# A Study of Adverse Drug Reactions in Paediatric FAERS

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*Abstract- The emergence of massive datasets in a FAERS presents both challenges and Opportunities in data analysis. This so called "big data" challenges and will increasingly require novel solutions customized from related domains. An advance in information and communication technology provides the most feasible solutions to big data analysis in terms of efficiency and scalability. The MapReduce programming framework important two tasks common in functional Programming: Map and Reduce. MapReduce is a new parallel processing framework and Hadoop is its open-source implementation on a single computing node or on clusters. The usage of MapReduce and Hadoop on a distributed system represents a significant advance in post marketing big data processing and utilization, and provides new opportunities in the emerging era of big data analytics. The main aim of this paper is to summarize the state-of-the-art efforts in post marketing Paediatrics big data analytics and highlight what might be needed to enhance the outcomes of these big data analytics tools. This paper is concluded by summarizing the potential usage of the Map Reduce programming framework and Hadoop platform to process huge volumes of data in FAERS data.*
*Keywords: Data mining, MapReduce, Hadoop, Big data, post marketing surveillance.*

## I. INTRODUCTION

Adverse drug reactions represent a severe problem worldwide. It refers to drug associated adverse incidents in which drugs are used at an appropriate dose and indication. It can complicate a patient's medical condition or contribute to increase morbidity, even death. Even though premarketing clinical trials are required for all new drugs before it is approved for marketing, trials are necessarily limited in size and duration and are not capable of detecting rare adverse drug reactions. If the event rate of a possible ADR is less than 0.1%, it cannot be recognized by the premarketing randomized controlled trials due to limitation in size. [1]

The safety of medication utilized in patients of an adult cannot be applicable to a paediatric group. [1] The pharmacokinetics and pharmacodynamics of several frequently used drugs vary considerably between these two age groups of patients.[2] Further, adverse drug reactions (ADRs) in kids will have a comparatively a lot of severe impact when put next to adults. Thus, the ADRs can lead to important morbidity among children.[3] It has been observed that ADRs in children not only cause in hospital admissions or prolonged hospitalization but also may lead to eternal disability or even death.[4] The information about the occurrence, severity and kinds of

drugs most frequently involved in adverse reactions in the paediatric age group is of particular interest, since pre-marketing clinical trials are done mainly in adults.[5] They constitute a reported incidence of 9.5%, including 2.1% of hospital admissions, with 39.3% of them being life-threatening [6] The safety profile of a drug thus marketed with its testing done on adults can differ significantly when utilized for children.[7]. Few studies were methodically addressed for spontaneous reports of post-market Surveillance.

## II.   METHODS
### A)  Postmarket Surveillance

Pharmacovigilance evaluates the protection of every drug to boost the protection profile of the drug over its period of time within the market [8]. One important step in this process is safety *signal detection*. Below we formally introduce relevant terminologies.

- Safety Signal Detection**.** WHO defines a *safety signal* as reported information on a possible causal relationship between an adverse event and a drug. Recently, the Council for International Organisations of Medical Sciences [9] extended this definition to cover any new potential causal relationship or a new aspect of a known association between a drug and an event, either adverse or beneficial.

A set of activities that, based on various sources of data, determines whether there is any safety concern regarding an active ingredient or medicinal product is called *signal management*. These activities include signal detection, signal validation, prioritisation and assessment, recommendation for action, and exchange of information with authorities [10]. *Signal detection* is the process of discriminating between safety signal and noise. We briefly explain most of the activities related to signal management, but our focus is on signal detection**.**

- Active versus Passive Surveillance.

Two different postmarket surveillance approaches are practised to ensure the safety of medications: passive and active. Passive approaches rely on individual reports of potential ADEs from different sources like health professionals or manufacturers. Active methods, however, seek to automatically generate such safety reports from all completely different knowledge sources, like patient health records, and medical and pharmacy claims. Ultimately, signals generated from these reports, passive or active, are confirmed using similar methods, which frequently need human specialists, to determine relation.

- Postmarket Surveillance Procedure.

To detect the harmful side effects that go undiscovered during clinical trials, multiple sources of information are consulted. Pharmaceutical companies continue to monitor for potential adverse effects, with regulatory bodies mandating these companies to report suspected adverse effect.

## III.   DATA SOURCES

Data were retrieved from the publicly accessible version of the US Authority FDA Adverse Event Reporting System (FAERS), which consists of results of sudden ADRs submitted by manufacturers, healthcare professionals, and patients. FAERS is one among the most important repositories of spontaneous reports within the world [11, 12]. The aim of pharmacovigilance is early recognition of adverse drug events so that correct treatment is given as early as possible. Many Spontaneous Reporting System (SRS) database are available to identify these adverse events. The structure of FDA_AERS database structure is shown in figure 1.
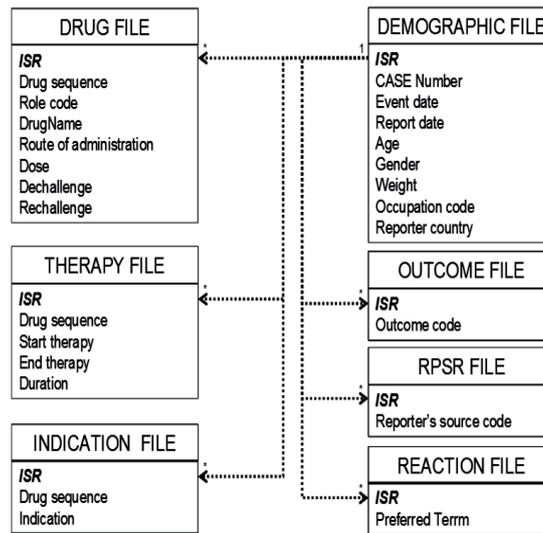
**Figure 1 FDA_AERS structure**

## IV.    DATA MINING TECHNIQUES IN ADVERSE DRUG REACTION DETECTION

A number of data and text mining methods have been developed to assist in the discovery of drug adverse effects from the data sources described above. Some of these methodologies deal with spontaneous reporting systems for passive ADR monitoring. Increasingly, however, newer methods are developed to *active monitoring* based on other types of data, such as administrative databases, medical literature, drug discussions in social media, and Electronic Health Records. As the amount of computer accessible ADR-related data grows, methods that integrate different types of data for ADR discovery become increasingly important. [13]. Figure2 shows data mining process in with FDA_AERS. Table1 describes the disproportionality calculation method.
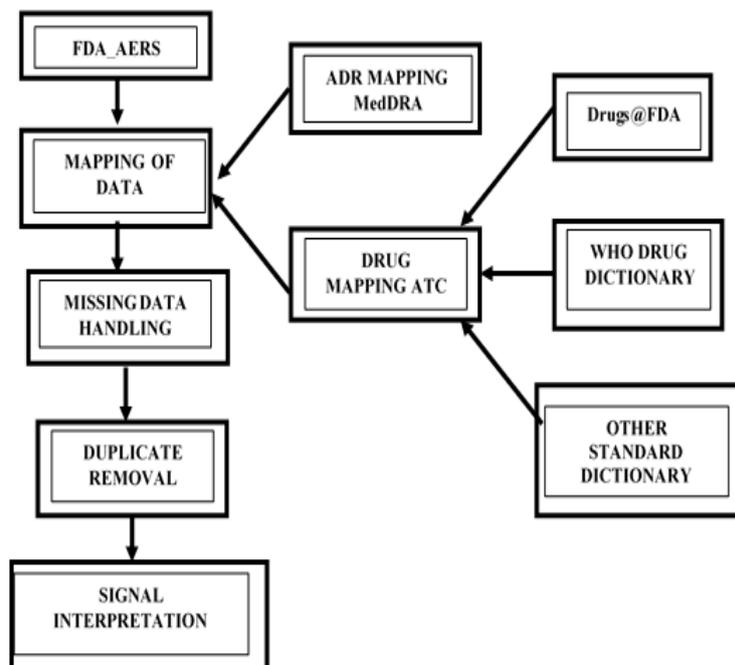


**Figure 2 Data mining process**

|  | Reports with ADE j | Reports without ADE j | Total |
|---|---|---|---|
| **Report with Drug i** | nij | ni − nij | ni |
| **Report without Drug j** | nj − nij | n − ni − nj + nij | n − ni |
| **Total** | nj | n − nj | n |

**Table 1 . A 2 × 2 Table for disproportionality calculation**

A total of 30 ADRs were documented among paediatric patients. Most of the ADRs (60%) occurred below the age of 1 year. Antibiotics comprised the major group of drugs causing ADRs (67%). Rashes and red weal's were the most general type of ADR (37%) followed by fever, anaphylactic shock, vomiting, chills, and rigors. A single case of death had been reported in the study period. There were additional occurrences of ADRs with several drugs compared to particular drug therapy. About 80% of the ADRs were of probable causality and 87% were of probable preventability. There were no mild reactions, with 77% of reactions being reasonable and 23% of reactions being cruel in the severity scale.[10]

| Age in Years | Common ADRs Reported |
|---|---|
| <1 | Rashes and urticaria, anaphylactic shock, Fever, vomiting, chills and rigors, acute dystonia, stevens Johnson syndrome |
| 1-3 | Fever, bradycardia, anaphylactic shock, rashes and urticaria, aphthous ulcer, diarrhoea |
| 4-6 | Vomiting, burning sensation, rashes and urticaria, chills and rigors death |

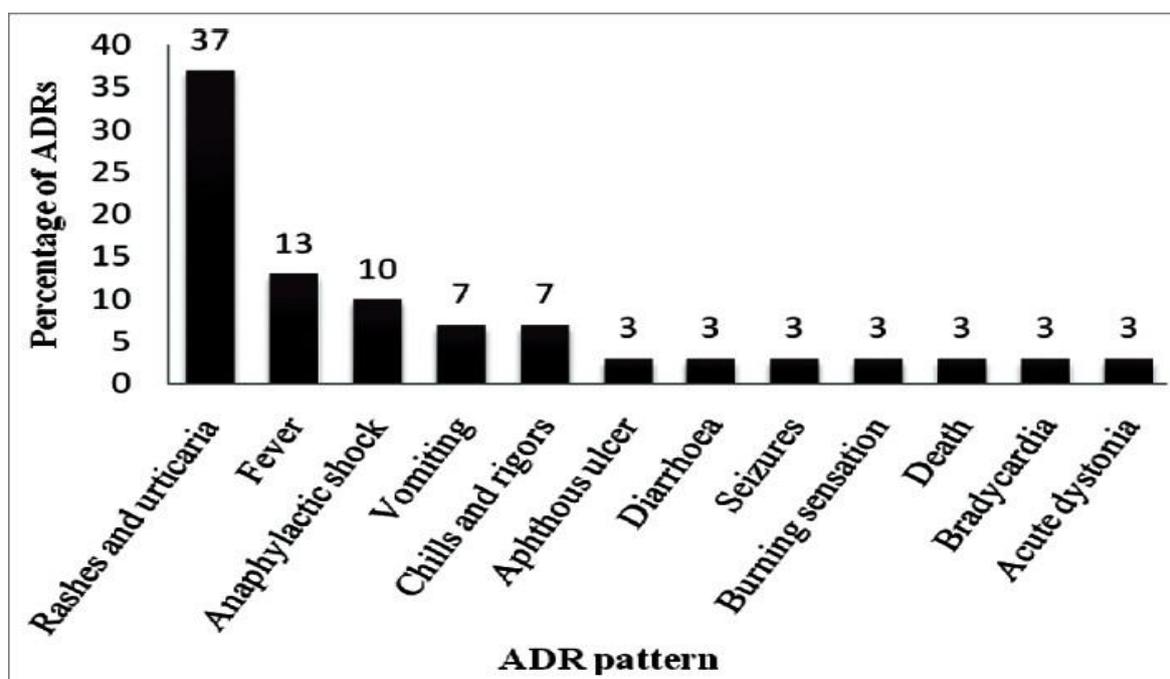**Table 2: Distribution of ADRs in different paediatric age groups**



**Figure 3 -ADR pattern in a paediatric population**

In a potential study done in 347 Indian children, it was identified that antibiotics particularly sulphonamides were linked with the adverse reactions and that skin rashes were the most general reactions reported. A single case of death was also reported in the period of the study which shows a alike ADR pattern depicted in the present study.[11]

### V. PUBLIC DATABASES

A MapReduce-based algorithm has been proposed for common adverse drug event (ADE) detection and has been tested in mining spontaneous ADE reports from the United States FDA. The purpose of this paper was to investigate the possibility of using the MapReduce framework to speed up biomedical data mining tasks using this pharmacovigilance case as one specific example. The distributed architecture of MapReduce and high dimensionality compression via Markov boundary feature selection [12] has been used to identify ADR on the World Wide Web. The response time was significantly reduced and a linear relationship was observed between the quantity of data and processing time in both a small and a very large dataset. The result shows that doubling the number of nodes resulted in a 47% decrease in processing time.

### VI. CONCLUSION

The study analysed about ADRs among children and antibiotics were more generally implicated. Many of the reactions were of reasonable severity. This shows the requirement of a rigid ADR monitoring among paediatric patients to guarantee safety of drug therapy. A variety of pharmacovigilance awareness programs should be conducted to enhance the spontaneous reporting of ADRs.

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