Reported drug induced acute kidney injury: a pharmacovigilance analysis

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Abstract number: 6ER-042 **Keywords (MeSH):** Acute Kidney Injury; Drug-Related Side Effects and Adverse Reactions; Pharmacovigilance; Pharmacoepidemiology; Risk Management; Patient Safety; Adverse Drug Reaction Reporting Systems.

Background

Acute Kidney Injury (AKI) is a condition that may result from various factors, including the exposure to nephrotoxic drugs. Exposure may occur in the outpatient setting, leading to hospital admission, but can also occur during hospitalization, extending its duration. The incidence of AKI among hospitalized patients varies, with underdiagnosis rates estimated to exceed 20% in developed countries and approximately 7% in developing countries.

Objective

To identify the drugs most frequently reported to the Portuguese Pharmacovigilance Database (PPV) associated with AKI in Portugal.

Study Design and Methods

Table 1 – Contingency table for the case-non-case analysis

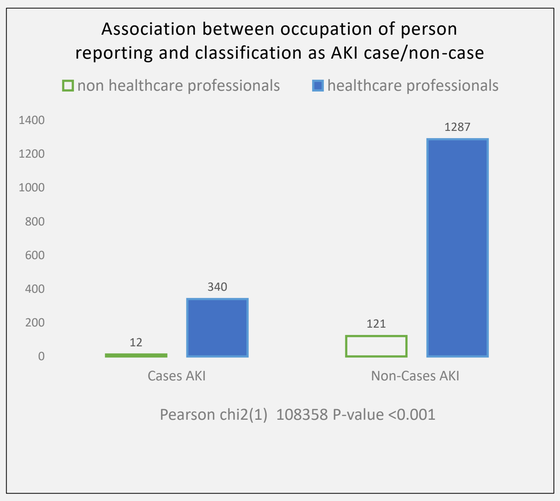
	ADRs of interest reported: "Cases"	Other ADRs reported: "Non-cases"
Drug of interest	a	b
Other drugs	c	d

ADR: Adverse drug reaction.

- ✓**Ratio case/non case** (1:4).
- ✓**Source** : PPV.
- ✓**Period**: 01/01/2009 - 31/12/2020.
- ✓**Outcome**: Reporting Odds Ratio (ROR), IC 95%.

Results

Our analysis focused on 53,505 reports, among which less than 1% were AKI cases (n=352). Nearly 10% led to death.



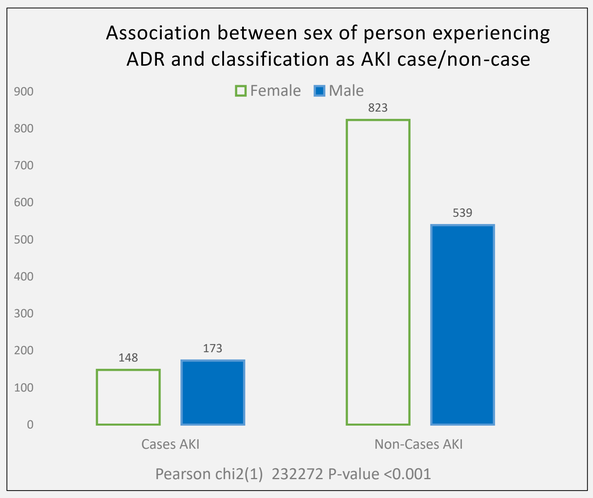


Table 2. Characteristics of patients, source of report and event characteristics

Characteristics	Cases AKI [a] (n=352) n (%)	Non-cases No AKI (n=1408) n (%)		P-value
Age			ANOVA F	
Years (mean ± SD)	(59.56 ± 21.6) [b]	(50.00 ± 22.1) [c]	31.776	**<0.001**
Outcome [d]			Pearson chi2(1)	
Death	32 (9.6)	69 (7.1)	2.1911	0.139
Hospitalization	170 (50.8)	261 (26.7)	65.5033	**<0.001**
Clinically important	215 (64.2)	639 (65.3)	0.1472	0.701
Life-threatening	26 (7.8)	82 (8.4)	0.1284	0.720
Disability	10 (3.0)	85 (8.7)	12.1049	**<0.001**
Congenital anomaly	1 (0.3)	0 (0.0)	2.9216	0.087

Abbreviations used - AKI: Acute Kidney injury

Data are n (%) unless otherwise indicated
[a] AKI in this table is the primary outcome in this study, which was defined with a narrow Standardized MedDRA Query of acute renal failure| [b] In Cases there were 150 (42.6%) reports with missing age | [c] In Non-cases there were 321 (22.7%) reports with missing age | [d]Each report can have more than one outcome

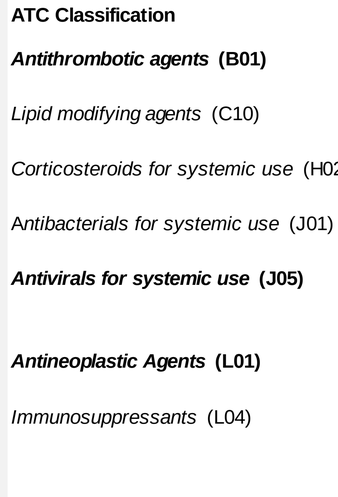
Table 3. Drugs involved in AKI events and respective ROR

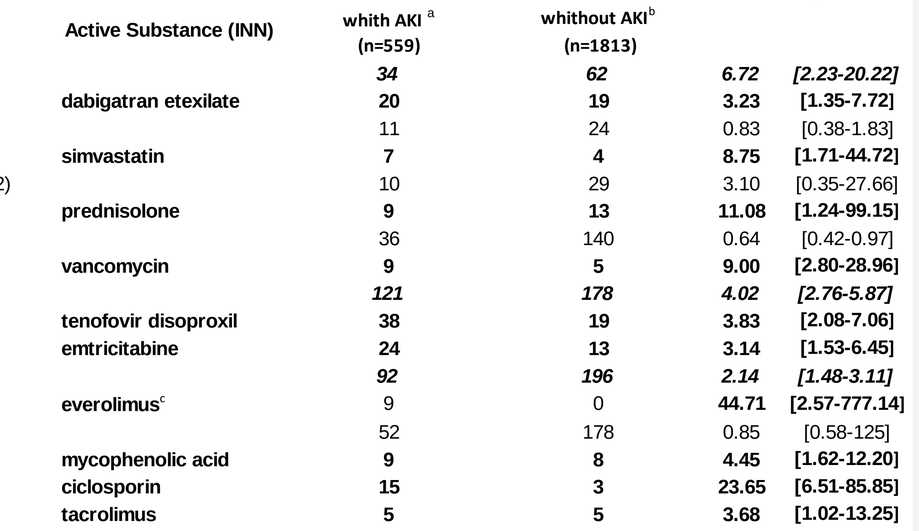
ATC Classification	Active Substance (INN)	Total number of ADRs whith AKI [a] (n=559)	Total number of ADRs whithout AKI[b] (n=1813)	ROR	[95%CI]
Antithrombotic agents **(B01)**		***34***	***62***	***6.72***	***[2.23-20.22]***
	dabigatran etexilate	**20**	**19**	**3.23**	**[1.35-7.72]**
Lipid modifying agents (C10)		11	24	0.83	[0.38-1.83]
	simvastatin	**7**	**4**	**8.75**	**[1.71-44.72]**
Corticosteroids for systemic use (H02)		10	29	3.10	[0.35-27.66]
	prednisolone	**9**	**13**	**11.08**	**[1.24-99.15]**
Antibacterials for systemic use (J01)		36	140	0.64	[0.42-0.97]
	vancomycin	**9**	**5**	**9.00**	**[2.80-28.96]**
Antivirals for systemic use **(J05)**		***121***	***178***	***4.02***	***[2.76-5.87]***
	tenofovir disoproxil	**38**	**19**	**3.83**	**[2.08-7.06]**
	emtricitabine	**24**	**13**	**3.14**	**[1.53-6.45]**
Antineoplastic Agents **(L01)**		***92***	***196***	***2.14***	***[1.48-3.11]***
	everolimus[c]	9	0	**44.71**	**[2.57-777.14]**
Immunosuppressants (L04)		52	178	0.85	[0.58-125]
	mycophenolic acid	**9**	**8**	**4.45**	**[1.62-12.20]**
	ciclosporin	**15**	**3**	**23.65**	**[6.51-85.85]**
	tacrolimus	**5**	**5**	**3.68**	**[1.02-13.25]**
All other therapeutic products **(V03)**		9	3	**46.50**	**[6.7-322.62]**
	deferasirox[3]	9	0	**133.00**	**[2.19-8082.55]**

Abbreviations used: ADR, Adverse Drug Reaction; ATC, Anatomical, Therapeutic and Chemical; AKI, Acute Kidney Injury; CI, Confidence Interval; PPVD, Portuguese National Pharmacovigilance Database; INN, International Nonproprietary Name; ROR, Reporting Odds Ratio

[a] In Cases there were 23 (4.1%) reports with missing ATC5
[b] In Non-cases there were 127 (7.0%) reports with missing ATC5
[c]Haldane correction statistical method

In total, eleven drugs were identified, with results suggesting a possible association with the occurrence of AKI (table 3).





Conclusion

In this study, we identified lesser-known drugs—dabigatran, simvastatin, emtricitabine, and mycophenolic acid—as being possibly implicated in AKI-through disproportionality analysis. However, further studies are needed to account for confounding factors. A key limitation is the reliance on spontaneous reports, which may lead to underreporting and an inaccurate estimation of ADR incidence. Nonetheless, our findings reinforce the need for vigilant monitoring of established AKI-associated drugs, emphasising the critical role of clinical pharmacy in assessing renal function in at-risk patients.

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