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Real-World Safety Signals of Drug-Induced Proteinuria: A Two-Decade Pharmacovigilance Study Using Multi-Indicator Detection and Multivariate Correction

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Abstract: Proteinuria is a critical biomarker for kidney damage and a key indicator in drug safety assessment. However, existing pharmacovigilance studies are often limited by single adverse event term detection and confounding factors inherent in spontaneous reporting systems, making it difficult to accurately identify the true risk of drug-induced proteinuria. We retrospectively analyzed data from the U.S. FDA Adverse Event Reporting System (FAERS) from the first quarter of 2004 through the fourth quarter of 2024. A multi-indicator detection framework was constructed using 17 MedDRA Preferred Terms related to proteinuria, encompassing 5,688 unique case reports. Signal-positive drugs were screened using four disproportionality analysis methods (ROR, PRR, EBGM, IC) with Bonferroni correction. Multivariable logistic regression models were applied to adjust for confounding factors including demographics, comorbidities, and concomitant medications. A total of 16 signal-positive drugs were identified. Antineoplastic agents accounted for the largest proportion (n = 8), with bevacizumab having the highest number of reported cases (n = 451) and tenofovir disoproxil showing the strongest disproportionality signal (ROR = 24.28). Immunomodulators (e.g., pembrolizumab, tacrolimus) and antiviral agents also demonstrated significant associations. The study population had a mean age of 53.7 years with a balanced sex distribution (50.7% male vs. 48.7% female). Antineoplastic and immunomodulatory agents are the primary risk sources for drug-induced proteinuria. The methodological framework proposed in this study, combining multi-indicator signal detection with multivariate correction, effectively enhances the reliability and accuracy of pharmacoepidemiological signals. Clinical monitoring of urinary protein is recommended for patients using high-risk medications to facilitate early identification of renal injury.

Keywords: Proteinuria; Pharmacovigilance; FAERS database; Signal detection; Nephrotoxicity; Multivariate analysis

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1. Introduction

Proteinuria is a pivotal biomarker for kidney damage, often detectable before tangible declines in glomerular filtration rate (GFR)[1]most commonly focal segmental glomerulosclerosis, minimal changes, membranous nephropathy, diffuse mesangial sclerosis and collapsing glomerulopathy. However, proteinuria of glomerular origin is frequently managed without biopsy; importantly, when the protein loss is mostly albumin, it is a direct readout of podocyte injury and a

strong predictor of cardiovascular events, kidney failure and reduced survival. Patients present with oedema and volume disturbances and are at risk of thromboembolism, serious infections and progressive kidney dysfunction. Aetiologically, podocytopathies arise from autoimmune, genetic, mechanical (hyperfiltration. It serves as an independent predictor of morbidity and cardiovascular risk, acting not merely as a consequence of pathology but as an active contributor to renal progression through inflammation and fibrosis[2]key domains of chronic kidney disease, have both been shown to be strong and independent risk factors for cardiovascular disease. Patients with kidney failure requiring dialysis are at highest risk for cardiovascular events (e.g., stroke or myocardial infarction. Consequently, identifying drug-induced proteinuria is a strategic imperative for pharmacovigilance. However, distinguishing true causal relationships from coincidental findings in post-marketing surveillance remains challenging due to the non-specific nature of proteinuria and the complexities inherent in spontaneous reporting data, such as reporting biases and confounding by indication.

To address these challenges with enhanced rigor and timeliness, we conducted a comprehensive pharmacovigilance study utilizing the FDA Adverse Event Reporting System (FAERS). Our analysis spans a twenty-year period from 2004 to 2024, encompassing 5,688 unique case reports of drug-associated proteinuria. This extensive temporal scope captures the dynamic evolution of the pharmaceutical market, including the rise of targeted therapies and biologics whose safety profiles were not fully established upon entry. The dataset size provides sufficient statistical power to identify meaningful associations across a broad array of medications, establishing a foundation for evaluating real-world renal risks.

Recognizing the heterogeneity of renal injury, we implemented a multi-indicator signal detection approach integrating 17 MedDRA Preferred Terms related to proteinuria. This allows for a more nuanced characterization of renal toxicity than binary classifications. Furthermore, to enhance validity, we employed rigorous multivariate logistic regression models. By systematically adjusting for potential confounders—including demographics, comorbidities, and concomitant medications—we aimed to isolate signals attributable to drug exposure rather than underlying patient characteristics, thereby strengthening causal inference.

By synthesizing a contemporary, large-scale dataset with advanced analytical approaches, this research provides a more accurate picture of the risk of drug-induced proteinuria. The integration of multi-indicator detection with comprehensive confounder adjustment strengthens the inferential power of the findings beyond conventional signal detection. Ultimately, this work aims to translate advanced analytical findings into tangible benefits for public health, informing regulatory benefit-risk assessments and guiding clinicians toward more targeted monitoring strategies for patients at risk of renal injury.

2. Methods

2.1. Data source and case identification

We retrospectively extracted all case reports of drug-associated proteinuria submitted to the U.S. Food and Drug Administration Adverse Event Reporting System (FAERS) from the first quarter of 2004 through the fourth quarter of 2024 (https://fis.fda.gov/extensions/FPD-QDE-FAERS/FPD-QDE-FAERS.html).

Proteinuria-related adverse events were identified based on 17 Preferred Terms (PTs) within the Medical Dictionary for Regulatory Activities (MedDRA) hierarchy: “PROTEINURIA,” “PROTEIN URINE PRESENT,” “MYOGLOBINURIA,” “URINE PROTEIN/CREATININE RATIO INCREASED,” “PROTEIN URINE,” “ALBUMINURIA,” “MICROALBUMINURIA,” “ALBUMIN URINE PRESENT,” “BENCE JONES PROTEIN URINE PRESENT,” “ALBUMIN GLOBULIN RATIO INCREASED,” “BENCE JONES PROTEINURIA,” “BETA-2 MICROGLOBULIN URINE INCREASED,” “GLOBULINURIA,” “ORTHOSTATIC PROTEINURIA,” “URINE ALBUMIN/CREATININE RATIO INCREASED,” “URINE PROTEIN/CREATININE RATIO ABNORMAL,” and “URINE PROTEIN, QUANTITATIVE.”

2.2. Data cleaning and deduplication

To ensure case uniqueness, a three-stage deduplication protocol was applied: (1) for duplicate case identifiers (case_id), only the record with the most recent FDA receipt date (fda_dt) was retained; (2) if both case_id and fda_dt were identical, the record with the larger primary identifier (primary_id) was selected; (3) a manual secondary review was conducted to identify and remove any residual duplicates. Reports with implausible patient characteristics—defined as age > 100 years or body weight > 200 kg—were excluded as potential data entry errors. After deduplication and quality filtering, a total of 5,688 valid reports were included in the analysis.

2.3. Data structure and variables

Each case report comprised seven standardized FAERS modules: (1) DEMO (demographics and administrative data), (2) REAC (MedDRA-coded adverse reactions), (3) DRUG (suspect and concomitant medications/biologics), (4) OUTC (patient outcomes), (5) RPSR (report source), (6) THER (drug start and end dates), and (7) INDI (MedDRA-coded indications/diagnoses for the reported drug). These modules provided comprehensive information on patient characteristics, drug exposures, clinical outcomes, and reporting context.

2.4. Statistical analysis

Signal detection was restricted to drugs with ≥ 50 reported cases to ensure statistical stability. Four established disproportionality measures were computed using standard 2 × 2 contingency tables **(Table 1-2)**: Reporting Odds Ratio (ROR), Proportional Reporting Ratio (PRR), Multi-item Gamma Poisson Shrinker (MGPS/EBGM), and Bayesian Confidence Propagation Neural Network (BCPNN/IC). Statistical significance was assessed using χ^2 tests with Bonferroni correction for multiple comparisons. Drugs meeting predefined signal criteria across these metrics were considered candidate nephrotoxic agents.

Table 1. Structure of the 2 × 2 contingency table used for disproportionality analysis.

	Target adverse events	All other adverse events
Target drug	a	b
All other drugs	c	d

The table defines the four core components (a, b, c, d) that form the basis for all disproportionality calculations. A safety signal is detected when the association between the target drug and the target adverse event (cell a) is disproportionately strong compared to the background reporting of all other drugs and events.

Table 2. Formulas and thresholds of ROR, PRR, BCPNN, and MGPS methods.

Method	Formula	Threshold
ROR	$ROR=\frac{a/c}{b/d}$ $SE(lnROR)=\sqrt{\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d}}$ $95\%CI=e^{\ln(ROR)\pm 1.96se}$	a ≥ 3 ROR ≥ 3 95%CI (lower limit) > 1

Table 2 (Continued)

Method	Formula	Threshold
PRR	$PRR=\frac{a/(a+b)}{c/(c+d)}$	a ≥ 3 PRR ≥ 2 95%CI (lower limit) > 1
	$SE(lnPRR)=\sqrt{\frac{1}{a}-\frac{1}{a+b}+\frac{1}{c}-\frac{1}{c+d}}$	
	$95\%CI=e^{\ln(PRR)\pm1.96se}$	
BCPNN	$IC=\log_2\frac{p(x,y)}{p(x)p(y)}=log_2\frac{a(a+b+c+d)}{(a+b)(a+c)}$	IC025 > 0
	$E(IC)=\log_2\frac{(a+\gamma 11)(a+b+c+d+\alpha)(a+b+c+d+\beta)}{(a+b+c+d+\gamma)(a+b+\alpha 1)(a+c+\beta 1)}$	
	$V(IC)=\frac{1}{(ln2)^2}[\frac{(a+b+c+d)-a+\gamma-\gamma 11}{(a+\gamma 11)(1+a+b+c+d+\gamma)}+\frac{(a+b+c+d)-(a+b)+a-\alpha 1}{(a+b+\alpha 1)(1+a+b+c+d+\alpha)}+\frac{(a+b+c+d+\alpha)-(a+c)+\beta-\beta 1}{(a+b+\beta 1)(1+a+b+c+d+\beta)}]$	
	$\gamma=\gamma 11\frac{(a+b+c+d+\alpha)(a+b+c+d+\beta)}{(a+b+\alpha 1)(a+c+\beta 1)}$	
	$IC-2SD=E(IC)-2\sqrt{V(IC)}$	
MGPS	$EBGM=\frac{a(a+b+c+d)}{(a+c)(a+b)}$	EBGM05 > 2
	$SE(lnEBGM)=\sqrt{\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d}}$	
	$95\%CI=e^{\ln(EBGM)\pm1.96se}$	

Note: ROR, reporting odds ratio; CI, confidence interval; PRR, proportional reporting ratios; BCPNN, Bayesian confidence propagation neural network; IC, information component; SD, standard deviation; MGPS, multi-item gamma poisson shrinker; EBGM, empirical Bayesian geometric mean.

To identify independent risk factors for drug-associated proteinuria, candidate drugs and relevant patient covariates—including demographics (age, sex, weight), comorbidities, concomitant medications, and reporting characteristics—were entered into a multivariable logistic regression model. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to quantify adjusted associations. Finally, descriptive statistics were used to summarize the clinical and demographic profiles of patients with reported drug-associated proteinuria. All analyses were performed using R software.

3. Results

3.1. Study population and reporting trends

A total of 5,688 unique case reports of drug-associated proteinuria were included in the analysis **(Table 3)**. Temporal assessment of reporting frequency from Q1 2004 to Q4 2024 revealed a general upward trend over time, accompanied by interannual fluctuations **(Figure 1A)**.

Table 3. Baseline characteristics of patients with reported Proteinuria in the FAERS database (2004–2024).

Characteristics		Proteinuria (N=5,688)
Gender		
F		2768 (48.7%)
M		2884 (50.7%)
Unknown		36 (0.6%)
Age		
Mean (SD)		53.7 (20.4)
Median [Min, Max]		58.0 [0, 100]
Weight		
Mean (SD)		71.9 (25.1)
Median [Min, Max]		69.8 [0.860, 200]
Country/Region of the reporter		
UNITED STATES	1,770	36.14%
JAPAN	979	19.99%
FRANCE	341	6.96%
GERMANY	318	6.49%
CHINA	287	5.86%
UNITED KINGDOM	277	5.66%
ITALY	143	2.92%
BRAZIL	106	2.16%
BELGIUM	86	1.76%
SPAIN	52	1.06%
SWITZERLAND	42	0.86%
SOUTH KOREA	41	0.84%
COLOMBIA	36	0.74%
NETHERLANDS	28	0.57%
AUSTRALIA	27	0.55%

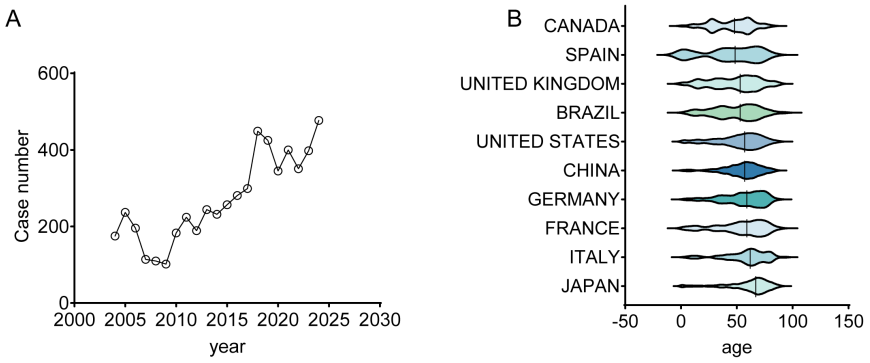

Figure 1. Characteristics of drug-related Proteinuria reports in FAERS.
Note: (A) Annual reporting trends (2004 Q1–2024 Q4); (B) Age distribution of patients in the top 10 reporting countries.

3.2. Patient demographics

The study population exhibited a balanced sex distribution: 2,768 (48.7%) female, 2,884 (50.7%) male, and 36 (0.6%) with unknown sex **(Table 3)**. The mean patient age was 53.7 ± 20.4 years. Body weight data were available for a subset of cases, with a mean of 71.9 ± 25.1 kg and a median of 69.8 kg **(Table 3)**.

3.3. Geographic distribution

Reports originated predominantly from the United States (1,770 cases, 36.14%), Japan (979 cases, 19.99%), France (341 cases, 6.96%), Germany (318 cases, 6.49%), and China (287 cases, 5.86%). Additional contributions came from the United Kingdom, Italy, Brazil, Belgium, and Spain **(Table 3)**. Among the top ten reporting countries, the mean age at onset of proteinuria increased in the following order: Canada, Spain, United Kingdom, Brazil, United States, China, Germany, France, Italy, and Japan **(Figure 1B)**.

3.4. Disproportionality analysis and signal detection

Signal detection was restricted to drugs with ≥ 50 reported cases to ensure statistical robustness. Using four complementary disproportionality measures—Reporting Odds Ratio (ROR), Proportional Reporting Ratio (PRR), Multi-item Gamma Poisson Shrinker (MGPS/EBGM), and Bayesian Confidence Propagation Neural Network (BCPNN/IC)—along with Bonferroni-adjusted χ^2 tests, we identified 16 drugs that met pre-specified signal criteria **(Table 4, Figure 2)**. These candidate agents were subsequently entered into multivariable logistic regression models to adjust for potential confounders, including patient demographics, comorbidities, and reporting characteristics.

Table 4. Drugs significantly associated with Proteinuria identified by disproportionality analysis.

Drug	CaseReports	ROR.(95.Cl.)	PRR(95.Cl)	PRR-χ^2	EBG.(EBGM05.)	IC.(IC025.)	pvalue	p_adjust
BEVACIZUMAB	451	17.25 (15.65 - 19.02)	16.77(16.68 - 16.87)	6169.93	15.52 (14.3)	3.96 (3.81)	0	0
LENVATINIB	235	14.78 (12.95 - 16.87)	14.42(14.29 - 14.54)	2817.98	13.86 (12.41)	3.79 (3.6)	0	0
ATEZOLIZUMAB	90	6.02 (4.89 - 7.43)	5.97(5.76 - 6.17)	366.93	5.89 (4.94)	2.56 (2.25)	1.01244E-80	7.05669E-78
EVEROLIMUS	88	8.28 (6.7 - 10.24)	8.17(7.96 - 8.38)	546.45	8.06 (6.75)	3.01 (2.7)	2.5625E-119	1.786E-116
MYCOPHENOLIC ACID	77	8.77 (6.99 - 11)	8.65(8.42 - 8.87)	514.58	8.54 (7.07)	3.09 (2.76)	2.7959E-112	1.9488E-109
TACROLIMUS	77	6.18 (4.93 - 7.75)	6.12(5.9 - 6.34)	325.96	6.05 (5.01)	2.6 (2.27)	9.16471E-72	6.3878E-69
TENOFOVIR DISOPROXIL	67	24.28 (18.98 - 31.06)	23.27(23.03 - 23.5)	1413.71	23.01 (18.72)	4.52 (4.16)	3.62613E-66	2.52741E-63
CICLOSPORIN	65	8.12 (6.35 - 10.39)	8.02(7.77 - 8.26)	395.33	7.94 (6.46)	2.99 (2.63)	1.8447E-86	1.28575E-83
PAZOPANIB	63	10.19 (7.93 - 13.09)	10.01(9.77 - 10.26)	506.38	9.91 (8.04)	3.31 (2.94)	3.3576E-110	2.3403E-107
AMLODIPINE	62	2.66 (2.07 - 3.42)	2.66(2.41 - 2.91)	63.46	2.64 (2.14)	1.4 (1.03)	3.75783E-15	2.61921E-12
DEFERASIROX	60	6.91 (5.35 - 8.92)	6.83(6.58 - 7.08)	296.03	6.77 (5.46)	2.76 (2.39)	4.35108E-65	3.0327E-62

Drug	CaseReports	ROR.(95.Cl.)	PRR(95.Cl)	PRR-χ^2	EBG.(EBGM05.)	IC.(IC025.)	pvalue	p_adjust
OXALIPLATIN	59	2.97 (2.3 - 3.84)	2.96(2.7 - 3.22)	75.94	2.94 (2.37)	1.56 (1.18)	7.79129E-18	5.43053E-15
SUNITINIB	56	3.49 (2.68 - 4.54)	3.47(3.21 - 3.74)	97.81	3.45 (2.76)	1.79 (1.4)	1.58007E-22	1.10131E-19
PEMBROLIZUMAB	53	2.98 (2.27 - 3.9)	2.97(2.7 - 3.24)	68.53	2.95 (2.35)	1.56 (1.16)	3.35442E-16	2.33803E-13
CABOZANTINIB	52	7.59 (5.76 - 9.99)	7.5(7.22 - 7.77)	290.6	7.44 (5.91)	2.89 (2.49)	9.23296E-64	6.43537E-61
ZOLEDRONIC ACID	50	3.04 (2.3 - 4.02)	3.03(2.75 - 3.3)	67.35	3.01 (2.38)	1.59 (1.18)	6.29324E-16	4.38639E-13

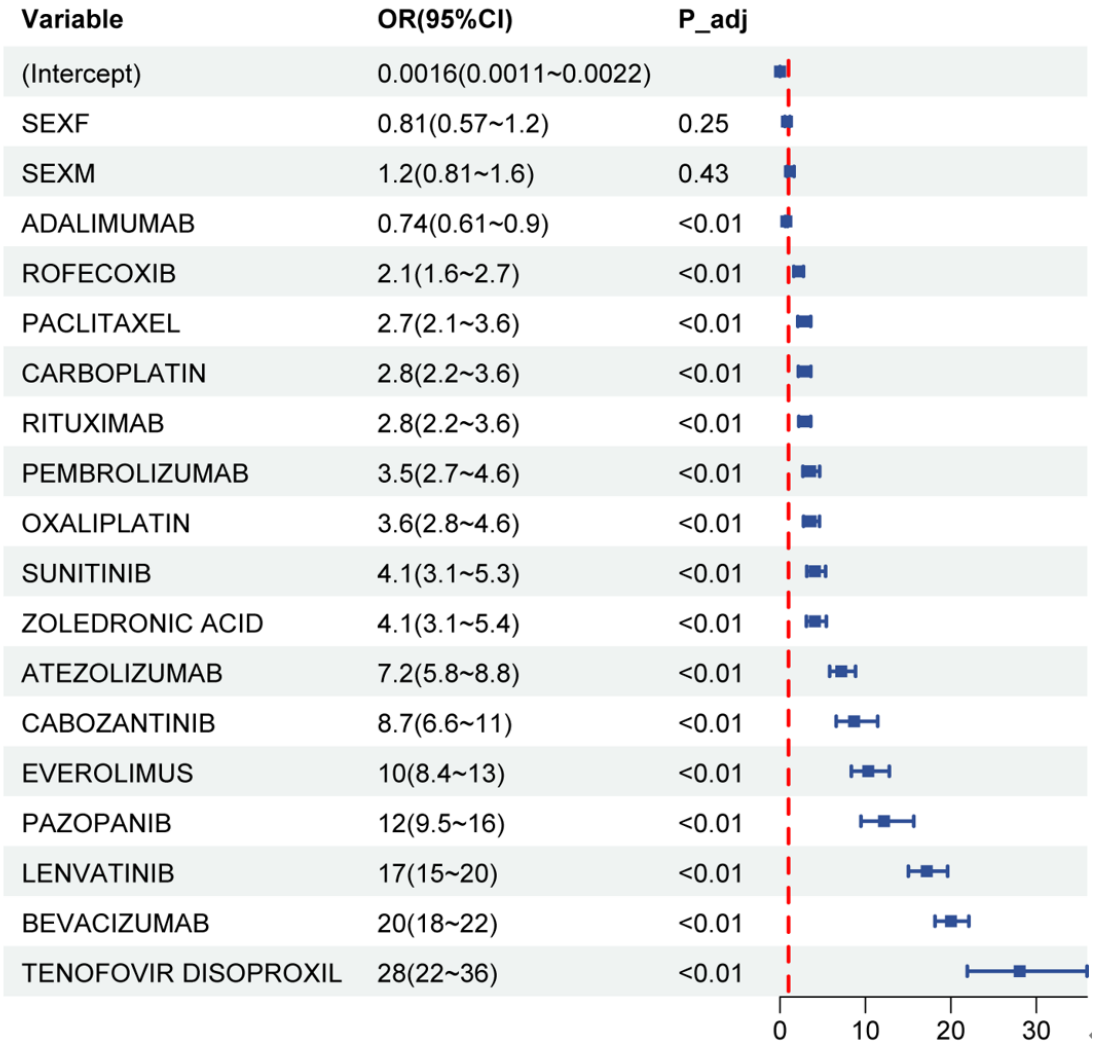

Figure 2. Multivariable logistic regression of drugs associated with Proteinuria.

3.5. Drug classification

The 16 flagged drugs were categorized by therapeutic class as follows **(Figure 3)**:

Antineoplastic agents (n = 8): bevacizumab, cabozantinib, everolimus, lenvatinib, oxaliplatin, paclitaxel, pazopanib (note: bevacizumab listed once)

Anti-infective agent (n = 1): tenofovir disoproxil

Bone metabolism agent (n = 1): zoledronic acid
Gastrointestinal agent (n = 1): rofecoxib
Immunomodulating agents (n = 2): adalimumab, pembrolizumab

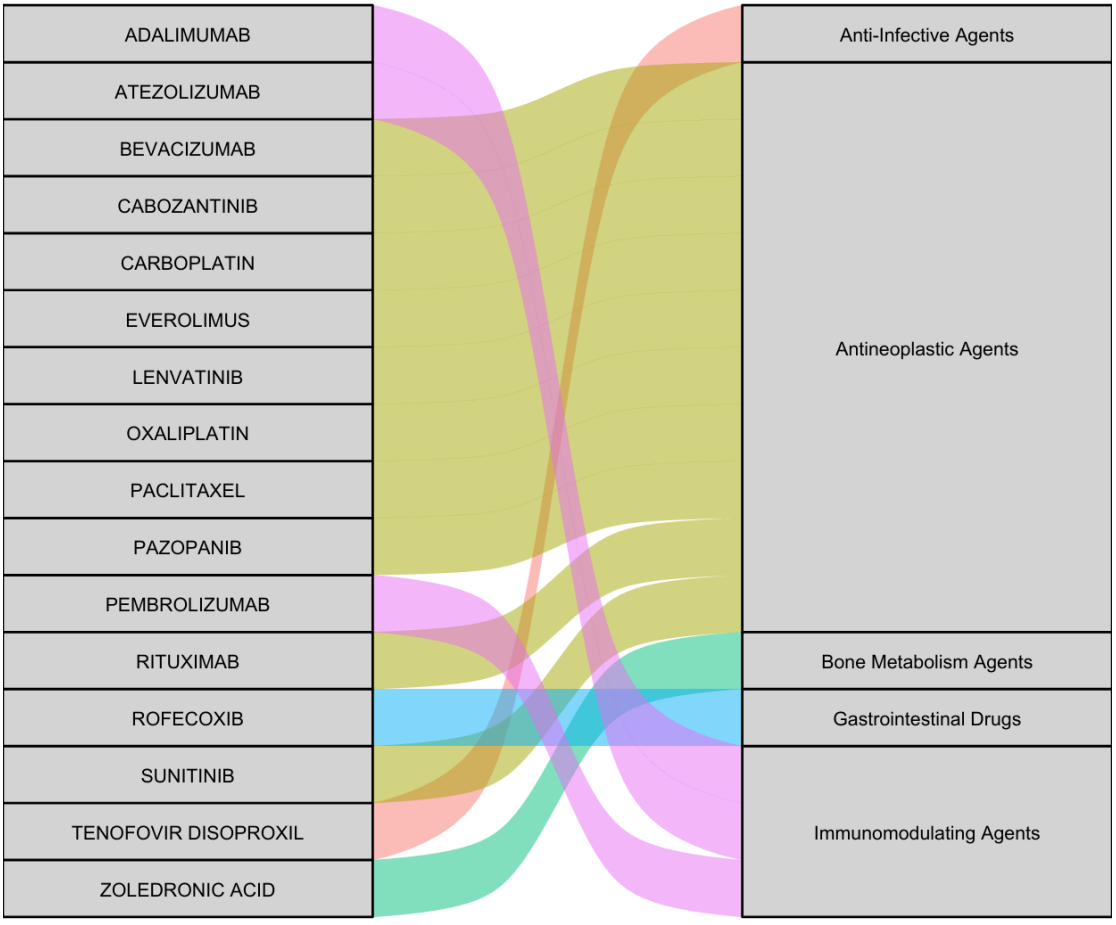

Figure 3. Pharmacological classification of positive drug

4. Discussion

4.1. Overall reporting trends and demographic characteristics

The temporal analysis revealed a general upward trend in proteinuria-related reports over the two-decade study period . This increase may reflect multiple factors, including expanding use of targeted therapies and immunotherapies, improved awareness of renal adverse events, enhanced pharmacovigilance practices, and greater global participation in FAERS reporting. Notably, the balanced sex distribution (48.7% female vs. 50.7% male) suggests that drug-associated proteinuria does not exhibit a marked sex predilection at the population level . The mean age of 53.7 years indicates that middle-aged and older adults constitute the predominant affected population, consistent with the demographic profile of patients receiving antineoplastic, immunomodulatory, and antiviral therapies.

Geographically, the majority of reports originated from the United States and Japan, followed by several European and Asian countries . This distribution likely reflects differences in drug utilization patterns, regulatory frameworks, healthcare infrastructure, and spontaneous reporting culture. The observed variation in mean age at onset across countries may also indicate heterogeneity in underlying disease epidemiology and prescribing practices.

4.2. Predominance of antineoplastic agents

Among the 16 signal-positive drugs, antineoplastic agents constituted the largest category (n = 8) . This predominance underscores the well-recognized nephrotoxic potential of contemporary cancer therapies. Bevacizumab and other vascular endothelial growth factor (VEGF) pathway inhibitors (e.g., lenvatinib, pazopanib, cabozantinib, sunitinib) demonstrated particularly strong disproportionality signals. Mechanistically, VEGF inhibition disrupts glomerular endothelial cell integrity and podocyte–endothelial crosstalk, leading to thrombotic microangiopathy, endothelial swelling, and increased glomerular permeability[3–5]with an associated mortality of up to 5%. The mechanisms underlying STEC-HUS and why the glomerular microvasculature is so susceptible to injury following systemic Stx infection are unclear.\nMETHODS: Transgenic mice were engineered to express the Stx receptor (Gb3. The high ROR and PRR values observed for bevacizumab and lenvatinib are therefore biologically plausible and align with established clinical observations.

Similarly, mTOR inhibitors such as everolimus showed significant associations. mTOR signaling plays a crucial role in podocyte homeostasis; its dysregulation can impair cytoskeletal organization and slit diaphragm function, thereby promoting protein leakage[6–8]amino acids and lipids are fundamental sources for the maintenance of essential cellular processes and homeostasis in all organisms. The nutrient-sensing kinases mechanistic target of rapamycin (mTOR. The detection of oxaliplatin and paclitaxel signals may reflect cumulative renal stress in oncology patients, although their mechanisms may be multifactorial, involving endothelial injury, oxidative stress, or indirect effects through systemic inflammation[9–11].

The strong signal observed for tenofovir disoproxil—an antiviral agent—also merits attention. Tenofovir is known to cause proximal tubular dysfunction via mitochondrial toxicity, which can manifest as proteinuria, particularly low-molecular-weight proteinuria. The high ROR and EBGM values suggest that this association remains clinically relevant despite increasing adoption of tenofovir alafenamide formulations with improved renal safety profiles.

4.3. Immunomodulators and immune-related renal injury

Immune checkpoint inhibitors (e.g., pembrolizumab, atezolizumab) and other immunomodulatory agents (e.g., adalimumab, mycophenolic acid, tacrolimus, ciclosporin) were also identified as signal-positive drugs . Immune checkpoint blockade can induce a spectrum of immune-related adverse events, including glomerulonephritis and interstitial nephritis, through loss of peripheral tolerance and autoreactive T-cell activation[12]. Proteinuria in this context may reflect immune-mediated glomerular injury rather than direct nephrotoxicity.

For calcineurin inhibitors (tacrolimus, ciclosporin), chronic nephrotoxicity is well documented and involves afferent arteriolar vasoconstriction, tubular atrophy, and interstitial fibrosis[13, 14]. The signals detected in our study reinforce the need for routine renal monitoring in transplant and autoimmune populations receiving these agents.

4.4. Other therapeutic classes

Zoledronic acid, deferasirox, and amlodipine also met signal criteria. Zoledronic acid has been associated with acute tubular necrosis and collapsing focal segmental glomerulosclerosis in rare cases[15]malignancy-associated metastatic bone lesions, and as a treatment for hypercalcemia. ZA is excreted almost entirely by the kidney; as a result, a reduction in renal clearance can lead to its accumulation and potential renal toxicity. Although uncommon, acute kidney injury (AKI. Deferasirox-related nephrotoxicity is believed to involve proximal tubular injury and altered iron handling[16]. The relatively lower magnitude of disproportionality for amlodipine suggests a weaker or potentially confounded association, which may be influenced by underlying hypertensive nephropathy in treated populations.

The inclusion of rofecoxib is notable, although its market withdrawal limits contemporary relevance. Cyclooxygenase-2 inhibition may impair renal hemodynamics by reducing prostaglandin-mediated vasodilation, thereby contributing to glomerular hyperfiltration injury in susceptible individuals[17].

4.5. Strengths and methodological considerations

A key strength of this study lies in the application of four distinct disproportionality algorithms combined with Bonferroni

correction, enhancing robustness and reducing false-positive signals . Restricting analyses to drugs with ≥ 50 reports further improved statistical stability. Additionally, multivariable logistic regression allowed adjustment for potential confounders, strengthening causal inference within the constraints of spontaneous reporting data .

However, inherent limitations of FAERS must be acknowledged. First, underreporting and reporting bias may distort true incidence. Second, lack of denominator data precludes estimation of absolute risk. Third, clinical details such as baseline renal function, proteinuria severity, biopsy findings, and temporal relationship to drug initiation are often incomplete. Confounding by indication is also possible, particularly for oncology and transplant populations with preexisting renal vulnerability.

4.6. Clinical implications and future directions

Despite these limitations, our findings have important clinical implications. The predominance of targeted therapies and immunotherapies among signal-positive drugs highlights the evolving landscape of drug-induced kidney injury. Routine monitoring of urinary protein excretion, early recognition of renal adverse events, and interdisciplinary collaboration between oncologists, nephrologists, and infectious disease specialists are essential to mitigate morbidity.

Future research should incorporate electronic health record–based cohort studies and mechanistic investigations to validate these signals and clarify pathophysiological pathways. Stratified analyses by age, comorbidity burden, and combination therapy may further refine risk prediction. Integration of pharmacogenomic data may also help identify susceptible subpopulations.

5. Conclusion

This comprehensive FAERS-based analysis identifies 16 drugs with significant signals for proteinuria, with antineoplastic and immunomodulatory agents representing the dominant categories. These results reinforce known nephrotoxic mechanisms while uncovering potential safety concerns warranting continued pharmacovigilance and prospective validation.

Disclosure statement

The author declares no conflict of interest.

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