

PROSPECTIVE DETECTION OF ADVERSE DRUG REACTIONS AMONG 2,263 HOSPITALISED CHILDREN OVER A 19 MONTH PERIOD - EREMI INTERMEDIATE REPORT -

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Background: Off-label and unlicensed (OLUL) drug use is a dominant practice in paediatrics. Recent observational studies suggest that OLUL drugs are more likely to be responsible for adverse drug reactions (ADRs) in children than licensed medicines (Santos 2008; ADRIIC 2014).

Purpose: EREMI study prospectively assess the relationship between OLUL drug use in children (0–15 years, ≥ 3 hospital days) and ADRs occurrence. This EREMI intermediate report describes ADRs detected over 19 months (September 2013 to March 2015) in our children's hospital.

Material and Methods: ADRs were detected by the EREMI team (physicians/pharmacists) analysing data extracted from the Hospital Information System (e-HIS): patient medical records, drug administrations, physiological parameters and biological outcomes. Suspected ADRs were validated with the clinical team.

RESULTS

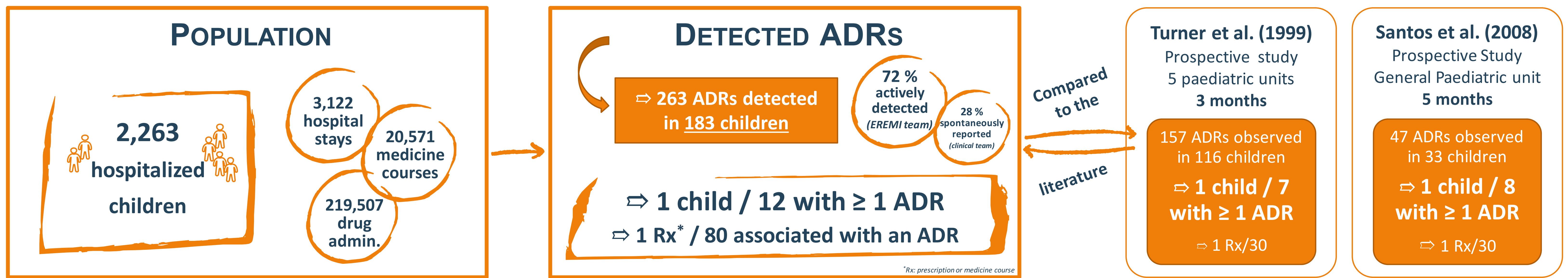


Table 1 – Frequency of observed ADRs within the 7 participating paediatric units.

Paediatric unit	Mean No. of Rx/child	Total No. of ADRs	Proportion of children experiencing ≥ 1 ADRs	Incidence of ADRs based on No. of children
1. Paediatric resuscitation	16	134	29 %	45 %
2. Nephrology / Rheumatology	15	32	10 %	15 %
3. Developmental psychopathology	1	19	9 %	12 %
4. Hepatogastroenterology	15	16	8 %	10 %
5. Neurology / Epileptology	11	25	8 %	9 %
6. Pulmonology	9	31	4 %	8 %
7. Endocrinology, General paediatrics	4	6	1 %	1 %

Table 2 – Observed ADRs coded by affected system organ class (MedDRA).

System organ class	Examples of ADRs	No. ADRs	% of ADRs
1. Metabolism and nutrition	hypokalaemia, decrease appetite	58	22 %
2. Nervous system	somnolence, extrapyramidal syndrome	28	11 %
3. Psychiatric	discontinuation syndrome, irritability	26	10 %
4. Vascular	blood pressure disorders, thrombosis	24	9 %
5. Hepatobiliary	increased transaminases	21	8 %
6. General and administration site	allergic reactions	19	7 %
7. Gastrointestinal	diarrhoea, pancreatitis	18	7 %
8. Blood and lymphatic system	anaemia, neutropenia	16	6 %
10. Skin and subcutaneous tissue	skin reaction	13	5 %
11. Renal and urinary	renal failure, urinary retention	13	5 %
12. Infection and infestations	opportunistic infections	9	3 %
13. Cardiac	cardiac rhythm disorders	8	3 %
14. Respiratory, thoracic and mediastinal	hypoxia	7	3 %
17. Musculoskeletal and connective tissue	tendinitis	2	1 %
19. Eye	corneal ulcer	1	0 %

Table 4 – Examples of ADRs responsible for hospital stay extended (44%)

ADRs	Suspected drugs
Acute pancreatitis (2)	⇔ hydrochlorothiazide, VPA
Allergic reactions (4)	⇔ vancomycin, piperacillin/tazobactam, tocilizumab
Interstitial tubulopathy (1)	⇔ carbamazepine

Table 5 – Examples of severe or life threatening ADRs (12%)

ADRs	Suspected drugs
Hypokalaemia (12)	⇔ diuretics
Corneal ulcer (1)	⇔ sufentanil+ midazolam + Nimbex® + Ketamine
Diabetes (1)	⇔ tacrolimus

Table 3 – Most commonly observed ADRs.

ADRs	No. of ADRs	%	Suspected drugs
1. Hypokalaemia	27	16 %	⇔ diuretics, topiramate, methylprednisolone, nalbuphine
2. Discontinuation syndrome	19	7 %	⇔ morphinics, ketamine
3. Somnolence	16	6 %	⇔ cyamemazine, nalbuphine, levetiracetam, vigabatrin
4. Cytolysis and cholestasis	16	6 %	⇔ mycophenolate, methotrexate, rituximab
5. Hypotension	15	6 %	⇔ diuretics, clonazepam, phenobarbital, midazolam
6. Skin reactions	14	5 %	⇔ vancomycin, lamotrigine + VPA

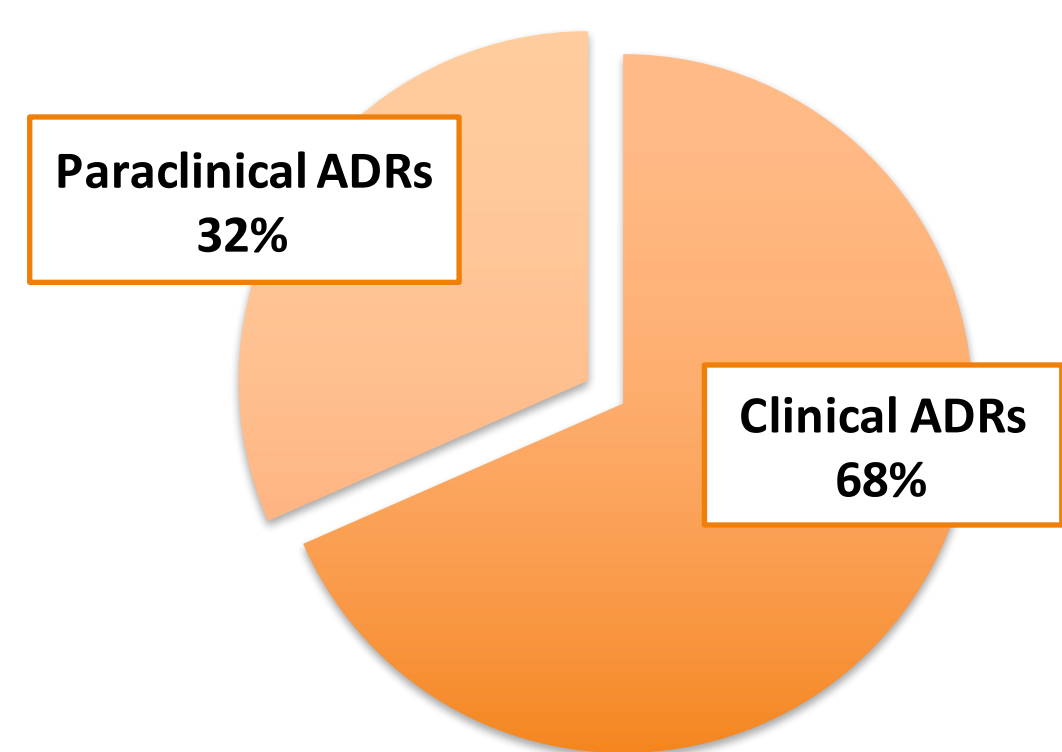


Figure 1 – Proportion of clinical and paraclinical ADRs

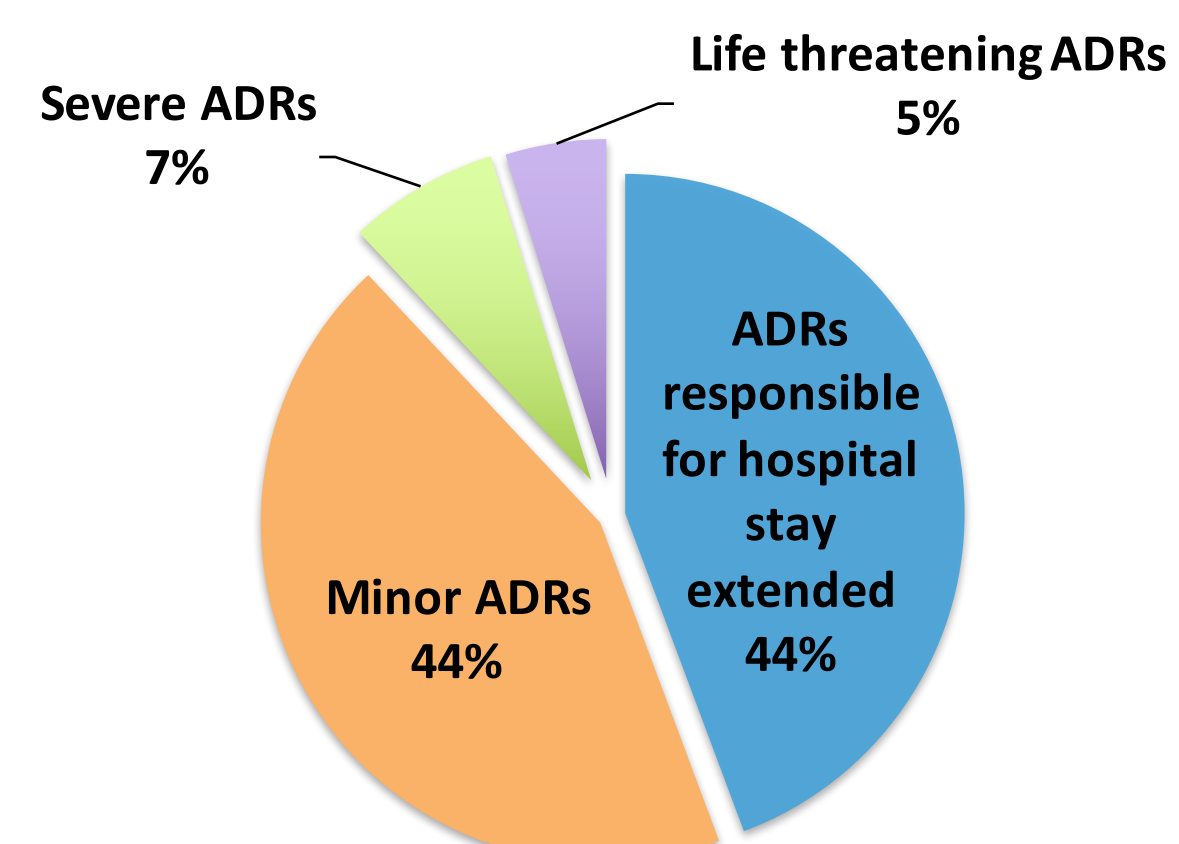


Figure 2 – Severity of detected ADRs

Discussion and Conclusion:

- ADRs in EREMI compared to the literature:
 - ✓ Almost twice as much children with ≥ 1 ADR;
 - ✓ Twice as much medicine courses per child;
 - ✓ Different units, longer ADR detection period in EREMI;
- As expected, great incidence of ADRs within the resuscitation ward (1 child/3 experiencing ≥ 1 ADR).
- Unanticipated high frequency of ADRs occurrence using psychiatric drugs in children.

Perspectives:

- Detected ADRs are being reviewed by our Regional Centre of Pharmacovigilance and the EREMI independent committee.
- Majority of ADRs were preventable (e.g.: hypokalaemia, discontinuation syndrome):
 - ⇒ Systematic warning of clinical staff for ADR risks would help in preventing ADRs.
 - ⇒ Collected information will be used to develop an automated tool for the detection of preventable ADRs.

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