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Research Article

Characteristics and Predictors of Serious Adverse Drug Reactions Reported to the Pharmacovigilance Unit, Anbar General Health Directorate, Iraq (2020–2025)

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Abstract

Background: Seriousness classification under ICH E2A criteria determines which adverse drug reaction (ADR) reports receive expedited regulatory attention; this has not previously been assessed in Iraqi regional pharmacovigilance data. ***Objectives***: To characterize the proportion, clinical basis, and independent predictors of serious ADR reporting among individual case safety reports (ICSRs) submitted to the pharmacovigilance section within the Anbar General Health Directorate, 2020–2025. ***Methods***: A retrospective analysis was conducted involving all ICSRs submitted through the VigiFlow platform. A case was classified as serious if at least one reaction met an ICH E2A criterion. Suspected medicines were harmonized to International Nonproprietary Names and classified by ATC level-1 group. Associations with seriousness were assessed using multivariable logistic regression, with adjusted odds ratios (aORs) and 95% confidence intervals reported. ***Results***: Of 3264 submitted reports, 3164(96.9%) had a recorded seriousness status, of which 978(30.9%) were serious (30% of all submitted reports). Life-threatening reactions were the commonest criterion (49.3%); 3.6% resulted in death. Anti-infectives were the leading ATC group among serious reports (36.1%), and ceftriaxone was the leading suspected medicine. Blood/blood-forming products, antineoplastic/immunomodulating agents, "various" products, and neonatal and infant age showed the strongest independent associations with seriousness (aORs=2.4–4.0), followed by nervous-system medicines, physician reporting, and increasing numbers of suspected drugs and reaction terms. ***Conclusions***: Nearly one-third of ICSRs submitted to the Anbar pharmacovigilance section met formal seriousness criteria. Blood products, antineoplastic agents, nervous-system medicines, and infant age were associated with seriousness, supporting risk-based pharmacovigilance and targeted safety monitoring in western Iraq.

Keywords: Adverse drug reactions; Anbar; Pharmacovigilance; Seriousness.

خصائص ومتنبئات ردود الفعل السلبية الخطيرة للأدوية تم الإبلاغ عنها إلى وحدة المراقبة الدوائية، مديرية الصحة العامة في الأنبار، العراق (2020–2025)

الخلاصة

الخلفية: تصنيف الجدية وفقا لمعايير ICH E2A يحدد أي تقارير التفاعلات السلبية للأدوية (ADR) تحظى باهتمام تنظيمي معجل؛ ولم يتم تقييم ذلك سابقا في بيانات اليقظة الدوائية الإقليمية العراقية. **الأهداف**: توصيف نسبة وأساس سريري ومستقل للتقارير الخطيرة عن ADR بين تقارير السلامة الفردية (ICSRs) المقدمة إلى قسم اليقظة الدوائية في إدارة الصحة العامة للأنبار 2020–2025. **الطرائق**: تم إجراء تحليل بأثر رجعي شمل جميع ICSRs المقدمة عبر منصة VigiFlow. تم تصنيف الحالة على أنها خطيرة إذا استوفى رد فعل واحد على الأقل معيار ICH E2A. تم توحيد الأدوية المشتبه بها مع أسماء دولية غير مملوكة وتصنيفها حسب مجموعة ATC المستوى 1. تم تقييم الارتباطات مع الجدية باستخدام الانحدار اللوجستي متعدد المتغيرات، مع الإبلاغ عن نسب احتمالات معدلة (aORs) وفواصل ثقة 95٪. **النتائج**: من بين 3264 تقريرا مقدما، كان 3164 (96.9٪) لديهم حالة خطورة مسجلة، منها 978 (30.9٪) كانت خطيرة (30٪ من جميع التقارير المقدمة). كانت ردود الفعل المهددة للحياة هي المعيار الأكثر شيوعا (49.3٪)؛ 3.6٪ أدت إلى الوفاة. كانت مضادات العدوى المجموعة الرائدة في مكافحة المراقبة بين التقارير الخطيرة (36.1٪)، وكان السيفترياكسون هو الدواء المشتبه به الرئيسي. أظهرت منتجات تكوين الدم، وعوامل مضادة للأورام العضلية/تعديل المناعة، ومنتجات "متنوعة"، وعمر حديثي الولادة والرضيع أقوى ارتباطات مستقلة مع الجدية (aORs=2.4–4.0)، تلتها أدوية الجهاز العصبي، وتقارير الأطباء، وزيادة أعداد الأدوية المشتبه بها ومصطلحات رد الفعل. **الاستنتاجات**: ما يقرب من ثلث ICSRs المقدمة إلى قسم اليقظة الدوائية في الأنبار استوفوا معايير الجدية الرسمية. ارتبطت منتجات الدم، وعوامل مضادة للأورام، وأدوية الجهاز العصبي، وعمر الرضيع بالجدية، مما دعم اليقظة الدوائية القائمة على المخاطر والمراقبة المستهدفة للسلامة في غرب العراق.

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INTRODUCTION

Spontaneous reporting systems remain the backbone of post-marketing medicine safety surveillance because they capture suspected adverse drug reactions (ADRs) as they occur in routine clinical practice, across a wide range of patients, comorbidities, and concomitant medicines that clinical trials cannot realistically represent [1]. The World Health Organization (WHO) defines pharmacovigilance as the science and activities related to the detection, assessment, understanding, and prevention of adverse effects or other medicine-related problems, with the important goal of improving patient care and public health [1]. Since spontaneous reporting systems cannot provide reliable incidence estimates in the absence of an appropriate exposure denominator, they remain important for detecting safety signals and characterizing patterns of reported ADRs [2,3]. Importantly, not all adverse drug reactions carry the same clinical significance. Under the International Council for Harmonization (ICH) E2A criteria, a serious adverse event or reaction can be defined as an event that results in death, is life-threatening, requires or prolongs hospitalization, causes persistent or

significant disability or incapacity, represents a congenital anomaly or birth defect, or constitutes another medically important event [4]. The regulatory concept of seriousness differs from clinical severity because some reports can describe severe but self-limiting reactions that do not meet any ICH E2A criteria. This distinction is important in pharmacovigilance because seriousness determines which reports require accelerated assessment, priority causality evaluation, and focused regulatory attention, particularly in resource-limited settings [4,5]. Although spontaneous reporting systems have been widely used to describe adverse drug reactions, relatively few studies have assessed seriousness as a primary outcome. A national analysis of pharmacovigilance data in Sweden demonstrated that age and sex were associated with patterns of ADR reporting, particularly when taking into account seriousness and drug utilization [6]. In Spain, a long-term pharmacovigilance program revealed that serious ADRs were associated with older age and drug-drug interactions [7]. However, comparable evidence from Iraq remains limited despite regional differences in disease burden, prescribing practices, and patterns of medicine use. Pharmacovigilance in Iraq has continued to develop within the WHO Program for International Drug Monitoring, of which Iraq has been a full member since 2010 [1,8]. The national system operates through pharmacovigilance sections established within each directorate of health, which collect ICSRs from affiliated healthcare settings and process them via VigiFlow, the individual case safety report (ICSR) management system developed and maintained by the Uppsala Monitoring Centre (UMC) for national pharmacovigilance centers participating in the WHO Programme for International Drug Monitoring—for subsequent submission to the WHO global database, VigiBase [8]. Within this framework, the pharmacovigilance section at the Anbar General Health Directorate serves healthcare institutions across Anbar, Iraq's largest governorate by geographical area, covering approximately one-third of the country's territory [9] and providing the data source for the present study. Although the pharmacovigilance section has operated for approximately a decade, reporting in earlier years was limited, and many ICSRs contained incomplete information. From 2020 onward, both the number and completeness of ICSRs increased markedly, providing a sufficiently robust dataset to characterize serious ADR reporting and evaluate the factors associated with seriousness. Accordingly, this study aimed to characterize the seriousness of ICSRs submitted to the pharmacovigilance section within the Anbar General Health Directorate from 2020 to 2025 and to identify factors associated with serious reporting. In particular, we assessed the frequency and clinical basis of serious ADRs, their clinical outcomes, the drug classes involved, and the reaction term patterns observed in serious reports. The findings provide regional evidence to support the prioritization of pharmacovigilance and safety monitoring in Anbar healthcare settings.

METHODS

Study design and setting

A retrospective study was conducted using individual case safety reports (ICSRs) submitted to the pharmacovigilance section of the Anbar General Health Directorate in Anbar governorate (western Iraq), covering ICSRs originating from health institutions across this governorate from January 2020 to December 2025. Reports were filtered and de-duplicated in Microsoft Excel by matching the VigiFlow worldwide unique case identifier; five records representing duplicate or follow-up submissions of the same ICSR were identified and removed, retaining the most recently updated version of each case. Missing values for individual variables were otherwise retained in the database and analyzed on an available-case basis for each variable.

Variables and definitions

The primary outcome was the categorization of ADR seriousness as serious or non-serious. The seriousness of the reported ADRs was characterized according to the criteria of the International Council for Harmonization (ICH E2A), which classifies a report as serious if it records at least one of the following: life-threatening events, death, congenital anomalies, sustained disabilities, hospitalization or prolonged hospitalization, and other medically important conditions. The variables identified at the individual report level included patient age and sex, clinical outcome, reporter qualification, number of suspected drugs, number of reported reaction terms, and reporting year. Age group was categorized as neonate (0–27 days), infant (28 days to <2 years), child (2 to <12 years), adolescent (12 to <18 years), adult (18 to <65 years), and elderly (≥65 years). Adverse reactions were classified using the Medical Dictionary for Regulatory Activities (MedDRA) version 28.1 at System Organ Classes (SOCs) and Preferred Term (PT) levels. Suspected medicines were standardized to active ingredients and International Nonproprietary Names (INNs) using the WHO Drug Dictionary (WHODrug Global, September 2025 release) linked to VigiFlow. Therapeutic grouping was based on the Anatomical Therapeutic Chemical (ATC) classification, a hierarchical system maintained by the WHO Collaborating Centre for Drug Statistics Methodology that classifies active substances in five levels from the anatomical main group (level 1) to the chemical substance (level 5). Level 1 comprises 14 main groups: alimentary tract and metabolism (A), blood and blood-forming organs (B), cardiovascular system (C), dermatological (D), genitourinary system and sex hormones (G), systemic hormonal preparations (H), anti-infectives for systemic use (J), antineoplastic and immunomodulating agents (L), musculoskeletal system (M), nervous system (N), antiparasitic products (P), respiratory system (R), sensory organs (S), and various (V). In this study, the reported medicines were classified into anatomical main groups using the first

level of the Anatomical Therapeutic Chemical (ATC) classification system.

Ethical considerations

The study was based on anonymized pharmacovigilance records collected during routine practice with no requirement for direct patient contact. Ethical approval was obtained from the scientific committee of the Anbar General Health Directorate, with written permission (No. 20250140), to access its pharmacovigilance database.

Statistical analysis

The data were analyzed using IBM SPSS software version 31 (IBM Corp., NY, USA). The variables were categorized and presented as frequencies and percentages. Multivariable logistic regression analysis was performed to explore factors independently associated with the seriousness of adverse drug reactions, and adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were calculated. Variables were selected for inclusion in the multivariable logistic regression model based on their clinical and pharmacovigilance relevance to ADR seriousness and their availability within the VigiFlow dataset, comprising patient-, reporter-, drug-, and report-level characteristics. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 3269 reports were initially identified and exported from Anbar pharmacovigilance data during the study period (2020–2025). After removing five duplicate reports, 3264 ICSRs were included in the final study. Of these, 3164 reports (96.9%) had a recorded seriousness status: 978 (30.0% of all reports; 30.9% of reports with known status) were classified as serious, and 2186 (67.0% of all reports; 69.1% of known-status reports) were non-serious. The remaining 100 reports (3.1%) had no recorded seriousness status and were excluded from seriousness-stratified analyses, as shown in the study flow diagram (Figure 1).

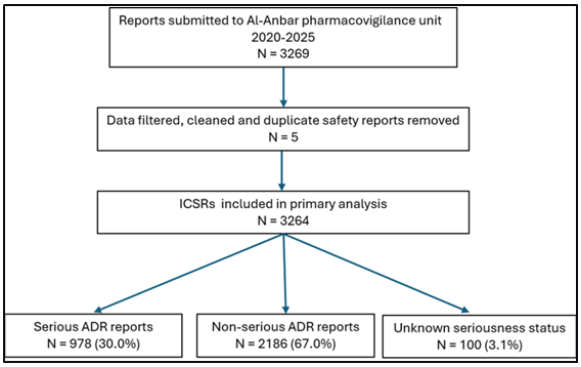


Figure 1: Study flow diagram for included individual case safety reports.

To evaluate the annual trend in submitted ICSRs with documented seriousness, the proportion of serious ADR reports across the six years was calculated, and the annual distribution is shown in Figure 2. The highest proportion of serious ADR reports was observed in 2020 (54.1%), whereas a fluctuating range of 20.7–38.9% was observed in subsequent years (Figure 2).

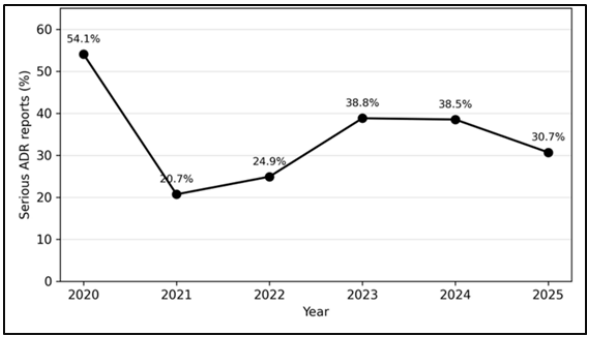


Figure 2: Annual proportion of serious ADR reports, 2020–2025.

The demographic and reporting characteristics of the ICSRs submitted to the pharmacovigilance section are summarized in Table 1.

Table 1: Demographic and reporting characteristics of ICSRs, classified by seriousness

Characteristic	All reports	Serious reports (n=978)	Non-serious reports (n=2186)
Age group (n=3097)		Available data* (n=945)	Available data* (n=2055)
Adult	2277(73.5)	631(66.8)	1591(77.4)
Child	222(7.2)	78(8.3)	135(6.6)
Elderly	224(7.2)	88(9.3)	130(6.3)
Infant	200(6.5)	96(10.2)	85(4.1)
Adolescent	134 (4.3)	39(4.1)	90(4.4)
Neonate	40(1.3)	13(1.4)	24(1.2)
Sex (n = 3239)		Available data* (n=975)	Available data* (n=2167)
Female	1795(55.4)	509(52.2)	1222(56.4)
Male	1444(44.6)	466(47.8)	945(43.6)
Reporter qualification (n = 3230)		Available data* (n=973)	Available data* (n=2166)
Pharmacist	2805(86.8)	854(87.8)	187 (86.7)
Physician	213(6.6)	77(7.9)	135(6.2)
Other health professional	140(4.3)	40(4.1)	83(3.8)
Consumer or other non-health professional	72(2.2)	2(0.2)	70(3.2)

Values are presented as frequency and percentage. * Percentages were calculated based on available data for each variable; reports with missing or unknown information were retained in the study database; the multivariable regression (Table 4) was restricted to complete cases. ICSR, individual case safety report.

Age group, sex, and reporter qualification were counted and compared between serious and non-serious reports. The majority of reported cases were in the adult age group (73.5%), and female patients accounted for a higher proportion of cases than males (55.4% *vs*. 44.6%). Most ICSRs were reported by pharmacists (86.8%), while a small number were submitted by physicians and other healthcare providers (6.6% and 4.3%, respectively). Serious ADR reports appeared to be more frequent among infant, elderly, and physician-reported cases than among their respective comparison groups (Table 1). Figure 3 illustrates the distribution of seriousness criteria among ICSRs classified as serious. Among serious reports, the most frequently recorded ICH E2A criterion was life-threatening (482; 49.3%). Other medically important conditions, as well as hospitalization or prolonged hospitalization, were also common, occurring in 27.9% and 23.2% of cases, respectively.

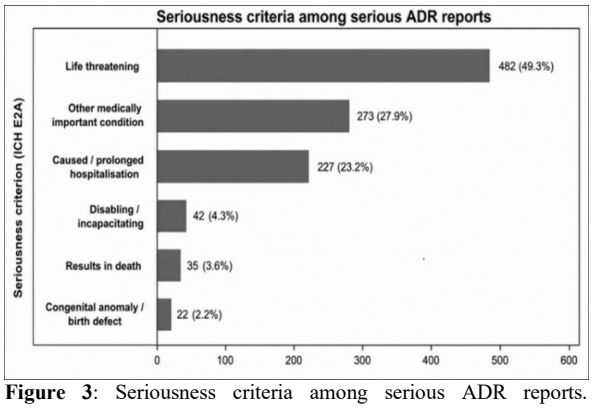


Figure 3: Seriousness criteria among serious ADR reports. Categories are not mutually exclusive, as a single ICSR could meet more than one ICH E2A seriousness criterion; percentages are therefore calculated as a proportion of serious reports (n = 978) and may sum to more than 100%.

Disability or incapacity was recorded in 42 case reports (4.3%), death in 35 reports (3.6%), and congenital anomaly or birth defect in 22 (2.2%). An ICSR could meet more than one seriousness criterion simultaneously. Among the 978 serious ICSRs, the most frequently recorded clinical outcome was "recovered/resolved" (641 cases; 65.5%), followed by "recovering/resolving" (129 cases; 13.2%), "unknown outcome" (77 cases; 7.9%), "not recovered/ongoing" (62 cases; 6.3%), "recovered with sequelae" (38 cases; 3.9%), and "fatal outcome" (31 cases; 3.2%) (Table 2).

Table 2: Clinical outcomes among serious ADR reports with known outcomes

Outcome among serious reports	n(%)
Recovered/Resolved	641(65.5)
Recovering/Resolving	129(13.2)
Unknown	77(7.9)
Not Recovered/Not Resolved/Ongoing	62(6.3)
Recovered/Resolved with Sequelae	38(3.9)
Fatal	31(3.2)

ADR: adverse drug reaction(s).

The death-related ICH E2A seriousness criterion was recorded in 35 ICSRs (3.6%), compared with 31 ICSRs (3.2%) documenting a fatal clinical outcome. Although these variables are recorded separately in VigiFlow, they overlapped in 28 reports. Of the remaining cases, seven met the death-related seriousness criterion but had a different recorded clinical outcome, whereas three had a fatal outcome without a corresponding death-related seriousness criterion. These results highlight the difference between seriousness criteria and reported clinical outcomes. Nearly two-thirds of serious cases were reported as recovered or resolved, suggesting that the ICH E2A seriousness criteria reflect the medical importance of an event at the time it occurs, rather than its long-term outcome. To characterize the clinical patterns underlying submitted serious ICSRs, and after excluding reaction rows without usable classification, reaction terms were assessed by MedDRA System Organ Class (SOC). The ten leading SOCs among serious reports are shown in Figure 4.

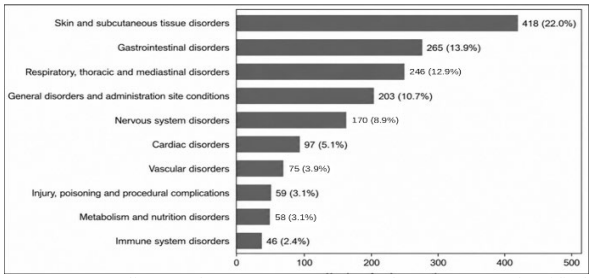


Figure 4: Leading MedDRA System Organ Classes among classified serious reaction rows (n = 1901).

Skin and subcutaneous tissue disorders were the most commonly reported SOC (418, 22.0%), followed by gastrointestinal disorders (265, 13.9%) and respiratory, thoracic, and mediastinal disorders (246, 12.8%). General disorders and administration-site conditions (203 reactions, 10.7%) and nervous system disorders (170 reactions, 9.0%) were also prominent. The remaining SOCs, including cardiac and vascular disorders, accounted for a smaller proportion of serious adverse reactions. After identifying the clinical patterns of serious ADRs, the therapeutic classes of the suspected medicines were evaluated using the Anatomical Therapeutic Chemical (ATC) classification system. The number of serious reports accounted for by each ATC group is shown in Figure 5.

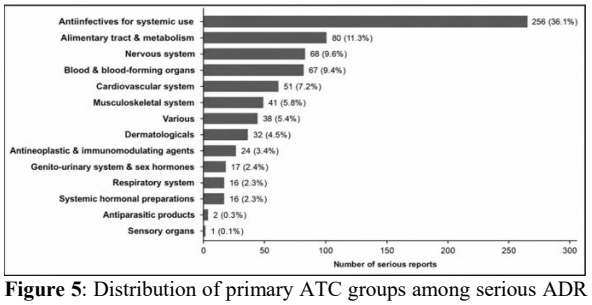


Figure 5: Distribution of primary ATC groups among serious ADR reports. Percentages are calculated among serious reports with classified ATC information (n= 709).

Anti-infectives for systemic use were the most frequent primary ATC group among the 709 serious reports with classifiable ATC information (256, 36.1%), substantially exceeding the other therapeutic classes. Alimentary tract and metabolism agents (80, 11.3%), nervous system medicines (68, 9.6%), blood and blood-forming organ products (67, 9.4%), and

cardiovascular medicines (51, 7.2%) were the next most frequently reported ATC groups (Figure 5). The therapeutic classes with the lowest proportion of serious reports were antiparasitic products and sensory-organ agents (0.3% and 0.1%, respectively). Among the standardized suspected medicines, ceftriaxone was the leading individual medicine implicated in serious reports, followed by a locally used herbal/mineral preparation. The leading suspected medicines implicated in serious ADRs are shown in Table 3.

A multivariable logistic regression analysis was performed to identify the independent predictors of ADR seriousness. Patient characteristics, reporter type, primary ATC group, and case-complexity indicators (number of suspected medicines and reaction terms) were incorporated into the analysis. The adjusted odds ratios, 95% confidence intervals, and p-values for all variables entered in the model (2241 reports with complete data, 695 of them serious), whether or not statistically significant ($p < 0.05$), are presented in Table 4 and shown graphically in Figure 6. Seriousness was independently associated with case complexity: each additional suspected medicine was associated with higher odds of a serious outcome (aOR 1.70, 95% CI 1.30–2.30), as did, to a lesser extent, a higher number of reaction terms (aOR 1.25, 95% CI 1.04–1.52). Physician-reported cases were more likely to be serious than those from other reporters (aOR 1.79, 95% CI 1.20–2.67). Infants (aOR 3.80, 95% CI 2.47–5.87) and children (aOR 1.93, 95% CI 1.37–2.72) demonstrated significantly higher odds than the reference. Age group, suggesting pediatric vulnerability. Among drug classes, antineoplastic/immunomodulating agents and blood/blood-forming organ products displayed the strongest associations (aOR 4.01, 95% CI 2.07–7.76 and aOR 3.93, 95% CI 2.68–5.78, respectively), followed by various/unclassified products (aOR 2.36, 95% CI 1.25–4.47) and nervous system (aOR 2.28, 95% CI 1.60–3.24), cardiovascular (aOR 1.75, 95% CI 1.15–2.55), alimentary tract/metabolism (aOR 1.75, 95% CI 1.20–2.40), and musculoskeletal (aOR 1.55, 95% CI 1.00–2.35) agents, all significantly associated with seriousness relative to the reference class.

Table 3: Fifteen most frequently reported suspected medicines/products underlying the 978 serious ICSRs

Standardized suspected INN	Serious reports (n)	% serious reports (n=978)
Ceftriaxone	129	13.2
Herbal/mineral product	35	3.6
Vancomycin	27	2.8
Levofloxacin	20	2.0
Amoxicillin	18	1.8
Amoxicillin + clavulanic acid	18	1.8
Iron sucrose	17	1.7
Paracetamol	13	1.3
Amikacin	13	1.3
Azithromycin	13	1.3
Diclofenac	12	1.2
Enoxaparin	11	1.1
Ciprofloxacin	11	1.1
Tozinameran	10	1.0
Heparin	10	1.0

*At the case level, a case may imply more than one medicine. INN, International Nonproprietary Name; ICSR, individual case safety report.

Table 4: Multivariable logistic regression for factors associated with serious ADR reporting (all variables included)

Predictor	Adjusted OR	95% CI	*p*-value
Case complexity			
Number of suspected medicines (per additional medicine)	1.70	1.30–2.30	<0.001
Number of reaction terms (per additional term)	1.25	1.04–1.52	0.019
Reporter qualification (reference: pharmacist)			
Physician	1.79	1.20–2.67	0.005
Other reporters	1.27	0.81–1.98	0.299
Age group (reference: adult)			
Neonate	3.04	1.08–8.53	0.035
Infant	3.80	2.47–5.87	<0.001
Child	1.93	1.37–2.72	<0.001
Adolescent	1.85	1.18–2.91	0.008
Elderly	1.52	1.09–2.14	0.015
Sex (reference: female)			
Male	1.19	0.99–1.45	0.069
Primary suspected-drug class, ATC level 1 (reference: J, anti-infectives for systemic use)			
Alimentary tract and metabolism (A)	1.75	1.20–2.40	0.003
Blood and blood-forming organs (B)	3.93	2.68–5.78	<0.001
Cardiovascular system (C)	1.75	1.15–2.55	0.008
Dermatological (D)	1.42	0.90–2.24	0.128
Genito-urinary system and sex hormones (G)	1.66	0.92–3.02	0.095
Systemic hormonal preparations (H)	1.62	0.83–3.18	0.159
Antineoplastic and immunomodulating agents (L)	4.01	2.07–7.76	<0.001
Musculoskeletal system (M)	1.55	1.00–2.35	0.048
Nervous system (N)	2.28	1.60–3.24	<0.001
Antiparasitic products (P)	1.56	0.27–8.93	0.617
Respiratory system (R)	1.16	0.60–2.22	0.659
Sensory organs (S)	0.58	0.06–5.26	0.629
Various (V)	2.36	1.25–4.47	0.009

OR: odds ratio; CI: confidence interval; ATC: Anatomical Therapeutic Chemical classification. All variables were entered simultaneously (complete-case analysis: n= 2241 reports, 695 serious). Reference categories: age group, adult; reporter, pharmacist; sex, female; drug class, anti-infectives for systemic use (ATC group J). The numbers of suspected medicines and reaction terms were modelled as continuous variables (per additional medicine or term). *Other reporters comprise other health professionals and consumers or other non-health professionals, combined because consumers (2 serious of 72 reports) could not be estimated separately.

These findings indicate that ICSR classification as serious is jointly associated with case complexity, reporter type, and primary suspected-drug class, warranting particular pharmacovigilance attention to pediatric patients and oncology/hematology-related agents.

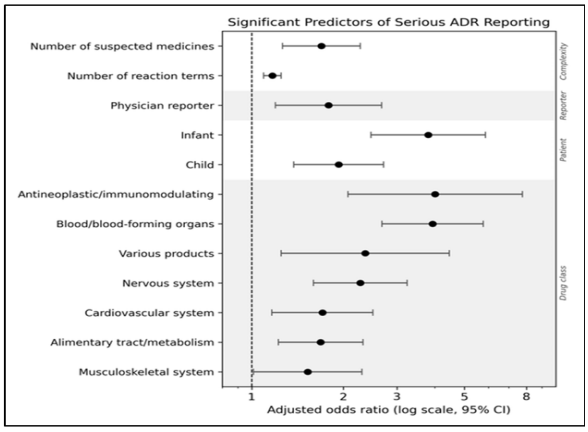


Figure 6: Multivariable logistic regression for independent predictors of serious ADRs. Points represent adjusted odds ratios (aORs), and horizontal lines indicate 95% confidence intervals (CIs), plotted on a logarithmic scale. The dashed vertical line denotes the null value (aOR = 1.0). Predictors are grouped by domain (case complexity, reporter type, patient characteristics, and primary suspect drug class), as indicated by the alternating shaded bands and right-hand axis labels. Categorical predictors are presented relative to their reference categories (age group: adult; reporter: pharmacist; drug class: anti-infectives for systemic use). Only statistically significant predictors ($p< 0.05$) are displayed. Exact adjusted odds ratios, 95% confidence intervals, and p-values for all predictors are reported in Table 4.

DISCUSSION

Serious adverse drug reactions are of particular concern in pharmacovigilance because they represent events with significant clinical implications, underscoring the attention required for signal assessment and safety monitoring. The current regional pharmacovigilance study found that serious ADRs accounted for 30.0% of all ICSRs submitted to the pharmacovigilance section of the Anbar General Health Directorate between 2020 and 2025. This considerable proportion, representing nearly one-third of all recorded reports in VigiFlow—the reporting system used by all healthcare settings in Iraq, including the Anbar pharmacovigilance section—emphasizes the important role of the regional reporting system in capturing the meaningful burden of clinically important medicine-safety events. The findings also provide evidence for local risk-prioritization efforts. The proportion of seriousness in the current study was lower than that reported in other countries. For instance, approximately half of spontaneously reported ADRs in a German pharmacovigilance study were identified as serious when compared with cases recorded in a parallel emergency department study [10]. Furthermore, a long-running hospital-based pharmacovigilance program in Spain demonstrated that more than 50% of reported ADRs were classified as serious [7]. The variation in the proportion of serious reports may arise from several factors, including healthcare settings, reporting practices, and interpretation of seriousness criteria. Additionally, the comparatively lower proportion of serious ADRs in Anbar healthcare settings may reflect the high contribution of pharmacists (86.8% of all submitted ICSRs) and the potential tendency of hospital pharmacists to preferentially report common, lower-severity reactions encountered during routine dispensing, as previous studies have suggested that the characteristics and seriousness of ADR reports may vary by reporter type [11,12]. Among reported serious reactions, life-threatening events accounted for nearly half of the cases, followed by other medically important conditions and hospitalization/prolonged hospitalization. This pattern demonstrates that reporting of serious cases in Anbar healthcare settings was not limited to fatal outcomes but also extended to events with immediate or potentially significant clinical consequences. The prominence of the "other medically important condition" criterion is notable because it relies more on clinical judgement than on specific events such as death or hospitalization. These findings emphasize the importance of distinguishing between seriousness and clinical severity and support the systematic follow-up of reports of life-threatening or other medically important events. The highest independent odds of serious classification among the age groups were attributable to the infant age group (aOR 3.80, 95% CI 2.47–5.87), followed by the neonatal age group (aOR 3.04, 95% CI 1.08–8.53; a wide interval reflecting few neonatal reports). This pattern is consistent with pediatric pharmacovigilance literature, which attributes the heightened vulnerability of infants and young children to the physiological immaturity of hepatic and renal drug-elimination pathways, incompletely developed blood–brain barrier function, and the widespread off-label or extrapolated dosing that characterizes pediatric prescribing [13]. Similar findings have been reported in other pediatric pharmacovigilance programs, where the youngest age subgroups accounted for a disproportionate share of serious reports [13,14]. Elderly patients also showed a numerically higher proportion of serious reports in the descriptive comparison (Table 1), and this age group was also independently associated with seriousness in the adjusted model (aOR 1.52, 95% CI 1.09–2.14). These results reinforce the value of age-stratified signal monitoring, with particular attention to neonates, infants, children, and the elderly at the Anbar Pharmacovigilance Section. The most frequently implicated primary ATC group among serious reports was anti-infectives for systemic use, with ceftriaxone alone accounting for the leading single suspected medicine among all serious reports (13.2%). These findings are consistent with reports from other national pharmacovigilance centers; for instance, a pharmacovigilance data analysis in Saudi Arabia showed that antimicrobial agents were important contributors to serious ADRs [15]. A previous study from an Iranian center reviewing a decade of ceftriaxone-related reports found that 5.8% of all reports with drug events recorded during this period were related to ceftriaxone, of which 30% were classified as serious, including cardiac arrest and anaphylactic reactions [16]. Similar patterns have been reported in Ugandan [17] and Syrian [18] pharmacovigilance data, including fatal anaphylactic reactions, and ceftriaxone has also featured prominently in recent global analyses of drug-associated anaphylaxis [19]. Ceftriaxone was the subject of a CDC/FDA multistate investigation into

serious adverse events, including cardiac arrest and death occurring within hours of administration, with 26 cases and 12 deaths identified across 22 United States healthcare facilities, as reported in a full 2026 publication [20]. The predominant reporting of ceftriaxone does not necessarily indicate a higher incidence or intrinsic risk than other antibiotics: reporting frequency is influenced by prescribing volume, route of administration, and the clinical recognizability of acute reactions such as anaphylaxis, which are more likely to prompt spontaneous reporting. Its higher reporting frequency among ICSRs submitted to the Anbar pharmacovigilance section therefore likely reflects a combination of high local exposure and a clinically important safety profile rather than drug-specific risk alone, particularly as the current analysis evaluates reported cases rather than exposure-adjusted incidence. Although anti-infectives were the predominant ATC class, blood/blood-forming products (aOR 3.93, 95% CI 2.68–5.78) and antineoplastic/immunomodulating agents (aOR 4.01, 95% CI 2.07–7.76) showed the strongest independent associations with seriousness among the evaluated drug classes. This finding is supported by recent international disproportionality studies, in which large Food and Drug Administration Adverse Event Reporting System (FAERS) analyses have documented significant safety signals for antineoplastic agents across multiple serious outcomes, including cardiac failure, hepatotoxicity, and neutropenia/agranulocytosis, reflecting the narrow therapeutic index and predictable dose-limiting toxicity of these agents [21–23]. Within the blood/blood-forming class, iron sucrose—a parenteral iron product—accounted for 17 serious reports in the present study. Despite the generally favorable safety profile of iron sucrose, intravenous iron administration remains a recognized cause of hypersensitivity and infusion-related reactions, including rare but fatal anaphylaxis. Recent international guidelines have highlighted the need for close clinical monitoring during intravenous iron administration [24]. Similarly, an FDA database analysis comparing subcutaneous anticoagulants, including enoxaparin (11 serious reports in the current study), found consistent bleeding- and thrombocytopenia-related safety signals across this ATC class, particularly among elderly patients [25]. Together with parenteral iron, these findings identify clinically important safety concerns within the blood/blood-forming organ class, consistent with the high-risk profile of this therapeutic group identified in an analysis of the Saudi Arabian pharmacovigilance database [26]. Nervous-system medicines (aOR 2.28, 95% CI 1.60–3.24) were also independently associated with seriousness in the present analysis; this finding is supported by a study of antiseizure medications recorded in the EudraVigilance database, which similarly found that a substantial proportion of reported reactions to older and newer central nervous system agents were serious, with the specific proportion varying by agent and system organ class [27]. The heterogeneous "Various" ATC group (aOR 2.36, 95% CI 1.25–4.47), which included herbal and mineral preparations, was also independently associated with seriousness. The present finding aligns with recent evidence that herbal and traditional medicines remain markedly under-monitored relative to their global use, particularly in low- and middle-income settings, despite an estimated 88% of the world's population relying on traditional and complementary medicine for primary healthcare [28]. Within this category, the single largest contributor was a herbal/mineral preparation locally known as Sagwa, a traditional remedy widely used across Iraq, particularly in rural households, to treat infant diarrhea and acute gastroenteritis [29]. Sagwa is a variably compounded, non-standardized mixture that may contain heavy metals and animal-derived material, and Iraqi case-control and surveillance studies have linked its use to substantial morbidity and mortality among infants with acute diarrhea, including life-threatening and fatal outcomes [29,30]. Because Sagwa is largely unrecognized outside Iraq, it does not appear as a signal in international pharmacovigilance databases, despite representing a locally significant and preventable cause of serious pediatric morbidity [31]. The association of serious reports with herbal medicine, particularly Sagwa, highlights the need for continued pharmacovigilance of this and other locally used traditional herbal remedies. Taken together, these findings support the development of a risk-based approach to pharmacovigilance in the Anbar General Health Directorate, with closer attention to reports involving infant/young child and elderly patient groups, physician-reported cases, and medicines associated with potentially serious ADRs. Furthermore, the widespread use of antimicrobials among patients with serious ICSRs indicates a need for targeted safety monitoring and antimicrobial stewardship, potentially through the integration of pharmacovigilance services in Anbar healthcare settings.

Strengths and Limitations

This study benefits from a substantial volume of six years of pharmacovigilance data, standardized classification of seriousness and outcomes, and multivariable analysis to identify independent predictors of serious ADR reporting. Several limitations should nonetheless be acknowledged. First, as with all spontaneous reporting data, this analysis describes reporting patterns rather than true incidence because denominators for drug exposure—such as drug utilization or dispensing data—were not available. Second, missing information, particularly for primary ATC classification and certain demographic variables, may have introduced misclassification or selection bias; a substantial minority of serious reports lacked a classifiable primary ATC group (269/978, 27.5%) or complete demographic information, which may bias estimates if missingness was not random with respect to seriousness. Third, the pronounced predominance of pharmacist reporting (86.8% of all ICSRs), with very few consumer or physician reports, limits the generalizability of these findings to reporter

populations with different clinical vantage points and mirrors a broader pattern of underreporting and limited pharmacovigilance awareness previously documented among healthcare professionals in Iraq [32,33]; the very low number of consumer and physician reports may itself reflect systemic underreporting rather than a true lower burden of seriousness in these groups. Fourth, no formal causality assessment (e.g., WHO-UMC or Naranjo algorithm) was applied at the case level; hence, this analysis characterizes regulatory seriousness rather than the strength of the drug-event causal relationship. Finally, because the study was conducted in a single Iraqi governorate, the findings may not generalize to other governorates, which may have different prescribing patterns or reporting cultures. Additionally, reporting year was not included as a covariate in the multivariable model; given the marked annual fluctuation in the proportion of serious reports (Figure 2), residual temporal confounding cannot be excluded.

Conclusion

Serious ADRs accounted for nearly one-third of ICSRs submitted to the Anbar pharmacovigilance section between 2020 and 2025, with life-threatening events representing the most frequent seriousness criterion. Antimicrobials, particularly ceftriaxone, accounted for the largest proportion of serious reports, while antineoplastic, blood/blood-forming, and nervous-system medicines were independently associated with higher odds of seriousness. Age group (neonatal, infant, child, adolescent, and elderly) and physician-submitted reports were also identified as independent predictors of seriousness in multivariable analysis. These findings provide regional evidence to inform pharmacovigilance priorities in western Iraq, supporting the need for targeted monitoring of high-risk medicines, greater attention to vulnerable age groups, and broader engagement of healthcare professionals in ADR reporting.

Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

The data that supports the findings of this study are available from the corresponding author upon a reasonable request.

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