Cutaneous adverse drug reactions: A four-year audit from a district hospital in Johor, Malaysia

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SUMMARY

Cutaneous adverse drug reactions (cADR) are common. However, only very few audits reported the clinical characteristics of cADR captured at district hospitals. We performed a 4-year audit on cADR reported to the Department of Pharmacy in Hospital Pakar Sultanah Fatimah between May 2012 and March 2016. It showed that the main adverse drug reaction (ADR) reporters were pharmacists (84.9%) where the majority of the reactions were clinical descriptions without dermatological diagnosis. Antibiotics (46.4%) were the commonest culprit drug followed by NSAIDs (22%). The most common reactions were immediate reactions, i.e. urticaria and angioedema contributing 55.7% of the cases; followed by maculopapular eruptions (41.8%). There were only six cases (1%) of severe cADR reported in this cohort. Reporting bias and the incomplete dermatological diagnosis were the main limitation of the reports.

Cutaneous adverse drug reaction (cADR) is defined as an unintended morphological skin change and encompasses all adverse events related to drug eruption, which predicts hazard from future administration and warrants prevention, or specific treatment, or alteration of the dosage regimen, or withdrawal of the drug.[1] Spontaneous reporting of adverse drug reactions (ADR) has been established in Malaysia since 1987. However, most of the published cADR audits were cases that presented to dermatology units. This audit aims to describe the pattern of cADR reaction and the associated medications from a district hospital ADR database.

This is a retrospective descriptive cross-sectional study comprises four-year data (May 2012 to March 2016) collected from the adverse drug reaction database, Department of Pharmacy, Hospital Pakar Sultanah Fatimah (HPSF), Johor, Malaysia. The database is built upon the reported ADR by the health care practitioners (HCP) in HPSF with the use of local adverse drug reporting form, which adheres to the World Health Organization (WHO) drug reporting guidelines.[1] The reports were then submitted to the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC). The ADR database was classified into cutaneous or non-cutaneous ADR and was subsequently analysed.

Out of 651 valid ADR captured from the Department of Pharmacy, HPSF, 591 cases (91.8%) were cADR. The mean age of the patients was 39.7 years old (range: two months to 94 years), and majority (85%) aged younger than 65 years. The ethnicity proportion was consistent with the national population data as shown in Table I. The main reporters were pharmacists where most of the reactions were not reported with dermatological diagnosis but merely clinical descriptions that were retrieved from the case notes of patients. The most common reactions reported were immediate reactions, i.e., urticaria and angioedema as shown in Figure 1.

Figure 2 demonstrated that the most frequent drug group responsible for cADR was antibiotic followed by non-steroidal anti-inflammatory drugs (NSAIDS). Among the antibiotics, penicillin/amoxicillin/ampicillin (55.8%) and cephalosporin (15.3%) were the main culprits followed by macrolides (8.8%), co-trimoxazole (5.1%), fluoroquinolone (4%) and others (9.8%). There was only a case of cADR following immunization reported in the past four years. Ten cases of cADR were related to mineral, vitamin and herbal supplements bought over the counter.

The demographic pattern of cADR and the responsible drugs were very much different from two other audits done in a tertiary hospital in Johor Bahru.[2,3] The two audits were reported by dermatologists where there was more severe cutaneous adverse drug reactions (SCARs) which included Stevens Johnson Syndrome (SJS), Toxic epidermal necrolysis (TEN), SJS-TEN overlapped, acute generalized exanthematous pustulosis (AGEP), and drug reaction, eosinophilia with systemic symptoms (DRESS). The rate of SCARs in the current audit was very low, which could be due to inability to recognise SCARs by HCP, selective reporting (as some SCARs might have been referred to tertiary centre, and reports were expected to be done at the receiving end) or under-reporting. In addition, we were not able to assess the causal relationship between the culprit drugs and the drug reactions in this cohort as the data was regrettably not captured in the database. This will be collected and evaluated in future.

Generally, the rate of cADR is predicted to be higher among the elderly.[4] This is due to polypharmacy resulted from the increasing prevalence of multiple comorbidities among elderly as well as the higher hospitalization rate. It is also well described in some studies, that the common skin disorders among the elderly, i.e. xerosis and chronic eczema, were related to the use of anti-hypertensive agents such as calcium-channel

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Table I: Demographic characteristics of cutaneous adverse drug reactions reported in current study (n=591)

Characteristics	n (%)
Mean age in years (±SD)	39.7 (22.3)
Age Groups	
Less than 65 years	502 (84.9)
More than 65 years	89 (15.1)
Gender	
Male	307 (51.9)
Female	284 (48.1)
Ethnic	
Malay	450 (76.1)
Chinese	120 (20.3)
Indian	16 (2.7)
Others	5 (0.8)
ADR Reporter	
Pharmacists	502 (84.9)
Doctors	88 (14.9)
Nurse	1 (0.2)

ADR -adverse drug reaction

blockers, diuretics, angiotensin-converting enzyme inhibitors and nitrates.[5-7] However, such pattern was not captured in our cohort, which likely attributed to reporting bias.

In addition, there was a very low number of cADR following immunisation reported in the current cohort. As reported by WHO, the estimated occurrence of injection site reactions and rash for measles vaccine is 17-30 in 100 doses and five in 100 doses respectively.[8] Therefore, higher number immunisation-related cADR is expected but it was not observed in the current audit, which is likely due to the inherent tendency to report only severe reactions.[9] Thus, HCP should be educated to actively report all forms of such cADR in any severity.

Clinicians reported only 10% of the cADR in this audit. The majority of the reporters were pharmacists who probably unable to provide an accurate dermatological diagnosis. Lack of drug testing, direct management, and follow-up of the reactions by reporters may greatly influence the reliability and the accuracy of the ADR, the likelihood of the

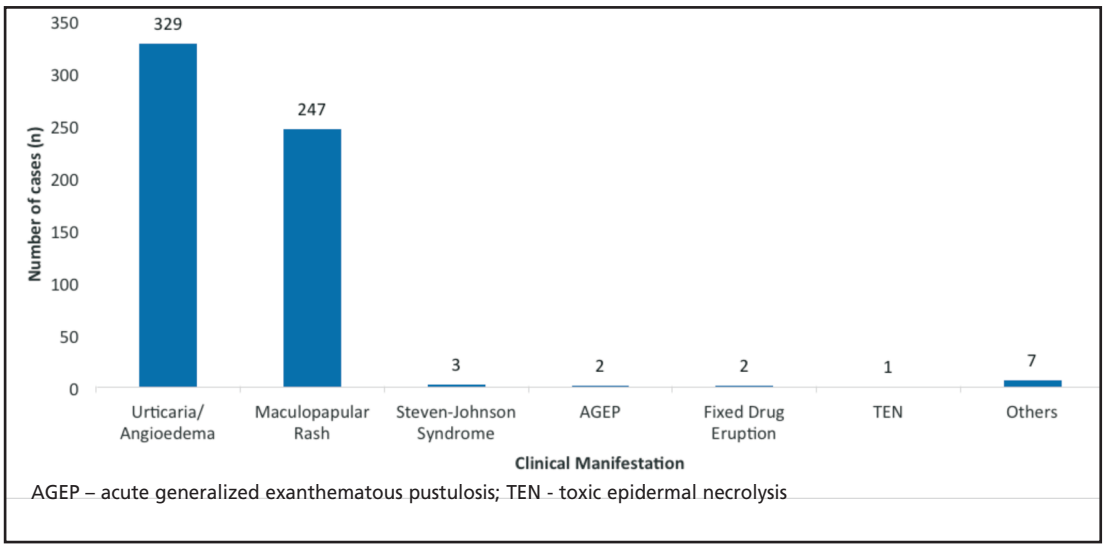

Fig. 1: Clinical manifestations of cutaneous adverse drug reactions (n=591).

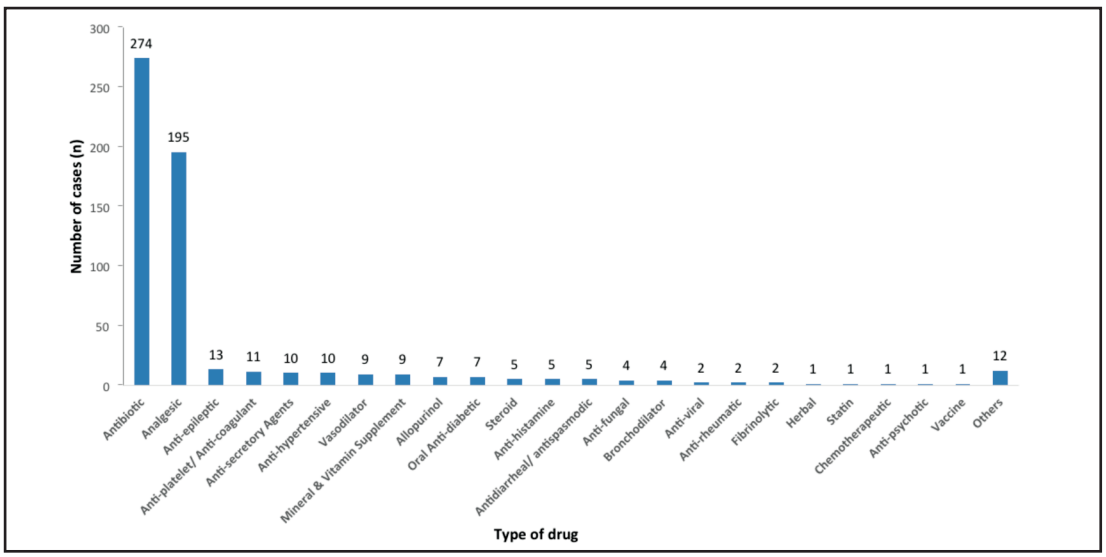

Fig. 2: Drug groups responsible for the cutaneous adverse drug reactions (n=591).

culprits reported and the outcome of the cADR. Clinicians should play a bigger role in reporting cADR. Continuous education and awareness campaign among clinicians and pharmacists are essential in order to improve the quality and accuracy of ADR reports.[10]

In conclusion, urticaria and maculopapular eruption were the most commonly reported cutaneous adverse reaction with NSAIDs and beta-lactam antibiotics being the main causative agents in Hospital Pakar Sultanah Fatimah, Johor. There is an urgent need for continuous education and training of the HCP to improve the quality of ADR reporting. All clinicians should actively report adverse drug reactions.

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