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Pharmacovigilance Evaluation of Amoxicillin Induced Adverse Drug Reactions

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Abstract:
Amoxicillin- Clavulanate is frequently prescribed to manage a wide range of bacterial infections in both outpatient and hospital setting. Although it is considered effective and reliable, its use may be associated with adverse drug reaction (ADRs). This review evaluates published studies and pharmacovigilance data to identify the nature, occurrence rate, severity, and causality of ADRs related to this medication. Reported reaction were systematically categorized according to the organ system involved, and their association with the drug was assessed using established causality assessment methods.
The analysis indicates that gastrointestinal disturbances, including diarrhea, nausea, and abdominal discomfort, are the most commonly observed reactions. Uncommon but clinically significant reaction such as hepatotoxicity and serious hypersensitivity reactions have also been reported. Appropriate prescribing practices and patient monitoring are necessary to enhance safety and reduce the adverse outcome.

Keywords: *Adverse Drug Reaction (ADRs); Amoxicillin-Clavulanate; Drug induced liver injury (DILI); Proportional reporting ratio (PRR); Reporting odds ratio (ROR*).

INTRODUCTION:

Pharmacovigilance is a vital field that focuses on tracking and preventing side effects, also known as adverse drug reactions (ADRs). Even when a medicine passes clinical trials, certain side effects might only show up once thousands of people start taking it in the real world. This is why constant monitoring is essential to keep patients safe and improve overall healthcare [1].
Amoxicillin is an antibiotic, It's a member of the penicillin family. It is frequently prescribed to treat bacterial infections by stopping the growth of bacteria. It is mainly work as if bacteria were a construction crew building a wall (the cell wall) to protect themselves, Amoxicillin shows up and steals their bricks. Without that wall, the bacteria can't survive or multiply, allowing your immune system to finish the job [2].
In pharmacovigilance, amoxicillin is important because its large-scale use means side effects must be carefully monitored. Most reactions are mild, such as nausea, diarrhea, or skin rash, but some patients may develop allergic reactions, including rare but serious anaphylaxis. Continuous monitoring and reporting of adverse drug reactions help ensure safe use and improve patient care [2].
The goal of this paper is to look at existing research to get a clear picture of the side effects caused by Amoxicillin-Clavulanate. By using charts and tables to organize this data, we hope to help doctors better understand the risks. Ultimately, this review aims to promote the safer use of antibiotics and highlight how important it is to keep tracking drug safety in everyday medical practice [3].

Literature Review:

Several studies have documented the occurrence of adverse drug reactions (ADRs) during treatment with amoxicillin. Although the drug is widely used and generally considered safe, a number of side effects have been reported in clinical practice. Among these, skin-related reactions such as rash, urticaria, and itching appear to be the most commonly observed. These reactions are often mild but can cause discomfort and may require discontinuation of the medication in some patients.
Gastrointestinal disturbances are also frequently associated with amoxicillin therapy. Symptoms such as nausea, vomiting, and diarrhea are commonly reported, particularly when the drug is taken for a longer duration or at higher doses. These effects are usually temporary and resolve after stopping the medication, but they remain an important consideration in patient management [2,9].

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Mechanism of Action:

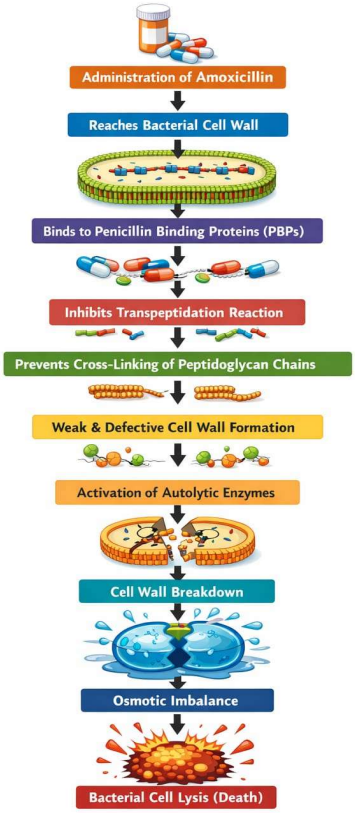

Figure 1: MOA of Amoxicillin-Clavulanate [6].

MATERIAL AND METHODS:

Study Design-
This review was designed as a systematic and statistical analysis of pharmacovigilance data related to Amoxicillin Clavulanate. The study focused on evaluating the pattern, frequency, severity, and causality of reported adverse drug reactions (ADR_S). The review followed a structured approach to collect, screen and analyze published and database derived safety data.

Data Sources-
Data were collected from published literature and recognized pharmacovigilance database. Electronic database such as PubMed, Scopus, Web of Science, and Embase were searched for relevant articles. In addition, publicly available adverse event reporting systems such as VigiBase and FAERS were reviewed to obtain statistical safety data. [2,4]

Inclusion and Exclusion Criteria-
Studies were included if they reported statistical data on ADR_S, case series, cohort studies, cross- sectional studies, or pharmacovigilance database analyses related to amoxicillin clavulanate. Case reports without statistical relevance, duplicate records, review articles without primary data, and non- English publications were excluded.

Data Extraction-
Relevant data were extracted using a standardized data collection from extracted variable included year of publication, country, study design, number of cases, patient demographic (age and gender), indication for use, type of ADRs, severity classification, and causality assessment. Seriousness of ADR_S was categorized based on hospitalization, life- threatening events, disability, or death.

Statistical Analysis-
Descriptive statistical methods were used to summarize the data. Frequencies and percentages were calculated for categorical variables. Where applicable, disproportionality analysis measure such as reporting odds ratio (ROR) or proportional reporting ratio (PRR) were considered for signal detection. Data were presented in tables and charts to demonstrate trends clearly and patterns of ADR reporting [5].

Ethical Consideration-
As this study was based on published literature and publicly available pharmacovigilance database, ethical approval was not required.

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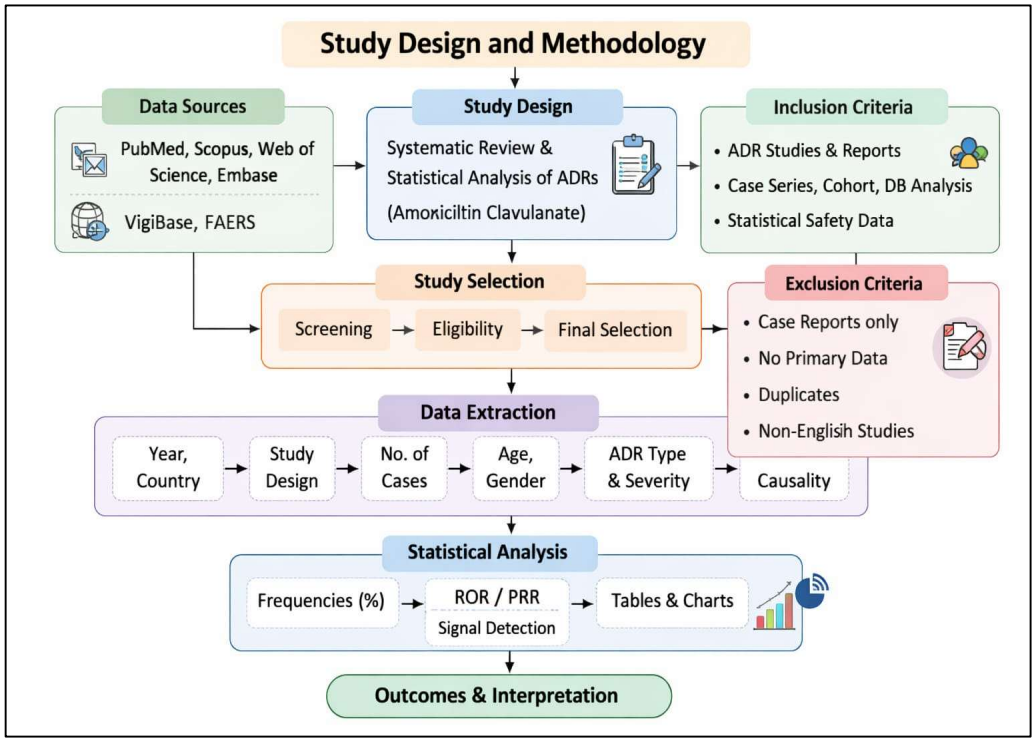


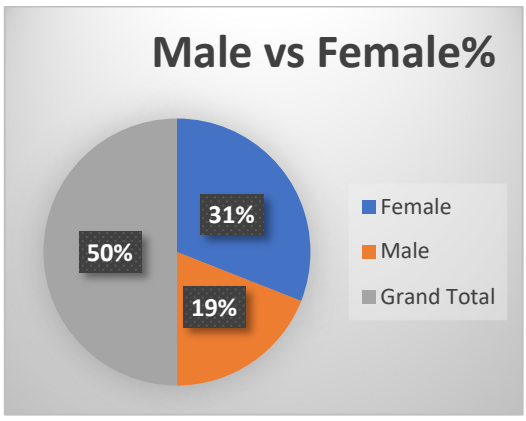
Figure 2: Material and Method [7,8].

RESULT:

A Comprehensive review of published pharmacovigilance studies and adverse event reporting databases related to amoxicillin and amoxicillin-clavulanate was conducted. The collected data were analyzed to identify the pattern, frequency, and severity of reported adverse drug reactions (ADRs).

Table 1: Gender Distribution.

Male Vs Female	Count	Male Vs Female %
Female	31	62.00%
Male	19	38.00%
Grand Total	50	100.00%



Graph 1: Pie chart of Gender Distribution.

Table 2: Age Distribution of ADRs

Age Group	Count of Patients
1 to 10	8
11 to 20	9
21 to 30	9
31 to 40	6
41 to 50	3
51 to 60	3
61 to 70	5
71 to 80	3
81 to 90	3

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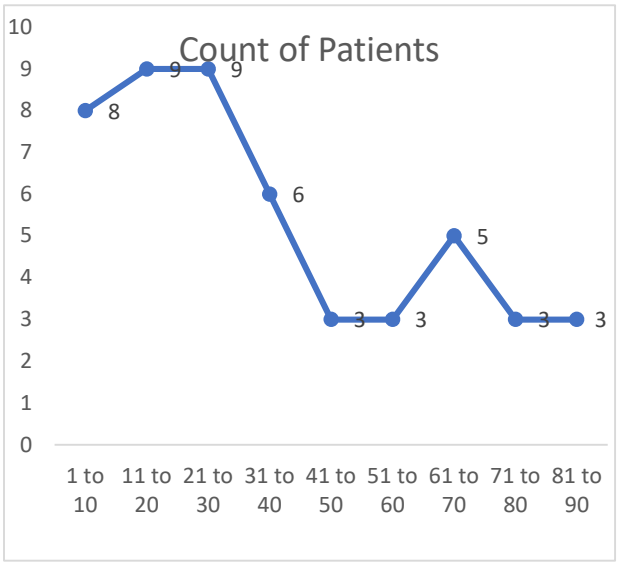
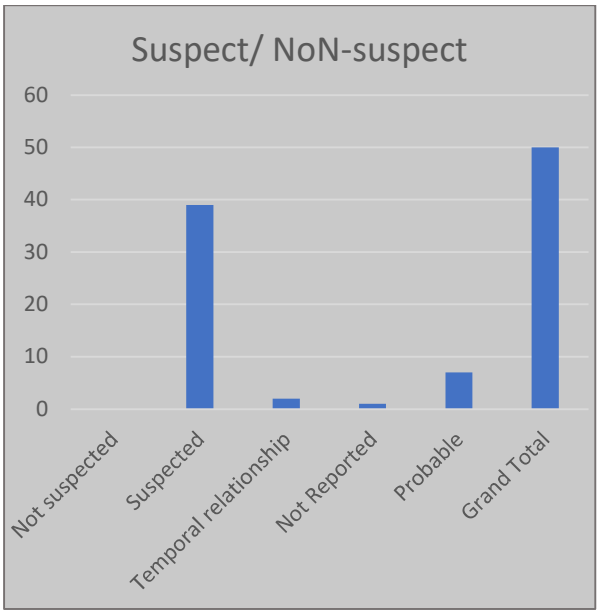


Graph 2: Line Graph (Line Chart) Age Group Percentage.



Graph 3: Bar Graph of Severity of ADRs

Table 3: Severity of ADRs.

Row Labels	Suspect/ NoN-suspect
Not suspected	0
Suspected	39
Temporal relationship	2
Not Reported	1
Probable	7
Grand Total	50

Table 4: Types of Adverse Drug Reactions.

Row Labels	Count of ADR	ADR %
Rash maculo-papular	15	29.41%
Drug Hypersensitivity	6	11.76%
Skin Lesion	4	7.84%
Acute Renal Failure	3	5.88%
Toxic Epidermal Necrolysis	2	3.92%
Hepatitis	2	3.92%
Renal Failure Acute	2	3.92%
Other single case ADR	1 each	1.96% each
Total	35	

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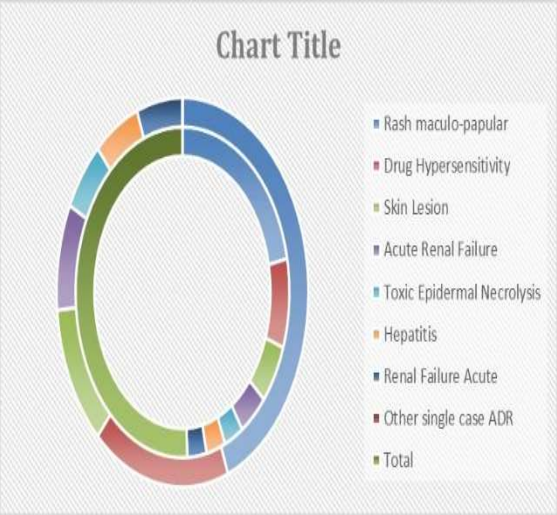

Graph 4: Pie chart of ADR Types

DISCUSSION:

This study examined the adverse drug reactions reported with the use of Amoxicillin. Amoxicillin is widely used for treating different types of bacterial infections and is generally considered a safe antibiotic [9]. However, the findings of this study show that some patients may still experience adverse reactions during treatment [10]. Among the different reactions observed, skin-related problems such as rashes and itching were reported more often than other types of reactions [11]. This may happen because certain patients develop allergic or hypersensitivity responses to beta-lactam antibiotics [12].

The study also showed that adverse drug reactions were slightly more common in males than in females. In addition, most of the reported cases were seen in young adults. One possible explanation is that young adults often receive antibiotic therapy for infections like respiratory tract infections, throat infections, or dental infections. As the use of antibiotics increases in this age group, the chance of observing adverse reactions may also increase [13].

Another important finding of the study was that most of the reactions were mild and improved after stopping the suspected medicine. This suggests that careful monitoring during antibiotic therapy is very important. If symptoms are identified early and the medicine is discontinued in time, serious complications can usually be avoided. Healthcare professionals therefore play an important role in identifying and managing such reactions [14].

The causality assessment indicated that many of the reported reactions were probably related to the use of Amoxicillin. These results highlight the importance of pharmacovigilance activities in clinical practice. Regular reporting of adverse drug reactions helps in improving the safety profile of commonly used medicines and supports better patient care [15].

MAIN TEXT:

Amoxicillin has been used in clinical practice for many years and continues to be one of the most prescribed antibiotics worldwide [16]. Because of its widespread use, monitoring its safety does not stop after approval. Clinical trials are conducted under controlled conditions and may not always capture rare or delayed adverse effects. Therefore, real-world safety monitoring becomes essential to understand how the drug behaves in a larger and more diverse patient population. Post marketing surveillance systems have provided useful insights in this regard. For instance, data collected through national adverse event reporting programs have identified reactions that were either uncommon or not clearly emphasized in official prescribing information [17].

Analysis of recent European safety databases has shown that a notable proportion of reported adverse reactions related to amoxicillin and its combinations were categorized as serious. Many of these reports involved significant skin reactions and gastrointestinal disturbances. Such observations indicate that although the drug is generally considered safe, careful monitoring remains necessary. A clear difference is observed when clavulanic acid is combined with amoxicillin [18,19]. The addition of clavulanic acid enhances antibacterial activity by inhibiting beta- lactamase enzymes, thereby extending its spectrum of action. However, this benefit appears to be associated with an increased frequency of liver related adverse events compared to amoxicillin used alone. This suggest that while the combination offers broader coverage, it may also carry additional safety considerations [20].

Side effect comparison: Amoxicillin vs Amoxicillin-Clavulanate.

Table 1: Side effect comparison**.**

Feature/ System	Amoxicillin (Alone)	Amoxicillin- Clavulanate (Combination)
Common Gastrointestinal	Mild nausea, vomiting or diarrhea.	Higher frequency of severe diarrhea and abdominal cramping.
Hepatobiliary (Liver)	Rarely associated with liver injury or jaundice.	Stronger signal for drug induced liver injury (DILI) and cholestatic jaundice.

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Dermatological	Standard maculopapular rash or urticaria (Hives).	Similar skin risks, through some studies suggest slightly higher incidence of severe reactions.
Allergic Reaction	Standard risk of type I hypersensitivity (Anaphylaxis).	Equivalent risk; allergic potential is primarily linked to the penicillin component.
Fungal Overgrowth	Risk of oral or vaginal candidiasis (thrush).	Increased risk due to the broader impact on the body's natural microflora.

CONCLUSION:

In conclusion, this review shows that amoxicillin is still one of the most commonly prescribed antibiotics and is generally safe and well tolerated by most patients. However, adverse drug reactions (ADRs) related to amoxicillin can occur and should not be ignored. These reactions usually range from mild effects such as stomach upset and skin rashes to rare but serious allergic reactions.

Most of the reported ADRs are mild to moderate in severity, and in many cases, they are categorized as probable or possible during causality assessment. These findings highlight the importance of carefully reviewing a patient's medical history, especially any previous drug allergies, before prescribing amoxicillin. Continuous pharmacovigilance and monitoring are also essential.

Early identification and proper management of ADRs can help prevent complications and improve patient safety. Therefore, rational prescribing, educating patients about possible reactions, and regular monitoring of ADRs are important steps to reduce risks while still maintaining the therapeutic benefits of amoxicillin.

Data Availability:

No new data were added in this review. All the information was taken from previously published research articles, and no new information was generated.

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