

SHORT COMMUNICATION

**ADVERSE EVENTS OF SPECIAL INTEREST (AESI) FOR
ACTIVE VACCINE SAFETY SURVEILLANCE IN BRUNEI.**

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Adverse Events of Special Interest (AESI) for Active Vaccine Safety Surveillance in Brunei

The introduction of COVID-19 vaccines requires systematic approaches for collecting safety data and details of adverse events following immunisation (AEFI). This requires clinicians to proactively report suspected AEFI to their national pharmacovigilance centers. However, it is known that globally, there is a need to improve AEFI reporting to improve the capacity of detecting and managing vaccine safety issues, particularly in low and middle-income countries. [1]

For mass-vaccination programmes of novel vaccines (such as the COVID-19 vaccines), active vaccine safety surveillance is an important consideration. This collects relevant data from all individuals within a well-defined population, minimizing under-reporting. This may help with signal detection of potential AEFI attributed to the vaccine, as well as relative risk and rates of the events. This strategy was used during a mass-vaccination campaign of a meningococcal A conjugate vaccine in Burkina Faso, identifying a rate of 12.83 AEFI cases per 100,000 vaccine recipients. While there were frequent reports of convulsions, urticarial and bronchospasm, these attack rates were similar to baseline rates in the same population over a similar time period a year earlier. [2] As there was no increase in incidence of these symptoms of concern after the immunisation programme, it is less likely that these side effects were due to the vaccine. Thus, it is important to monitor for baseline rates of specific conditions to assist with signal detection and causality assessment for issues arising post-vaccination.

These conditions are called adverse events of special interest (AESI), which can be identified through a pro-active approach, reported, investigated and analysed to identify signals of potential harm. An AESI is defined as a 'pre-specified medically significant event that has the potential to be causally associated with a vaccine

product that needs to be carefully monitored and confirmed by further special studies'. These are shortlisted based on associations with immunisations, vaccine platforms or adjuvants, or theoretical concerns based on immunology or pre-clinical studies. AESI conditions include anaphylaxis, generalized convulsions, Guillain-Barre syndrome, meningoencephalitis, coagulation disorders, aseptic arthritis and cutaneous vasculitis. [3]

Brunei is a small country with a population of over 420000 people. [4] The national electronic clinical records system (Bru-HIMS) was used to obtain the baseline rates of specific AESI, which will be monitored after vaccine roll-out. Figure 1 illustrates the number of patients with selected AESI for the years 2018-2020, with approximate baseline rates that can be appreciated. Note that for neurological conditions such as encephalomyelitis and Guillain-Barre syndrome, the reduced rates in 2020 can be explained by the national neurology service being moved to a different center, with delayed implementation of the Bru-HIMS system. For the national population of 420000, it is expected that there will be approximately 10 patients with encephalomyelitis, 30 with anaphylaxis, 20 with erythema multiform, 30 with cutaneous vasculitis and 10 with Guillain-Barre syndrome annually. Any significant increase in baseline rates for these AESI in 2021 may represent a signal of possible AEFI from COVID-19 vaccines.

Another consideration for AESI is to evaluate the accuracy of the diagnosis. The Brighton Collaboration provides case definitions and guidelines to ensure that investigations of AESI will only include patients with correct diagnoses. For example, if anaphylaxis AESI requires further evaluation, a case definition is available, which outlines major and minor criteria, as well as levels of diagnostic certainty. [5]

For the 2020 data, there were 29 patients coded as anaphylaxis. There were 14 (48.3%) males and 15 (51.7%) females. Among these, 15 had previous allergies and 14 had previous immunisations. Event classification according to Brighton Collaboration case definitions of anaphylaxis are summarized in Table 1. Overall, only 79.3% of the patients met level 1 to 3 criteria for the diagnosis of anaphylaxis.

In summary, obtaining baseline rates of AESI is an important task for active vaccine safety surveillance to pick up potential signals of harm after introduction of COVID-19 vaccines. The feasibility of this in Brunei was illustrated using data obtained from national electronic health records in Brunei. If specific AESI warrants further investigation, it is crucial to ensure there is diagnostic certainty using case definitions before inclusion in case numbers.

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Conflict of Interest

The author has no conflicts of interests to declare.

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Ethical approval was not obtained as the data was necessary for public health surveillance during a public health emergency, following the principles of minimal risk, non-identifiable data and sharing of information that will be useful for public health purposes. (WHO Guidance for managing ethical issues in infectious disease outbreaks, 2016)

Table 1. Event Classification for anaphylaxis cases in 2020 using Brighton Collaboration Case Definitions

Event Classification	N (%)
Level 1 criteria	15 (51.7%)
Level 2 criteria	7 (24.1%)
Level 3 criteria	1 (3.4%)
Reported anaphylaxis but insufficient evidence to meet case definition	2 (6.9%)
Not a case of anaphylaxis	2 (6.9%)
Follow-up case (incident from previous years)	2 (6.9%)

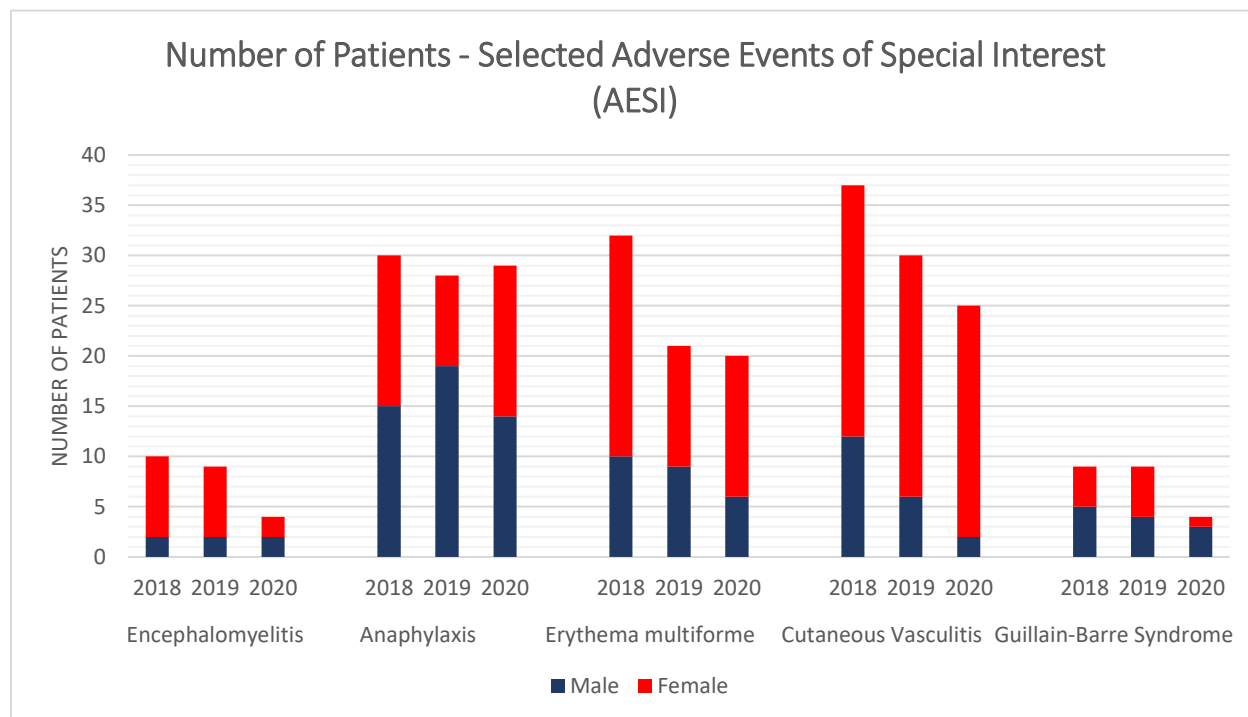


Figure 1: Number of patients and selected adverse events of special interest (AESI) for 2018 to 2020

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