldwide problems tackled by Pharmacovigilance (PV) systems (Nebeker et al., 2004).

An adverse drug event is an untoward medical occurrence after exposure to a medicine, which is not necessarily caused by that medicine (European Medicines Agency). An ADR is 'a response to a medication that is noxious and unintended used in man to treat' (World Health Organization, 2002). A meta-analysis estimated that 8.7% of hospital admissions in the elderly were due to ADR and proposed that a great burden of disease is due to medications that are supposed to heal (Oscanoa et al., 2017). On the other hand, ME is an error that can lead to an ADR and it potentially stems from a higher-than-needed dose of a medication or an interaction with another drug (Zafar et al., 2008). An expert opinion on drug safety revealed that the global prevalence of MEs is approximately 3%, with the highest rates observed in elderly care settings (11%) and intensive care units (7%) (Al Meslamani, 2023b). Following the thalidomide scandal of 1961, countries strengthened PV systems, establishing robust regulatory frameworks, particularly in high-income countries (Fornasier et al., 2018). For example, countries such as Australia and EU member states have developed robust PV systems, with detailed ADR reporting mechanisms supported by regulatory agencies (Khan et al., 2023; Linger & Martin, 2018).

PV is a worldwide master key for drug safety and monitoring (Jeetu & Anusha, 2010). The World Health Organization (WHO) defines PV as a vital pharmacological science and activities 'relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems' (World Health Organization, 2025). It is the fourth Phase of drug development which is the post-marketing surveillance/data-gathering studies (Chavan & Gawade, 2024). Before approval by regulatory authorities, every drug must undergo comprehensive clinical trials and evaluations to confirm its safety and efficacy and to identify any adverse reactions (Chavan & Gawade, 2024; Garashi et al., 2022).

Post-marketing PV is fundamental to the limitations of pre-marketing phases, which involve a limited number of participants for a short period which may not be considered as an accurate representation of a bigger population (Deore et al., 2019; Klein & Bourdette, 2013). Unidentified ADRs during clinical trials can occur after the drug has been distributed to a more diverse group of people including a specific population (people with comorbidities, pregnant women and children) for a longer period (Deore et al., 2019). It is therefore imperative that post-marketing surveillance be treated with the same importance as other phases of drug development (Abbas et al., 2023).

In Lebanon, the prevalence of ADEs presents a significant drug safety challenge, worsened by systemic issues such as underreporting, particularly among vulnerable populations. Studies have shown that women are more likely to report ADEs, yet they often face barriers such as limited access to healthcare, cultural stigmas, and financial constraints that hinder comprehensive reporting (Al Meslamani, 2023a).

The existing disparities in drug safety, particularly in developing countries, further complicate the landscape of ADEs and MEs. Research conducted in regions such as Jordan's Syrian refugee camps, Iran, Brazil, and Malawi reveals that women, the elderly, and marginalised populations, including refugees, are especially vulnerable to drug safety issues. Factors such as socioeconomic status, geographic location, and gender significantly influence access to safe medications. In rural areas, inadequate healthcare infrastructure and limited resources contribute to higher error rates, compounded by cultural barriers and the absence of strong pharmacovigilance systems (Al Meslamani, 2024a).

Moreover, the region faces significant challenges due to a lack of outcome-based drug safety studies (OBDSSs), which are essential for understanding the real-world impact of ADEs, including ADRs and MEs. While these studies are vital for assessing the incidence and severity of ADEs, operational difficulties such as data collection challenges, resistance from healthcare facilities, and patient recruitment hinder their effectiveness. Additionally, discrepancies in data across diverse healthcare settings complicate the assessment of medication safety (Al Meslamani, 2024b).

The public health implications of underreported ADEs and MEs in Lebanon are significant. Global estimates indicate that underreporting can exceed 90%, driven by factors including fear of repercussions, lack of knowledge about reporting processes, ineffective reporting systems, and organisational cultures that discourage transparency (Al Meslamani, 2023b).

While developed countries benefit from robust healthcare infrastructure, developing countries such as the Arab countries are engaging in remarkable activities, though there is variability in the maturity of the PV systems (Alshammari et al., 2019; Garashi et al., 2022). In Jordan, exhaustive work

has been implemented by the Jordanian Food and Drug Administration (JFDA) to increase awareness and promote safety reporting (Alshammari et al., 2019). One of the main strengths is the establishment of Jordanian PV regional centers setting room for more effective ADR monitoring with great precision.

Despite established reporting mechanisms, many healthcare professionals are reluctant to report ADEs due to concerns about litigation or reputational damage, compounded by inadequate training and support. This lack of reporting not only delays the identification of medication-related safety issues but also obscures systemic flaws in healthcare delivery, emphasising the urgent need for multifaceted strategies to enhance awareness, provide training, and create more user-friendly reporting systems (Al Meslamani, 2023b).

On the other hand, in Lebanon, despite the existence of guidelines on good PV practices, there is still room for the harmonisation of PV requirements in terms of healthcare regulation systems, awareness, and applications (Abbas et al., 2023; Alshammari et al., 2019). In Lebanon, the Ministry of Public Health (MoPH) is responsible for implementing quality standards related to the safety of drugs monitored by the Lebanese National Pharmacovigilance Program (LNPVP). The LNPVP works by collecting and managing Lebanon's national ADE database. However, it was not until 2018 that the MoPH took serious decisions to develop strategic plans. PV operational plans are designed to outline activities, objectives, regulations, collaborators and timescales, all of which are executed through 2025 (Ministry of Public Health (MoPH)).

In light of these challenges, focusing on the significant drug safety issues that persist in the region is critical. Neighbouring countries report a 6.7% dispensing error rate in community pharmacies, highlighting the need for improved pharmacist training and electronic safety systems to reduce similar risks in Lebanon (Ibrahim et al., 2020).

The disparities in ADRs highlight the pressing need for gender-specific research and inclusive strategies that consider the intersections of gender, socioeconomic status, and healthcare access to ensure equitable drug safety practices. Bridging these gaps requires global collaboration, enhanced healthcare infrastructure, and improved regulatory oversight which are essential to advancing drug safety in Lebanon and similar contexts (Al Meslamani, 2024a).

The objective of this paper is to (1) evaluate the prevalence of detected ADEs within the Lebanese population in a descriptive analysis providing insights into the frequency and patterns of adverse reactions associated with pharmaceutical products authorised for use in Lebanon and (2) to describe the operational process employed at the LNPVP for the systematic collection and management of ADE reports.

Methods

Study design and setting

This retrospective descriptive study examines spontaneous ADE case reports submitted to the LNPVP by Marketing Authorization Holders (MAHs) between 2018 and 2023. Data collection began following the issuance of Ministerial Decisions #180 and #181 by the MoPH in March 2021 (Ministry of Public Health (MoPH), 2021). These decisions mandated that all MAHs submit ADE data retroactively starting from 2018. This led to the active submission of Individual Case Safety Reports (ICSRs) to the LNPVP, which served as the basis for this study's analysis. The study includes ADEs reported to the LNPVP for all marketed medications and medications in the pre-marketing phase as part of clinical trials in Lebanon.

Data collection tools and processes

The ADE reporting tool used in this study was developed following international pharmacovigilance standards, adhering to the ICH E2B (R2 & R3) guidelines for electronic transmission of Individual Case Safety Reports (ICSRs). The tool collects comprehensive data on ADEs, including patient demographics, drug-related details, and detailed case narratives. Before full implementation, the tool underwent a validation process through pilot testing with actual MAH data submitted to ensure its reliability and accuracy.

MAHs submitted ICSRs in XML format via email to the LNPVP, which were then imported into VigiFlow, a web-based ICSR management system. Upon import, ICSRs were categorised as successfully imported, flagged for follow-up, or excluded due to missing essential criteria. The LNPVP team applied a rigorous data cleaning process to ensure completeness and accuracy, identifying and rectifying any irrelevant, incomplete, or incorrect information (World Health Organization, 2024).

Operational definitions

The following terms are used throughout the study to maintain clarity and consistency:

- *Adverse Drug Reactions (ADRs):* Harmful and unintended reactions to a medicinal product, whether expected or not, and irrespective of their inclusion in the product's labeling (World Health Organization, 2015).
- *Medication Errors (MEs):* Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, healthcare products,

procedures, and systems, including prescribing, order communication, product labeling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use (World Health Organization, 2022).
- *Individual Case Safety Reports (ICSRs):* Documents detailing one or more suspected ADEs related to a medicinal product in a single patient (International Council for Harmonisation (ICH), 2013).
- *Causality Assessment:* The process of determining the relationship between a drug and an adverse reaction, based on the WHO-UMC Causality Assessment System (World Health Organization, 2013).

Inclusion and exclusion criteria

The study applied specific criteria to ensure the relevance and quality of the data analysed:

- ***Inclusion Criteria***: ICSRs submitted by MAHs concerning marketed or pre-marketed medications in Lebanon between 2018 and 2023. All reports of suspected ADRs, including serious and non-serious reactions, expected or unexpected, were considered, regardless of the source (e.g. spontaneous reports, literature, digital media).
- ***Exclusion Criteria:*** ICSRs that did not adhere to the reporting standards set in Ministerial Decisions #180 and #181 were excluded from the analysis. These excluded reports related to medications not procured in Lebanon and reported missing essential data elements such as patient identifiers, drug details, or appropriate reaction classification.

Data management and validation

Upon receipt, ICSRs were organised by month and by the company before being imported into VigiFlow. Reports not meeting the minimum criteria, such as lacking mandatory data elements (e.g. patient identifiers, drug information, MedDRA-coded reactions), were excluded or merged with follow-up reports when applicable (European Medicines Agency). Data cleaning involved verifying that essential fields, such as medication start/stop dates, reaction outcomes, and seriousness criteria, were properly documented. The LNPVP team also reviewed case narratives for consistency with structured data fields to ensure that the clinical information was accurately captured.

Causality assessment

The causality assessment process, conducted using the WHO-UMC Causality Assessment System, classified suspected ADRs as Certain, Probable, Possible,

Unlikely, Conditional, or Unclassifiable. This assessment allowed for a systematic evaluation of the relationship between the suspected drug and the reported ADRs, ensuring consistency in data interpretation (World Health Organization, 2023).

Statistical analysis

Descriptive statistics summarised the collected data, reporting results as counts and percentages. A bivariate analysis was conducted to assess the relationship between patient demographics (age and gender) and the incidence of ICSRs. The statistical analysis was performed using SPSS software (version 23.0), and categorical variables were compared using Pearson's χ^2 test. Statistical significance was set at $p < 0.05$.

Results

The received ADE case reports are presented by count, type, patient demographics, reaction classification by System Organ Class (SOC) and Preferred Term (PT), and suspect drug classification by Anatomical Therapeutic Chemical (ATC) classification. Reflection on the type of reported medication errors is also presented.

Reports count

Since its initiation, the LNPVP has received and processed a total of 21,631 ICSRs; 3,855 of which were excluded on the following grounds: 1,546 cases were duplicates and /or follow-ups, which were merged with the original case; 1,329 cases corresponded to drugs purchased outside of Lebanon; and 980 cases didn't meet the minimum criteria for reporting. The remaining 17,776 ICSRs are the subject of this paper and correspond to 37,768 ADEs associated with medications authorised for use in Lebanon (Figure 1), acknowledging that a single ICSR may contain multiple ADEs.

Figure 2 details the monthly distribution of ICSRs received from MAHs between March 2021 and November 2023 and reflects the 5-year worth of reports. A steady monthly reporting rate is noticeable after the initial flow of reports corresponding to the implementation of ministerial resolutions #180 and 181 starting in March 2021. The two subsequent increases in activity (November 2021 and March 2023) are linked to heightened reporting from two MAHs due to an error in their submission process. This was rectified by a bulk retransmission of the concerned XML files.

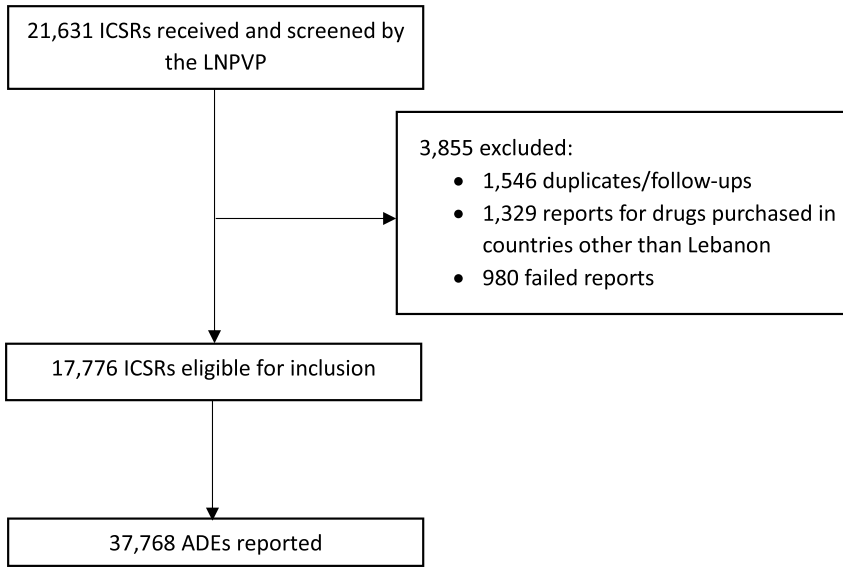

Figure 1. Data screening of ICSRs received from 2018 till 2023.

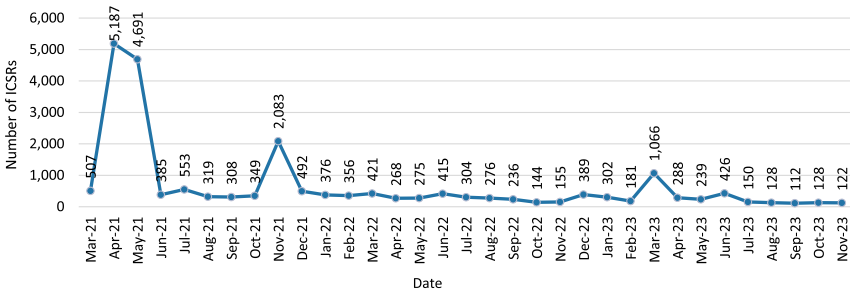

Figure 2. Monthly number of ICSRs received by the LNPVP between March 2021 and November 2023.

Type of reports

Solicited reports, which include cases sent from studies such as Patient Support Programs (PSPs) or clinical trials, were the most common type of reporting during the study period with 11,227 ICSRs (63.2%). As for the remaining 6,549 (36.8%) ICSRs, they were spontaneous reports.

Demographic characteristics of the received reports

Among the 17,776 reported cases, a demographic breakdown reveals that 9,828 cases (55.3%) pertained to females, whereas 6,737 cases (37.9%) were associated with males.

Table 1. Demographic distribution of ICSRs received between 2018 and 2023.

	ICSRs	
Gender	Count (N)	Percentage (%)
Female	9,828	55.3
Male	6,737	37.9
Missing information	1,211	6.8
Age Range (years)		
0–1	163	0.9
2–11	386	2.2
12–17	336	1.9
18–44	4,669	26.3
45–64	4,297	24.2
65–74	1,528	8.6
≥75	1,038	5.8
Missing information	5,359	30.1
Mean Age ± SD*	**46.81 ± 19.043**	
Total	17,776	100.00

*SD: Standard Deviation.

The age distribution of the received ICSRs indicates a predominant occurrence among patients aged 18–44 years, constituting 26.3% of the total cases, closely followed by the age group between 45 and 64 years, accounting for 24.2% of cases. Subsequently, the category covering patients aged 65–74 years contributed to 8.6% of the cases. The mean age in years across all reported cases was determined to be 46.8 ± 19.043.

It is worth emphasising that a considerable portion of the cases lacked information on the gender (6.8%) and the age (30.1%) of the patients. This highlights the significance of ongoing awareness initiatives to reinforce the minimum criteria for a comprehensive and successful report (Table 1).

In addition, a bivariate analysis was conducted to ascertain the correlation between age and gender concerning the incidence of ICSRs. The results reveal a statistically significant higher incidence of ICSRs among male patients up to the age of 17 years old, after which the prevalence transitions to female patients (Table 2).

Table 2. Correlation between the gender and age of the ICSRs received between 2018 and 2023.

	Gender			
Age Range (years)	Females *N* (%)	Males *N* (%)	Total (*N*)	*p*-value*
0–1	55 (37.9)	90 (62.1)	145	<0.001
2–11	176 (47.8)	192 (52.2)	368	
12–17	157 (48.2)	169 (51.8)	326	
18–44	2,728 (58.8)	1,914 (41.2)	4,642	
45–64	2,643 (62.1)	1,615 (37.9)	4,258	
65–74	857 (56.9)	649 (43.1)	1,506	
≥75	556 (54.3)	468 (45.7)	1,024	
Total	7,172 (58.5)	5,097 (41.5)	12,269**	

*$p < 0.05$ indicates statistical significance.
**This total excludes the cases with missing information on gender and/or age.

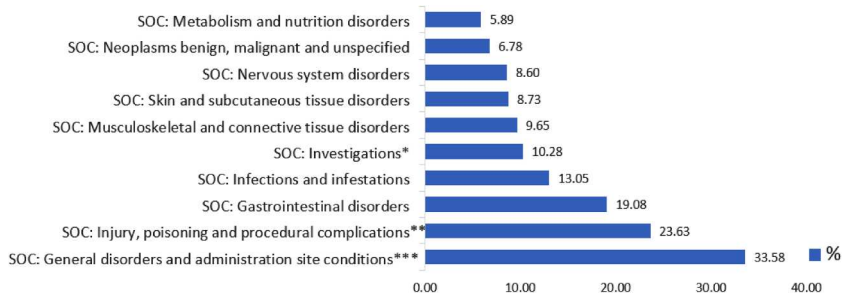

Figure 3. SOC classification of the ADRs received between 2018 and 2023.

*SOC: Investigations: An investigation is a clinical laboratory test concept (including biopsies), radiologic test concept, physical examination parameter, and physiologic test concept. (Lower-level HLGTs include cardiac and vascular investigations, respiratory and pulmonary investigations, lipid analyses, etc. …) (Medical Dictionary for Regulatory Activities, 2023). **SOC: Injury, poisoning and procedural complications: A class of events where an injury, poisoning, procedural, or device complication factor is significant in the medical event being reported. (Lower-level HLGTs include medication errors and other product use issues, exposure to chemicals and poisoning, and procedural-related injuries and complications etc. …) (Medical Dictionary for Regulatory Activities, 2023). ***SOC: General disorders and administration site conditions: A class of disorders that encompasses conditions of a general kind that result from a disease, the treatment of disease or administration of treatment at a particular site and are manifested by a characteristic set of symptoms and signs (Lower-level HLGTs include body temperature conditions, administration site reactions, etc. …) (Medical Dictionary for Regulatory Activities, 2023).

Adverse drug events per system organ class

Figure 3 summarises the received ADEs per SOC, which is the highest level of the Medical Dictionary for Regulatory Activities (MedDRA) terminology, grouped by anatomical or physiological system, etiology or purpose (Medical Dictionary for Regulatory Activities). To note, a given case report can contain multiple ADEs i.e. multiple SOCs.

Adverse drug events per preferred term

Figure 4 summarises the ADEs by their Preferred Term (PT), which is the second most specific level in the MedDRA hierarchy, and that is a distinct descriptor (single medical concept) for a symptom, sign, disease diagnosis, indication, investigation, surgical or medical procedure, and medical social or family history characteristic (Medical Dictionary for Regulatory Activities). To note, a given case report can contain multiple ADEs i.e. multiple PTs. The most reported PT was 'Drug ineffective' accounting for 10.17% of the received case reports, followed by 'Off-label use' which accounted for 8.53% of the total, and thirdly nausea which accounted for 5.36%. Although terms like 'Drug ineffective' and 'Off-label use' are not classic ADEs but rather fall under product use issues or therapeutic failures, they are still in line with the study's methodology and the reporting structure within pharmacovigilance systems. These terms were included in the analysis as healthcare professionals and consumers within the ADE reports frequently report them.

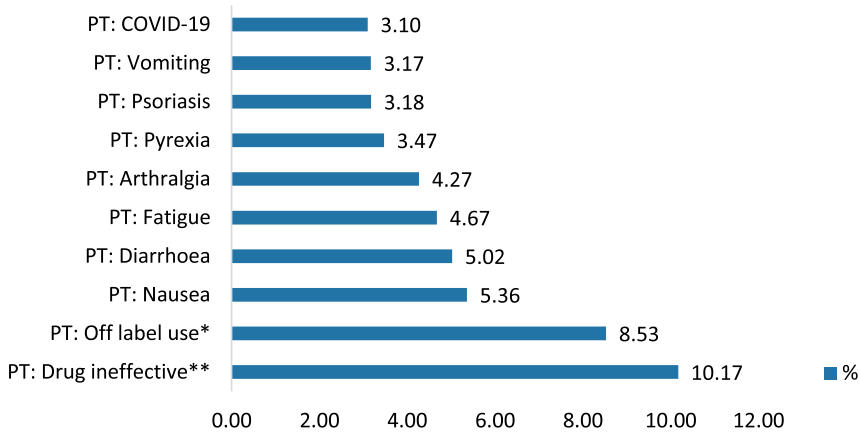

Figure 4. PT classification of the ADEs received between 2018 and 2023.

*PT: Off-label use: situations where a healthcare professional intentionally prescribes, dispenses, or recommends a product for a medical purpose not per the authorised product information (Medical Dictionary for Regulatory Activities, 2023). **PT: Drug Ineffective: therapeutic ineffectiveness includes drug interactions, resistance, tolerance and tachyphylaxis, as well as pharmaceutical defects such as substandard, adulterated, and counterfeit drugs (Medical Dictionary for Regulatory Activities, 2023).

Moreover, MedDRA categorises these terms under product-related issues, which, although not classical ADEs (such as unexpected side effects), still provide a critical understanding of drug performance and usage in real-world settings. 'Drug ineffective' indicates a lack of therapeutic effect, which can have significant clinical implications, while 'Off-label use' highlights deviations from approved usage that can affect patient safety. Including these terms aligns with pharmacovigilance practices, where both therapeutic failures and inappropriate product use are closely monitored due to their potential impact on patient outcomes.

Classification of the reported suspect drugs by anatomical therapeutic chemical classification

Between 2018 and 2023, the reported 37,768 ADEs were associated with 700 Active Pharmaceutical Ingredients (APIs). A useful API classification system is the WHO's Anatomical Therapeutic Chemical (ATC) classification system, where the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties (World Health Organization). In the ATC classification system, the active substances are classified in a hierarchy with five different levels. The system has 14 main anatomical/pharmacological groups or 1st levels. Each ATC main group is divided into 2nd levels which could be either pharmacological or therapeutic groups. The 3rd and 4th levels are

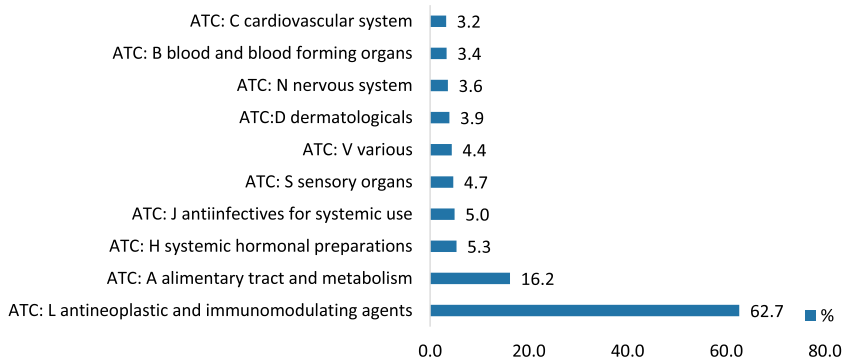

Figure 5. Distribution of ADEs by ATC classification.

chemical, pharmacological or therapeutic subgroups and the 5th level is the chemical substance (World Health Organization). Figure 5 displays the top 10 identified ATCs (Level 1) between 2018 and 2023. The most frequently identified ATC (Level 1) was 'Antineoplastic and immunomodulating agents (L)' (62.7%), followed by 'Alimentary tract and metabolism (A)' (16.2%), and thirdly by 'Systemic hormonal preparations (H)' (5.3%).

Therapeutic subgroups and their associated adverse drug events by preferred term

Table 3 displays the top reported therapeutic subgroup (2nd-level ATC classification of the reported APIs) identified from the received cases

Table 3. Top 5 reported therapeutic subgroups and their associated ADE preferred terms.

Therapeutic Sub-group (2nd level ATC classification)	ADEs (%) ($N = 37,768$)	ADE Preferred Terms (PTs)
L04 = Immunosuppressants	12,698 (33.09)	Arthralgia, Influenza, Psoriasis, Infection, Crohn's disease, Injection site erythema, Maternal exposure during pregnancy, Rash, Condition aggravated, Herpes zoster
A10 = Drugs Used in Diabetes	4,234 (11.07)	Nausea, Drug ineffective, Weight loss poor, Diarrhea, Vomiting, Off-label use, Abdominal pain upper, Constipation, Fatigue, Headache
L01 = Antineoplastic Agents	2,297 (6)	Off-label use, White blood cell count decreased, Platelet count decreased, Neoplasm progression, Anemia, Immune system disorder responsiveness, Malignant neoplasm progression, Drug ineffective
S01 = Ophthalmological	1,229 (3.21)	Vision blurred, Eye hemorrhage, Intentional product misuse, Drug ineffective, Fatigue, Cataract, Product availability issue*, Dyspnea, Pyrexia, Infection
H05 = Calcium Homeostasis	979 (2.55)	Nausea, Arthralgia, Dizziness, Headache, Fall, Pruritus, Asthenia, Pain, Vomiting, Decreased appetite

*Product availability issue: LLTs in this class include: drug shortage, drug delivery device unavailable, product unavailable due to pandemic …

between 2018 and 2023. It also provides insights into the associated ADEs for each subgroup. The top reported therapeutic subgroups confirm the above ATC classification, with immunosuppressors (ATC class L04) being the top reported class contributing to 33.09% of the total cases. This was followed by drugs used in diabetes (ATC class L01) (11.07%), then antineoplastics (6%).

Medication errors

A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is under the control of a healthcare provider, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures and systems, including prescribing, order communication, product labeling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use (World Health Organization, 2022).

Understanding and documenting medication errors is an essential aspect of pharmacovigilance with significant implications for patient safety. This information is central to identifying trends, assessing the impact on patient outcomes, and formulating targeted interventions to enhance the safety and efficacy of medication practices nationwide. The inherent preventability of medication errors highlights the critical need for heightened awareness among both healthcare providers and patients.

Within the MedDRA classification system adopted by the LNPVP, medication errors fall under the 'Injury, poisoning and procedural complications' System Organ Class (SOC). This category covers various lower-level classifications that precisely delineate the specific types of errors (Medical Dictionary for Regulatory Activities, 2023).

Table 4 offers a comprehensive overview of medication errors reported in Lebanon between 2018 and 2023. Out of the received adverse event reports, 1,961 were suspected to have occurred secondary to a medication error. However, these incidents may or may not have been associated with an adverse reaction.

Discussion

This retrospective study aims to evaluate the prevalence and distribution of detected ADEs from 2018 to 2023 within Lebanon. Once the requirements for a functional PV system were implemented, the LNPVP started efficiently operating to collect and manage all ADE reports.

A steady monthly reporting rate was seen (Figure 2) in ADE from 2021 to 2023. Higher ICSR numbers observed in April and May 2021 could be the effect of the sensitisation programme since Lebanon became a full

Table 4. Reported medication errors between 2018 and 2023.

Medication Errors (HLGT)	Count (N = 37,768)	Percentage (%)
HLT: Product administration errors and issues **(PT: expired product administered, product dose omission issue, contraindicated product administered …)**	1,048	2.77
HLT: Medication errors, product use errors and issues not elsewhere classified **(PT: wrong dose, wrong patient, wrong route …)**	779	2.06
HLT: Product storage errors and issues in the product use system **(PT: wrong product stored, intercepted product storage error …)**	57	0.15
HLT: Product prescribing errors and issues **(LLT: written prescription illegible, drug prescribed for unapproved population …)**	38	0.10
HLT: Accidental exposures to product **(PT: accidental device ingestion, accidental exposure to product packaging …)**	10	0.03
HLT: Product preparation errors and issues **(LLT: inappropriate dilution of medication, inappropriate reconstitution technique …)**	10	0.03
HLT: Product dispensing errors and issues **(PT: product transcribing errors, device dispensing error …)**	7	0.02
HLT: Product monitoring errors and issues **(PT: drug monitoring not performed, labelled drug-food interaction …)**	6	0.02
HLT: Product confusion errors and issues **(PT: product label confusion, device use confusion …)**	3	0.01
HLT: Product selection errors and issues **(LLT: wrong product selected, wrong strength selected …)**	2	0.01
HLT: Product transcribing errors and communication issues **(LLT: patient misunderstanding instructions to product use, product data entry error …)**	1	0.00
Total	1,961	5.2%

Member of the WHO PIDM (Program for International Drug Monitoring) in February 2021.

The demographic data from this study is consistent with the existing literature, reflecting gender disparities in ADE reporting. Among the 17,776 cases received, 55.3% were female and 37.9% were male, which aligns with global trends showing a higher rate of ADE reports among women (Al Meslamani, 2024a). This gender disparity may be due to women's more frequent engagement with healthcare systems, reproductive health needs, and their propensity to report ADEs more often than men, as seen in previous studies (De Paepe et al., 2013; Harugeri et al., 2011; Sneha et al., 2019; Watson et al., 2019). Interestingly, our bivariate analysis revealed a statistically significant shift in ADE reporting patterns by age. Males had a higher incidence of reports in younger age groups (up to 17 years), while females accounted for the majority of reports in adulthood (ages 18 and above). This age-related gender transition may reflect differing health-seeking behaviours and social norms between genders across life stages. However, the lack of information in a notable percentage of cases (6.8% for gender and 30.1% for age) highlights the ongoing

challenge of incomplete reporting, highlighting the need for enhanced efforts to raise awareness of the importance of comprehensive data submission in pharmacovigilance systems. These findings support the call for more inclusive strategies in ADE reporting, particularly among underserved populations, as well as targeted initiatives that address the gender and age disparities observed in this study (Al Meslamani, 2024a).

At the time of this study, the most frequently identified ATC was 'antineoplastic and immunomodulating agents (L)' with a rate of 62.7% followed by 'alimentary tract and metabolism (A)', a finding consistent with other studies (Alsbou et al., 2017; Ozcan et al., 2016). Medications categorised as Antineoplastic and immunomodulating agents are licensed to treat a spectrum of cancer types and immune-related disorders. However, their usage imposes a burden of serious and harmful adverse drug reactions (Hussain & Khan, 2022). A previous study examining patients' behaviours towards anti-cancer drugs elucidated that ADRs are readily detected and obvious compared to many other types of ADRs that patients may struggle to identify and report, rendering them more conspicuous for reporting purposes (Aagaard & Hansen, 2013). The PV team effectively delineated the subgroup-specific side effects of each category of ADEs (Table 3), with immunosuppressors being the top reported class contributing to 33.09% of the total cases including adverse effects such as arthralgia, influenza, psoriasis, infection, Crohn's disease, injection site erythema and others. In addition, antineoplastic agents ranked 3rd (Table 3) with a rate of 6% of total ADEs with ADRs such as white blood cell & platelet count decreased, neoplasm progression, anemia, and drug ineffectiveness. However, some differences are notable between Lebanon and Mumbai PV schemes on the prominence of antibiotics and vaccines in the latter (Thakare et al., 2022). The observed differences may be due to the varied ADE reporting practices in addition to differences in the most administered ATC groups within these countries.

The results of our analysis provide several perceptions about the pattern of ADE reporting. Among the different organs or systems affected (Figure 4), 'General disorders and administration site conditions' are most commonly involved (33.58%), these would include low-level Group terms such as body temperature conditions, administration site reactions, asthenia, and chest pain. This is consistent with a previous study that showed that SOC 'General disorders and administration site conditions' accounted for 54% of ADRs reported by European consumers for antineoplastic and immunomodulating agents (Aagaard & Hansen, 2013). A plausible justification for it might be that antineoplastic and immunosuppressants are often administered via intravenous infusion or injections (Aagaard & Hansen, 2013; Hussain & Khan, 2022) which makes ADRs (such as localised reactions at the injection site e.g. pain, erythema, or swelling) easily detectable by both patients and healthcare providers, making them more prone to be reported.

The analysis of MEs in Lebanon between 2018 and 2023 highlights several key areas that align with global findings (Hodkinson et al., 2020). The 1,961 reported cases suspected as MEs in Lebanon emphasise the widespread nature of these preventable events and their potential to cause patient harm. The most common MEs, such as product administration errors and wrong dose or route issues, reflect similar patterns found in international studies, where prescribing and administration errors are prevalent (Hodkinson et al., 2020). These errors may be exacerbated during crises like the COVID-19 pandemic due to system overload, staff burnout, and rapidly changing clinical guidelines (Al Meslamani, 2023a). The high incidence of product administration errors (2.77%) and wrong dose/patient errors (2.06%) signals the critical need for improved education, monitoring, and system-level interventions to reduce the risk of MEs, particularly during times of increased healthcare complexity.

Similarly, a recent WHO paper reported the same findings, suggesting that the most common types of MEs are incorrect dosage with a rate of 34.7%, omission of a dose with a rate of 40%, and wrong administration speed of 7% (Breuker et al., 2021; Key Facts about Medication Errors (MEs) in the WHO European Region, 2022). As stated by the WHO (The Urgent Need to Reduce Medication Errors in Hospitals to Prevent Patient and Second Victim Harm, n.d.; World Health Organisation. Patient Safety. The Third WHO Global Patient Safety Challenge: Medication Without Harm. [Online] 2017., n.d.), MEs occur when unreliable medication systems and/or human factors such as fatigue and increased workload affect the practice of prescribing, dispensing, and administering medication, with significant consequences for patients in terms of morbidity and mortality (Jin et al., 2023).

In light of both the global and local data, integrating technology, fostering inter-professional collaboration, and enhancing medication safety protocols are critical strategies to mitigate these risks. Such interventions would ensure that medication practices are resilient, even during pandemics or other healthcare challenges (Al Meslamani, 2023a).

We acknowledge the limitations of this study, as not all ADEs may have been reported to the LNPVP database, where underreporting is a widespread issue in PV (García-Abeijon et al., 2023). Underreporting, which can exceed 90%, affects both MEs and ADRs, delaying the identification of drug safety issues and contributing to patient harm. Barriers to reporting include fear of litigation, reputational damage, lack of understanding of reporting processes, and ineffective reporting tools (Al Meslamani, 2023b). In this study, ICSRs with incomplete documentation were excluded, resulting in a lower number of cases analysed. Additionally, some ICSR cases lacked critical information, such as patient gender (6.8%) and age (30.1%), underlining the need for improved awareness, comprehensive training, and technological solutions. Inconsistent documentation highlights the importance of reinforcing

minimum information requirements for clearer, more complete reports. User-friendly reporting systems and innovative methods like electronic health records and data mining could help capture unreported ADRs (Al Meslamani, 2023b). Continuous efforts to improve report completeness and accuracy are crucial for enhancing medication safety and patient outcomes.

Another limitation of this study is the predominant distribution of reports among patients aged 18–44 years (26.3% of total cases) and this can cause unnoticed or underreported ADEs from other age groups leading to incomplete understanding of the drug's safety profile. Moreover, the retrospective nature of our study heavily relies on the accuracy of the reports: errors in data entry and misclassification of events could affect the reliability of findings. The significant number of spontaneous reports (36.8%) suffer from the limitation of low data quality, as well as lack of information of the correct diagnosis, all of which may affect proper causality assessment analysis.

Conclusion

In conclusion, this study is the first regional survey of ADEs conducted in Lebanon by the PV team that gives an overall picture of 5-year worth of ICSR cases. The overview of ADE reporting shows that in Lebanon antineoplastic and immunomodulating agents are the most commonly (62.7%) monitored and reported on for adverse events, demonstrating their commitment to thorough safety evaluations and transparency in patient care. Moreover, MEs were found to have a significant rate of 5.2% of total reported AEs. This emphasises the PV systems' responsibility to promote drug safety and ensure the comprehensive monitoring of adverse events. In adhering to our study objectives, we established the importance of ensuring a strong and efficient PV system to detect the safety of medicines. Hence, additional research should explore potential factors impacting medication errors, aiming to mitigate their associated risks to the utmost extent.

Acknowledgements

The authors would like to thank all patients who participated in this study.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Data availability statement

All data generated or analysed during this study are not publicly available. The dataset supporting the conclusions is available upon request to the corresponding author.

Author contributions

RK and AZ were involved in the study design. RK, AZ, SS, AI wrote the manuscript; SS and AI were responsible for the data collection. SH was involved in data analysis and interpretation. AZ revised the paper for intellectual content. All authors approved its final version.

ORCID

Rita Karam http://orcid.org/0000-0002-1977-2778
Sarah Reda El Sayed http://orcid.org/0000-0002-6556-8583
Aya Ibrahim http://orcid.org/0000-0003-1408-7322
Souheil Hallit http://orcid.org/0000-0001-6918-5689
Abeer Zeitoun http://orcid.org/0000-0002-2720-413X

References

Aagaard, L., & Hansen, E. (2013). Side Effects of Antineoplastic and Immunomodulating Medications Reported by European Consumers. *Journal of Research in Pharmacy Practice*, 2(1): 44.

Abbas, H., Zeitoun, A., Watfa, M., & Karam, R. (2023). Implementation of a pharmacovigilance system in a resources-limited country in the context of COVID-19: Lebanon's success story. *Therapeutic Innovation & Regulatory Science*, *57*(2), 178–185. https://doi.org/10.1007/s43441-022-00460-7

Al Meslamani, A. Z. (2023a). Medication errors during a pandemic: What have we learnt? *Expert Opinion on Drug Safety*, *22*(2), 115–118. https://doi.org/10.1080/14740338.2023.2181954

Al Meslamani, A. Z. (2023b). Underreporting of adverse drug events: A look into the extent, causes, and potential solutions. *Expert Opinion on Drug Safety*, *22*(5), 351–354. https://doi.org/10.1080/14740338.2023.2224558

Al Meslamani, A. Z. (2024a). Adverse drug event reporting among women: Uncovering disparities in underserved communities. *Expert Opinion on Drug Safety*, *23*(5), 543–545. https://doi.org/10.1080/14740338.2024.2337745

Al Meslamani, A. Z. (2024b). Why are outcome-based drug safety research studies scarce? Insights into operational challenges and potential solutions. *Expert Opinion on Drug Safety*, *23*(2), 145–148. https://doi.org/10.1080/14740338.2024.2305368

Alsbou, M., Abdeen, G., Batarseh, A., Bawaresh, N., Jaber, J., Qawasmi, G., Maqatef, T., Banat, H., & Batayneh, A. (2017). Analysis of the national pharmacovigilance database in Jordan (2010-2014). *Biomedical and Pharmacology Journal*, *10*(1), 319–328. https://doi.org/10.13005/bpj/1112

Alshammari, T. M., Mendi, N., Alenzi, K. A., & Alsowaida, Y. (2019). Pharmacovigilance systems in Arab countries: Overview of 22 Arab countries. *Drug Safety*, *42*(7), 849–868. https://doi.org/10.1007/s40264-019-00807-4

Breuker, C., Macioce, V., Mura, T., et al. Medication Errors at Hospital Admission and Discharge: Risk Factors and Impact of Medication Reconciliation Process to Improve Healthcare. J Patient Saf. 2021;17:e645–e652. https://doi.org/10.1097/PTS.0000000000000420

Chavan, G., & Gawade, V. (2024). The stages of drug discovery And development process. *International Journal of Pharmaceutical Sciences*, *2*(3), 474–482. https://doi.org/10.5281/zenodo.10603065

Deore, A. B., Dhumane, J. R., Wagh, R., & Sonawane, R. (2019). The stages of drug discovery and development process. *Asian Journal of Pharmaceutical Research and Development*, *7*(6), 62–67. https://doi.org/10.22270/ajprd.v7i6.616

De Paepe, P., Petrovic, M., Outtier, L., Van Maele, G., & Buylaert, W. (2013). Drug interactions and adverse drug reactions in the older patients admitted to the emergency department. *Acta Clinica Belgica*, *68*(1), 15–21. https://doi.org/10.2143/ACB.68.1.2062714

European Medicines Agency. Adverse event. https://www.ema.europa.eu/en/glossary-terms/adverse-event

European Medicines Agency. Individual case safety report. https://www.ema.europa.eu/en/glossary/individual-case-safety-report

Fornasier, G., Francescon, S., Leone, R., & Baldo, P. (2018). An historical overview over pharmacovigilance. *International Journal of Clinical Pharmacy*, *40*(4), 744–747. https://doi.org/10.1007/s11096-018-0657-1

Garashi, H. Y., Steinke, D. T., & Schafheutle, E. I. (2022). A systematic review of pharmacovigilance systems in developing countries using the WHO pharmacovigilance indicators. *Therapeutic Innovation & Regulatory Science*, *56*(5), 717–743. https://doi.org/10.1007/s43441-022-00415-y

García-Abeijon, P., Costa, C., Taracido, M., et al. (2023). Factors Associated with Underreporting of Adverse Drug Reactions by Health Care Professionals: A Systematic Review Update. Drug *Safety*, *46*, 625–636.

Harugeri, A., Parthasarathi, G., Ramesh, M., Guido, S., & Basavanagowdappa, H. (2011). Frequency and nature of adverse drug reactions in elderly in-patients of two Indian medical college hospitals. *Journal of Postgraduate Medicine*, *57*(3), 189–195. https://doi.org/10.4103/0022-3859.85201

Hodkinson, A., Tyler, N., Ashcroft, D. M., Keers, R. N., Khan, K., Phipps, D., Abuzour, A., Bower, P., Avery, A., Campbell, S., & Panagioti, M. (2020). Preventable medication harm across health care settings: A systematic review and meta-analysis. *BMC Medicine*, *18*(1), 313. https://doi.org/10.1186/s12916-020-01774-9

Hussain, Y., & Khan, H. (2022). Immunosuppressive Drugs. *Encyclopedia of Infection and Immunity*, *4*, 726–740. https://doi.org/10.1016/B978-0-12-818731-9.00068-9

Ibrahim, O. M., Ibrahim, R. M., Meslamani, A. Z. A., & Mazrouei, N. A. (2020). Dispensing errors in community pharmacies in the United Arab Emirates: Investigating incidence, types, severity, and causes. *Pharmacy Practice*, *18*(4), 2111. https://doi.org/10.18549/PharmPract.2020.4.2111

International Council for Harmonisation (ICH). (2013). International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Efficacy guidelines. https://www.ich.org/page/efficacy-guidelines.

Jeetu, G., & Anusha, G. (2010). Pharmacovigilance: A worldwide master key for drug safety monitoring. *Journal of Young Pharmacists*, *2*(3), 315–320. https://doi.org/10.4103/0975-1483.66802

Jin, H., Yao, J., Xiao, Z., et al. (2023). Effects of Nursing Workload on Medication Administration Errors: A Quantitative Study. *Work*, *74*, 247–25.

Khan, M. A. A., Hamid, S., & Babar, Z. U. (2023). Pharmacovigilance in high-income countries: Current developments and a review of literature. *Pharmacy*, *11*(1), 10. https://doi.org/10.3390/pharmacy11010010

Klein, E., & Bourdette, D. (2013). Postmarketing adverse drug reactions: A duty to report? *Neurology Clinical Practice*, *3*(4), 288–294. https://doi.org/10.1212/CPJ.0b013e3182a1b9f0

Linger, M., & Martin, J. (2018). Pharmacovigilance and expedited drug approvals. *Australian Prescriber*, *41*(2), 50–53. https://doi.org/10.18773/austprescr.2018.010

Medical Dictionary for Regulatory Activities. MedDRA Hierarchy. Retrieved December 7, 2023. https://www.meddra.org/how-to-use/basics/hierarchy.

Medical Dictionary for Regulatory Activities. (2023). Introductory Guide MedDRA Version 26.1. https://admin.meddra.org/sites/default/files/guidance/file/intguide_26_1_English.pdf

Ministry of Public Health (MoPH). Pharmacovigilance in Lebanon. https://www.moph.gov.lb/en/Pages/4/44742/pharmacovigilance-system-lebanon#/en/Pages/4/44742/pharmacovigilance-system-lebanon

Ministry of Public Health (MoPH). (2021). PV Clarifications—Ministerial Decisions 180 and 181: https://www.moph.gov.lb/userfiles/files/Quality&Safety/PharmacovigilanceSystemInLebanon/PVClarifications-MinisterialDecisions180and181.pdf

Nebeker, J. R., Barach, P., & Samore, M. H. (2004). Clarifying adverse drug events: A clinician's guide to terminology, documentation, and reporting. *Annals of Internal Medicine*, *140*(10), 795–801. https://doi.org/10.7326/0003-4819-140-10-200405180-00009

Oscanoa, T., Lizaraso, F., & Carvajal, A. (2017). Hospital admissions due to adverse drug reactions in the elderly. A meta-analysis. *European Journal of Clinical Pharmacology*, *73*(6), 759–770. https://doi.org/10.1007/s00228-017-2225-3

Ozcan, G., Aykac, E., Kasap, Y., Nemutlu, N. T., Sen, E., & Aydinkarahaliloglu, N. D. (2016). Adverse drug reaction reporting pattern in Turkey: Analysis of the national database in the context of the first pharmacovigilance legislation. *Drugs - Real World Outcomes*, *3*(1), 33–43. https://doi.org/10.1007/s40801-015-0054-1

Sneha, S. G., Simhadri, K., Subeesh, V. K., & Sneha, S. V. (2019). Predictors of adverse drug reactions in geriatric patients: An exploratory study among cancer patients. *South Asian Journal of Cancer*, *8*(2), 130–133. https://doi.org/10.4103/sajc.sajc_218_18

Thakare, V., Patil, A., Jain, M, V. Rai, & D. Langade. (2022). Adverse Drug Reactions Reporting: Five Years Analysis from a Teaching Hospital. *Journal of Family Medicine and Primary Care*, *11*, 7316–7321. https://doi.org/10.4103/jfmpc.jfmpc_1043_22

Watson, S., Caster, O., Rochon, P. A., & den Ruijter, H. (2019). Reported adverse drug reactions in women and men: Aggregated evidence from globally collected individual case reports during half a century. *EClinicalMedicine*, *17*, 100188. https://doi.org/10.1016/j.eclinm.2019.10.001

World Health Organization. Anatomical therapeutic chemical (ATC) classification. https://www.who.int/tools/atc-ddd-toolkit/atc-classification

World Health Organization. WHO collaborating centre for drug statistics methodology. ATC Classification—Structure and principles. Retrieved January 5, 2024. https://www.whocc.no/atc/structure_and_principles/

World Health Organization. (2002). Safety of medicines. https://iris.who.int/bitstream/handle/10665/67378/WHO_EDM_QSM_2002.2.pdf?sequence=1

World Health Organization. (2013). The use of the WHO-UMC system for standardized case causality assessment. https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf

World Health Organization. (2015). Glossary of terms. https://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/glossary/en/

World Health Organization. (2022). Medication without harm. https://www.who.int/initiatives/medication-without-harm

World Health Organization. (2023). Uppsala monitoring centre. https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance/networks/vaccine-safety-net/vsn-members/umc

World Health Organization. (2024). The backbone of medicines and vaccines safety monitoring. https://who-umc.org/pv-products/vigiflow/

World Health Organization. (2025). Pharmacovigilance. https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance

Zafar, A., Hickner, J., Pace, W., & Tierney, W. (2008). An adverse drug event and medication error reporting system for ambulatory care (MEADERS). *AMIA Annual Symposium Proceedings*, *2008*, 839–843.