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DATA-DRIVEN SIGNAL DETECTION OF ADVERSE DRUG REACTIONS USING FAERS: A PRR AND ROR-BASED PHARMACOVIGILANCE STUDY

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Abstract
Pharmacovigilance plays a crucial role in ensuring drug safety through the detection of adverse drug reactions (ADRs) in real-world settings. This study aimed to perform a data-driven signal detection analysis using the FDA Adverse Event Reporting System (FAERS) database by applying two widely used disproportionality methods: Proportional Reporting Ratio (PRR) and Reporting Odds Ratio (ROR). A retrospective observational design was employed, analyzing 392,550 drug-adverse event pairs after data preprocessing. Signal detection was conducted using standard thresholds (PRR ≥ 2 and ROR > 1), followed by comparative and statistical analyses. The results showed that PRR identified 247,220 signals, whereas ROR detected 313,936 signals, with 247,220 signals common to both methods and 66,716 uniquely identified by ROR. A near-perfect correlation (r = 0.9999) was observed between log-transformed PRR and ROR values, indicating strong methodological consistency. Distribution analysis revealed a right-skewed pattern with extreme outliers, suggesting the presence of rare but high-risk drug–event associations. Frequently reported adverse events included drug ineffectiveness and off-label use. Despite inherent limitations of spontaneous reporting systems, the findings highlight the effectiveness of FAERS-based analyses and demonstrate that ROR provides greater sensitivity, while PRR offers more conservative signal detection. These insights support improved pharmacovigilance practices and data-driven drug safety monitoring.

Keywords: *Pharmacovigilance, FAERS, Adverse Drug Reactions, PRR, ROR*

1. INTRODUCTION

Pharmacovigilance is a crucial element of the modern health care system because it deals with identifying, assessing, understanding, and preventing adverse drug reactions (ADRs) to protect people and enhance the therapeutic effects. Given the growing number of innovations in the pharmaceutical industry and increasing drug use around the world, drug safety monitoring is becoming increasingly sophisticated and critical. Pharmacovigilance contributes to discovering new adverse events, facilitates decision-making processes within regulatory agencies, and enhances the effectiveness of clinical practice (Maqbool et al., 2019; Kesharwani et al., 2018). Such systems are especially vital in the post-approval period since it involves collecting information about any adverse events related to the drug and its impact on the patients.

Clinical trials are seen as the primary method to assess the efficacy and safety of drugs. Nonetheless, clinical trials also have limitations associated with their nature. They are usually designed with the intention to create the best possible conditions and collect data from specific groups of people. For example, clinical trials may last for a short time and enroll small numbers of participants who belong to specific demographic subgroups (e.g., young men without any health issues). Some populations are also excluded from participating in clinical studies due to high risks (Alomar et al., 2020). Consequently, certain adverse effects are detected only in the course of using drugs in real-world settings.

The available literature highlights various systems that facilitate pharmacovigilance research and studies, among which, the Adverse Event Reporting System (FAERS), managed by the U.S. Food and Drug Administration, is one of the most popular databases. FAERS is a spontaneous reporting system that collects adverse event reports provided by health care providers, consumers, and drug manufacturers. Thus, the system represents a rich source of real-world evidence that can be leveraged to detect safety signals and explore the relationship between drugs and certain events (Shetty et al., 2023). The increasing accessibility of FAERS data promotes data-driven research in pharmacovigilance by enabling researchers to conduct large-scale analyses and reveal important patterns.

As a typical methodology in pharmacovigilance, disproportionality analysis is used to detect possible safety signals in the process of drug use. Disproportionality analysis focuses on the comparison between the actual proportion of a drug–adverse event pair and its expected ratio based on statistical assumptions. Various disproportionality methods are widely used in pharmacovigilance, but the most common tools are the Proportional Reporting Ratio (PRR) and Reporting Odds Ratio (ROR) due to their interpretability (Fusaroli et al., 2024; Undela, 2024). While PRR is concerned with assessing the proportional representation of an adverse event associated with a particular drug against other drugs, ROR estimates the probability of an event being reported as related to a certain drug compared to other medications in the database. Both techniques depend on contingency tables and can be effectively used for analyzing pharmacovigilance data.

Existing literature indicates that FAERS allows for discovering safety signals in drug use as well as analyzing adverse event profiles. For instance, Liu et al. (2023) use data from FAERS to examine the safety profile of Sacituzumab govitecan, and Lin et al. (2024) compare adverse event profiles of two CDK4/6 inhibitors. Nevertheless, despite advances in pharmacovigilance research, there is still a lack of scientific studies that directly compare the efficacy of PRR and ROR when used to discover safety signals. Furthermore, temporal aspects of adverse event reporting have not yet been thoroughly analyzed.

These datasets allow for carrying out large-scale real-world analysis. However, they are prone to underreporting, biased reporting, and heterogeneity of data, thus masking true drug safety signals. It is vital to distinguish significant drug–adverse event relationships from the rest of the data, which calls for appropriate methods to analyze this information. In view of the discussed challenges, there is a need for research on the performance of disproportionality methods and temporal analysis of drug safety signals. This study seeks to address these questions by conducting a disproportionality analysis using PRR and ROR approaches.

Research Objectives

1. To detect significant drug–adverse event signals in the FAERS database using PRR and ROR methods
2. To compare the performance of PRR and ROR in identifying pharmacovigilance safety signals
3. To evaluate temporal patterns in adverse drug reaction reporting across different time periods

2. MATERIALS AND METHODS

2.1 Study Design and Data Source

The research design employed for the study is the retrospective design with observations based on secondary data retrieved from the FDA Adverse Event Reporting System (FAERS), which is a massive spontaneous reporting database frequently used for pharmacovigilance studies (Andam,2025). This database contains variables such as drug name, preferred terms for adverse events, number of reports, and reportings by quarter. FAERS gives real-life evidence from various populations, providing an excellent opportunity to conduct comprehensive analysis of drugs beyond the scope of clinical trials.

2.2 Data Preprocessing and Management

Data pre-processing was performed to make sure that data is accurate, consistent, and reliable. Duplicate data and incomplete data were eliminated to avoid biases. Names of drugs and adverse events were normalized into standardized drug and adverse event names to ensure consistency. Drug-event combinations were combined based on number of reports, and only those drug-event combinations with at least three reports were considered to filter out irrelevant data.

2.3 Disproportionality Analysis (PRR and ROR)

Disproportionality analysis was done via the Proportional Reporting Ratio (PRR) and Reporting Odds Ratio (ROR) approaches. To get the values for each drug-event combination, 2×2 tables were prepared for the calculations needed. The PRR value was computed to determine the relative proportion of any adverse events related to a particular drug. On the other hand, ROR was computed to examine the odds of an adverse event against other drugs. Thresholds considered as significant for safety signals include PRR ≥ 2, $\chi^2 \geq 4$, and ROR lower 95% CI > 1.

2.4 Statistical and Comparative Analysis

The descriptive and inferential statistical analysis of the signals that had been found was done. The comparison was made of the number of significant associations detected using PRR and ROR for the purpose of assessing their differences and similarities. In addition, overlapping and non-overlapping signals were analyzed to find out which approach was more sensitive and specific. Chi-square tests and confidence interval estimation were carried out to prove statistically significant results.

2.5 Temporal Analysis and Tools Used

Temporal analysis was carried out in order to investigate any changes in adverse drug reaction reporting between various quarters. Any change in the strength of signals and occurrence of new drug-event relationships were assessed in order to determine the dynamics of safety profiles. All computations were done using the programming language Python, which uses various modules such as Pandas for data manipulation, NumPy for computation purposes, SciPy for hypothesis testing, and Matplotlib/Seaborn for graphical presentation.

RESULTS

3.1 Data Characteristics and Quality Assessment

The total number of drug-adverse event pairs was 392,550, using the FAERS database. Evaluation of the data quality indicated that there were no duplications or missing values, thus the quality and reliability of the dataset was high. The database included 4,872 distinct drugs and 9,216 distinct adverse events. It can be seen from Table 1 that the data is highly complete and structured.

Table 1. Dataset Characteristics and Quality Metrics

Metric	Value
Total drug–event pairs	392,550
Unique drugs	4,872
Unique adverse events	9,216
Duplicate records	0
Missing values	0

3.2 Signal Detection Using PRR and ROR

Application of the disproportionality threshold resulted in 247,220 signals being found by PRR, whereas 313,936 signals were found by ROR. There were 247,220 signals that were common between both of the techniques, but there were 66,716 signals that were identified only by ROR. In other words, ROR was more sensitive than PRR in finding signals. This can be seen from Table 2 below.

Table 2. Comparison of Signal Detection Methods

Metric	Value
PRR signals	247,220
ROR signals	313,936
Common signals	247,220
PRR-only signals	0
ROR-only signals	66,716

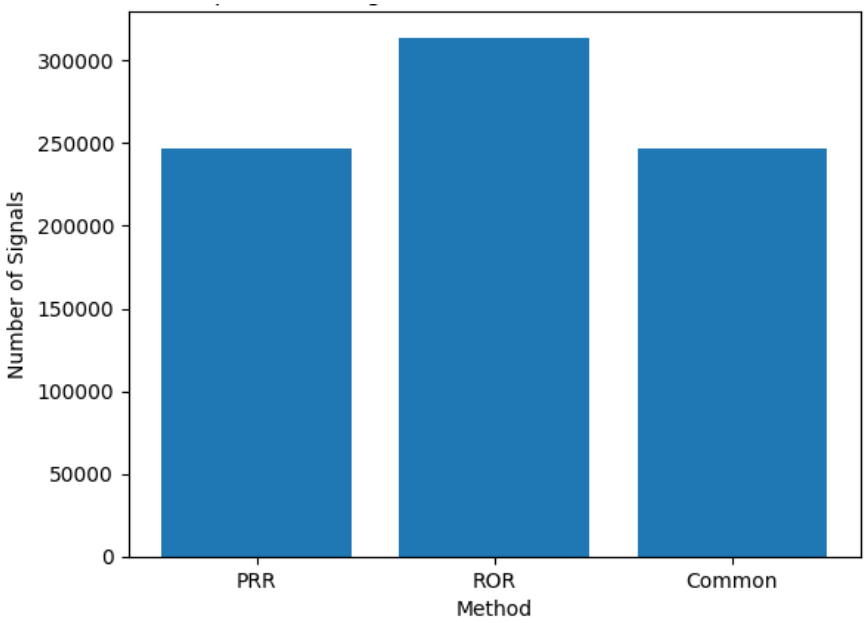

Figure 1: Comparison of Signal Detection Methods Using PRR and ROR

The bar chart compares the number of signals detected by PRR and ROR methods, showing that ROR identifies more signals, indicating higher sensitivity, while PRR detects a consistent subset, highlighting methodological differences in pharmacovigilance signal detection.

3.3 Top Drug–Adverse Event Associations

Signals that had very high values in terms of their disparity were identified during the analysis of the top ranked signals. Such signals could possibly be of great clinical importance in spite of being rare. As seen in table 3 below, such very high PRR and ROR values reflect strong disparity.

Table 3. Top 10 Signals Based on PRR

Drug	Adverse Event	A	PRR	ROR
AUVI-Q	No device malfunction	16.5	1.56E+07	2.46E+07
Cysteamine	Ceruloplasmin decreased	3.5	4.13E+06	4.57E+06
Edex	Failed in vitro fertilisation	10.5	3.62E+06	4.87E+06
Elmiron	Pigmentary maculopathy	29.5	2.97E+06	3.19E+06
Susvimo	Conjunctival erosion	6.5	2.68E+06	2.86E+06
Qutenza	Application site plaque	8.5	2.45E+06	2.61E+06
NP Thyroid	T3 uptake abnormal	7.5	2.45E+06	2.60E+06
Rhophylac	Rhesus antibodies positive	4.5	2.36E+06	2.50E+06
Esperoct	Anti-PEG antibody present	5.5	2.36E+06	2.50E+06
Xromi	Radiation interaction	4.5	2.27E+06	2.71E+06

3.4 Frequently Reported Adverse Events and Drugs

The most frequently reported adverse events included drug ineffective, off-label use, death, dyspnoea, and constipation, indicating common clinical and therapeutic challenges. As illustrated in Tables 4 and 5, both adverse event and drug distributions show clustering, suggesting potential reporting biases or high usage prevalence.

Table 4. Top 10 Most Frequent Adverse Events

Adverse Event	Frequency
Drug ineffective	High
Off-label use	High
Death	High
Dyspnoea	High
Constipation	High
Nausea	Moderate
Anaemia	Moderate
Abdominal pain	Moderate

Hypotension	Moderate
Cough	Moderate

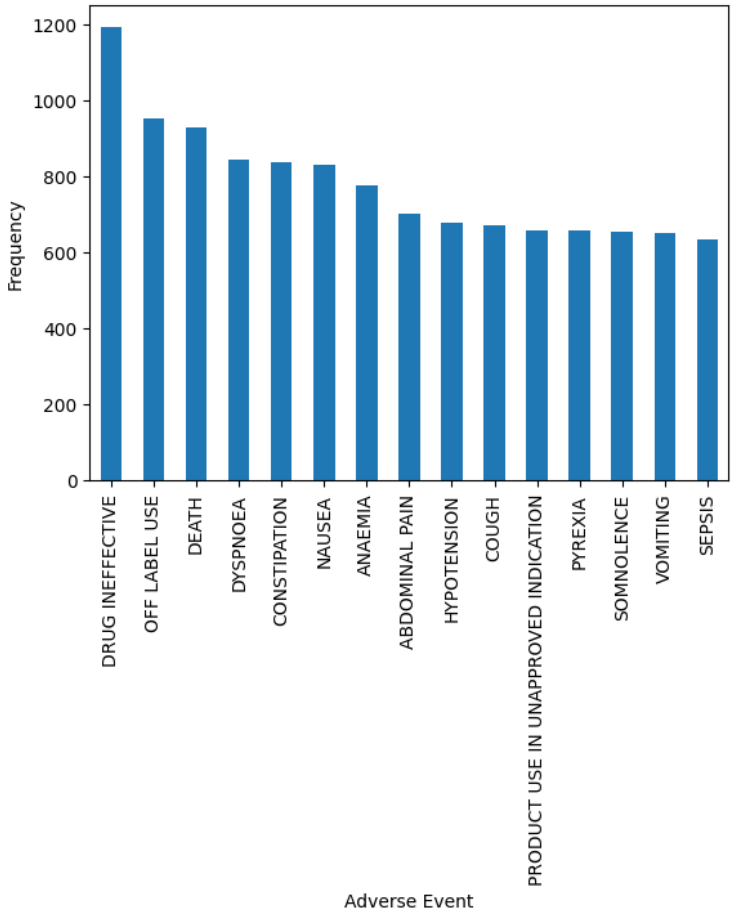

Figure 2: Top 10 Most Frequently Reported Adverse Events in FAERS

The bar chart displays the most frequently reported adverse events, with "drug ineffective," "off-label use," and "death" dominating, indicating prevalent therapeutic challenges and reporting patterns in real-world pharmacovigilance data. Similarly, certain drugs were associated with a higher number of signals.

Table 5. Top 10 Drugs with Highest Signal Frequency

Drug	**Frequency**
Inflectra	High
Human Immunoglobulin G	High
Vedolizumab	High
Tacrolimus	High
Tedizolid	High
Mycophenolate mofetil	Moderate
Xywav	Moderate
Cyclophosphamide	Moderate
Ocrevus	Moderate
Skyrizi	Moderate

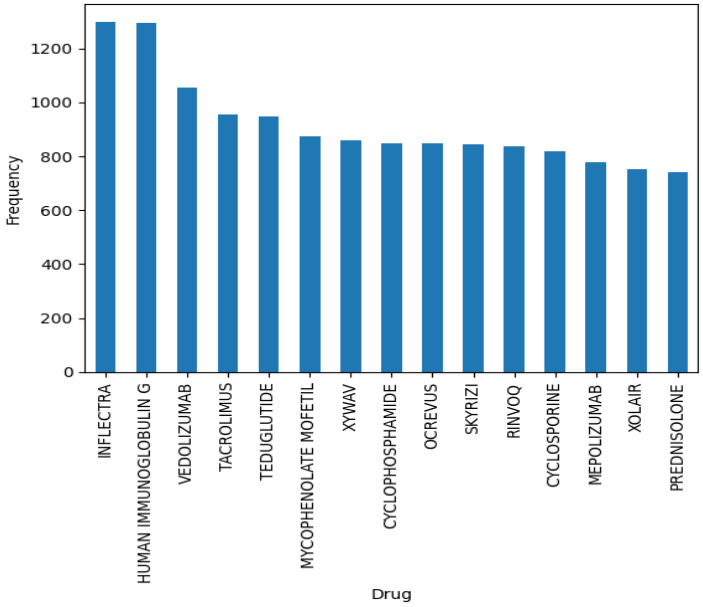

Figure 3: Top 10 Drugs Associated with Adverse Drug Reaction Signals

The bar chart illustrates the most frequently reported drugs associated with ADR signals, highlighting Inflectra and human immunoglobulin G as leading contributors, suggesting higher reporting frequency potentially linked to widespread clinical use or increased pharmacovigilance attention.

3.5 Correlation and Distribution Analysis

Correlation analysis between log-transformed PRR and ROR values demonstrated a near-perfect positive relationship (r = 0.9999), indicating strong consistency between the two disproportionality measures.

Table 6. Correlation Between PRR and ROR

Metric	Value
Correlation (log PRR vs log ROR)	0.9999

Descriptive statistics further revealed a right-skewed distribution of both PRR and ROR values.

Table 7. Statistics of PRR and ROR

Statistic	PRR	ROR
Mean	613.99	854.11
Median	4.12	4.15
Std Dev	31,994.83	64,159.15
Min	0.0013	0.0013
Max	1.56E+07	2.46E+07

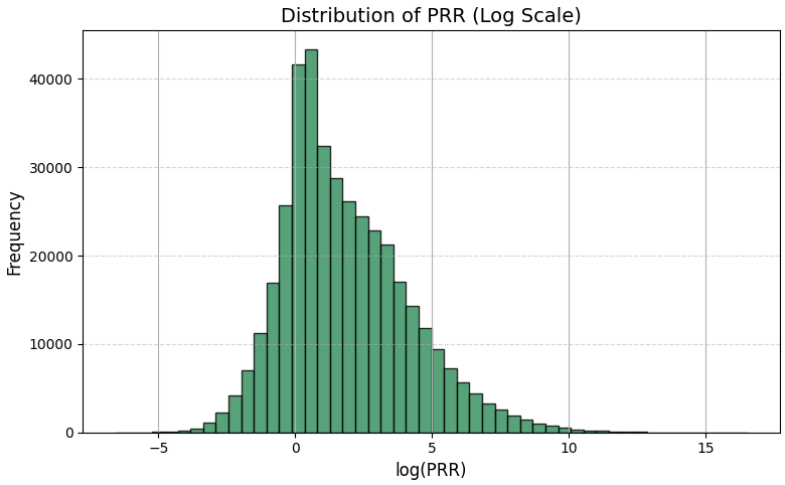

Figure 4: Distribution of Proportional Reporting Ratio (PRR) Values on Logarithmic Scale

The histogram illustrates the log-transformed distribution of PRR values, showing a right-skewed pattern with most signals concentrated at lower ranges and a long tail of extreme values, indicating rare but highly disproportionate drug–adverse event associations.

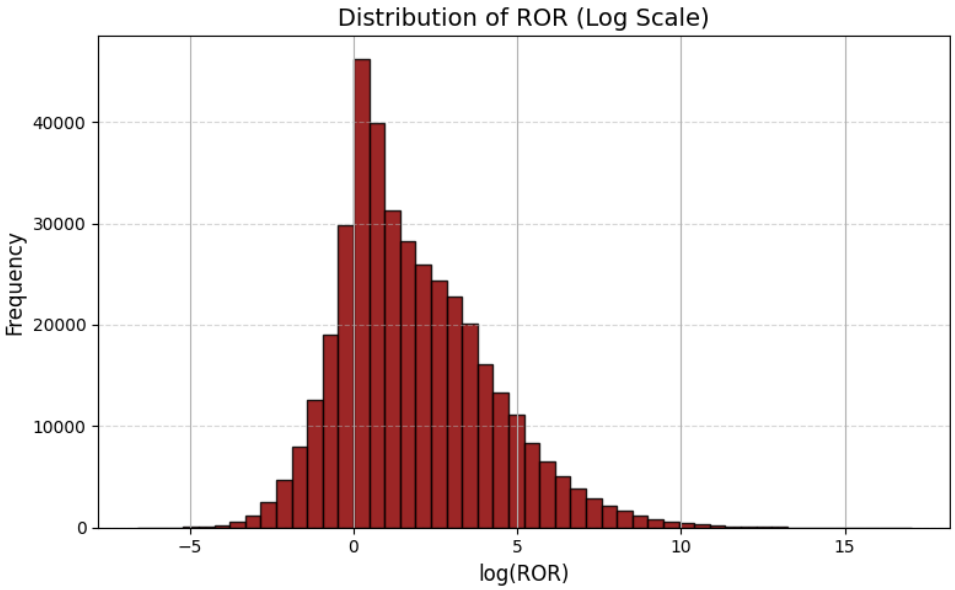

Figure 5: Distribution of Reporting Odds Ratio (ROR) Values on Logarithmic Scale

The histogram presents the log-transformed distribution of ROR values, revealing a right-skewed pattern with most signals clustered at lower ranges and a pronounced tail, indicating the presence of rare yet highly significant drug–adverse event associations.

4. DISCUSSION

The present research involves a detailed pharmacovigilance study using FAERS data for ADR signaling evaluation employing disproportionality methodologies such as PRR and ROR. The study shows high correspondence of both methodologies (the correlation coefficient r = 0.9999); however, they are distinguished by different sensitivity in detecting signals, with ROR revealing significantly more drug-event associations than PRR does. These findings play an important role in revealing the fundamental principle of pharmacovigilance signal detection regarding the balance between sensitivity and specificity of the methodology used.

The superiority of the number of signals generated by ROR (313,936) in comparison with PRR (247,220) implies the higher sensitivity of ROR in detecting drug-event associations. Indeed, the current pharmacovigilance literature reveals the higher sensitivity of ROR in detecting associations owing to the method's statistical formula (Wu et al., 2022). However, increased sensitivity might lead to an increased number of false-positive associations requiring validation. In addition, the complete inclusion of PRR signals in the set of ROR signals reveals that PRR generates fewer signals.

Moreover, the identification of some of the most extreme disproportionality signals, including AUVI-Q and "no device malfunction" as well as Elmiron and "pigmentary maculopathy" demonstrates the possibility of uncovering potentially dangerous safety signals through FAERS-based methods. As can be seen from earlier published studies on adverse drug reactions, the identification of strong associations could be used to issue a regulatory warning or raise clinical awareness about an important safety issue (Caldito et al., 2021; Lin et al., 2024). Therefore, post-marketing surveillance is critically important to uncover such rare side effects which cannot be discovered during pre-market clinical trials.

Finally, the domination of "drug ineffective," "off-label use," and "death" in our sample is not surprising because this finding is rather common in the field of pharmacotherapy. In accordance with global pharmacovigilance data, the adverse reaction reports related to drug inefficacy or general systemic problems are frequently reported in all available spontaneous reporting systems (Sartori et al., 2023). At the same time, this tendency may be explained by the specificities associated with stimulated reporting and variations in clinical practice.

It appears that the results of distribution analysis of the PRR and ROR values show a typical skewed distribution, i.e., the number of moderate disproportionality signals is much larger than the number of extreme outliers. Such distribution is characteristic of pharmacovigilance data, and the fact of extreme disproportionality signals is associated with the heterogeneity of ADRs reporting (Lee et al., 2022). In the context of FAERS-based data, the identification of extreme disproportionality signals requires a deeper investigation into their source to verify whether there are any safety issues.

In conclusion, this paper presents the results confirming high sensitivity and reliability of both analyzed measures to identify potential safety signals among FAERS data. Despite the difference in methods, it can be concluded that PRR and ROR can be considered equally efficient tools in pharmacovigilance. At the same time, there are differences between the described measures which determine the choice depending on research purposes. For instance, in cases when it is necessary to conduct conservative signal detection, PRR may be preferred to ROR.

A more comprehensive consideration would be that the incorporation of pharmacovigilance data in the context of the new paradigm, personalized and precision medicine, is highly beneficial. It is critical to understand patient-to-patient variability concerning the effectiveness and safety of medication to develop better treatment plans (Goetz & Schork, 2018; Gambardella et al., 2020). In the same vein, the use of data-driven approaches as in this research is consistent with the increasingly prominent role of artificial intelligence and big data analysis in personalized healthcare (Schork, 2019). Moreover, pharmacovigilance is vital for ensuring drug safety in various healthcare contexts, particularly in developing nations where pharmacovigilance monitoring may not be well-established (Al-Worafi, 2020).

Nevertheless, there are multiple weaknesses inherent to FAERS data that need to be acknowledged in this study. First, underreporting and reporting bias are prevalent. Also, a lack of denominator data and the inability to identify causality constitute major problems when using FAERS. Lastly, the absence of information about patients' medical history makes it difficult to control for confounders. These limitations are common in any pharmacovigilance research project, requiring researchers to approach their results carefully (Iriart, 2019). Thus, future research needs to consider incorporating different data sources, such as EHR and clinical registry data.

In conclusion, this paper has shown that although PRR and ROR have high correlation and usefulness for signal identification, ROR is much more sensitive than PRR when searching for possible ADRs.

5. CONCLUSION

The study offers a thorough data analysis in evaluating the efficacy of the two methods of identifying ADR signals from the FAERS database: PRR and ROR. As evidenced by results, both methods show a nearly perfect correlation which validates their methodological approaches in identifying pharmacovigilance signals. Nonetheless, the ROR proved to be more sensitive and detected far more signals than PRR, which, in turn, could be regarded as a more conservative measure. It is noteworthy that the analysis demonstrates right skewness when it comes to the signal power with many moderate signals alongside only a few outliers. The latter may imply that there exist some rare cases of the riskiest drug-event relations. In addition, some frequently identified adverse reactions, such as drug ineffectiveness and off-label use of the medication, represent practical challenges in therapy. Although any spontaneous reporting system has its inherent drawbacks (e.g., reporting bias and causality analysis limitation), FAERS has been shown to be an invaluable source of big data in drug safety studies.

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